European Journal of Cancer

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# Abstract Book

EBCC 10
European Breast Cancer Conference

## Amsterdam, 9–11 March 2016

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# European Journal of Cancer

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## Thursday, 10 March 2016



## Friday, 11 March 2016

# Late Breaking Abstracts

## Wednesday, 9 March 2016 14:45–16:15

PLENARY SESSION

# Keynote Lecture and Late-Breaking Abstracts

**1LBA** Late Breaking Oral

### Two-stage implant-based breast reconstruction is safer than immediate one-stage implant-based breast reconstruction augmented with an acellular dermal matrix: a multicentre randomized controlled trial

R. Dikmans[1], V. Negenborn[1], M.B. Bouman[1], W. Hay[1], J. Twisk[2], Q. Ruhé[3], M. Mureau[4], J.M. Smit[5], S. Tuinder[6], Y. Eltahir[7], N. Posch[8], M. Meesters-Caberg[9], M. Ritt[1], M. Mullender[1]. *[1]VU University Medical Center, Plastic- Reconstructive and Hand Surgery, Amsterdam, Netherlands; [2]VU University Medical Center, Department of Epidemiology & Biostatistics, Amsterdam, Netherlands; [3]Meander Medical Centre, Plastic- Reconstructive and Hand Surgery, Amersfoort, Netherlands; [4]Erasmus MC Cancer Institute, Plastic- Reconstructive & Hand Surgery, Rotterdam, Netherlands; [5]Alexander Monro Breast Cancer Hospital, Plastic- Reconstructive & Hand Surgery, Bilthoven, Netherlands; [6]Maastricht University Medical Centre, Plastic- Reconstructive and Hand Surgery, Maastricht, Netherlands; [7]University Medical Centre Groningen, Plastic- Reconstructive and Hand Surgery, Groningen, Netherlands; [8]Haga Ziekenhuis, Plastic- Reconstructive and Hand Surgery, The Hague, Netherlands; [9]Orbis Medical Centre, Plastic- Reconstructive and Hand Surgery, Sittard, Netherlands*

**Background:** The evidence justifying the use of acellular dermal matrices (ADMs) in implant-based breast reconstruction (IBBR) is limited. The aim of this prospective randomized trial was to compare the outcomes of direct IBBR augmented with an ADM (Strattice™, LifeCell Cooperation) with those of two-stage IBBR. We report on the first results on the safety outcomes of the two procedures.

**Material and Methods:** A non-blinded randomized controlled trial was conducted at eight hospitals in the Netherlands. Patients who intended to undergo skin-sparing mastectomy and immediate IBBR were randomized to one of two procedures for IBBR: one-stage ADM-assisted IBBR or two-stage IBBR. The primary endpoint was quality of life. In the present article, we assessed the effect of the procedure on the occurrence of adverse outcomes. Analyses were performed with logistic regression and the general linear model. The trial is registered in the Dutch National Trial Register (NTR TC 5446) and the public CCMO register in the Netherlands (NL41125.029.12). The inclusion of patients is completed.

**Results:** Between April 14, 2013, and May 29, 2015, 140 patients were enrolled in the study. Eventually, 59 patients (91 breasts) in the one-stage IBBR group and 59 (87 breasts) in the two-stage IBBR group were included for analysis. The overall medical complication rates (38.5% vs 10.3%, OR = 6.28, p = 0.001), the medical re-operation rates (32.6% vs 9.6%, OR = 3.96, p = 0.009) and the implant explantation rates (27.0% vs 2.4%, OR = 15.17, p = 0.001) were significantly higher in the one-stage group. This remained the case after controlling for multiple confounding factors (p < 0.001).

**Conclusions:** Immediate one-stage ADM-assisted IBBR was associated with a significantly higher rate of post-operative complications compared with two-stage IBBR. There was no evidence of adverse tissue reactions to the ADM itself. These results indicate that immediate one-stage ADM-assisted IBBR should be considered very carefully.

**No conflicts of interest**

**2LBA** Late Breaking Oral

### Long-term outcome of cardiac dysfunction in a population-based cohort of breast cancer survivors

L.M. Boerman[1], P. Van der Meer[2], J.A. Gietema[3], J.H. Maduro[4], Y.M. Hummel[2], M.Y. Berger[1], G.H. De Bock[5], A.J. Berendsen[1]. *[1]University Medical Center Groningen, General Practice, Groningen, Netherlands; [2]University Medical Center Groningen, Cardiology, Groningen, Netherlands; [3]University Medical Center Groningen, Medical Oncology, Groningen, Netherlands; [4]University Medical Center Groningen, Radiation Oncology, Groningen, Netherlands; [5]University Medical Center Groningen, Epidemiology, Groningen, Netherlands*

**Background:** Chemotherapy and radiotherapy for breast cancer increase survival, but may lead to cardiac dysfunction. Prevalence of long-term cardiac dysfunction in breast cancer survivors in an unselected population is unknown.

**Method:** We performed a population-based cross-sectional study in which 350 women treated for breast cancer with chemotherapy and/or radiotherapy at least 5 years previously were included. These patients were compared to 350 age-matched women without oncological diagnosis. The primary outcome was systolic or diastolic dysfunction on echocardiography, defined as a left ventricle ejection fraction <54% or an age-dependent decreased e′ septal or e′ lateral. Data on cardiovascular risk factors were collected from electronic files of general practitioners and reported by participants at inclusion. Breast cancer patients were divided into two groups: (1) patients treated with chemotherapy with or without radiotherapy (N = 175) and (2) patients treated with radiotherapy only (N = 173).

**Results:** Prevalence of CV risk factors at diagnosis was similar for chemotherapy-treated survivors compared to controls, and radiotherapy-treated patients compared to controls. Mean age at time of diagnosis was 49 (26−66) in the chemotherapy-group and 53 (32−79) in the radiotherapy-group. Median follow-up was 9 years (range 5−33). Systolic dysfunction was present in 25 (14.7%) patients in the chemotherapy-group and in 11 (6.6%) of their controls, diastolic dysfunction in 80 (46.8%) respectively 63 (39.1%). In the radiotherapy-group 28 (16.6%) had systolic dysfunction compared to 13 (7.8%) of their controls, with diastolic dysfunction in 69 (40.6%) resp. 65 (38.9%). Chemotherapy-treated patients and radiotherapy-treated patients had a two times increased risk of developing systolic dysfunction compared to controls, OR 2.2 (95% CI 1.1−4.5) respectively OR 2.3 (95% CI 0.9−2.1), and had no increased risk of diastolic dysfunction, OR 1.4 (95% CI 0.9−2.1) resp. OR 1.1 (95% CI 0.7−1.7).

**Conclusion:** Breast cancer survivors treated with chemotherapy with or without radiotherapy or treated with radiotherapy only have an increased risk of systolic dysfunction on the long-term after breast cancer treatment.

**No conflicts of interest**

**3LBA** Late Breaking Oral

### Interim results of the Adjunct Screening with Tomosynthesis or Ultrasound in Mammography-negative Dense Breasts (ASTOUND) trial

A. Tagliafico[1], M. Calabrese[2], G. Mariscotti[3], M. Durando[3], S. Tosto[2], F. Monetti[2], S. Airaldi[4], B. Bignotti[4], J. Nori[5], A. Bagni[6], A. Signori[4], M.P. Sormani[4], N. Houssami[7]. *[1]University of Genova, Experimental Medicine, Genova, Italy; [2]IRCCS AOU San Martino-IST, Radiology, Genova, Italy; [3]Azienda Ospedaliero-Universitaria Città della Salute e della Scienza di Torino, Radiology, Torino, Italy; [4]University of Genova, Department of Health Sciences DISSAL, Genova, Italy; [5]Azienda Ospedaliero-Universitaria Carreggi, Diagnostica Senologica, Firenze, Italy; [6]Ospedale Bufalini, U.O. Radiologia Ausl, Cesena, Italy; [7]University of Sydney, Screening and Test Evaluation Program- Sydney School of Public Health- Sydney Medical School, Sydney, Australia*

**Background and Purpose:** Mammographic breast density is a risk factor in the context of breast cancer (BC) screening for two reasons: (1) density has a masking effect on BC detection increasing the risk of a missed cancer; (2) density is an independent risk factor for BC. Indeed, in some settings legislation requires that women be informed about their mammography-density and about adjunct imaging. After a negative mammographic screen, ultrasound or tomosynthesis can detect additional BCs. However, these modalities have not been directly compared in prospective trials. The purpose of this study is to report interim results of a trial of adjunct screening that compares, within the same screening participants, incremental BC detection by tomosynthesis and ultrasound in mammography-negative dense breasts.

**Patients and Methods:** Adjunct screening with tomosynthesis or ultrasound in women with mammography-negative dense breasts (ASTOUND) is a prospective multicentre study started in December 2012 (registered as NCT02066142). ASTOUND recruited asymptomatic women with mammography-negative screens and dense breasts (BI-RADS 3 or 4). Eligible women had both tomosynthesis and ultrasound with independent interpretation of adjunct imaging. Outcome measures included cancer detection rate (CDR), number of false-positive (FP) recalls, and incremental CDR for tomosynthesis and ultrasound − these were compared using McNemar's test for paired binary data. Pre-planned interim analysis at around 3000 screens was done for adaptive sampling informed by incremental detection of both modalities.

**Results:** Amongst 3,231 mammography-negative screening participants (median age 51 years, interquartile range 44−78) with dense breasts, 24 additional BCs were detected (23 invasive): 13 tomosynthesis-detected BCs (incremental CDR 4.0/1000 screens; 95% CI: 1.8−6.2) versus 23 ultrasound-detected BCs (incremental CDR 7.1/1000 screens; 95% CI:

4.2−10.0), P = 0.006. Mean tumour size was15.2 mm (SD 6.1 mm) for tomosynthesis-detected cancers and 15.1 mm (SD 4.8 mm) for ultrasound-detected cancers. Incremental FP-recall occurred in 107 (3.33%; 95% CI 2.72–3.96%): FP-recall (any testing) did not differ between tomosynthesis (FP = 53) and ultrasound (FP = 65), P = 0.26; FP-recall (biopsy) also did not differ between tomosynthesis (FP = 22) and ultrasound (FP = 24), P = 0.86.

**Conclusion:** ASTOUND's interim analysis showed that ultrasound has better incremental BC detection than tomosynthesis in mammography-negative dense breasts. Estimates for additional FP-recall were comparable. Given that tomosynthesis detected >50% of the additional BCs in these women, implications are that it could potentially be the primary mammography screening modality without necessitating adjunct imaging.

**No conflicts of interest**

**4LBA** Late Breaking Oral

**Partial breast radiotherapy for women with early breast cancer: First results of local recurrence data for IMPORT LOW (CRUK/06/003)**

C. Coles[1], R. Agrawal[2], M.L. Ah-See[3], H. Algurafi[4], A. Alhasso[5], A.M. Brunt[6], C. Chan[7], C. Griffin[8], A. Harnett[9], P. Hopwood[8], A. Kirby[10], E. Sawyer[11], I. Syndikus[12], J. Titley[8], Y. Tsang[13], D. Wheatley[14], M. Wilcox[15], J. Yarnold[16], J.M. Bliss[8], on behalf of IMPORT TMG. *[1]Cambridge University Hospitals NHS Foundation Trust, Oncology, Cambridge, United Kingdom; [2]Shrewsbury and Telford Hospitals NHS Trust, Oncology, Shrewsbury, United Kingdom; [3]Mount Vernon Cancer Centre, Breast Cancer Research Unit, London, United Kingdom; [4]Southend University Hospital NHS Foundation Trust, Oncology, Southend, United Kingdom; [5]Beatson West of Scotland Cancer Centre, Oncology, Glasgow, United Kingdom; [6]University Hospitals of North Midlands and Keele University, Oncology, Stoke-on-Trent, United Kingdom; [7]Nuffield Health Cheltenham, Surgery, Cheltenham, United Kingdom; [8]The Institute of Cancer Research, Clinical Trials and Statistics Unit, London, United Kingdom; [9]Norfolk and Norwich University Hospital, Oncology, Norwich, United Kingdom; [10]The Royal Marsden NHS Foundation Trust, Radiotherapy and imaging, London, United Kingdom; [11]Kings College London- Guys Hospital, Research Oncology/Biomedical research centre, London, United Kingdom; [12]Clatterbridge Cancer Centre NHS Foundation Trust, Oncology, Bebington, United Kingdom; [13]Mount Vernon Cancer Centre, Radiotherapy, London, United Kingdom; [14]Royal Cornwall Hospitals NHS Trust, Oncology, Truro, United Kingdom; [15]Independent Cancer Patients Voice, London, United Kingdom; [16]The Institute of Cancer Research, Radiotherapy and imaging, London, United Kingdom*

**Background:** IMPORT LOW is a randomised, multi-centre phase III trial testing partial breast radiotherapy (RT) using intensity modulated RT in women with low risk early stage breast cancer, for whom late complications of RT are the dominant hazard rather than local recurrence (LR).

| Year 5 assessments | n (%) | | |
|---|---|---|---|
| | Control | Test 1 | Test 2 |
| **Photographs − change in breast appearance (comparison with pre-RT baseline)** | | | |
| Number available | 262 | 264 | 279 |
| None | 202 (77) | 205 (78) | 229 (82) |
| Mild | 52 (20) | 45 (17) | 43 (15) |
| Marked | 8 (3) | 14 (5) | 7 (3) |
| P | – | 0.71* | 0.18* |
| **Clinician − worst adverse event (shrinkage, induration, telangiectasia & oedema)** | | | |
| Number available | 445 | 469 | 463 |
| None | 239 (54) | 267 (57) | 266 (58) |
| Mild | 149 (34) | 154 (33) | 151 (33) |
| Moderate | 49 (11) | 42 (9) | 42 (9) |
| Marked | 8 (2) | 6 (1) | 4 (1) |
| P | – | 0.19* | 0.12* |
| **Patient reported outcome measures (PROMS): change in appearance of breast** | | | |
| Number available | 295 | 325 | 331 |
| None | 78 (26) | 88 (27) | 93 (28) |
| Mild | 137 (46) | 171 (53) | 190 (57) |
| Moderate | 59 (20) | 44 (14) | 36 (11) |
| Marked | 21 (7) | 22 (7) | 12 (4) |
| P | – | 0.25* | 0.005* |

*$\chi^2$ test for trend compared to control.

**Materials and Methods:** Women age ⩾50 who had breast conservation surgery, for invasive adenocarcinoma (excluding classical lobular carcinoma) pT1−2 (⩽3 cm) N0−1, any grade, with minimum microscopic margins of ⩾2 mm, were eligible. Patients were randomised (1:1:1) to 40Gy/15F to whole breast (control); 36Gy/15F to whole breast and 40Gy/15Fr to partial breast (test 1); or 40Gy/15F to partial breast (test 2). The primary endpoint is local tumour control in the ipsilateral breast. 1935 patients were required to exclude 2.5% inferiority for each test group (80% power, one-sided alpha 2.5%) assuming 2.5% local recurrence (LR) rate at 5 years in the control group. Key secondary endpoints were late adverse effects measured using a combination of clinical, photographic and patient self-assessments. Analysis was by intention to treat.

**Results:** 2018 patients were recruited from 05/2007 to 09/2010 from 30 UK RT centres (675 control, 674 test 1, 669 test 2). Baseline characteristics were balanced with median age 63 (IQR 58−68); 43%, 47% and 10% were tumour grade 1, 2 and 3; 3% were pN+. Median follow-up is 68.3 (IQR 60.3–73.4) months. The 5-year rate of LR was 1.1% (95% CI 0.5, 2.3), 0.2% (95% CI 0.02, 1.2) and 0.5% (95% CI 0.2−1.4) in the control, test 1 and test 2 groups respectively. Absolute treatment differences in LR with control compared with test 1 is −0.83% (95% CI −1.04, 0.18) and −0.69% (−0.99, 0.44) compared with test 2. For each of the test groups non-inferiority, assessed against the pre-specified 2.5% threshold was demonstrated.

**Conclusions:** At 5 years, partial breast RT was shown to be non-inferior to whole breast RT in women with low risk early breast cancer. LR rates were very low in all treatment groups and moderate and marked normal tissue events were also low across all groups. Follow-up is ongoing and 10 year LR rates will be reported.

**No conflicts of interest**

**5LBA** Late Breaking Oral

**A RCT to evaluate the value of automated remote monitoring of symptoms between clinic visits for women receiving chemotherapy for breast cancer**

K. Mooney[1], S. Beck[1], S. Latimer[1], G. Donaldson[2]. *[1]University of Utah, College of Nursing, Salt Lake City, USA; [2]University of Utah, Anesthesiology- School of Medicine, Salt Lake City, USA*

**Background:** Patient-reported outcomes are often electronically captured during oncology clinic visits. Similar technology can be extended for remote home monitoring between treatment visits. Utilizing a prospective randomized controlled trial, we tested the efficacy of an automated remote monitoring system in reducing symptoms for women with breast cancer beginning a course of chemotherapy.

**Materials and Methods:** Prospectively 152 women beginning chemotherapy for breast cancer were randomized to the Symptom Care at Home (SCH) intervention (n = 83) or usual care (UC) (n = 69). Their mean age was 52.5, (SD = 11.4) and all cancer stages were included. After randomization all women, regardless of assignment, called the SCH telephone-based automated system daily reporting the presence and severity of 11 common symptoms. In addition SCH patients received automated, tailored, self-care messages based on their specific reported symptom pattern. Alerts for moderate or greater severity symptoms for SCH patients were also sent to a study nurse practitioner who called patients and, utilizing a decision support system based on guidelines, intensified symptom care. The primary endpoints were symptom severity across all symptoms and the number days with severe or moderate intensity symptoms. Secondary endpoints included symptom severity for individual symptoms. Mixed modeling and negative binominal regressions were used to compare SCH with UC.

**Results:** The most common symptoms reported at moderate or severe levels (4 or greater 0−10 scale) included fatigue (86%), trouble sleeping (80%), pain (73%), nausea (57%), depressed mood (47%), trouble thinking (46%) and anxiety (45%). SCH patients had significantly less symptom severity across all symptoms than UC (p = 0.031). The benefit occurred early and was sustained. Symptom burden reduction for SCH was 3.98 severity points lower than UC at 30 days from baseline (p = 0.001). SCH also had significant reductions compared with UC in moderate and severe symptom days − a 38% reduction in moderate (4−7 rating) days (p = 0.011) and a 48% reduction in severe (8−10 rating) days (p = 0.006). At 30 days from baseline, 7 of 11 individual symptoms were significantly decreased compared to UC. Moderate or severe intensity days for individual symptoms were also decreased compared to UC including 51% fewer pain days, 72% fewer numbness/tingling days, 66% fewer anxiety days, 61% fewer nausea days and 37% fewer fatigue days.

**Conclusion:** Remote automated monitoring of patient-reported symptoms between breast cancer chemotherapy visits significantly improves symptom outcomes. These results demonstrate that automated telemonitoring systems that efficiently extend cancer symptom care into the home

are very effective in achieving better symptom outcomes for women with breast cancer and should be considered for adoption in routine oncology care.

**No conflicts of interest**

## Thursday, 10 March 2016 16:00−17:30

**CLINICAL SCIENCE SYMPOSIUM**

# HER 2 Positive Breast Cancer

**6LBA** Late Breaking Oral

**Effects of perioperative lapatinib and trastuzumab, alone and in combination, in early HER2+ breast cancer − the UK EPHOS-B trial (CRUK/08/002)**

N. Bundred[1], D. Cameron[2], A. Armstrong[3], A. Brunt[4], A. Cramer[5], D. Dodwell[6], A. Evans[7], A. Hanby[6], S. Hartup[6], A. Hong[8], K. Horgan[6], I. Khattak[9], J. Morden[10], J. Naik[11], S. Narayan[12], J. Ooi[13], A. Shaaban[14], R. Smith[12], M. Webster-Smith[10], J. Bliss[10], Submitted on behalf of the EPHOS-B Investigators. *[1]University Hospital of South Manchester NHS Foundation Trust, Academic Department of Surgery, Manchester, United Kingdom; [2]University of Edinburgh and NHS Lothian, Edinburgh Cancer Centre, Edinburgh, United Kingdom; [3]The Chrtistie NHS Foundation, Manchester, United Kingdom; [4]University Hospitals of North Midlands NHS Trust and Keele University, Stoke-on-Trent, United Kingdom; [5]The Christie Pathology Partnership, Manchester, United Kingdom; [6]Leeds Teaching Hospital, Leeds, United Kingdom; [7]Poole Hospital NHS Foundation Trust, Poole, United Kingdom; [8]Royal Devon & Exeter NHS Foundation Trust, Exeter, United Kingdom; [9]Betsi Cadwaladr University Health Board, Bangor, United Kingdom; [10]The Institute of Cancer Research, ICR-CTSU, Clinical Studies, United Kingdom; [11]Mid Yorkshire Hospitals NHST, Wakefield, United Kingdom; [12]University Hospitals of North Midlands NHS Trust, Cancer Clincial Trials, Stoke-on-Trent, United Kingdom; [13]Bolton NHS FT, Bolton, United Kingdom; [14]University Hospitals Birmingham NHS Foundation Trust, Department of Cellular Pathology, Birmingham, United Kingdom*

**Background:** Optimal management of HER2+ cancers remains unclear. The window between diagnosis and definitive surgery provides an opportunity to assess biological drug effects in a treatment naïve primary breast cancer (BC) population. EPHOS-B was designed to measure the effect of 10−12 days' pre-operative anti-HER2 therapy on proliferation and apoptosis in HER2+ BC patients.

**Patients and Methods:** EPHOS-B is a multicentre, 2-part randomised trial in patients with operable newly diagnosed HER2+ primary BC. In Part 1 patients were randomised (1:2:2) to no perioperative treatment (control), trastuzumab only (6 mg/kg on days 1 & 8 pre-surgery) or lapatinib only (1500 mg/day). Emerging evidence on the efficacy of combination anti-HER2 therapy led to amendment to Part 2 where patients were allocated to control, trastuzumab only (as above) or combination of lapatinib (1000 mg/day) and trastuzumab (1:1:2). Analyses of Part 1 and Part 2 are presented.

Primary endpoint is change in Ki67 and/or apoptosis. Response is defined as a drop in Ki67 of ⩾30% or a rise in apoptosis of ⩾30% from baseline.

Tissue samples were taken at diagnostic core biopsy and surgery and analysed centrally for Ki67, apoptosis (activated caspase 3) and PgR, by immunohistochemistry (IHC). As an exploratory analysis, patients with insufficient tumour at surgery were categorised using pathological reports obtained from centres, blinded to randomised treatment allocation as having either pathological complete response in the breast (pCR), minimal residual disease (MRD, defined as <5 mm invasive tumour), or other. Full central pathology review with analysis of samples for Ki67/apoptosis is due for completion end of February 2016.

| | Control (N = 51) | Lapatinib (N = 51) | Trastuzumab (N = 89) | Combination (N = 66) |
|---|---|---|---|---|
| **Part 1** | N = 22 | N = 51 | N = 57 | – |
| Tumour size (cm) at entry, median (IQR) | 2.0 (1.3−2.5) | 2.5 (1.3−3.0) | 2 (1.5−3.3) | – |
| Breast pCR | 0 (0%) | 0 (0%) | 1 (1.8%) | – |
| MRD | 0 (0%) | 0 (0%) | 1 (1.8%) | – |
| **Part 2** | N = 29 | – | N = 32 | N = 66 |
| Tumour size (cm) at entry, median (IQR) | 1.8 (1.5−2.3) | – | 1.6 (1.3−2.7) | 1.7 (1.2−2.7) |
| Breast pCR | 0 (0%) | – | 0 (0%) | 7 (10.6%) |
| MRD | 0 (0%) | – | 1 (3.1%) | 11 (16.7%) |

(Please note: complete table to follow).

**Results:** 257 patients were recruited (130 in Part 1 and 127 in Part 2); all were HER2+ (91% IHC 3+ and 9% amplified by FISH, locally assessed). Median age was 52 years (IQR 48−62); 48% had tumours >2 cm and 51% were grade 3 on biopsy at entry. According to local assessment, 67% were ER+ and 40% PgR+.

Response by treatment group is shown in the table.

**Conclusion:** The early reduction or absence of invasive disease in approximately quarter of patients after only 11 days' preoperative combination HER2 therapy identifies cancers addicted to the HER2 pathway. Using preoperative antiHER2 therapy offers potential to personalise therapy for these patients. Further trials are required to determine which patients may need only antiHER2 combination therapy continued thus avoiding chemotherapy.

**Conflict of interest:** Other Substantive Relationships: J. Bliss, Educational grant received by ICR in relation to EPHOS-B Trial from GSK. Advisory boards: J. Naik for Astra Zeneca and Novartis and I provided some paid training for Roche employees.

## Friday, 11 March 2016 09:45–11:15

**PLENARY SESSION**

# Keynote Lecture and Late-Breaking Abstracts

**7LBA** Late Breaking Oral

**Global status of advanced/metastatic breast cancer (ABC/mBC): A Decade Report 2005−2015**

F. Cardoso[1], M. Beishon[2], M.J. Cardoso[3], D. Corneliussen-James[4], J. Gralow[5], S. Mertz[6], E. Papadopoulos[7], D. Paonessa[8], F. Peccatori[9], K. Sabelko[10], N. Sakurai[11], D. Spence[12], M. Mayer[13]. *[1]European School of Oncology & Breast Unit, Champalimaud Clinical Center, Lisbon, Portugal; [2]European School of Oncology & Cancer World, London, United Kingdom; [3]MamaHelp & Breast Unit, Champalimaud Clinical Center, Lisbon, Portugal; [4]METAvivor, Annapolis, USA; [5]Seattle Cancer Care Alliance, Washington, USA; [6]Metastatic Breast Cancer Network, New York City, USA; [7]Europa Donna, Europa Donna Cyprus, Nicosia, Cyprus; [8]Liga Argentina de Lucha Contra el Cancer, Buenos Aires, Argentina; [9]European School of Oncology & Fertility & Procreation Unit, European Institute of Oncology, Milan, Italy; [10]Susan G. Komen, Dallas, US; [11]Hope Project NPO, Tokyo, Japan; [12]Breast Cancer Network Australia, Secondary Breast Cancer Strategy, Camberwell, Australia; [13]AdvancedBC.org, New York, USA*

**Background:** To provide a global overview of the progress made in the past decade in the field of metastatic BC (mBC), assess the current status of research and treatment, and identify ways to improve the treatment of these patients.

**Materials and Methods:** A multilayered approach was used to assess the status of mBC with a focus on patient care perspectives, the environmental landscape, and the scientific landscape. Primary research conducted in 2015 included 3 global surveys of the general population, patient support organizations, and BC centers, spanning about 15,000 individuals in 34 countries. Responses were gathered online, by telephone, or through face-to-face interviews. Secondary research included analysis of peer reviewed literature, patient survey reports and online articles.

**Results:** Despite efforts over the past decade, significant gaps remain in communication, public understanding, and scientific progress in mBC. 48−76% of the general public believed that mBC is curable, and 18−49% indicated that patients with mBC should keep their disease a secret. Although varied, the greatest identified needs of mBC patients were support (79%) and quality of life (QoL) (79%); QoL had limited improvement over the past decade. Though 83% of health care providers (HCPs) recognize the need for training to bring difficult news to patients and families, less than 50% reported having received such training, and 65% of end-of-life discussions were held too late. Further, nearly half of mBC patients had not told their HCPs about their therapy goals. The worldwide burden of BC is expected to rise dramatically, with an estimated 43% increase in the absolute number of deaths by 2030. However, scientific advances have not kept up with several other tumor types, with only 4 approved targeted therapies compared with 6 in melanoma and 7 in lung cancer, in the past decade. The 5 year survival rate for mBC is still about 25%. However, there is now a robust pipeline of mBC drugs, with 21 currently in phase 3 trials. Data on societal

perspectives of mBC, with a focus on community/workplace settings, are being analyzed by the project steering committee and will also be presented.

**Conclusions:** Improvements in mBC have been small and slow to achieve, with the exception of HER-2 positive disease. mBC is still an incurable disease, with a median survival of 2–3 years. Understanding the global landscape of this disease and what has been achieved in the past decade provides the evidence to develop a call to action that will be implemented worldwide, through the collaboration of the scientific and advocacy communities. The report was developed in collaboration with the European School of Oncology and Pfizer. The underlying surveys and report were sponsored by Pfizer.

**Conflict of interest:** Consultant: Astellas/Medivation, AstraZeneca, Celgene, Daiichi-Sankyo, Eisai, GE Oncology, Genentech, GlaxoSmithKline (GSK), Merck-Sharp, Merus BV, Novartis, Pfizer, Pierre-Fabre, Roche, Sanofi, Teva.

**8LBA** Late Breaking Oral

**Prospective WSG phase III PlanB trial: Clinical outcome at 5 year follow up and impact of 21 Gene Recurrence Score result, central/local-pathological review of grade, ER, PR and Ki67 in HR+/HER2− high risk node-negative and -positive breast cancer**

O. Gluz[1], U. Nitz[1], M. Christgen[2], R. Kates[3], M. Clemens[4], S. Kraemer[5], B. Nuding[6], B. Aktas[7], S. Kümmel[8], T. Reimer[9], F. Lorenz-Salehi[10], P. Krabisch[11], M. Just[12], D. Augustin[13], C. Liedtke[14], C. Svedman[15], S. Shak[16], R. Würstlein[17], H. Kreipe[2], N. Harbeck[18]. *[1]West German Study Group, Clinical Research, Mönchengladbach, Germany; [2]MHH Hannover, Pathology, Hannover, Germany; [3]West German Study Group, Statistics, Mönchengladbach, Germany; [4]Mutterhaus Trier, Oncology, Trier, Germany; [5]University Clinics Cologne, Gynecology and Obstetrics, Cologne, Germany; [6]EVK Bergisch Gladbach, Gynecology and Obstetrics, Bergisch Gladbach, Germany; [7]University Clinics Essen, Gynecology and Obstetrics, Essen, Germany; [8]Kliniken Essen Mitte, Breast Centre, Essen, Germany; [9]Klinikum Südstadt, Gynecology and Obstetrics, Rostock, Germany; [10]HSK Wiesbaden, Gynecology and Obstetrics, Wiesbaden, Germany; [11]Klinikum Chemnitz, Gynecology and Obstetrics, Chemnitz, Germany; [12]Oncology Practice, Bielefeld, Germany; [13]Klinikum Deggendorf, Breast Centre, Deggendorf, Germany; [14]University Clinics Lübeck, Gynecology and Obstetrics, Lübeck, Germany; [15]Genomic Health Inc, Redwood, USA; [16]Genomic Health Inc, Redwood, USA; [17]LMU Munich, Gynecology and Obstetrics- Breast Centre, Munich, Germany; [18]LMU Munich, Gynecology and Obstetrics, Munich, Germany*

**Background:** The 21-gene Recurrence Score (RS) assay, nodal status, grade, and immunohistochemical markers are recommended for chemotherapy decision making in HR+/HER2− early breast cancer (EBC). The phase III PlanB trial, prospectively used RS to define a low-risk subset of patients with node negative disease with high risk traditional parameters and patients with node positive disease (HR+, HER2−) who could be treated with adjuvant endocrine therapy alone. We have previously reported the prospectively planned interim analysis at 3-years of clinical outcome and substantial discordance between central and local grade, Ki67 and RS. Here, we report for the first time 5-year outcome data from the trial.

**Material and Methods:** A central tumor bank was prospectively established within PlanB. Following an early amendment, HR+, pN0−1 patients with RS $\leqslant$ 11 were recommended to omit adjuvant chemotherapy (CT). Patients with RS of 12 or above were randomized to 6$\times$ TC vs. 4$\times$ EC- 4$\times$ Docetaxel chemotherapy. Primary endpoint of the study was disease free survival (DFS), defined as relapse (invasive and non-invasive), secondary malignancy or death. Reported survival percentages were based on the Kaplan-Meier estimator. Univariate and multivariate Cox proportional hazard models for DFS were performed.

**Results:** From 2009 to 2011, PlanB enrolled 3198 patients; median age of 56 years; 41.1% had node-positive and 32.5% grade 3 disease. In 348 patients (15.3%), CT was omitted based on RS $\leqslant$ 11. After 55 months median follow-up, 5-year DFS in patients with RS $\leqslant$ 11 and endocrine therapy alone was estimated as 94% vs. 94% (RS 12–25) and 84% (RS > 25) in CT-treated patients ($p < 0.001$). Nodal status, central and local grade, Ki-67, ER, PR, tumor size, and RS were univariate prognostic factors for DFS; only pN2–3, both central and local grade, tumor size >2 cm, and fractionally ranked RS were independent multivariate factors.

**Conclusions:** WSG PlanB for the first time shows excellent 5-year DFS of 94% in a population of high risk node-negative and node-positive (pN1) early BC patients (HR+ HER2−) who omitted adjuvant CT based on RS $\leqslant$ 11. Together RS and classical clinical-pathological markers, despite of substantial heterogeneity in their assessment, provided independent prognostic information. These 5 year outcome data from a prospective trial incorporating the RS support the incorporation of the assay in combination with nodal status, grade and tumor size for adjuvant treatment decisions in early HR+ HER2− BC.

**Conflict of interest:** Advisory Board: Genomic Health.

## Friday, 11 March 2016 14:00–15:30

**CLINICAL SCIENCE SYMPOSIUM**

# What is New in the Biology of Breast Cancer?

**9LBA** Late Breaking Oral

**The molecular landscape of high-risk early breast cancer: comprehensive biomarker analysis of a phase III adjuvant population**

T. Wilson[1], J. Yu[2], X. Lu[2], J. Spoerke[1], Y. Xiao[2], C. O'Brien[1], H. Savage[1], L. Huw[1], W. Zou[2], H. Koeppen[3], W. Forrest[4], J. Fridlyand[2], F. Ling[1], R. Tam[1], E. Schleifman[1], T. Sumiyoshi[1], L. Molinero[1], G. Hampton[1], J. O'Shaughnessy[5], M. Lackner[1]. *[1]Genentech, Oncology Biomarker Development, South San Francisco, USA; [2]Genentech, Biostatistics, South San Francisco, USA; [3]Genentech, Pathology, South San Francisco, USA; [4]Genentech, Bioinformatics, South San Francisco, USA; [5]US Oncology, Baylor Sammons Cancer Center, Dallas, USA*

**Background:** Breast cancer is a heterogeneous disease and patients are managed clinically based on ER, PR, HER2 expression and key risk factors. We sought to characterize the molecular landscape of high-risk breast cancer patients enrolled onto an adjuvant study to understand how disease subsets and tumor immune status impact survival.

**Materials and Methods:** DNA and RNA were extracted from 1539 breast cancer samples from patients enrolled onto the United States Oncology trial 01062 (clinicaltrials.gov/show/NCT00089479). Samples were characterized using multiplex gene expression, copy number and qPCR mutation assays.

**Results:** HR+ patients with a PIK3CA mutant tumor had a favorable outcome (HR 0.66, $P = 0.052$), however, the prognostic effect was specific to luminal A patients (Luminal A: HR 0.67, $P = 0.1$; Luminal B: HR 1.01, $P = 0.98$). The basal subtype within TNBC cancers trended to have an improved 5-year DFS with the addition of capecitabine (HR 0.75. $P = 0.26$). Further TNBC molecular subtyping suggested that the mesenchymal subtype had the worst prognosis whereas the immunomodulatory subtype had the best prognosis. Profiling of immunologic genes revealed that TNBC tumors displaying an activated T cell signature had a longer DFS following adjuvant chemotherapy (HR 0.59, $P = 0.044$), while a distinct set of immune genes was associated with DFS in HR+ cancers. Utilizing a discovery approach, we identified genes (e.g. PDCD4 and MAP3K1) associated with a high risk of recurrence in HR+ patients, which were validated in an independent data set.

**Conclusions:** Molecular classification based on PAM50 and TNBC subtyping stratified clinical high-risk patients into distinct prognostic subsets. Patients with high expression of immune-related genes showed superior DFS in both HR+ and TNBC. These results may inform patient management and drug development in early breast cancer.

**Conflict of interest:** Ownership: TW, JY, XL, JS, YX, COB, HS, LH, WZ, HK, WF, JF, LF, RT, ES, TS, LM, GM and ML are employed by Genentech and have stock ownership in Roche.

## 9–11 March 2016

POSTER SESSION

# Late-Breaking Posters

**400LBA** Late Breaking Poster

### The long term follow up of patients undergoing oncotype Dx testing in a multicenter study in southwest Wales, UK

S. Khawaja[1], S. Udayasankar[1], A. Munir[1], D. Thomas[1], A. Huws[1], Y. Shariaha[1], S. Holt[1]. [1]*Prince Philip Hospital, Breast Unit, Llanelli, United Kingdom*

**Background:** A multicentre prospective trial took place in southwest Wales on oncotype Dx testing in the year 2010. Chemotherapy decision making was initially determined with adjuvant online and revised if needed with the recurrence score results. The purpose of this study was to determine the long term five year follow up of this patient cohort in terms of the number of patients who recurred either locally or systemically.

**Materials and Methods:** A total of 142 patients were involved in the trial of oncotype Dx testing in Southwest Wales in the year 2010. All patients who had estrogen receptor positive and node negative breast cancer were consented to enter the trial. Four hospital sites were involved in the recruitment of these patients. The oncologist initially discussed the role of chemotherapy based on adjuvant online. The oncotype Dx test was then requested, and the patient was seen again with the recurrence score result. The decision of chemotherapy remained either the same or was altered. Long term five year follow up of these patients was documented on their last clinic visit.

**Results:** The age of the patients was from 34 years to 72 years with a mean of 55 years. The initial chemotherapy decision based on adjuvant online was no in 84 patients and yes in 55 patients. After the oncotype test results, the final chemotherapy decision was no in 100 patients and yes in 39 patients. Three patients had insufficient tissue for testing. There was a total of 5 recurrences in the 5 year follow up period. Two patients had in breast local recurrences in a different quadrant from the surgical site, while 3 patients had systemic recurrence. The two patients with a local recurrence had a recurrence score of 14 and 23. Both patients had no plan for chemotherapy prior to and after testing. The third patient had lung metastases with an initial grade 2 infiltrating lobular carcinoma of 30 mm and being PR negative. Initially not planned for chemotherapy and received it with a recurrence score of 39. The fourth patient with lung and liver metastases had a recurrence score of 24 with a 19 mm grade 2 infiltrating ductal carcinoma which was PR positive. The patient was planned for chemotherapy from the start and received FEC. The fifth patient had lung, liver, bones and axillary metastases with a grade 3 invasive ductal cancer of 20 mm with it being PR negative. The recurrence score was 40, and the patient was planned for chemotherapy from the start with FEC. Out of the five patients with recurrence, only one had a low risk score on oncotype Dx testing with the other four having either an intermediate or high score.

**Conclusion:** After the present five year follow up, one can conclude that our change of chemotherapy decision making based on the oncotype Dx results was effective management in this trial group of patients.

**No conflicts of interest**

**402LBA** Late Breaking Poster

### First results of an pre-planned interim analysis of a national multicenter Patient Reported Outcome Study (PRO-Bra) in breast reconstruction following mastectomy with titaniferously coated polypropylene mesh (TiloopBra)

S. Paepke[1], E. Klein[1], D. Paepke[1], M. Kiechle[1], M. Dieterich[2], J.U. Blohmer[3], R. Ohlinger[4], M. Warm[5], M. Thill[6], C. Schumacher[7], A. Faridi[8], A. Meiré[7]. [1]*Klinikum rechts der Isar – Technische Universität München, Frauenklinik und Poliklinik der TU München, München, Germany;* [2]*Universitätsfrauenklinik Rostock, Südstadt Krankenhaus, Rostock, Germany;* [3]*Klinik für Gynäkologie CCM- Charité, Brustzentrum der Charité, Berlin, Germany;* [4]*Klinik und Poliklinik der Universitätsmedizin Greifswald, Frauenheilkunde und Geburtshilfe, Greifswald, Germany;* [5]*Brustzentrum Köln-Holweide, Brustzentrum, Köln, Germany;* [6]*Agaplesion Markus Krankenhaus, Klinik für Gynäkologie und Geburtshilfe, Frankfurt am Main, Germany;* [7]*St. Elisabeth-Krankenhaus Köln-Hohenlind, Brustzentrum/Senologie, Köln, Germany;* [8]*Vivantes Klinikum Am Urban, Brustzentrum, Berlin, Germany*

**Background:** In the majority of interdisciplinary breast centers of Germany implant based, mesh-supported operations constitute a total of approximately 50–60% of reconstructive techniques. The vast majority of mesh-supported reconstructive breast surgery is performed with the titanized polypropylene mesh TiLoop®Bra [Zoche H; 2014]. The BreastQ [Pusic AL; 2006] is the most valid and reliable measurement of quality of life aspects in important domains used in clinical routine.

**Material and Method:** Because the patient reported outcome is the most relevant factor reflecting the overall satisfaction from a patient perspective a prospective single arm non-randomized surveillance study with BreastQ-scales at 12 months as primary endpoint was conducted (2013). Overall 205 breasts of 153 pts. were treated between 12/2013 and 9/2015. A pre-planned analysis of the first 60 pts. with completion of the BreastQ after 6 months (secondary endpoint) was done.

**Results:** Most frequent indication was BC. Almost all surgeries were primary reconstructions (96.6%) and nipple-skin-sparing mastectomies (97.1%). A expander exchange is planned for 20 pts. The most frequent incision was inframammary (n = 115), followed by T-shaped (n = 45). The average of the pts. was 50 y (19–77); BMI was 22 (17–33), 77.3% were non-smokers. Percentage of neoadjuvant chemotherapy was 23%, of prior radiotherapy was 12%. Radiotherapy showed no significant influence of the BreastQ. Severe events occurred in 46 cases. The most frequent complications were necrosis (n = 12), hematoma (n = 12); 9 pts. dropped out. The mean score of BreastQ was equal pre- and postoperative after 6 months (67±16 to 65±15); satisfaction with breast from 67±22 to 61±14; psycho-social well-being from 71±17 to 73±18; sexual well-being from 62±17 to 60±19; satisfaction with outcome was 75±18 and satisfaction with surgeon 90±15. 88.3% were very satisfied, 10.0% somewhat satisfied, only 1.7% somewhat dissatisfied, 0% very dissatisfied.

**Conclusion:** The first analysis of the PROBra-study shows positive results in all outcome parameters. The study will continue until the complete recruitment of the pre-planned 267 pts. within a follow up of at least two years.

**Conflict of interest:** Other Substantive Relationships: Honoraria, Consulting, travel costs by PFM Medical AG, Wankelstraße 60, 50996 Köln, Germany.

**403LBA** Late Breaking Poster

### Elevated ANXA1 levels predict trastuzumab resistance in HER2-positive breast cancer

K. Berns[1]. [1]*Antoni van Leeuwenhoek – Netherlands Cancer Institute, molecular carcinogenesis, Amsterdam, Netherlands*

**Background:** Despite the substantial progress in the development of targeted anti-cancer drugs, treatment failure due to primary or acquired resistance is still a major hurdle in the effective treatment of most advanced human cancers. Understanding these resistance mechanisms will be instrumental to improve personalized cancer treatment.

**Methods:** Genome wide loss-of-function genetic screens were performed to identify genes implicated in resistance to HER2/PI3K/mTOR targeting agents in HER2+ breast cancer cell lines. Expression and adjuvant trastuzumab response data from the HER2+ breast cancer trials FINHER and Responsify were used to validate our findings in patient series.

**Results:** We find that reduced ARID1A expression confers resistance to several drugs that inhibit the HER2/PI3K/mTOR signaling cascade at different levels. We demonstrate that ARID1A loss activates AnnexinA1 (ANXA1) expression, which is required for drug resistance through its activation of AKT. Consistent with these in vitro data, we find in two independent $HER2^{+}$ breast cancer patient series that high ANXA1 expression is associated with resistance to adjuvant trastuzumab based therapy.

**Conclusion:** Our findings provide a rationale for why tumors accumulate ARID1A mutations and identify high ANXA1 expression as a predictive biomarker for trastuzumab-based treatment. Our findings also suggest strategies to treat breast cancers with elevated ANXA1 expression.

**No conflicts of interest**

**404LBA** Late Breaking Poster

### Data managers: A survey of the European Society of Breast Cancer Specialists (EUSOMA) in certified multidisciplinary breast Centres

A. Ponti[1], L. Marotti[2], T. Tarasco[2], D. Casella[1], G. Schnapper[3], M.P. Mano[4], R. Mansel[5]. [1]*AOU Citta della Salute e della Scienza, CPO Piemonte, Torino, Italy;* [2]*EUSOMA, Florence, Italy;* [3]*Comprensorio Sanitario di Bolzano, Surgery, Bolzano, Italy;* [4]*University of Turin, CPO Piemonte, Torino, Italy;* [5]*Cardiff University, School of Medicine, Cardiff, United Kingdom*

**Background:** According to an European Parliament deliberation, multidisciplinary breast Centres should be established throughout Europe by 2016. The EUSOMA document "The requirements of a specialist breast centre"

defines data managers (DM) as "trained and dedicated persons responsible for breast data management" and includes them in the multidisciplinary core team. However, the characteristics and actual role of these emerging professionals are little known.

**Materials and Methods:** A 44-questions web questionnaire was submitted to the DM of all EUSOMA certified breast Centres in October, 2015. The last response was received in December.

**Results:** 23 of 28 Centres (82%) and 24 DM from Italy, The Netherlands, Belgium, Germany and Switzerland responded. They were in prevalence (21 of 24) females of a wide range of ages. The majority were highly educated: 67% held a PhD or a Master degree while 12% completed education with a high school diploma. Some are nurses, a few physicians, others are software specialists or have been trained as clinical trials managers or for administrative positions. All stated to be proficient in at least one foreign language.

More than half of DM held their post for more than 5 years and for all except one this was not their first job. Two thirds held it as the only job while the remaining have another work activity, equally distributed between administrative tasks in the Health sector, a clinical job, and activities not related to health. Of 24, eight only worked full time in the breast Centre as data managers.

All DM but one have a clinical supervisor. Half declared to have no direct contact with patients. All Centres have a clinical data base, which is fed in 29% of cases contemporaneous to patients' management. 70% of responders reported to attend weekly multidisciplinary meetings and 88% to be responsible for organising the annual (38%) or biannual (54%) performance and clinical review meetings, including preparatory data analysis and the monitoring of quality indicators. Forty per cent present personally the results to the team.

Forty-two per cent of DM reported to have received less than 10 hours of specific training in the breast Centre regarding their work. Eighty per cent declared that an European document proposing a core-curriculum for breast Centres DM would be useful.

Most DM (88%) report being satisfied or very satisfied with their work.

**Conclusions:** Breast Centres data managers are highly educated individuals with a variety of backgrounds carrying out, more frequently part-time, a job for which they received little specific training. They represent an important added value in the specialist breast Centres model and are instrumental for assuring and improving quality and as an aid to research. Their role would probably be even more beneficial if a core curriculum and job title were agreed at European and Country levels.

**No conflicts of interest**

# Oral Abstracts

## Thursday, 10 March 2016 09:45–11:15

CLINICAL SCIENCE SYMPOSIUM

# Controversial Issues With the Neo-Adjuvant Approach

1 Oral

**Baseline MRI for breast cancer patients receiving neoadjuvant chemotherapy leads to additional biopsies and unnecessary cost**

R. Lancaster[1], M. Seagren[1], R. Mukhtar[2], E. Price[3], J. Wong[1], C. Ewing[1], L. Esserman[1], M. Alvarado[1]. [1]*University of California San Francisco, Breast Surgical Oncology, San Francisco CA, USA;* [2]*Kaiser Permanente, General Surgery, San Francisco, USA;* [3]*University of California San Francisco, Radiology, San Francisco CA, USA*

**Background:** To evaluate extent of disease and allow monitoring of chemotherapy response, women with locally advanced breast cancer often undergo a pre-therapy MRI that can cost between 5,000–8,765 USD. Furthermore, MRI guided biopsies can cost between 13,762–15,261 USD.

**Materials and Methods:** Evaluating data from the University of California San Francisco Breast Cancer Registry, we retrospectively identified women treated for locally advanced breast cancer from October 2010 to January 2014. We identified 147 consecutive patients with unilateral, non-recurrent breast cancer that received a baseline MRI at the onset of neoadjuvant chemotherapy.

**Results:** Median age at diagnosis was 49.8 years. The majority of patients were Caucasian (70.7%). Sixty-two (42.1%) were hormone receptor positive-HER2 negative, thirty-nine (26.5%) were hormone receptor positive-HER2 positive, twelve (8.1%) were hormone receptor negative-HER2 positive, and thirty-four (23.1%) were triple negative. Baseline MRI identified contralateral findings (BIRADS 4 or 5) in 39 patients. 23.8% of baseline MRIs resulted in either a successful (33) or an attempted contralateral breast biopsy (2). A majority (76.4%) of these contralateral breast biopsies occurred via MR guidance with the other biopsies occurring via US guidance (17.6%) or operative excision (5.8%). The majority of contralateral biopsies were benign 29 (87.8%), 3 were invasive and 1 was DCIS. There was no association between index tumor receptor subtypes and the incidence of contralateral MRI findings, the incidence of a contralateral biopsy, or the pathology associated with the contralateral biopsy. There was no association between index tumor receptor subtype and the surgery performed. A contralateral breast biopsy was associated with an increased incidence of bilateral surgery ($p = 0.017$).

**Conclusions:** We estimate that over 1.2M USD was spent to obtain 147 baseline MRIs leading to 33 contralateral biopsies. 76% of these additional biopsies occurred via MR guidance with an additional cost of approximately 400K USD. Overall, baseline MRI detected clinically relevant contralateral pathology in only 4/147 (2.7%) cases. In the current climate of healthcare cost consciousness, efforts should focus on a more selective approach to MRI utilization and on identifying ways to limit contralateral biopsy. Our findings highlight the importance of both the surgeon and radiologist in making thoughtful decisions regarding contralateral breast biopsies on lesions found on MRI as it potentially subjects patients to unnecessary procedures and additional costs. Surgeons must remain cognizant that a contralateral finding on MRI or a contralateral biopsy, regardless of the pathology finding, has the potential to influence their surgical decision-making.

**No conflicts of interest**

2 Oral

**Pattern of care using breast MRI in patients undergoing neoadjuvant chemotherapy: Dutch population based study in 4,796 breast cancer patients**

I.J.H. Vriens[1], M.B.I. Lobbes[2], A.C.M. Van Bommel[3], G.A.P. Nieuwenhuijzen[4], M.L. Smidt[5], L. Boersma[6], C.H. Smorenburg[7], H. Struikmans[8], S. Siesling[9], A.C. Voogd[1], V.C.G. Tjan-Heijnen[1]. [1]*Maastricht University Medical Center+, Medical Oncology, Maastricht, Netherlands;* [2]*Maastricht University Medical Center+, Radiology, Maastricht, Netherlands;* [3]*Leiden University Medical Center, Surgery, Leiden, Netherlands;* [4]*Catharina Ziekenhuis Eindhoven, Surgery, Eindhoven, Netherlands;* [5]*Maastricht University Medical Center+, Surgery, Maastricht, Netherlands;* [6]*Maastro Clinic, Radiotherapy, Maastricht, Netherlands;* [7]*Antoni van Leeuwenhoek Ziekenhuis, Medical Oncology, Amsterdam, Netherlands;* [8]*Medisch Centrum Haaglanden, Radiotherapy, 's Gravenhage, Netherlands;* [9]*Comprehensive Cancer Center The Netherlands, Research, Utrecht, Netherlands*

**Background:** Previously, we reported that in patients who underwent immediate surgery breast Magnetic Resonance Imaging (MRI) use was associated with less primary and secondary mastectomies in the treatment of invasive lobular cancer (ILC), in contrast to an increased number of primary mastectomies in patients with invasive ductal cancer (IDC). MRI was further associated with an almost fourfold higher incidence of contralateral breast cancer (SABCS 2015). So far, regarding the impact of breast MRI use in the neoadjuvant setting, only limited data are available.

**Patients and Methods:** All patients that underwent NAC for stage I-III invasive breast cancer in The Netherlands in the years 2011–2013 were identified through the Netherlands Cancer Registry. Using multivariate analyses, we analysed which parameters were associated with MRI use in patients treated with NAC and whether MRI use was related to type of surgery, surgical margin involvement and diagnosis of synchronous contralateral breast cancer.

**Results:** MRI was performed in 3,651 (76.1%) out of 4,796 patients treated with NAC. Younger patients more often had a breast MRI: Odds Ratio (OR) 10.31 (95% Confidence Interval (CI) 8.15–13.05) in patients $\leqslant$50 years and OR 5.92 (95% CI 4.73–7.40) in patients 50−69 years of age as compared to those of 70 years and older. Moreover, larger tumour stage (cT2 OR 1.88; 95% CI 1.53–2.31; cT3−4 OR 1.84; 95% CI 1.47–2.31 as compared to cT1 tumours), higher nodal status (cN+ OR 1.30; 95% 1.11–1.52 as compared to cN0), multifocality (OR 1.45; 95% CI 1.21–1.73 as compared to no multifocality) and lobular histology (OR 1.41; 95% CI 1.12–1.78 as compared to ductal) were all significantly associated with increased breast MRI use in patients treated with NAC. Use of breast MRI in patients treated with NAC was associated with a decrease in number of mastectomies as first surgical procedure (OR 0.80; 95% CI 0.64–0.94). No significant association was found between the use of MRI and the risk of a positive surgical margins (OR 0.70; 95% CI 0.42–1.18) and the number of secondary mastectomies (OR 1.30; 95% CI 0.58–2.92). No significant association was found between MRI use and the frequency of being diagnosed with contralateral breast cancer in patients treated with NAC (OR 1.21; 95% CI 0.78–1.88).

**Conclusion:** Younger age was the most important parameter associated with breast MRI use in patients treated with NAC. Breast MRI use was associated with a decrease in primary mastectomies, fortunately not at the expense of an increased risk of positive surgical margin in those patients who had breast conserving surgery.

**No conflicts of interest**

## Thursday, 10 March 2016 09:45–11:15

CLINICAL SCIENCE SYMPOSIUM

# Genes, Families and Other Risk Factors

3 Oral

**Pre- and post-pregnancy cigarette smoking and the risk of premenopausal breast cancer**

P. Gradowska[1], M. Hauptmann[1], M. Rookus[1]. [1]*Netherlands Cancer Institute, Epidemiology and Biostatistics, Amsterdam, Netherlands*

**Background:** Several studies reported increased breast cancer risks for smoking before but not after a first full time pregnancy (FFTP), although these studies mainly included postmenopausal women. We evaluated smoking before and after a FFTP among mainly premenopausal women.

**Materials and Methods:** We analyzed a Dutch population-based case–control study including 918 patients diagnosed with a first primary breast cancer in 1986–1989 at 20−54 years of age and 918 individually age- and area-matched controls. Information on lifetime smoking history, known or suspected breast cancer risk factors, and reproductive events was obtained by personal interview. Conditional logistic regression was used to estimate odds ratios (ORs) and confidence intervals (CIs).

**Results:** Among 1,558 parous women, 600 of the 758 cases were premenopausal. Accounting for age at FFTP, lifetime cigarette smoking was associated with an increased breast cancer risk (OR per 10 pack-years of smoking, 1.2; 95% CI, 1.0−1.3). The OR was elevated for smoking after FFTP (OR per 10 pack-years of smoking, 1.2; 95% CI, 1.1−1.5), but not for prepartum smoking (OR per 10 pack-years of smoking, 0.9; 95% CI, 0.6−1.4). The association was stronger for premenopausal breast cancer, while no association was observed for postmenopausal breast cancer. After FFTP, smoking 1−3, 4−9, 10−16, and 17 or more pack-years versus not smoking yielded ORs of 1.6 (95% CI, 1.1−2.4), 1.3 (95% CI, 0.9−1.9), 1.7 (95% CI, 1.1−2.5) and 1.8 (95% CI, 1.1−3.0), respectively (p-trend=0.019). Further adjustment for body mass index or other established or suspected risk factors did not alter the results.

**Conclusions:** Our results suggest that cigarette smoking increases premenopausal breast cancer risk. The observed association seems to be mainly driven by smoking after a FFTP.

**No conflicts of interest**

**4** Oral

**Ethnicity and the tumour characteristics of breast cancer in a large nationally representative sample of women in England**

T. Gathani[1], V. Beral[1], G. Reeves[1], K. Pirie[1], I. Barnes[1]. [1]*University of Oxford, Cancer Epidemiology Unit, Oxford, United Kingdom*

**Background:** There is limited information about differences in the tumour characteristics of breast cancer in women of different ethnic minorities in the United Kingdom. Complete data on tumour characteristics by ethnicity are available for over 68,000 breast cancers registered in England between 2006 and 2013 and are reported here.

**Methods:** The data analysed includes information about patient characteristics including age at diagnosis, region of residence, deprivation, and ethnicity and about tumour characteristics including size, grade, nodal status, oestrogen (ER) and Herceptin (HER2) receptor status. For each tumour characteristic, a logistic regression model was used to estimate the odds ratio (OR) and 95% confidence interval by ethnicity adjusting for age, region, deprivation, and all other tumour characteristics.

**Results:** There were 66,192 breast cancers in White women, 1233 in South Asian women and 641 in Black women. The mean age at diagnosis was significantly lower in both South Asians (55.0 years) and Blacks (54.6 years) compared to Whites (60.4 years). 50% of Blacks were in the lowest socioeconomic quintile, compared with 40% of South Asians and less than 15% of Whites.

In unadjusted analyses, both South Asian and Black women were more likely than White women to have had higher risks of more biologically aggressive tumour factors including higher grade, larger size, ER negativity and node positive tumours. However on multivariate analyses and allowing for all factors listed above there were fewer differences. For example, compared to White women, the unadjusted and adjusted OR for tumours >5 cm was 1.23 and 1.03 (not significant) for South Asian women, and 2.06 and 1.55 for Black women. Similarly, compared to White women, the unadjusted and adjusted OR for node positive cancers was 1.32 and 1.16 for South Asian women and 1.6 to 1.2 for Black women. No differences were seen in the risk of HER2 positive tumours across different ethnic groups.

**Conclusions:** This study provides nationally reliable data in England on the association between ethnicity and different tumour characteristics of breast cancer. Much of the apparent differences in tumour characteristics by ethnicity is due to confounding by age and socioeconomic factors, together with the intercorrelation between the characteristics. Simultaneous adjustment for all these factors substantially reduces the differences by ethnicity.

**No conflicts of interest**

## Thursday, 10 March 2016 11:30−12:30

**BEST ORAL ABSTRACT SESSION**

# Best Oral Abstracts

**5** Oral

**Dose-dense adjuvant chemotherapy, treatment-induced amenorrhea and overall survival in premenopausal breast cancer patients: A pooled analysis of the MIG1 and GIM2 phase III studies**

M. Lambertini[1], M. Ceppi[2], P. Bruzzi[2], G. Cavazzini[3], F. Cognetti[4], M. De Laurentiis[5], S. De Placido[6], A. Michelotti[7], G. Bisagni[8], A. Durando[9], E. Valle[10], T. Scotto[11], A. De Censi[12], A. Turletti[13], M. Benasso[14], S. Barni[15], F. Montemurro[16], F. Puglisi[17], C. Bighin[1], L. Del Mastro[18]. [1]*IRCCS AOU San Martino − IST, Department of Medical Oncology − U.O. Oncologia Medica 2, Genova, Italy;* [2]*IRCCS AOU San Martino − IST, Unit of Clinical Epidemiology, Genova, Italy;* [3]*Ospedale "Carlo Poma", Oncologia, Mantova, Italy;* [4]*Istituto Regina Elena per lo Studio e la Cura dei Tumori, Department of Medical Oncology, Rome, Italy;* [5]*Istituto Nazionale Tumori − IRCCS Fondazione Pascale, Medical Oncology, Naples, Italy;* [6]*Azienda Ospedaliera Universitaria Federico II, Medical Oncology, Naples, Italy;* [7]*Azienda Ospedaliero − Universitaria Pisana, Oncologia Medica 1, Pisa, Italy;* [8]*IRCCS Arcispedale S. Maria Nuova, Medical Oncology, Reggio Emilia, Italy;* [9]*Citta' della Salute e della Scienza- ASO S. Anna, Breast Unit, Turin, Italy;* [10]*Ospedale Oncologico "A. Businco", Oncologia Medica, Cagliari, Italy;* [1]*Ospedale Civile, U.O. Oncologia Medica, Sassari, Italy;* [12]*Ospedali Galliera, Medical Oncology, Genova, Italy;* [13]*ASLTO1, Medical Oncology, Turin, Italy;* [14]*Ospedale S. Paolo, Medical Oncology, Savona, Italy;* [15]*Azienda Ospedaliera Treviglio, UOC Oncologia Medica, Treviglio, Italy;* [16]*Fondazione del Piemonte per l'Oncologia/Candiolo Cancer Center IRCCS, Investigative Clinical Oncology, Candiolo, Italy;* [17]*Azienda Ospedaliera di Udine, Department of Oncology, Udine, Italy;* [18]*IRCCS AOU San Martino − IST, Department of Medical Oncology − U.O. Sviluppo Terapie Innovative, Genova, Italy*

**Background:** No evidence exists to recommend a specific chemotherapy (CT) regimen for premenopausal breast cancer (BC) patients (pts). No prospective data are available on the impact of dose-dense (DD) CT on the risk of developing treatment-induced amenorrhea (TIA). With a pooled analysis of two large randomized DD adjuvant studies, we aim to evaluate the efficacy of DD CT in the subgroup of premenopausal BC pts and its impact on the risk of developing TIA.

**Material and Methods:** In the MIG1 study, node positive or high-risk node negative BC pts were randomized to receive 6 cycles of fluorouracil/epirubicin/cyclophosphamide (FEC 600/60/600 mg/m$^2$) every 2 (DD) or every 3 (standard interval [SI]) weeks (Venturini et al, JNCI 2005). Using a 2×2 factorial design, the GIM2 study randomized node positive early BC pts to receive 4 cycles of DD or SI EC or FEC followed by 4 cycles of DD or SI paclitaxel (T) (Del Mastro et al, Lancet 2015). The same number of cycles (4 EC or FEC and 4 T) and doses (F 600 mg/m$^2$, E 90 mg/m$^2$, C 600 mg/m$^2$, T 175 mg/m$^2$) were used in all treatment arms.

TIA was defined as absence of menses after the end of CT, after 3 to 6 months in the MIG1 study and after 12 months in the GIM2 study.

Using individual patient data, the hazard ratio (HR) of DD or SI CT for overall survival (OS) by means of a Cox regression model and the odds ratio (OR) of DD or SI CT for TIA through a logistic regression model were calculated for each study. We then performed a meta-analysis of the two studies and report the parameter estimates of the random effect model.

**Results:** A total of 1,549 pts were included in the present analysis, 528 out of 1,214 from the MIG1 study and 1,021 out of 2,091 from the GIM2 study. Median age was 44.1 years (interquartile range: 39.6–48.0).

In the DD arm and in the SI arm respectively, 10-year OS were 84.9% and 79.1% (HR=0.72, 95% confidence intervals [CI] 0.47–1.11; p = 0.137) in the MIG1 study, and 88.0% and 77.3% (HR=0.71, 95% CI 0.48–1.04; p = 0.079) in the GIM2 study. The pooled analysis showed that DD CT improved significantly OS as compared to SI CT (HR=0.71, 95% CI 0.54–0.95; p = 0.021; test for heterogeneity p = 0.953).

Overall, 39 pts were not evaluable for the TIA analysis. In the DD arm and in the SI arm respectively, 160 (59.9%) and 159 (60.9%) pts in the MIG1 study (OR=1.15, 95% CI 0.78–1.70; p = 0.484), and 229 (46.3%) and 235 (44.7%) in the GIM2 study (OR=1.01, 95% CI 0.79–1.30; p = 0.925) developed TIA. The pooled analysis showed that DD CT was not associated with an increased risk of developing TIA (OR=1.05, 95% CI 0.85–1.30; p = 0.646; test for heterogeneity p = 0.592).

**Conclusions:** DD adjuvant CT in premenopausal BC pts is associated with a significant improved OS without increasing the risk of developing

TIA. Subgroup analyses and evaluation of the prognostic effect of TIA are underway and will be reported at the conference.

**No conflicts of interest**

**6** Oral

**Effect of event-free years on the 5-year risk of regional recurrence in cT1−2N0 breast cancer in relation to biologic subtypes**

M. Moossdorff[1], M. Vane[1], R. Bretveld[2], T. Van Nijnatten[3], B. Goorts[1], L. Van Roozendaal[4], E. Heuts[1], L. Strobbe[5], M. Smidt[1]. *[1]Maastricht University Medical Center, Surgery, Maastricht, Netherlands; [2]Netherlands Comprehensive Cancer Organisation IKNL, Utrecht, Netherlands; [3]Maastricht University Medical Center, Surgery/Radiology, Maastricht, Netherlands; [4]Zuyderland Medical Center, Surgery, Heerlen, Netherlands; [5]Canisius-Wilhelmina Hospital, Surgery, Nijmegen, Netherlands*

**Background:** Regional recurrence (RR) is an endpoint in several recent and ongoing trials of reducing axillary treatment in cT1−2N0 breast cancer patients. Topics of debate regarding these trials are adequate follow-up time and whether subtypes such as triple negative breast cancer are adequately represented. The risk of RR may decrease with each subsequent event-free year, affecting the yield and usefulness of longer follow-up. The aim of this study is to determine risk of RR as a first event within 5 years after diagnosis (a common time for first analysis of results) in subtypes of breast cancer, conditional to being event-free for 1, 2, 3, and 4 years.

**Methods:** From the Dutch National Cancer Registry, all cT1−2N0M0 epithelial breast cancers diagnosed in 2005–2008 were analyzed. RR risk was calculated with Kaplan–Meier analysis. Conditional RR (assuming *x* event-free years) was determined by selecting patients without an event at *x* years, and calculating the risk of RR within 5 years after diagnosis.

**Results:** Between 2005 and 2008, 24655 cT1−2N0 (all pN stages) new breast cancers were available for analysis. Overall, 5-year RR as a first event occurred in 1.1% (See Table). After 1, 2, 3, and 4 event-free years, the risk of RR within 5 years after diagnosis, decreased to 0.9%, 0.7%, 0.4%, and 0.2%. The risk of RR at diagnosis varied between subtypes; it was highest for triple negative (3.0%) and lowest for ER+PR+Her2− tumours (0.7%) The risk of RR as a first event within 5 years after diagnosis decreased in all subtypes when more event-free years had passed. After 3 event-free years, the risk of RR within 5 years after diagnosis was 0.4% overall.

**Conclusions:** The risk of RR as a first event within 5 years of follow-up after 3 event-free years is almost negligible. Thus, the absolute yield of additional follow-up until 5 years will be low: for every 250 event-free patients still in the trial, 1 RR can be expected. This suggests that longer follow-up is of limited value for RR, although it may be required for other outcomes.

**No conflicts of interest**

**7** Oral

**Pathologic prognostic factors of male breast cancer: results of the EORTC 10085/TBCRC/BIG/NABG International Male Breast Cancer Program**

M.A. Vermeulen[1], L. Slaets[2], F. Cardoso[3], S. Giordano[4], S. Aebi[5], J. Bayani[6], P.J. Van Diest[1], J. Fraser[7], T. Goulioti[8], C. Kelly[9], E. Van Leeuwen-Stok[10], B. Linderholm[11], J. Martens[12], S. Peeters[13], P. Porter[14], I. Rubio[15], C. Schroder[16], K. Tryfonidis[17], J.M.S. Bartlett[18], C.H.M. Van Deurzen[19]. *[1]University Medical Center Utrecht, Pathology, Utrecht, Netherlands; [2]European Organisation for Research and Treatment of Cancer, Statistics, Brussels, Belgium; [3]Champalimaud Cancer Center, Breast Unit, Lisbon, Portugal; [4]University of Texas MD Anderson Cancer Center, Health Services Research and Breast Medical Oncology, Houston, USA; [5]Swiss Group for Clinical Cancer Research, SAKK, Bern, Switzerland; [6]Ontario Institute for Cancer Research, Transformative pathology, Toronto, Canada; [7]Beatson West of Scotland Cancer Centre, Breast Unit, Glasgow, United Kingdom; [8]Breast International Group, BIG, Brussels, Belgium; [9]ICORG, All Ireland Cooperative Oncology Research Group, Ireland; [10]Dutch Breast Cancer Research Group, BOOG, Amsterdam, Netherlands; [1]Sahlgrenska University Hospital and Swedish Association of Breast Oncologists SABO, Oncology, Gothenburg, Sweden; [12]Erasmus Medical Center, Oncology- Breast Cancer Genomics and Proteomics lab, Rotterdam, Netherlands; [13]UZ Leuven, Oncology & Radiotherapy, Leuven, Belgium; [14]Fred Hutchinson Cancer Research Center, Human Biology and Public Health Sciences and Department of Pathology, Seattle, USA; [15]Hospital Universitario Vall d'Hebron, Breast Surgical Unit, Barcelona, Spain; [16]University Medical Center Groningen, Medical Oncology, Groningen, Netherlands; [17]European Organisation for Research and Treatment of Cancer, EORTC, Brussels, Netherlands; [18]Ontario Institute for Cancer Research and University of Edinburgh, Transformative pathology, Toronto, Canada; [19]Erasmus Medical Center, Pathology, Rotterdam, Netherlands*

**Background:** Male breast cancer (MBC) is an uncommon disease that shares several similarities with female breast cancer (FBC), but also differs in many ways. Several prognostic histologic features have been well established in FBC, but it is unknown whether these prognostic features can be extrapolated to MBC. Therefore, the aim of this study was to describe the association of several histologic features in MBC with outcome in the presence of locoregional and adjuvant treatments according to physician's choice (non-uniform treatments).

**Material and Methods:** Central pathology review was performed for 1203 out of 1483 MBC patients from the Part 1 (retrospective joint analysis) of the EORTC 10085 MBC Program. These patients were treated between 1990 and 2010 in 23 centers from 9 countries. Pathology review included histologic subtype, grade, mitotic activity index (MAI)/2 $mm^2$, the presence of a fibrotic focus and density of tumor infiltrating lymphocytes (TILs). These features were correlated with all cause relapse-free and overall survival (RFS and OS). Only OS results are reported below since both endpoints showed similar trends. Hazard ratios are based on univariate Cox Models and p-values on unadjusted log rank tests, after exclusion of patients with distant metastases. Additionally, we investigated the relationship between TILs and fibrotic focus with cancer subtypes based on immunohistochemical surrogates (ER, PR, Her2, Ki-67).

**Results:** Median follow-up for OS was 7.1 years. The majority (85%) of carcinomas were classified as ductal carcinomas, mainly grade two (50%). Histologic grade was not significantly associated with OS ($p = 0.129$,

Table (abstract 6): Risk of 5-year regional recurrence as a first event in cT1−2N0 breast cancer of different subtypes, conditional to a number of event-free years

| Breast cancer subtype [a] | No. of patients | Risk of 5-year regional recurrence | | | | |
|---|---|---|---|---|---|---|
| | | At diagnosis | After 1 event-free year | After 2 event-free years | After 3 event-free years | After 4 event-free years |
| All | 24,655 | 1.1% | 0.9% | 0.7% | 0.4% | 0.2% |
| ER+PR+Her2− | 13,587 | 0.7% | 0.6% | 0.5% | 0.3% | 0.2% |
| ER+PR−Her2− | 2,838 | 1.1% | 0.9% | 0.7% | 0.4% | 0.2% |
| ER+Her2+ | 1,714 | 1.5% | 1.3% | 1.1% | 0.6% | 0.1% |
| ER−Her2+ | 964 | 1.9% | 1.4% | 0.8% | 0.6% | 0.1% |
| Triple negative | 2,438 | 3.0% | 2.2% | 1.2% | 0.7% | 0.2% |

RR, regional recurrence; ER, estrogen receptor; PR, progesterone receptor; Her2, Her2Neu receptor.
[a] Subtype unknown for 3114 (12.6%).

HR=1.27 for grade II vs I, 95% CI 0.95–1.70 and HR=1.39 for grade III vs grade I, 95% CI 1.00–1.93), nor when analyzed in a subgroup analysis by disease stage and chemo- and endocrine therapy administration. MAI however, which is one of the components of grading, was correlated with unfavorable OS (p = 0.006, HR 1.02 for 1-unit increase, 95% CI 1.01–1.03). The presence of a fibrotic focus was also correlated with an unfavorable OS (p = 0.004, HR=1.39, 95% CI 1.11–1.74), as was a low density of TILs (p = 0.011, HR=0.71 for moderate versus minimal, 95% CI 0.49–1.03 and HR=0.68 for mild versus minimal, 95% CI 0.53–0.87). We observed a higher density of TILs for HER2 positive cancers compared to luminal Her2 negative subtypes, an effect that was not seen for the presence of a fibrotic focus.

**Conclusions:** In MBC, overall histologic grade was not significantly correlated with outcome, unlike what is known in FBC, although MAI strongly correlated with OS. Fibrotic focus and a limited amount of TILs were associated with unfavorable outcome, an effect that is also seen in FBC. This descriptive study contributes to our understanding of MBC and may facilitate the optimization of risk stratifications and treatment decisions.

**No conflicts of interest**

**8** Oral

**Nipple sparing mastectomy: Surgical and oncological outcomes from a national multicentric registry with 913 patients (1006 cases) over a six year period**

L. Orzalesi[1], D. Casella[1], C. Santi[1], R. Murgo[2], S. Rinaldi[3], L. Regolo[4], C. Amanti[5], M. Roncella[6], M. Serra[7], G. Meneghini[8], M. Bortolini[9], V. Altomare[10], C. Cabula[11], F. Catalano[12], A. Cirilli[13], F. Caruso[14], M.G. Lazzaretti[15], L. Cecconi[16], L. Cataliotti[1], M. Bernini[1]. *[1]Breast Unit Surgery, Careggi Hospital, Firenze, Italy; [2]Breast Unit Surgery, San Giovanni Rotondo Hospital, Foggia, Italy; [3]Breast Unit Surgery, San Paolo Hospital, Bari, Italy; [4]Breast Unit Surgery, Maugeri Hospital, Pavia, Italy; [5]Breast Unit Surgery, Sant'Andrea Hospital, Rome, Italy; [6]Breast Unit Surgery, Cisanello Hospital, Pisa, Italy; [7]Breast Unit Surgery, Sant'Orsola Hospital, Bologna, Italy; [8]Breast Unit Surgery, Montecchio Maggiore Hospital, Vicenza, Italy; [9]Breast Unit Surgery, Valdese Hospital, Turin, Italy; [10]Breast Unit Surgery, Campus Biomedico Hospital, Rome, Italy; [1]Breast Unit Surgery, Businco Hospital, Caglairi, Italy; [12]Breast Unit Surgery, Cannizzaro Hospital, Catania, Italy; [13]Breast Unit Surgery, Policlinico Hospital, Bari, Italy; [14]Breast Unit Surgery, Humanitas Hospital, Catania, Italy; [15]Breast Unit Surgery, Policlinico Hospital, Carpi, Italy; [16]Statistics, of Statistics- Informatics and Application "G. Parenti"- University of Florence, Florence, Italy*

**Background:** Nipple sparing mastectomy is surgically and oncologically safe, with appropriate indications. Results from literature come from reviews of single Institution series. This study aims at evaluating indications and results of NSM on a large multi-institutional scale, by means of the Italian National registry.

**Methods:** In July 2011 a panel of Italian specialists agreed upon and designed a National database of nipple sparing mastectomy. Any center with at least 150 cancers per year could participate on a voluntary basis. In March 2015 analysis of data was accomplished. Dataset for this study consists of cases extracted in the period between January 1st 2009 and December 31st 2014. Last follow-up update was performed on March 31st 2015.

**Results:** 913 women were analyzed. Mean tumor diameter was 2.95 cm. Centers adopted different tumor to nipple distance cut-offs. Prophylactic mastectomies were 124 (12.3%). MRI was performed in 46.9% of cases. Intraoperative frozen-section NAC examination was accomplished in 84.0% of confirmed carcinomas. NAC necrosis rate was 4.8%. Larger skin-flap necrosis rate was 2.3%. Loco-regional recurrences rate was 3.1%, NAC recurrence 0.8%. Systemic recurrence rate was 1.1%. Six deaths (0.6%) were registered.

**Conclusion:** Patients selection criteria are still very different from center to center. MRI is gaining more importance over time. Intraoperative frozen-section is commonly used. Surgical and oncological results show that NSM is effective. This National multicentric analysis enables a comparison of results with no geographical differences and a "safe" state of the art of NSM in Italy.

**No conflicts of interest**

## Thursday, 10 March 2016 14:00–15:30

**CLINICAL SCIENCE SYMPOSIUM**

# Luminal Breast Cancer

**9** Oral

**Concurrent versus sequential adjuvant endocrine therapy in early stage breast cancer patients with hormone-receptor positive disease: A systematic review and meta-analysis**

F. Poggio[1], M. Ceppi[2], M. Lambertini[1], A. Levaggi[1], A. D'Alonzo[1], M. Vaglica[1], S. Giraudi[1], E. Blondeaux[1], S. Pastorino[1], A. Abate[1], G. Iacono[1], P. Bruzzi[2], C. Bighin[1], P. Pronzato[1], L. Del Mastro[3]. *[1]IRCCS AOU San Martino − IST, U.O. Oncologia Medica 2, Genova, Italy; [2]IRCCS AOU San Martino − IST, Epidemiologia Clinica, Genova, Italy; [3]IRCCS AOU San Martino − IST, U.O. Sviluppo Terapie Innovative, Genova, Italy*

**Background:** The optimal timing of adjuvant chemotherapy (CT) and endocrine therapy (ET) in patients with hormone-receptor positive breast cancer has not been clearly defined yet. To better clarify this issue we conducted a systematic review and meta-analysis of randomized studies evaluating the difference between the two modalities of administrations in terms of disease-free survival (DFS) and overall survival (OS).

**Material and Methods:** Relevant studies were identified by searching PubMed, Web of Knowledge and the proceedings of the major conferences with no date restriction up to March 2015. Eligible studies were those that randomized hormone-receptor positive breast cancer patients to receive endocrine therapy concomitantly or sequentially to adjuvant chemotherapy.

The summary risk estimates (pooled hazard ratio [HR] and 95% confidence intervals [CI]) for DFS and OS were calculated using random effect models (DerSimonian and Laird method).

**Results:** Three randomized studies were included (Pico et al, Ann Oncol 2004; Albain et al, Lancet 2009; Bedognetti et al, JNCI 2011). A total of 2,021 breast cancer patients were enrolled in these trials: 1,019 received sequential chemotherapy and endocrine therapy and 1,002 started endocrine therapy concurrently to chemotherapy.

Overall, 771 DFS events were observed, 370 in the sequential arm and 401 in the concomitant arm, with a pooled HR of 0.99 (95% CI, 0.78–1.25; p = 0.442). No difference between treatment modalities was observed in terms of OS (HR=0.95; 95% CI, 0.80–1.12; p = 0.529). The heterogeneity between studies was not significant in both DFS and OS (p = 0.123 and p = 0.385 respectively).

**Conclusions:** Our pooled analysis of randomized studies showed no significant difference in terms of DFS and OS among the concurrent and sequential administration of adjuvant treatments. In view of the small number of published trials, the lack of data on timing of taxane and aromatase inhibitors as adjuvant treatment, this topic still remain controversial and further studies on this issue are warranted.

**No conflicts of interest**

**10** Oral

**Association between multifocal disease and the risk of distant metastasis as assessed by the 70-gene signature in clinical low-risk breast cancer patients − results from the EORTC 10041/BIG 03-04 MINDACT trial**

K. Aalders[1], A. Kuijer[2,3], M. Straver[2], L. Slaets[4], G. Viale[5], L. Van 't Veer[6], A. Glas[7], M. Delorenzi[8], K. Tryfonidis[1], M. Piccart[9], F. Cardoso[10], E. Rutgers[11], on behalf of the TRANSBIG Consortium & the MINDACT Investigators. *[1]European Organization for Research and Treatment of Cancer EORTC, Medical Department, Brussels, Belgium; [2]Diakonessenhuis, Department of Surgery, Utrecht, Netherlands; [3]University Medical Center Utrecht, Department of Radiology, Utrecht, Netherlands; [4]European Organization for Research and Treatment of Cancer EORTC, Department of Statistics, Brussels, Belgium; [5]European Institute of Oncology and University of Milan, Department of Pathology, Milan, Italy; [6]UCSF Helen Diller Family Comprehensive Cancer Center, Department of Laboratory Medicine, San Francisco, USA; [7]Agendia, Department of Product Development and Support, Amsterdam, Netherlands; [8]Swiss Institute of Bioinformatics, Bioinformatics Core Facility, Lausanne, Switzerland; [9]Institut Jules Bordet, Medicine Department, Brussels, Belgium; [10]Champalimaud Cancer Center, Breast Cancer Unit, Lisbon, Portugal; [1]Netherlands Cancer Institute/Antoni van Leeuwenhoek, Department of Surgery, Amsterdam, Netherlands*

**Background:** Current guidelines recommend basing adjuvant systemic treatment (AST) decisions in multifocal (MF) disease on the prognostic

characteristics of the largest lesion. In patients considered as low risk based on clinical assessment of this lesion, it might result in omission of AST. As MF disease has been suggested to be a sign of high tumor load, disregarding multifocality as a prognosticator may result in under treatment. We assessed the association between MF disease and the 70-gene signature (70-GS) in clinical low-risk breast cancer (BC) patients enrolled in the EORTC 10041/BIG 03−04 MINDACT trial.

**Patients and Methods:** The analyzed population consisted of enrolled BC patients in the Mindact trial with clinical low-risk disease, defined by a modified Adjuvant! Online cut-off for the 10-year risk of recurrent disease or death. Presence of MF disease was deducted from the CRF-question for sum of diameter for all invasive tumor foci. In case of MF breast cancer, characteristics of the largest lesion were considered for analysis. Clinicopathological characteristics (including age, stage, grade, ER, PgR, HER2, histology, Ki67) and gene expression of patients with unifocal and MF disease were compared and the association between MF disease and the risk of distant metastasis, as determined by the 70-GS, was assessed (Fisher's exact test for association). With 3088 clinical low risk patients with unifocal and 238 with MF disease, we have 97% power to detect that the percentage 70-gene signature high-risk tumors is doubled in patients with MF compared to unifocal disease, from 7% to 15%, at a significance level of 5%.

**Results:** The study included 3088 clinical low-risk patients with unifocal and 238 patients with MF disease. There is a significant association between genomic risk and multifocality in the group of clinically low risk Mindact patients. The percentage of genomic high risk increased from 17.3% for unifocal to 22.7% for MF tumors. This corresponds to an absolute increase by 5.4% and a relative increase of 31%. Apart from an absolute increase in the frequency of lobular tumors by 10% (17.9% vs. 7.8% by central and 21.8% vs. 10.8% by local pathology), we do not observe any differences in tumor and patient baseline characteristics for MF vs. unifocal tumors. In multivariable regression analysis MF disease remained significantly associated with a high-risk 70-GS result (OR 1.64, 95% CI 1.03–2.08, p = 0.035).

**Conclusion:** In the group of enrolled Mindact patients with a clinical low risk, defined by a modified Adjuvant! Online cut-off, MF tumors are more likely to have a high genomic (70-gene) risk profile compared to unifocal tumors. This association between multifocality and genomic risk, 22.7% genomic high risk for multifocal vs. 17.3% genomic high risk for unifocal tumors, is statistically significant, albeit smaller than hypothesized.

**Conflict of interest:** Ownership: LV is a founder of Agendia and has stock ownership. Corporate-sponsored Research: KA, LS and KT are employees of the EORTC which receives funding for the study. Other Substantive Relationships: AG is an employee of Agendia; GV has received consultancy fees/honorarium from Agendia; MP has received consultancy fees from Sanofi-Aventis, Novartis and Roche, honorarium from Roche and research grant from Roche and Novartis; FC has received consultancy fees/honorarium from Novartis, Sanofi-Aventis and Roche.

## Thursday, 10 March 2016 16:00–17:30

**CLINICAL SCIENCE SYMPOSIUM**

# Controversial Issues in Radiotherapy

**11** Oral

### Validation of the web-based IBTR! 2.0 nomogram to predict for ipsilateral breast tumour recurrence after breast conserving therapy

I. Kindts[1,2], A. Laenen[3], S. Peeters[1,2], H. Janssen[1,2], T. Depuydt[1,2], E. Van Limbergen[1,2], C. Weltens[1,2]. *[1]KU Leuven − University of Leuven, Department of Oncology, Leuven, Belgium; [2]University Hospitals Leuven, Department of Radiation Oncology, Leuven, Belgium; [3]KU Leuven − University of Leuven, Leuven Biostatistics and Statistical Bioinformatics Centre L-Biostat, Leuven, Belgium*

**Background:** A nomogram to predict the 10-years ipsilateral breast tumour recurrence (IBTR) after breast conserving therapy (BCT) for breast cancer (BC) was developed by Sanghani et al (JCO 2010). The IBTR! 2.0 is based on seven literature-derived clinicopathologic variables with risk ratios estimated from a British Columbia Cancer Agency (BCCA) cohort. Validation in an independent cohort showed a concordance index (C-index) of 0.66. The aim of this study was to evaluate the performance of this algorithm in a large independent patient cohort.

**Material and Methods:** In the University Hospitals of Leuven (UZL), 1863 eligible BC patients who underwent BCT from 2000 to 2007 were retrospectively identified. Clinicopathologic factors and the nomogram performance were assessed for the 1898 cases with data for the nomogram variables. Two definitions of IBTR were considered where simultaneous regional or distant recurrence were either censored (conform IBTR! 2.0) or included as event.

The prognostic value of patient, tumour and treatment characteristics was evaluated in univariable analysis. Validation comprises discrimination and calibration. Discrimination, i.e. the extent to which patients predicted to be at higher risk exhibit higher event rates than those deemed at lower risk, was assessed by the concordance probability estimate (CPE) and Harrell's C-index based on a Cox model with time to IBTR as outcome and the nomogram prediction as the only covariate. Calibration reflects prediction accuracy, i.e. the absence of over- or underestimation of the actual risk. The mean predicted and observed 10-year estimates were compared for the entire cohort and for four risk groups predefined by nomogram-predicted IBTR risks and a calibration plot was drawn.

**Results:** Median follow-up was 10.9 years. The 10 years Kaplan–Meier estimated IBTR-free rates were 98.7% and 97.9%, according to the two definitions of IBTR. Patients in the UZL cohort had less negative section margins, less lymphovascular invasion and a larger tumour size. The foremost difference is that 81.5% of the patients in the UZL cohort received hormonal therapy versus 39.4% of the patients in the BCCA cohort. In univariable analysis, a younger age (p = 0.002) and a positive nodal status (p = 0.048) were significantly associated with IBTR with a trend for the omission of hormonal therapy (p = 0.061).

The CPE and C-index vary between 0.57 to 0.67 for the two definitions of IBTR. In all four risk groups, the model overestimates the IBTR risk. A limited differentiation between the risk groups is suggested by the calibration plot, in particular between the highest-risk groups.

**Conclusions:** The IBTR! 2.0 predictive model for IBTR in BC patients lacks accuracy in this large study population with an overestimation in all risk groups.

**No conflicts of interest**

**12** Oral

### Optimal treatment of the axilla after positive sentinel lymph node biopsy in primary invasive breast cancer patients (surgery versus radiotherapy). Final results of the OTOASOR trial. 10 years follow-up of a randomized clinical trial

A. Sávolt[1], Z. Mátrai[1], C. Polgár[2], N. Udvarhelyi[3], I. Sinkovics[4], E. Kovács[5], G. Péley[6]. *[1]National Institute of Oncology, Department of Breast and Sarcoma Surgery, Budapest, Hungary; [2]National Institute of Oncology, Department of Radiotherapy, Budapest, Hungary; [3]National Institute of Oncology, Department of Pathology, Budapest, Hungary; [4]National Institute of Oncology, Department of Nuclear Medicine, Budapest, Hungary; [5]National Institute of Oncology, Department of Diagnostic Imaging, Budapest, Hungary; [6]Norfolk and Norwich University Hospital, Department of General Surgery, Norwich, United Kingdom*

**Aims:** The National Institute of Oncology, Budapest conducted a single centre randomized clinical study. The OTOASOR (Optimal Treatment of the Axilla − Surgery or Radiotherapy) trial compares completion axillary lymph node dissection (cALND) to axillary nodal irradiation (ANI) in patients with sentinel lymph node (SLN)-positive primary invasive breast cancer.

**Patients and Methods:** Patients with primary invasive breast cancer (clinically lymph node negative and less than or equal to 3 cm in size) were randomized before surgery for cALND (arm A-standard treatment) or ANI (arm B-investigational treatment). SLNB was performed by the radioguided method. The use of blue-dye was optional. SLNs were investigated with serial sectioning at 0.5 mm levels by haematoxylin and eosin staining. In the investigational treatment arm patients received 50 Gy ANI instead of cALND. Adjuvant treatment was recommended and patients were followed up according to the actual institutional guidelines.

**Results:** Between August 2002 and June 2009, 2106 patients were randomized for cALND (arm A-standard treatment, 1054 patients) or ANI (arm B-investigational treatment, 1052 patients). SLN was identified in 2073 patients (98.4%) and was positive in 526 patients (25.4%). Fifty-two SLN-positive patients were excluded from the study (protocol violation, patient's preference). Out of the remaining 474 patients, clinical and tumor characteristics were similar between 244 patients randomized to cALND and 230 randomized to SLNB plus ANI. Primary endpoint of the study is axillary recurrence and secondary endpoints are overall survival, breast cancer specific survival, disease-free survival, distant disease-free survival.

We note high correlations by non parametric correlation matrix analysis between palpability with type of breast procedure, histological tumour size, pT category and SLN metastasis category. Mean length of follow-up is at the moment 107 months, 76–153 months on arm A and 75–152 on arm B (p=NS). Axillary recurrence (primary endpoint) was 1.6% vs. 1.7% (p=NS). The 9.1 year overall survival was 84.9% vs. 91.2%; 10-year disease-free survival was 79.9% with cALND and 85.6% with SLND plus ANI.

**Conclusions:** The 10 years follow-up datas of our OTOASOR trial suggest that ANI without cALND does not increase the risk of axillary failure in SLN+ patients.

**No conflicts of interest**

## Thursday, 10 March 2016 16:00–17:30

CLINICAL SCIENCE SYMPOSIUM

# Breast Density − How Thick is the Fog?

**13** Oral

### The association of physical activity with mammographic density: A register-based cohort study

S. Azam[1], A.R. Aro[1], M. Von Euler-Chelpin[2], I. Vejborg[3], A. Tjønneland[4], E. Lynge[2], Z.J. Andersen[2]. [1]*Syddansk Universitet, Health promotion research, Esbjerg, Denmark;* [2]*Copenhagen University, Center for Epidemiology and Screening, Copenhagen, Denmark;* [3]*Copenhagen University Hospital, Diagnostic Imaging Centre, Copenhagen, Denmark;* [4]*Danish Cancer Research Center, Danish Cancer Society, Copenhagen, Denmark*

**Background:** Physical activity is recognized as a modifiable lifestyle risk factor in prevention of breast cancer. Mammographic density (MD) is increasingly used as a biomarker of breast cancer risk, as it is one of the strongest risk factors. Studies on the association between physical activity and MD have reported inconsistent results. The purpose of this study is to evaluate the association of leisure, transport related and occupational physical activity with MD.

**Material and Methods:** For 5,703 (1,202 pre- and 4,501 post-menopausal) women who participated in the Danish Diet, Cancer and Health cohort (1993–1997) and attended mammographic screening in Copenhagen (1993–2001), we used MD assessed at the first screening after cohort entry. MD was defined as either mixed/dense or fatty. Participation and duration (hours/week) in leisure-time physical activities: sports, walking, cycling (leisure and to-and from work), and gardening; as well as occupational physical activity (sedentary, standing, manual, heavy manual), and potential confounders were assessed by questionnaire at the cohort baseline. The association between physical activities and MD was analysed by logistic regression with adjustment for confounders.

**Results:** 56.3% women had mixed/dense MD, 47.5% participated in sports, 70.1% cycled, 52.2% did gardening and 92.7% walked. We found a significant positive association between participation in sports (odds ratio (OR) with 95% confidence interval (CI): 1.17; 1.05–1.30), cycling (1.19; 1.06–1.33) and odds of having mixed/dense MD, which attenuated (1.08; 0.96–1.22 and 1.10; 0.97–1.25) in a fully adjusted model. We found no association between walking and MD (0.98; 0.79–1.22) and weak association between gardening and MD (1.06; 0.94–1.18) in fully adjusted model. We found no dose-response relationship between time spent on activities and MD, and no association of occupational physical activity with MD.

**Conclusions:** Physical activity does not affect MD. Our results suggest that the protective effect of physical activity on breast cancer risk is not mediated by MD.

**No conflicts of interest**

## Friday, 11 March 2016 09:45–11:15

PLENARY SESSION

# Keynote Lecture, Oral and Late-Breaking Abstracts

**14** Oral

### Cost-effectiveness of shifting breast cancer surveillance from a hospital setting to a community-based national screening programme setting

K. De Ligt[1], A. Witteveen[2], S. Siesling[1], L. Steuten[3]. [1]*Comprehensive Cancer Centre The Netherlands IKNL, Department of Research, Utrecht, Netherlands;* [2]*University of Twente, Health Technology and Services Research, Enschede, Netherlands;* [3]*Fred Hutchinson Cancer Research Center, HICOR: Hutchinson Institute for Cancer Outcomes Research, Seattle WA, USA*

**Background:** In the Netherlands, breast cancer surveillance after breast conserving surgery (BCS) takes place in a hospital setting for at least five years to detect possible recurrences in early stage. As breast cancer incidence rises and mortality decreases, surveillance expenses increase. This study explores the effectiveness and cost-effectiveness of BCS surveillance as delivered in a hospital setting versus providing BCS surveillance as part of the community-based National Breast Cancer Screening Program (NBCSP). We hypothesise that the NBCSP-based strategy leads to lower costs and a lower proportion of true test results (TTR) compared to the hospital-based strategy and determine to what extent potential lower effectiveness may be balanced with expected cost savings.

**Materials and Methods:** Both strategies are compared on effectiveness and cost-effectiveness in a decision tree from a healthcare perspective over a 5-year time horizon. Women aged 50−75 without distant metastases that underwent BCS in the years 2003–2006 with complete 5 year follow-up were selected from the Netherlands Cancer Registry (n = 14,093). Key input variables were mammography sensitivity and specificity, risk of loco regional recurrence (LRR), and direct healthcare costs. The primary outcome measure was the overall predictive value (measured in true test results). Secondary effectiveness measures were the positive predictive value (PPV) (LRRs detected or true positive test results) and the negative predictive value (NPV) (true negative test results) detected within five years post-treatment. Results are presented for low and high risk patients separately and expressed in incremental cost-effectiveness ratios (ICERs).

**Results:** For low risk patients (with grade 1 tumours, no node involvement, and hormonal treatment), the PPV and NPV for the NBCSP strategy were 3.31% and 99.88%, and 2.74% and 99.95% for the hospital strategy respectively. For high risk patients (grade 3 tumours, over three nodes involved, without hormonal treatment), the PPV and NPV for the NBCSP strategy were 64.1% and 98.9%; and 51.0% and 99.7% for the hospital strategy respectively. For low risk patients the NBCSP saves €202 per patient leading to an ICER of €109/accurate test result. For high risk patients the cost savings are €72 per patient, leading to an ICER of €43/accurate test result.

**Conclusion:** Although the NBCSP-based strategy is cheaper, it cannot replace the hospital-based strategy, since it leads to only half of the accurate test results compared to hospital-based strategy. This contradicts the goal of early detection of LRRs and improving outcomes.

**No conflicts of interest**

**15** Oral

### Hospital organizational factors affect the use of immediate breast reconstruction after mastectomy for breast cancer

K. Schreuder[1,2], A.C.M. Van Bommel[3], K.M. De Ligt[1], J.H. Maduro[4], M.T.F.D. Vrancken Peeters[5], M.A.M. Mureau[6], S. Siesling[1,2]. [1]*Netherlands Comprehensive Cancer Organisation, Department of research, Utrecht, Netherlands;* [2]*University of Twente, Department of Health Technology and Services Research- MIRA Institute for Biomedical Technology and Technical Medicine, Enschede, Netherlands;* [3]*Leiden University Medical Center, Department of surgery, Leiden, Netherlands;* [4]*University of Groningen- University Medical Center Groningen, Department of radiation oncology, Groningen, Netherlands;* [5]*Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital, Department of surgery, Amsterdam, Netherlands;* [6]*Erasmus MC Cancer Institute- University Medical Center Rotterdam, Department of plastic and reconstructive surgery, Rotterdam, Netherlands*

**Background:** Aims of the current study were to identify which hospital organizational factors determine the variation in the use of immediate breast reconstruction (IBR) after mastectomy for ductal carcinoma in situ (DCIS) or invasive breast cancer and to investigate whether these factors explain the variation in IBR between hospitals in the Netherlands.

**Material and Methods:** From the NABON Breast Cancer Audit (NBCA) patients with DCIS or primary invasive breast cancer without distant metastatic disease, diagnosed between January 1, 2011 and December 31, 2013 were selected. Hospital organizational factors were identified with an online web-based survey on different organization factors such as the number of weekly multidisciplinary team (MDT) meetings, number of (breast and plastic) surgeons in the hospital and the presence of plastic surgeons in weekly MDT. Logistic regression analyses were used to analyze whether the identified organizational factors significantly affected IBR rates. Patient, tumor and hospital organizational factors that demonstrated to significantly affect IBR rates in univariate analyses were included in the multivariate analyses.

**Results:** In total, 72 hospitals (78% of all Dutch hospitals) participated in the survey. In these hospitals 16,471 female patients were treated with a mastectomy for DCIS (n = 1,980) or non-metastatic breast cancer (n = 14,491) during the study period. In total 20% (n = 3,244) of these patients underwent IBR for DCIS (mean, 42%; hospital range, 0−80%) or invasive breast cancer (mean, 17%; hospital range, 0−62%). Patients who underwent a mastectomy in a teaching (OR=2.6, 95% CI: 1.8−3.7) or university hospital (OR=10.8, 95% CI: 5.7–20.5) or in an intermediate

volume (OR=2.0, 95% CI: 1.5−2.8) or high volume hospital (OR=3.0, 95% CI: 2.0−4.5) had a significantly higher chance of receiving IBR compared to patients treated in a district or low volume hospital, respectively. More often IBR was performed in hospitals having 3−4 MDT meetings/week organized compared to hospitals with 1−2 MDT meetings/week (OR=1.4, 95% CI: 1.1−1.8). The number of plastic surgeons in-house did not significantly affect the chance of IBR. In almost 70% of the hospitals, a plastic surgeon structurally attended the weekly MDT meeting, which was prognostic for performing more IBRs compared to MDTs with no or incidental plastic surgeon attendance (OR=3.89, 95% CI: 3.00–5.04).

**Conclusion:** Hospital organizational factors affect the use of IBR and consequently could be subject for improvement to make IBR available to more breast cancer patients.

**No conflicts of interest**

## Friday, 11 March 2016 14:00–15:30

**CLINICAL SCIENCE SYMPOSIUM**

# What is New in the Biology of Breast Cancer?

**16** Oral

### Prediction of the 70-gene signature in early breast cancer patients using computer-derived DCE-MRI features of the tumor and intramammary blood vessels

B.H.M. Van der Velden[1], A.M.T. Schmitz[1], H.M. Chan[1], C.E. Loo[2], K.G.A. Gilhuijs[1]. [1]*University Medical Center Utrecht, Image Sciences Institute, Utrecht, Netherlands;* [2]*the Netherlands Cancer Institute–Antoni van Leeuwenhoek Hospital, Radiology, Amsterdam, Netherlands*

**Background:** Molecular assays such as the Mammaprint or Oncotype DX are increasingly used as prognostic indicators to select chemotherapy in individual patients. These assays are typically derived from postoperative excision specimens and require several weeks to complete. Assessment prior to surgery, i.e. during breast cancer diagnosis, may open new therapeutic windows to tailor primary therapy to individual patients. Although molecular assays may be derived from biopsied tissue, tumor heterogeneity may cause uncertainty. Dynamic contrast-enhanced MRI (DCE-MRI) depicts some of the hallmarks of cancer that are tested by these molecular essays. The goal of this study was to develop a preoperative prediction model of the postoperatively derived 70-gene signature using computer-derived DCE-MRI features of the breast.

**Material and Methods:** Seventy-two breast cancer patients with limited axillary load (<4 positive lymph nodes) received a preoperative MRI and a postoperative 70-gene signature assay between 2003 and 2006. Twenty-three features were used for the model: two clinical features (age at diagnosis and immunohistochemical subtype) and twenty-one DCE-MRI features (twelve tumor features and nine from intramammary blood vessels). Principle component analysis was used to remove correlations between features. The components containing 90% of the variation were used to construct a model to predict the 70-gene signature (low-risk or high-risk). For this purpose, the least absolute shrinkage and selection operator (LASSO) was used, and the model was internally validated using bootstrap validation with 1000 iterations. Two operating points were examined: one to predict a positive 70-gene signature with high certainty (i.e., at high positive predictive value (PPV)) and one to predict a negative signature with high certainty (i.e., at high negative predictive value (PPV)).

**Results:** The average patient age at diagnosis was 48 years (range: 32−58). The low-risk signature was found in 43/72 (60%) patients and the high-risk signature in 29/72 (40%). Components selected by the LASSO involved the initial enhancement of the ipsilateral blood vessels, the tumor size, and the immunohistochemical subtype. The prediction model after bootstrap validation achieved a median AUC of 0.82 (interquartile range 0.77–0.86). At the 95%-sensitivity operating point (specificity 46%), a negative predictive value of 95% was achieved. At the 95%-specificity operating point (sensitivity 38%), a positive predictive value of 84% was achieved.

**Conclusion:** Computer-derived features from the tumor and intramammary blood vessels at DCE-MRI of the breast have potential to predict the 70-gene signature. In an enriched subpopulation containing half the number of patients with a negative 70-gene signature, approximately 95% was correctly identified.

**No conflicts of interest**

## Friday, 11 March 2016 14:00–15:30

**CLINICAL SCIENCE SYMPOSIUM**

# The New Mammography

**17** Oral

### Parenchymal enhancement of the contralateral breast in DCE-MRI and outcome of patients with early breast cancer: complementary value of the 70-gene signature

B.H.M. Van der Velden[1], C.E. Loo[2], K.G.A. Gilhuijs[1]. [1]*University Medical Center Utrecht, Image Sciences Institute, Utrecht, Netherlands;* [2]*the Netherlands Cancer Institute–Antoni van Leeuwenhoek Hospital, Radiology, Amsterdam, Netherlands*

**Background:** Low parenchymal enhancement of the contralateral breast on dynamic contrast-enhanced (DCE) MRI was shown to be associated with inferior long-term survival in patients with breast cancer. Another method for stratification of patient survival is the 70-gene signature. The potential relationship between contralateral parenchymal enhancement and the 70-gene signature is currently unknown. The aim of this study was to investigate the complementary value of the 70-gene signature and contralateral parenchymal enhancement in the stratification of survival in patients with early breast cancer.

**Material and Methods:** Sixty-nine breast cancer patients with limited axillary load (<4 positive lymph nodes) received a preoperative MRI in study setting and a postoperative 70-gene test between 2003 and 2006. The contralateral parenchymal tissue was automatically segmented from MRI in 3D to objectively quantify the enhancement. The relative enhancement between the first and last post-contrast scan was calculated, and the mean of the top-10% most enhancing voxels in the parenchyma was dichotomized on a previously published threshold. Fisher's exact test was employed to investigate the relationship between parenchymal enhancement (low-risk vs high-risk) and the 70-gene signature (low-risk vs high-risk). Patients at risk of inferior invasive-disease free survival (IDFS) according to both tests were identified. Kaplan–Meier estimators and log-rank tests were used.

**Results:** The average age at diagnosis was 47 years (range 32−58) and the average largest tumor diameter on MRI was 1.9 cm (range 0.5−4.6). The median follow-up time was 86 months (range 12–110), 64/69 (93%) patients had IDFS. Twenty-six of 69 (38%) patients were in the high-risk MRI group, 28/69 (41%) patients had a high-risk 70-gene signature. The ratio between the low-risk test results and the high-risk results based on the 70-gene signature was not different between the MRI risk groups ($P = 0.461$). Patients in the high-risk MRI group had significantly worse cumulative survival at 9 years (74%) than those in the low-risk MRI group (98%) ($P = 0.033$). In the high-risk group according to both the MRI and the 70-gene test (9/69 patients, 13%) the cumulative survival at 9 years was even worse (61%) compared to the subgroup were at least of one the tests was negative (96%) ($P = 0.004$).

**Conclusions:** Contralateral parenchymal enhancement appears to be complemented by the 70-gene signature to identify patients with relatively inferior invasive disease-free survival.

**No conflicts of interest**

# Poster Abstracts

## Wednesday, 9 March 2016

**POSTER SESSION**

# Advocacy

**103** Poster

### How women cope with HER-2 ABC

M. Miklavcic[1]. [1]*Europa Donna, Europa Donna Slovenia, Ljubljana, Slovenia*

Breast cancer is the most common cancer among European women and has the highest mortality of any cancer in women worldwide. That is why breast cancer patients and all women are the one who we advocating for. Among breast cancer patients one of the diagnoses is also BC with HER + advanced breast cancer.

From the patient's perspective coping with the disease is very difficult, regardless of the type of disease. In recent years patients are getting more involved in education, information and also clinical trials and decision making policy, because patients are getting more self-awareness and self-regulation with having more and more knowledge about the disease. The same is with the breast cancer patients with HER 2+ advanced breast cancer.

For better understanding of HER2+ BC patients we did a short questionnaire research among HER 2+ BC patients in Slovenia, where we asked them if they think that they were sufficiently informed about treatment, which treatment they received and how they felt during treatment, were they aware about consequences or side effects and what are their personal proposals for maintaining their health.

From patient's perspective, no matter the type of disease, the rules and standards about treatment must be very clear and understandable for anyone. But from patients' perspective coping with the disease is something very personal, feelings and consequences are personal and need to be taken into account and all medical staff need not only listen, but also hear the patient's voice, which is powerful and important and must be heard.

All of the above shows that personalized treatment, what we are advocating for, is very important and informing the patient too. As recent guidelines shows personalized medicine is a future in BC as well.

**No conflicts of interest**

**104** Poster

### Understanding and eliminating the stigmatism and myths associated with male breast cancer

H. Wagner[1]. [1]*A Man's Pink, CEO, Brooksville- Florida, USA*

As an eleven year male breast cancer (MBC) survivor, founder and CEO of A Man's Pink, a MBC advocacy organization that supports our website www.malebreastcancer.ca, our mission is to promote MBC awareness, increase early detection, optimize and bring the survival rates for men diagnosed with breast cancer into the 21st century. In the 1980's extensive promotional campaigns to increase female breast cancer awareness significantly increased early detection with a corresponding dramatic enhancement in the survival rates for women diagnosed with this disease. Up until the early 1980's, many MBC patients diagnosed with estrogen receptor-positive tumors (80−90% of MBC patients) with metastatic or inoperable cancer underwent removal of their testicles in order to prevent further growth of the tumor (20% of male body estrogen is produced in the testicles). One definite reason why men did not want to talk about MBC. Identification of the "estrogen receptor" eliminated this treatment option. Today's talk will also include MBC occurrence data, prognosis and treatment options, myths about MBC, difficulties encountered by patients and survivors during their treatment and recovery, as well as suggesting, from a survivors point of view, how to best promote and increase MBC awareness. Input will also be solicited, in a survey form from the medical professional audience, as to their thoughts and suggestions on how to best increase MBC awareness, early detection, survival rates and to improve the journey for men, in Europe and globally, with their battle with breast cancer.

**No conflicts of interest**

**105** Poster

### Patient participation for better shared decision-making

L. Steinmeijer[1], H. Van Veenendaal[2]. [1]*Dutch Breast Cancer Association, Shared Decision Making- Patient Advocacy, Utrecht, Netherlands;* [2]*Van Veenendaal Advies, Shared Decision Making, Wijk bij Duurstede, Netherlands*

In the Netherlands patients' experiences are implemented to improve shared decision-making (SDM) in the doctor-patient relationship. This is done by preparing the patient for consultations with the clinician, by providing extra time to reflect at the beginning of the process and by assisting clinicians with the implementation of SDM. On the basis of patient experiences the Dutch breast cancer patient organization (BVN) has made an extensive question prompt, B-bewust (Be aware), enabling patients to reflect on what is important for them, as a first step to taking control when discussing the treatment plan with the physician. Voluntary BVN patient advocates (PAs) stimulate doctors and nurses to introduce B-bewust during consultations with patients. This fosters SDM, which makes the care more personal, more informative and causes less regret for decisions taken.

B-bewust (www.b-bewust.nl) offers checklists and medical information for patients to prepare for consultations with clinicians. B-bewust has been set up with patients and clinicians. First experiences show that right after the diagnosis, patients deal with information in a limited way. Creating time to reflect may help, as may the degree in which clinicians involve patients in SDM. A 'time-out consultation', combined with SDM stimulates patients to take an active role when making preferential decisions. The point is that there is not one best option for diagnosis and treatment, but that patients can make their own fitting choices from equal options.

In 2015 and 2016 B-bewust will be implemented and evaluated in 20 hospitals with the help of PAs. PAs are experience experts with a knowledge of breast cancer care, trained to deploy the patient perspective for improved quality of care. They keep in touch with the care teams of breast cancer uinits which want to consciously embed B-bewust in their procedures and to motivate patients to take control and SDM. Additonally, in 2016 a group of hospitals are starting a 'time-out consultation' combined with SDM. There will be an evaluation whether this leads to more patient participation in decision making, different choices, adapted guidelines and/or cooperation between hospitals in 1 region and costs.

At the end of 2015 and in the course of 2016 B-bewust results will be available regarding the timing of introducing B-bewust to the patient, how to motivate clinicians and what works with implementation by PAs. The implementation of a 'time-out consultation' will start in 2016 with a zero measurement and an investigation into how 'time-out consultation' combined with SDM can be introduced.

**No conflicts of interest**

**106** Poster

### Optimizing breast cancer care in developing countries: Current problems with and way forward for research on epidemiology and delivering screening, treatment, supportive and survivor care services

R.V. Kumar[1], A. Mandava[1], D.M. Gangaiah[2], L.N. Kashyapa[1], S. Bhasker[3], D.S. Nihanthy[1], C.S. Rao[1]. [1]*Kidwai Memorial Institute of Oncology, Radiation Oncology, Bangalore, India;* [2]*Kidwai Memorial Institute of Oncology, Surgical Oncology, Bangalore, India;* [3]*All India Institute of Medical Sciences, Radiation Oncology, New Delhi, India*

**Background:** With more than half of global burden of breast cancer, it is the commonest cancer among women in developing countries. Lack of infrastructure, knowledge along with sub-standard and sub-optimal technology, technique and infrastructure to assess the epidemiology, to screen, diagnose, work-up and stage, for treating and following-up, to provide supportive care and to address survivorship issues of the breast cancer patients may contribute to delay in diagnosis, increasing burden of advanced stage disease, poorer outcome and quality of life (QoL).

**Methods and Materials:** Discrete hospital-based data of breast cancer patients treated during specific time period at two regional cancer centres of India, i.e., All India Institute of Medical Sciences, New Delhi and Kidwai Memorial Institute of Oncology, Bangalore were analyzed. Analysis of published literature of epidemiology and screening of breast cancer patients was carried-out.

**Results:** Epidemiology of breast cancer is quite different from that of those of affluent industrialized nation. Breast self-examination may still have relevance in early detection of breast cancer in contrary to evidence from developed countries. Newer modalities of screening and initial work-up may not be feasible and accessible in developing world. Need to select patients for breast conservation therapy, optimizing chemotherapy regime (CMF/CAF regime over epirubicin-/docetaxel-based chemotherapy) and radiotherapy techniques (conventional body-contouring directed cobalt-60 radiotherapy technique over intensity-modulated radiotherapy) after considering the cost-benefit and cost-effectiveness of these modalities. Follow-up interval and investigations should be prescribed to patients with Common Terminology Criteria for Adverse Events Reporting (CTCAE v4.0) grade 2 or higher symptoms. Distress screening and tool to measure distress has to be optimized based on the resources available in developing countries. Everyday travel to radiotherapy centre may push patients into poverty and advocacy for free travel pass may be essential in these under-developed regions of the world. Personalization of investigations and therapy and quality of life issue should consider not only tumor-related factors, but also the patients- and health-care-related factors.

**Conclusion:** Epidemiology of breast cancer and its care in developing countries appears to be slightly different from that of developed affluent industrialized nations. There is need to design studies to uncover the actual risk factors of breast cancer and optimize the screening and care component by development of appropriate protocol for breast cancer management in developing countries. Cancer centers in developing countries should be encouraged to be part of multi-centric policy research/ studies to evolve relevant breast cancer management guidelines.

**No conflicts of interest**

**107** Poster

**PATI: Patient Accessed Tailored Information: A pilot study to evaluate the effect on preoperative breast cancer patients of information delivered via a mobile application**

N. Foley[1], E. O'Connell[1], V. Livingstone[1], B. Maher[2], E. Lehane[3], T. Cil[4], N. Relihan[1], M. Bennett[1], H. Redmond[1], M. Corrigan[1]. *[1]Cork University Hospital, Breast Research Centre, Cork, Ireland; [2]University College Cork, School of Medicine, Cork, Ireland; [3]University College Cork, Catherine McAuley School of Nursing and Midwifery, Cork, Ireland; [4]University of Toronto, Division of General Surgery, Toronto- Ontario, Canada*

**Background:** The information needs of cancer patients are highly variable. Literature shows improved ability to cope, increased patient involvement with decision making, greater satisfaction with treatment choices and reduced anxiety levels in cancer patients who have access to information. The aim of this project was to evaluate the effects of a mobile application on the anxiety levels of patients undergoing surgery for breast cancer.

**Materials and Methods:** An application was developed for use with Apple iPad containing information on basic breast cancer biology, different treatments used and surgical techniques. Content and face validity studies were performed following consultation with patient and professional representatives. A randomized control trial was set up, with a 1:1 allocation. Data collected include basic demographics and type of surgery. Questionnaires used included: the hospital anxiety and depression scale (HADS), mini-mental adjustment to cancer (Mini-MAC), information technology familiarity and information satisfaction.

**Results:** To date 39 women have taken part. Thirteen women had access to an iPad containing additional information and 26 women acted as controls. The mean age was 54 and technology familiarity was similar among both groups. Anxiety scores at seven days were significantly lower in control patients without access to the additional information provided by the mobile application ($p = 0.033$).

**Conclusion:** Anxiety and depression in breast cancer patients is both multifactorial and significant, with anxiety levels directly correlating with reduced quality of life. Although intuitively information should improve anxiety levels, we have demonstrated that surgical patients with less information reported significantly reduced anxiety. We advise thoroughly testing and auditing of information initiatives in breast cancer patients.

This project was supported by a financial grant provided from the TRAP (translational Research Access Programme) Medical School Research Committee, University College Cork.

**No conflicts of interest**

**108** Poster

**Health literacy and the perception of risk in a breast cancer family history clinic**

E. Rutherford[1], J. Kelly[1], E. Lehane[1], V. Livingstone[1], B. Cotter[1], A. Butt[1], M. O' Sullivan[1], F. O' Connell[1], P. Redmond[1], M. Corrigan[1]. *[1]Cork Breast Research Centre- Cork University Hospital- Cork- Ireland., Surgery, Cork, Ireland*

**Background:** Breast cancer is one of the most common cancers in women, and as such is the focus of extensive research and significant media attention. Despite this, considerable misperception exists regarding the risk of developing breast cancer. This carries evident implications for delivering care. This study aims to examine the accuracy of risk perception of women attending a breast cancer family history clinic, and to explore any relationship between risk perception accuracy and health literacy.

**Methods:** A cross-sectional study of women attending a breast cancer family history clinic ($n = 86$) was carried out, consisting of a patient survey and a validated health literacy assessment. Patients' perception of personal and population breast cancer risk was compared to actual risk as calculated by a commonly used risk assessment tool.

**Results:** Significant discordance between real and perceived risks was observed. The majority (83.7%) of women overestimated their personal lifetime risk of developing breast cancer, as well as that of other women of the same age (89.5%). Health literacy was considered potentially inadequate in 37.2% of patients; there was a correlation between low health literacy and increased risk perception inaccuracy across both personal ten-year ($r_s$=0.224, $p = 0.039$) and general ten-year population estimations. ($r_s$= 0.267, $p = 0.013$). Accuracy of estimation of BRCA mutation population prevalence was also associated with higher health literacy scores ($r_s$= 0.348, $p < 0.001$).

**Conclusion:** Inaccuracy in risk perception is highly prevalent in women attending a breast cancer family history clinic. Health literacy inadequacy is significantly associated with this inaccuracy.

**No conflicts of interest**

**109** Poster

**Overcoming ageism bias in the treatment of breast cancer: Standard and non-standard strategies in the elderly**

A. Parvaiz[1], B. Isgar[2]. *[1]Peterborough City Hospital, Oncoplastic Breast Surgery, Peterborough, United Kingdom; [2]New Cross Hospital, Breast Surgery, Wolverhampton, United Kingdom*

**Background:** About 30% of all breast cancers occur in women aged over 70. The primary challenge of caring for older cancer patients is providing treatment options that maximize long-term survival while accounting for comorbidities, life expectancy, and effects of treatment.

**Materials and Methods:** All breast cancer patients aged over 70 in the last five years were included. Preoperative fitness assessment segregated patients into two groups.

**Results:** See the table. Reasons for inclusion in group B (non-standard treatment) included medically unfit (50), mental health issues (3), patients choice (14) and unknown (6).

**Conclusion:** Patients in group A were relatively younger, healthier, had a significantly longer survival and longer time to death. Mortality was significantly higher in group B. With appropriate selection of patients into standard and non-standard treatment groups, elderly breast cancer patients can be treated to maximize long-term survival. These favourable clinical findings should help clinicians counter highly prevalent 'ageism' bias in the breast cancer treatment.

**No conflicts of interest**

Table (abstract 109).

| | All | Group A (Standard treatment) | Group B (Non-standard treatment) | p value |
|---|---|---|---|---|
| Number of patients | 262 | 192 (73%) | 70 (27%) | |
| Age range (median) | 70−97 (79) | 70−95 (78) | 71−97 (84) | <0.0001 |
| Surgery | | 192 Surgery under general anaesthesia (69 mastectomies, 123 wide local excisions) | 12 Wide local excision under local anaesthesia | |
| Adjuvant treatment | | 14 chemotherapy, 146 radiotherapy, 161 hormone treatment, 7 trastuzumab (Herceptin) | 60 primary endocrine treatment, 6 palliative radiotherapy | |
| Surviving patients | 215 (82%) | 173 (90%) | 42 (60%) | <0.0001 |
| Mortality | 47 (18%) | 19 (10%) | 28 (40%) | <0.0001 |
| Follow-up, range (median) | 0−59 (30) months | 0−59 (29) | 4−58 (32) | |
| Time to death, range (median) | 0−58 (20) months | 3−58 (24) | 0−47 (19.5) | <0.0001 |

**110** Poster

**Factors influencing the decision to pursue immediate breast reconstruction after mastectomy for breast cancer**

M. Weenk[1], P. Wunschel[2], E. Heine[3], L. Strobbe[4]. [1]*Radboudumc, Surgery, Nijmegen, Netherlands;* [2]*Gelderse Vallei, Urology, Ede, Netherlands;* [3]*Canisius Wilhelmina Ziekenhuis, Plastic Surgery, Nijmegen, Netherlands;* [4]*Canisius Wilhelmina Ziekenhuis, Surgery, Nijmegen, Netherlands*

**Background:** Immediate breast reconstruction (IBR) after mastectomy has shown to be oncologically safe and to improve quality of life in breast cancer patients. However, most women undergoing mastectomy do not undergo IBR. In this study, we aim to identify surgeon-related factors in considering IBR and factors affecting patients' decision to choose for IBR.

**Materials and Methods:** In this retrospective study, we analyzed all records of breast cancer patients who underwent mastectomy with or without IBR between 2010 and 2013. We documented all information whether or not a patient underwent IBR after mastectomy. In patients who did not undergo IBR, we searched for documentation about the reason for refraining from IBR.

**Results:** Of 437 patients, 97 (22.2%) underwent IBR. The majority (89.8%) received tissue expanders, followed by deep inferior epigastric flaps (5.1%) and implants (4.1%). Patients who did not undergo IBR (340; 77.8%) had a higher age (62.2 versus 51.9 years, $p < 0.001$) and higher BMI (27.0 versus 24.3, $p < 0.001$).

In 49.1% of the patients who did not undergo IBR, the decision-making process was documented. Fifty two patients declined IBR. However, in most patients reasons for refraining IBR were not specified. In the remaining 115 documented cases, the surgeon did not offer IBR, mostly because of the predicted need for postmastectomy radiation.

**Conclusions:** A substantial proportion of the breast cancer patients might not be appropriately informed about IBR. In the documented cases, anticipated radiation, higher age and higher BMI were important surgeon-related factors in refraining from IBR.

**No conflicts of interest**

**111** Poster

**The association of waiting times from diagnosis to initiation of treatment with survival in women with breast cancer at a tertiary cancer centre in Western India**

N. Gupta[1], A. Deshpande[1], R. Cs[1], M. Sharrma[2], M. Patel[3]. [1]*Resident, Surgical Oncology, Ahmedabad, India;* [2]*Assistant Professor, Surgical Oncology, Ahmedabad, India;* [3]*Associate Professor, Surgical Oncology, Ahmedabad, India*

**Background:** Currently there is no agreement on the optimal time to treatment of breast cancer; however, given the considerable emphasis on early detection, one would expect a similar emphasis on early treatment. The purpose of our study was to assess the time interval between the first medical consultation and the beginning of treatment amongst women with breast cancer. This study was done at a tertiary care cancer centre in western India to analyse the waiting time for breast cancer treatment and its effect on survival.

**Materials and Methods:** We retrospectively reviewed the records of breast cancer patients who underwent surgery at our centre in 2011 and 2012. Waiting time was calculated by dividing it into 3 groups: Time interval 1 − Interval when the patient first visited a general physician and was suspected of having carcinoma breast to the time the patient first came to our centre; Interval 2 − the time when the patient came to our centre and was confirmed to have breast cancer; Time interval 3 − the time after diagnosis to the initiation of treatment at our centre. The patients records were analysed to check for age, stage, receptor status, surgical and adjuvant treatment given, follow up, recurrence and survival. The data were compiled and the results analysed.

**Results:** In our study, we analysed 119 patients who were operated for breast cancer at our institute and the median age was 47.4 years. We have excluded patients with metastatic disease and those undergoing toilet mastectomies. Amongst these patients, 12 underwent breast conservative surgery, 111 underwent modified radical mastectomy and one patient underwent axillary dissection only as she had undergone a wide local excision of breast lump outside the institute. The total mean waiting time (interval 1+2+3) between the first medical consultation outside our centre and the beginning of treatment was 32.6 days. The mean waiting time (Interval 1) when the patient first visited a general physician and was suspected of having carcinoma breast to the time the patient first came to our centre was 11.4 days. After coming to the centre, the mean waiting time (Interval 2) to confirm the diagnosis of breast cancer was 3.2 days and the waiting time till start of the treatment after diagnosis (Interval 3) was 8.4 days. The mean waiting time from first visit to the institute to start of treatment (Interval 2+3) was 13.93 days. The mean disease free survival was 1143 days and the mean waiting time did not have any effect on survival.

**Conclusion:** The waiting times for breast cancer treatment in our centre is 13.93 days and in comparison to data from western world. Also, waiting time did not have any statistically significant effect on disease free and overall survival of breast cancer.

**No conflicts of interest**

## Wednesday, 9 March 2016

**POSTER SESSION**

# Lifestyle, Prevention including Secondary Prevention

**112** Poster

**Validation and assessment of a technology familiarity score in patients attending a symptomatic breast clinic**

C. O'Brien[1,2], J. Kelly[1], E. Lehane[3], V. Livingstone[1], B. Cotter[1], A. Butt[1], L. Kelly[1], M. Corrigan[1]. [1]*Cork Breast Research Centre- Cork University Hospital, Department of Academic Surgery, Cork, Ireland;* [2]*University College Cork, School of Medicine, Cork, Ireland;* [3]*University College Cork, Catherine McAuley School of Nursing and Midwifery, Cork, Ireland*

**Introduction:** New media (computers, mobile phones and the internet) have the potential to transform the healthcare information needs of patients with breast disease. However, patients' current level of use and their willingness to accept new media for education and communication remain unknown.

**Materials and Methods:** This was a single-centre clinic-based prospective cross-sectional study. A previously developed instrument was modified, validated and tested on patients attending a symptomatic breast clinic.

**Results:** The instrument was evaluated on 200 symptomatic breast patients. The commonest outlets for education were staff (95%), leaflets (69%) and websites (59%). Websites are more likely to be consulted by younger patients (<47 years), and patients who were working, students or homemakers ($p < 0.05$). Patients rated usefulness of information media in this order: (1) print, (2) phone, (3) website, (4) email, (5) text and (6) apps. Patients who were new to the clinic were more likely to find text messaging and emailing useful ($p < 0.05$). Younger patients (<47 years) are more likely to find text messages, apps, websites and email useful ($p < 0.05$). Urban patients are more likely to find websites and email useful ($p < 0.05$). Patients with higher education were more likely to favour apps, websites and email ($p < 0.05$). Smartphone owners were significantly more likely to rate text messaging, apps, websites and email as useful media ($p < 0.05$).

**Conclusion:** This study demonstrates that new media technology use among breast patients is expanding as expected along generational trends. As such its further integration into healthcare systems can potentially ameliorate patient education and communication.

**No conflicts of interest**

**113** Poster/Poster Spotlight

**Examining the knowledge and perception of the lifestyle risk factors for cancer development among cancer survivors in Ireland and development of an educational tool**

M.G. Kelly[1], J. Richmond[1]. [1]*Letterkenny General Hospital, Oncology, Co Donegal, Ireland*

**Background:** The cancer landscape is changing and the picture emerging is a complex one that recognizes some cancers as preventable. Previous research has explored the public's knowledge of cancer risk based on lifestyle, but to date no research in Ireland had explored cancer survivors' knowledge of the lifestyle risk factors for developing cancer. As knowledge is one prerequisite for behavior change, this research aimed to investigate cancer survivors' knowledge of lifestyle risk factors for cancer, perception of their personal lifestyle risk and motivation for change.

**Methodology:** Based on literature that identified lifestyle risk factors for cancer, a questionnaire was developed. Significant testing demonstrated reliability of the questionnaire. Construct validity was shown to be high. Subsequently the questionnaire was administered to 620 cancer survivors in Ireland using a non-experimental design. Response rate was 69.5% ($n = 414$), 60% of whom were breast cancer survivors.

**Results:** Tobacco use was universally accepted as a risk factor most likely as a result of government policy and health education in Ireland. Participants recognized diet, alcohol consumption and physical exercise to

be risks factors however many did not perceive their own personal risk to be linked to these variables. Two thirds of the breast cancer survivors' respondents were either overweight or obese and 40% did not exercise as per recommended guidelines. Since their cancer diagnosis, participants tried to improve some aspects of their lifestyle. 64% of breast cancer survivors reported to eat healthier; 13% stopped smoking after their cancer diagnosis; of the people who drank alcohol 26% reduced alcohol intake after their cancer diagnosis. Despite stress not being a recognized risk factor for cancer, participants overwhelmingly endorsed it. Myths abounded relating to other risk factors for cancer development including the effects of multi-vitamins, fish and red meat, confusion surrounding caffeine intake, use of deodorant, use of hormones, breast feeding, condom use and other aspects of lifestyle.

**Conclusion:** This study identifies major knowledge deficits and personal disconnect regarding lifestyle adaptation for cancer prevention. In response to this need, a web based app was developed: www.stopcancer.support. This tool targets a wide audience of cancer survivors and the public. It can be used by health professionals as a health promotion tool. The web-based app is appropriate to patients' needs and should improve knowledge of cancer prevention and will assist with health education strategies.

**No conflicts of interest**

**114** Poster

**Hot infusions and risk of breast cancer: A case–control study in Uruguay**

A. Ronco[1], E. De Stefani[2], B. Mendoza[3], E. Abbona[4], H. Deneo-Pellegrini[2]. *[1]Pereira Rossell Women's Hospital, Unit of Oncology and Radiotherapy, Montevideo, Uruguay; [2]Clinicas Hospital-School of Medicine- UdelaR, Pathology Department, Montevideo, Uruguay; [3]Clinicas Hospital- School of Medicine- UdelaR, Endocrinology and Metabolism Department, Montevideo, Uruguay; [4]Pereira Rossell Women's Hospital, Department of Nutrition, Montevideo, Uruguay*

**Background:** Several epidemiologic studies showed a risk increase for the intake of 'maté' (infusion of Ilex Paraguariensis herb) on some cancer sites, particularly of the upper aerodigestive tract. There are no conclusive evidences about possible roles of tea and coffee consumption in the risk of breast cancer (BC), as well as there are no published specifically designed studies on the role of 'maté' infusion, to our knowledge. In order to know the associations of 'mate', tea and coffee and the risk of BC in Uruguayan women, we conducted a case–control study in women residents in the capital city Montevideo, who were affiliated to the private healthcare system.

**Material and Methods:** The study sample included 111 BC incident cases and 222 non-hospitalized controls having normal mammograms, which were age-frequency matched to cases. Women were interviewed with a specific questionnaire featured by a food frequency questionnaire of 120 items, as well as with sociodemographic, reproductive, lifestyle and medical variables. The study was focused on the intake of hot beverages (daily intake, age at start, age at quit, duration of habit, intensity of intake). Odds Ratios (OR) and their 95% confidence intervals (95% CI) were calculated through unconditional logistic regression, adjusting for potential confounders.

Table 1. Adjusted Odds Ratios of BC for each analyzed variable

| Variable | Intake tertile [a] | Controls | Cases | Adjusted [b] OR (95% CI) | p-value for trend |
|---|---|---|---|---|---|
| Tea | ⩽149 | 32 | 35 | 1.00 | |
| | 150 | 124 | 49 | 0.45 (0.22–0.92) | |
| | ⩾151 | 66 | 27 | 0.40 (0.19–0.86) | 0.001 |
| Maté | 0 | 63 | 54 | 1.00 | |
| | 100–1000 | 123 | 47 | 0.31 (0.17–0.57) | |
| | >1000 | 36 | 10 | 0.21 (0.08–0.52) | 0.001 |
| Coffee | 0 | 70 | 45 | 1.00 | |
| | 1–100 | 71 | 34 | 0.99 (0.53–1.86) | |
| | >100 | 81 | 32 | 0.73 (0.38–1.39) | 0.22 |
| Tea + maté | Low | 17 | 23 | 1.00 | |
| | Mid | 137 | 70 | 0.37 (0.16–0.85) | |
| | High | 68 | 18 | 0.14 (0.05–0.38) | <0.001 |

[a] In ml/day.

[b] Logistic regression model adjusted for: age, education years, age at menarche, menopausal status, age at first delivery, number of live births, months of breastfeeding, oral contraception, family history of BC, body mass index, total energy from diet, total meat, total fruits and smoking status.

**Results:** The highest tertiles of 'maté' (OR=0.21, 95% CI 0.08–0.52) and tea (OR=0.40, 95% CI 0.19–0.86) intakes were associated with significant reductions of BC risk. High consumers of both infusions exhibited an additive risk reduction (OR=0.14, 95% CI 0.05–0.38). Conversely, coffee intake did not show a significant association.

**Conclusions:** Our study found evidence of an inverse association for intakes of tea and 'maté' drinks and the risk of BC. To our knowledge, this is the first study reporting results on 'maté' intake and the quoted disease.

**No conflicts of interest**

**115** Poster

**Lifestyle and breast cancer**

A. Fatima[1]. *[1]Fatima Jinnah Medical College/University, MBBS, Lahore, Pakistan*

**Objective:** To evaluate the knowledge, screening and pre disposition of breast cancer risk factors among undergraduate students.

**Methods:** A cross sectional study was carried out at Punjab University from March 2015 to July 2105. About 500 female students between 20−24 years of age were requested to fill a questionnaire designed to assess the knowledge about the breast cancer in association with its risk factors, signs and symptoms, screening methods, self-breast examination and treatment. The questionnaire was divided into parts. The first compromise the qualification of the respondent. The second part contained the questions which depicts the knowledge of respondent about risk factors, symptomology, screening tools and treatment modalities of breast cancer. The third part of the questionnaire was directed towards female respondent's own practices regarding screening, specifically BSE. The questionnaire was distributed in person, informed consent was obtained, an immediate response was requested for and the questionnaires collected back.

**Results:** More than 250 students had good knowledge about self-breast examination, risk factors associated with breast cancer. More than 100 students agreed that breast cancer can be easily cured if it is detected in its early stage and about 150 students thought that a surgeon rather than an oncologist should be consulted first if lump is palpable. Almost 175 students had a knowledge of mammography screening.

**Conclusion:** This study reveals that students are not fully aware about the risk factors, signs, symptoms associated with breast cancer. There were very few students who had the knowledge of mammography screening and Breast self-examination. However majority were unaware of the importance of ultrasound and MRI as screening modalities. The practicing attitude of BSE is not observed by majority of females. Women believe that chemotherapy and radiation therapy is the key to success in treatment of breast cancer. Education and awareness programs are required to educate people about the morbidity and mortality of breast cancer.

**No conflicts of interest**

**116** Poster

**The knowledge and attitudes of breast cancer, breast self-examination and mammography among female faculty students in Hafr Al Batin**

F. Aldhafeeri[1]. *[1]University of Hafr Albatin, College of Applied Medical Sciences, Hafr Albatin, Saudi Arabia*

**Background:** Breast cancer has been ranked as one of the top ten causes of death for females in the Kingdom of Saudi Arabia (KSA) in 2010. Breast self-examination (BSE) and mammography ensure early diagnosis and a better chance for treatment and recovery. The main purpose of this study was to evaluate health beliefs concerning breast cancer risk factors, BSE and mammography among a sample of female faculty students in University of Hafr Albatin.

**Materials and Methods:** This is a descriptive cross-sectional study. It was conducted in college of Applied Medical Sciences, University of Hafr Albatin. The study sample included 100 undergraduate female students. The questionnaire included socio-demographic variables, knowledge of BSE and risk factors for breast cancer form and BSE practice form were used to collect data.

**Results:** The age range of the target population was between 20 to 30 years with the mean age 21 years. Only 37% of respondents believe that BSE is important to early diagnose breast cancer. Only 48% of the respondents believe that mammogram has an important role to diagnose breast cancer at early stages. However, 50% of the sample has no idea about what is mammogram. 67% of the students believe that age is a risk factor increasing the chance of occurrence. 80% of them accept that family history of breast cancer is a risk factor. 42% of the respondents indicated that puberty at less than 11 years has no effect on breast cancer occurrence while 37% have no idea.

**Conclusion:** There is a need to increase knowledge of female faculty students about the risks of breast cancer and benefits of early detection. Health care providers should develop effective breast health programs to encourage good health behavior in women from their youth.

**No conflicts of interest**

**117** Poster

**Utilising a nurse led holistic lifestyle intervention in reducing sexuality concerns in women after breast cancer − The Pink Women's Wellness Program results**

J. Porter-Steele[1], D. Anderson[1], A. McGuire[1], C. Seib[1]. [1]*Queensland University of Technology, Nursing, Brisbane Qld, Australia*

The impact of a cancer diagnosis and treatment on women is profound. With earlier diagnosis and improved multi-modal treatments for cancer women are generally living longer although their quality of life particularly in the sexual health domain is often poor. There is evidence that health professionals are reluctant to discuss sexuality concerns with their patients, reasons cited for this are many and varied and include embarrassment or the patient not expressing concerns and so clinicians assuming there is no issue. Often by the time a patient realises sexuality concerns are a problem, treatment has finished and they have less contact with the health care team and less access to specialist support to gain support in this area of their lives.

This study tested a 12-week multi-modal intervention, The Pink Women's Wellness Program (Anderson and Graham 2011) delivered by specialist breast care nurses that aimed to decrease negative sexuality symptoms for women following breast cancer treatment. Self-report data were collected at two time-points baseline (T1), and post intervention (T2) to measure quality of life (FACT-B, SF-12 v2) and sexual function − Female Sexual Function Index (FSFI).

Results indicate the majority of women in this study had common concerns in relation to sexual function following breast cancer diagnosis and treatment. 86.4% of women reported FSFI scores less than or 26.5, which is the cut-point for female sexual disorder (Rosen, 2000). Overall the FSFI scores in the intervention group showed a statistical and clinical improvement over the duration of the study (T1: M=11.1, SD 9.8; T2: M=14.0, SD=10.0) while the mean difference in the control group was 0.3, which was not significant.

This study demonstrates that compared to usual care, women who received the intervention showed a significant reduction in sexuality symptoms. This pilot study highlights the need for further research to efficiently manage sexual function in this population and a larger multi-centre RCT with women in this population is in progress in Australia (see www.wwacp.com.au).

**No conflicts of interest**

**118** Poster

**Women's perceptions on personalised risk-based breast cancer screening and primary prevention: A systematic review**

L. Rainey[1], A. Jervaeus[2], D. Van der Waal[1], Y. Wengström[2], M. Broeders[1]. [1]*Radboud University Medical Centre Nijmegen, Health Evidence, Nijmegen, Netherlands;* [2]*Karolinska Institutet, Neurobiology-Care Sciences and Society, Stockholm, Sweden*

**Background:** To counter the increasing burden of breast cancer, better strategies for primary and secondary prevention are urgently needed. Personalised risk-based approaches may help target screening and prevention for breast cancer to women who will benefit most while reducing harms among women who would experience less benefit. However, little is known about the acceptability of personalised approaches, and the challenges of implementation. Therefore, a systematic review was performed to study women's perceptions regarding personalised risk-based breast cancer screening and primary prevention.

**Material and Methods:** Electronic databases Pubmed, Embase and PsycInfo were systematically searched for studies evaluating perceptions of women 1) at population risk of developing breast cancer on personalised risk-based mammography screening, and 2) at increased risk due to familial predisposition on primary prevention for breast cancer. All titles, abstracts and full-text articles were systematically screened by two independent researchers. The methodological quality of the included studies was assessed using the Critical Appraisal Skills Programme (CASP) tool.

**Results:** The search strategy identified 5271 unique publications, of which 54 were selected. Several perceived benefits of risk-based breast cancer screening were identified, i.e. reassurance, empowerment, the possibility to detect breast cancer at a younger age, and more efficient screening strategies with a reduced burden for low risk women. Barriers to risk-based screening included lack of knowledge, insurance coverage, potential insurance or employer discrimination or stigmatization, anxiety, and worry.

Regarding primary breast cancer prevention, prophylactic bilateral mastectomy (PBM) was considered by women who perceived themselves to be at high risk. However, loss of 'womanhood', and expected adverse reaction of the spouse hindered the acceptance of PBM for prevention. Barriers to the uptake of chemoprevention were possible side-effects, difficulty in comprehending risk-information, cost of treatment, and drug interactions, whereas incentives included an increased sense of control and a physician's expert advice. Acceptance of lifestyle advice depended on the factors age, weight, and level of education. Data analysis is still ongoing, with the intention to include a meta-analysis of the results.

**Conclusions:** Generally, most women appear to have an accepting attitude towards the possibility of personalised risk-based breast cancer screening and primary prevention. However, this study identified several factors that need to be taken into account when considering the implementation of this new screening paradigm. Further research is required to qualitatively and quantitatively evaluate the identified factors with the target population, ultimately developing a model of acceptance.

**No conflicts of interest**

**119** Poster

**Reaching out to rural women to screen for breast cancer: A step to reduce the burden of breast cancer in a rural area of central India**

A. Mudey[1], S. Nayak[1], M. Khapre[1], R. Goyal[1]. [1]*Jawaharlal Nehru Medical College, Sawangi Meghe, Community Medicine, Wardha, India*

**Background:** In India, breast cancer is the most common cancer in urban areas while it is second most (after cervical cancer) in rural areas. Breast cancer accounts for 25% to 32% of all female cancers in all cities. This implies, practically, one fourth of all female cancer cases are breast cancers. It has led to 90,659 breast cancer deaths in 2010. According to National Cancer Registry Programme projections, the number of breast cancer deaths in India will climb to 106,124 in 2015 and to 123,634 in 2020.

Keeping in mind all these facts we have started this project with an aim to reduce the mortality due to breast cancer by screening females above 30 years with short-term objectives to create breast cancer awareness among females above 30 years.

**Material and Methods:** Study was conducted in 31 adopted villages of our Institute during July to October 2015. Health workers were given skill training about the basics of breast cancer, procedure of self-examination and screening methods. They were to go house to house to collect the information of females above 30 years and screen them by mammography after obtaining the informed written consent.

In health education session, awareness regarding breast and its importance was highlighted. Breast awareness implies familiarity with one's own breast. They were motivated to do self-examination monthly during bath, best time being just at the end of menses. This will help to keep in notice any irregularity, any lumps, the skin, the nipple etc. Participants found to be positive were to further undergo diagnostic test on opinion of expert doctor.

**Results:** During study period, in all 520 females from different villages were contacted by health workers. As the issue of diseases related with breast is sensitive among the rural females and it's very difficult to convince them, only 190 (36.53%) were convinced to get mammography done. Out of 190, 32 (16.84%) had BI-RAD's category II−IV. Out of these 32 females, 30 (93.75%) patients had come for follow-up and got histo-pathologically investigated. Three cases got operated and their histo-path reports were benign. However 01/190 mammography done is suspicious of malignancy and under follow-up. Significant improvement was found in pre and post test score after health education session.

**Conclusion:** Though the incidence of breast cancer is much lower in rural area, the patient reports in very advanced stage when only palliative care is an option. Lack of health care facilities, lack of transportation, long distance, and poor income combined with lack of awareness of symptoms leads to underdiagnosis of breast cancer in rural area.

So the *need of the hour* is breast awareness, beginning from 30 years of age, and regular screening from a qualified doctor, so that we can detect the cancer early and treat it in earlier stages thereby giving a chance of longer life for the patient.

**No conflicts of interest**

**120** Poster

**Breast cancer, awareness and screening programme in Mumbai**

P. Dyavarishetty[1], S. Kowali[1]. [1]*K. J. Somayya Medical College- Sion Mumbai, Community Medicine, Mumbai- Maharashtra, India*

**Background:** In India the incidence of breast cancer is rising especially in the cities and has now overtaken cervical cancer. Lack of awareness, fear of the disease and low priority accorded to health translates into poor health seeking behaviour, with woman usually coming in very late stages to the health care provider. Also regular health check-up and screening for diseases is a concept that is not usually practiced in India. Opportunistic screening for diseases is something that is feasible but is usually not practiced because of heavy patient load, and lack of privacy.

The aim of the project is to create awareness amongst the community, regarding breast cancer, and motivate the women aged 40 years and above to conduct regular self-breast examination, undergo annual clinical breast examination and mammography once in two years.

**Material and Methods:** Study area: A low socio-economic group in the city of Mumbai.

Implementation:

- Sensitization of community and enumeration of household members
- Health education on breast cancer
- Teaching beneficiaries self-breast examination
- Assessing risk for breast cancer
- Weekly OPD for Clinical breast examination and reminder visits for CBE
- Mammography for women above 50 years through mobile mammography unit
- Accompanied referral and follow up services for women identified with abnormalities detected in clinical breast examination
- Quarterly follow up on whether women are doing self-breast examination

**Results:** Of the 455 cases (54% of eligible women) undergoing clinical breast exam, 49 (10.8%) were found to have some breast related abnormalities by the primary care physician. A large proportion of cases (36), i.e. almost 74% cases, did not visit the surgeon or did not complete the investigations requested. Only 13 patients (26%) completed the referrals successfully. 44% of the eligible women underwent mammography. No case of breast cancer was detected in year one.

**Conclusion:** Creating awareness in the community and motivating the women through reminder and follow-up visits does result in participation in breast cancer screening programme even in a community where such behaviour does not prevail.

**No conflicts of interest**

**121** Poster

**Patient preferences for oncoplastic breast surgery in early breast cancer: A discrete choice experiment**

N. Gonen[1], M. Menke[2], E. De Bekker-Grob[3]. *[1]Sykehuset i Vestfold, Breast and Endocrine Surgery, Tonsberg, Norway; [2]Albert Schweitzer Ziekenhuis, Oncologic Surgery, Dordrecht, Netherlands; [3]ErasmusMC, Public Health, Rotterdam, Netherlands*

**Background:** Oncoplastic breast surgery for larger lesions has been widely developed with good oncological and cosmetic results. However, the desicion making for the type of oncoplastic breast surgery in early breast cancer patients does not give room for patients to express their preferences. Surgeons are usually subjective in providing information on treatment options, often influenced by patient characteristics, in particular age. It is known that health professionals and patients may or may not share the same preferences related to the treatment options. Discrete choice experiments (DCEs) have been increasingly used in health care as an approach to elicit patients' preferences. The aim of this study is to quantify patient's preferences for oncoplastic breast surgery in early breast cancer.

**Methods:** Between 2013–2015 a two-centered DCE was conducted among patients who had been treated for early breast cancer with breast conserving surgery in the past. Patients were asked on their preferences for aspects of breast reconstructive surgery using scenarios based on: breast symmetry, shape, cup size, location and number of scarring, and number of operations. Data was analyzed using a panel latent class model.

**Results:** A total of 136 patients, aged 35−90 years old, responded to the DCE survey. All above mentioned aspects proved to influence patients' preferences for oncoplastic breast surgery, except for the shape of the breast. Although breast symmetry was the most important aspect determining oncoplastic breast surgery, significant preference heterogeneity was observed. Two latent classes of preference patterns were found. Class 1 individuals were most likely to prefer cosmetic outcome (breast symmetry, and similar cup size for both breasts), whereas class 2 individuals were more focused on the invasiveness of the surgery (number of scarring, and number of operations. Patients' age, marital status or educational level however did not explain the difference between both classes.

**Conclusion:** Although, breast symmetry has the highest preference in patients after breast conserving surgery regarding cosmetic results, substantial preference heterogeneity existed among respondents. The preference for cosmetic result was not significantly influenced by age or marital status in this study. Therefore, the decision making for breast conserving therapy in patients with early breast cancer should be tailored for each patient, regardless of age.

**No conflicts of interest**

**122** Poster

**Screened versus symptomatic breast cancer patients in middle Hungarian region: A long term follow-up**

M. Ujhelyi[1], D. Pukancsik[1], P. Kelemen[1], M. Bidlek[2], E. Kovacs[2], I. Kenessey[3], N. Udvarhelyi[4], M. Bak[5], M. Kasler[6], T. Kovacs[7], Z. Matrai[1]. *[1]National Institute of Oncology, Breast and Sarcoma Surgery, Budapest, Hungary; [2]National Institute of Oncology, Radiological Diagnostics, Budapest, Hungary; [3]National Institute of Oncology, National Cancer Registry, Budapest, Hungary; [4]National Institute of Oncology, Surgical and Molecular Tumor Pathology Centre, Budapest, Hungary; [5]National Institute of Oncology, Department of Cytopathology, Budapest, Hungary; [6]National Institute of Oncology, Director, Budapest, Hungary; [7]Guy's Hospital, Breast Unit, London, United Kingdom*

**Background:** Breast cancer is a multifarious disease. Stage at diagnosis and breast cancer subtypes are the most powerful prognostic factors, which together with the oncology treatments determine the overall and disease free survival of the breast cancer patients. Many clinical randomized controlled trials (RCTs) have confirmed that mammography screening in women age 40 years and older reduces breast cancer mortality by 17% to 32%. But these trials were conducted before the era of multidisciplinary breast cancer units and before chemotherapy, adjuvant trastuzumab therapy and hormonal therapy became widely used in breast cancer treatment. Contrary, some recent studies deny the impact of the nonpalpable early stage tumor detection on mortality reduction. The goals of this study to compare the clinical outcome of a group of patients undergoing a breast cancer screening with that of a synchronous non-screened symptomatic group of patients matched for age and follow-up period and investigate the role of early diagnosis in breast cancer survival.

**Patients and Method**: Inclusion period was from 2002 to 2009. Data collection was performed from the database of National Institute of Oncology, Hungary. Screened breast cancer patients discovered by organized nationwide mammography screening program were collected prospectively. The symptomatic breast cancer patients were collected randomly and prospectively. Medical records and pathology reports were reviewed retrospectively. According to the international ESMO guideline all patients received multidiscipline oncology treatments in the National Institute of Oncology, Hungary.

**Results:** 47 718 women were examined by screening program and 298 breast cancer patients were discovered. 331 symptomatic non-screened breast cancer patients were randomly selected who were discovered by self-examination or other medical breast examination along this period. The screened group presented a significantly lower median tumor size than non-screened patients ($P < 0.00001$). Incidence of negative nodes was significantly higher in screened than that in non-screened group ($P < 0.0006$). Incidence of chemotherapy was 17% greater in non-screened group than in screened group ($P = 4 \times 10^{-5}$). Screened group did not show significantly better overall ($P = 0.717$) and disease-free survival rates ($P = 0.081$) than non-screened patients.

**Conclusion:** In our investigation the mammography screening had not brought any significant overall and disease free survival in the early stage brest cancer patients comparing to the symptomatic non-screened group. Due to the discovery of specific prognostic and predictive biomarkers that enable the application of more individualized therapies to different molecular subgroups and it might indeed have reduced breast cancer mortality in symptomatic breast cancer patients.

**No conflicts of interest**

**123** Poster

**Studying impact of screening: Large differences in stage distribution irrespective of varying definitions of advanced breast cancer**

L. De Munck[1], S. Siesling[1], J. Fracheboud[2], G. De Bock[3], M. Broeders[4]. *[1]Netherlands Comprehensive Cancer Organisation, Department of Research, Utrecht, Netherlands; [2]Erasmus Medical Centre- University Medical Center Rotterdam, Department of Public Health, Rotterdam, Netherlands; [3]University of Groningen- University Medical Center Groningen, Department of Epidemiology, Groningen, Netherlands; [4]Radboudumc and Dutch Reference Centre for Screening, Department for Health Evidence, Nijmegen, Netherlands*

**Background:** The effect of a breast cancer screening programme on the stage distribution of breast cancer has been described several times. However, as studies used different definitions of advanced breast cancer, results are difficult to compare. The aim of this study is to evaluate the impact of the Dutch breast cancer screening programme on stage distribution of screen-detected, interval, and non-screen-related breast cancers, using three commonly applied definitions of advanced breast cancer.

**Methods:** All women, 49−75 years of age, diagnosed with breast cancer (invasive or DCIS) between 2006 and 2011 were selected from the Netherlands Cancer Registry. Their data were linked to data from the Dutch national breast cancer screening programme. This included data of screened women between 2004 and 2011 to cover a period of at least 2 years before breast cancer diagnosis. Each breast cancer was categorized as screen-detected, interval, or non-screen-related cancer. Screen-detected cancers were defined as breast cancers diagnosed within 12 months after a suspect screen examination. Interval cancers were defined as women diagnosed with breast cancer within 24 months after a non-suspect screen examination. All other breast cancers were defined as non-screen-related cancers. Advanced stage was defined as: (1) Stage III and stage IV breast cancers (versus Stage 0, I, II); (2) All tumours with positive lymph nodes and/or metastasis (versus negative nodes without metastasis); (3) Tumours ⩾15 mm in size (versus <15 mm). The proportion of advanced breast cancer was calculated.

**Results:** In total 72619 breast cancers were included, of which 32193 were screen-detected cancers, 11955 interval cancers and 14807 non-screen-related cancers. Table 1 shows the differences in proportion advanced breast cancer per definition. When stage III and stage IV were defined as advanced stage, 5% of screen-detected cancers were advanced. Using tumours with positive lymph nodes and/or metastasis (N+ and/or M+), 21% advanced cancers were found. Exact tumour size was available for 45,718 cancers in total. When cancers ⩾15 mm in size were defined as advanced stage, 42% of screen-detected cancers were advanced. Irrespective of the definition used, screen-detected cancers were less often advanced stage compared to interval cancers and non-screen-related cancers (Table 1).

Table 1. Proportion advanced breast cancer per definition

| | Stage III, IV | N+ and/or M+ | ⩾15 mm |
|---|---|---|---|
| Screen-detected* | 5% | 21% | 42% |
| Interval* | 21% | 44% | 72% |
| Non-screen-related* | 23% | 41% | 64% |

*$p < 0.001$.

**Conclusion:** Screen-detected cancers were less often advanced stage, irrespective of the definition used. As different definitions for advanced breast cancer can lead to significant different estimates in the proportion advanced cancers, we recommend that in the evaluation of a breast cancer screening programme, the definition of stage is clearly stated.

**No conflicts of interest**

**124** Poster

**Differences between cancers detected in prophylactic mastectomy specimens, screen detected cancers and true interval cancers in women participating in an intermediate and high risk screening program**

S. Vreemann[1], A. Gubern-Mérida[1], S. Lardenoije[1], N. Karssemeijer[1], R. Mann[1]. [1]*Radboudumc, Radiology and Nuclear Medicine, Nijmegen, Netherlands*

**Background:** Intensive screening with annual mammography and MRI is offered to women at high risk for the development of breast cancer. Although most cancers are screen detected, screening does not prevent breast cancers from occurring and some are still detected between screening rounds (true interval cancers). Consequently, some women opt for prophylactic mastectomy rather than intensive screening since this reduces the incidence of breast cancer. Unfortunately, detection of cancer in a prophylactic mastectomy specimen (incident cancers) is not a rare occurrence. It is unsure whether these cancers should be considered as interval cancers. This study evaluates the prognostic factors of cancers stratified by the mode of tumor detection in these women.

**Material and Methods:** Review of our intermediate and high risk screening program from 2003 to 2013 identified 177 cancers. Of these, 136 were detected in screening, 15 cancers were true interval carcinomas detected due to symptoms, and 26 cancers were detected in prophylactic mastectomy specimens. Patient- and cancer characteristics (invasive versus in-situ disease, grade, pT-stage, age, menopausal state, cancer receptor status and pN-stage) between these three groups were compared using a Pearson's chi-square test for categorical variables or one-way ANOVA for continuous variables.

**Results:** The fraction of invasive disease was 8/26 (30.8%), 109/136 (80.1%) and 15/15 (100%) for cancers in prophylactic mastectomy specimens, screen detected cancers and interval cancers, respectively ($p < 0.001$). The fraction of cancers larger than two centimeters was 1/26 (3.8%), 24/136 (17.6%) and 3/15 (20.0%), respectively. A similar increase was observed for the overall pT-stage ($p < 0.001$). Moreover, tumor grade was higher in true interval cancers than in cancers detected in prophylactic mastectomy specimens ($p = 0.001$). Most cancers were node negative ($p = 0.233$). There were no significant differences in patient age, menopausal state, cancer receptor status, and pN-stage between true interval cancers and prophylactic mastectomy specimens.

**Conclusions:** True interval cancers are more often invasive, generally larger, and commonly of higher grade than screen detected cancers or cancers in prophylactic mastectomy specimens. The prognosis of cancers detected in prophylactic mastectomy specimens is particularly good as most of these lesions are in situ cancers only. Therefore, these incident cancers should not be regarded as interval cancers.

**Conflict of interest:** Ownership: Nico Karssemeijer: Shareholder Matakina Ltd Consultant, shareholder QView Medical Inc Director, shareholder ScreenPoint Medical BV. Other Substantive Relationships: Ritse Mann: Speaker: Bayer AG.

**125** Poster

**The dietary intake of breast cancer patients during chemotherapy**

M. Van den Berg[1], R. Winkels[1], E. Dik[1], Y. De Vries[1], A. De Kruif[2], J. De Vries[1], M. Visser[2], H. Van Laarhoven[3], E. Kampman[1]. [1]*Wageningen University, Human Nutrition, Wageningen, Netherlands;* [2]*VU University Amsterdam, Health Science, Amsterdam, Netherlands;* [3]*Academic Medical Center, Medical Oncology, Amsterdam, Netherlands*

**Background:** Weight gain during chemotherapy for women with breast cancer is highly prevalent. The increase in weight mainly seems to consist of increases in fat mass with loss or no change in muscle mass. These changes in body composition increase the risks of disease recurrence, cardiovascular disease and diabetes and can affect quality of life. Multiple reasons for this weight gain have been suggested, such as changes in menopausal status, changes in physical activity and changes in dietary intake. However, limited research is available regarding the dietary intake of breast cancer patients during chemotherapy.

The objective of this project is to investigate whether the energy intake and macronutrient intake of breast cancer patients during chemotherapy differs from the intake of women without breast cancer. A secondary objective is to assess whether the energy intake and macronutrient intake of breast cancer patients varies over de course of a chemotherapy cycle.

**Materials and Methods:** In this observational study, 160 patients with newly diagnosed, breast cancer (I-IIIA), scheduled for initiating (neo)adjuvant chemotherapy were recruited. 120 women without breast cancer, of the same age as the patient group (range, +/− 2 years) were recruited for the control group. To assess dietary intake, two 24 hour recalls on randomly chosen days were acquired during chemotherapy for the patients group and in a half year after baseline for the comparison group.

**Results:** In the first 150 participants, average daily energy intake of patients was 1778±652 kcal compared to 1948±480 kcal in the control group ($p > 0.005$). The energy intake of breast cancer patients was lowest in the first week after chemotherapy (1668±808 kcal), and was higher in week 2 and 3 (1794±561 and 1831±568 kcal, respectively). However these differences were not significant. No statistically significant differences were found in the intake of macronutrients.

**Conclusion:** Preliminary results of the first 150 participants did not show a statistically significant difference in energy and macronutrient intake between patients and the control group. No significant differences in energy intake were found during the course of a chemotherapy cycle. These preliminary results suggest that energy and macronutrient intake does not account for the often reported increase in weight in breast cancer patients. As this study is currently ongoing, updated numbers will be presented during the conference.

**No conflicts of interest**

**126** Poster

**The impact of diabetes and metformin usage on the outcome of HER2 positive primary breast cancer patients. Analysis from the ALTTO phase III randomized trial**

A. Sonnenblick[1,2], D. Agbor-Tarh[3], I. Bradbury[3], S. Di Cosimo[15], J.A. Zujewski[4], H.A. Azim Jr.[1], J. Judith[5], M. Andersson[6], T. Cufer[7], S. Simon[8], P. Salman[9], M. Toi[10], L. Harris[11], J. Gralow[12], K. Macoon[13], A. Moreno-Aspitia[14], M. Piccart[1], E. De Azambuja[1]. *[1]Institut Jules Bordet, Br.E.A.S.T. Data Centre, Brussels, Belgium; [2]Sharett Institute of Oncology- Hadassah − Hebrew University Medical Center, Oncology, Jerusalem, Israel; [3]Frontier Science Scotland Ltd, Frontier Science, Kingussie, United Kingdom; [4]National Cancer Institute, National Cancer Institute, Bethesda, USA; [5]BOOG, Dutch Breast Cancer Trialists' Group, BOOG, Netherlands; [6]DBCG, Danish Breast Cancer Cooperative Group, Danish Breast Cancer Cooperative Group, Denmark; [7]EORTC, breast group, Brussels, Belgium; [8]GBECAM, The Brazilian Breast Cancer Study, The Brazilian Breast Cancer Study, Brazil; [9]GOCCHI, The Chilean Cooperative Group for Oncological Research, GOCCHI, Chile; [10]JBCRG, Japan Breast Cancer Research Group, Japan Breast Cancer Research Group, Japan; [1]CALGB, CALGB, CALGB, USA; [12]SWOG, SWOG, SWOG, USA; [13]ICORG, Ireland Cooperative Oncology Research Group, Dublin, Ireland; [14]Mayo clinic, Oncology, Jacksonville, USA; [15]Fondazione IRCCS, Istituto Nazionale dei Tumori, Milan, Italy*

**Background:** Previous studies have suggested an association between metformin use and improved outcome in diabetic patients with breast cancer. In the current analysis, we aimed to explore this association in HER2 positive primary breast cancer in the context of a large phase III adjuvant trial.

**Methods:** The ALTTO trial randomized patients with HER2 positive breast cancer to receive either one year of trastuzumab, one year of lapatinib, their sequence or their combination. In this observational sub-study, we focused on patients who had diabetes at study entry and received or not metformin as anti-diabetic agent. Patients who did not have diabetes served as the comparator group. We evaluated whether diabetes and metformin treatment were associated with disease-free (DFS), distant disease free survival (DDFS) and overall survival (OS). This was tested in a multivariate model adjusted for treatment arm, body mass index status, tumour size and trial stratification factors.

**Results:** A total of 8,381 patients were included in the current analysis; of whom 7,935 patients (94.7%) had no history of diabetes at diagnosis. 186 patients (2.2%) had diabetes with no metformin treatment while 260 (3.1%) were treated with metformin. Median follow-up was 4.5 years, at which 1,205 (14.38%), 929 (11.08%) and 528 (6.3%) patients experienced a DFS, DDFS and OS event, respectively. Patients with diabetes and no metformin treatment experienced worse DFS (multivariate HR: 1.40; 95% CI: 1.01–1.94, p = 0.043), DDFS (multivariate HR 1.56; 95% CI: 1.10–2.22, p = 0.012) and OS (multivariate HR: 1.83; 95% CI: 1.20–2.79, p = 0.005). No significant differences were observed between diabetic patients treated with metformin relative to non-diabetic patients in DFS (multivariate HR: 1.02; 95% CI: 0.74–1.41, p = 0.90), DDFS (multivariate: HR: 0.97; 95% CI: 0.66–1.42, p = 0.88) and OS (multivariate HR: 1.25; 95% CI: 0.79–1.96, p = 0.34).

**Conclusions:** These data suggest that metformin treatment may reverse the poor prognosis that is associated with diabetes in primary HER2 positive breast cancer patients.

**Conflict of interest:** Dr Evandro De Azambuja: GSK, travel grants, research grant; Roche, travel grant and honoraria. Azim Hatem: Consultant, received honoraria from GSK and Novartis. Martine Piccart: declares consultancy/honoraria with Roche-Genentech. All other authors have no conflict on interest.

**127** Poster

**The usefulness of flat panel detector (FPD) mammography in tele-mammographic screening compared with computed radiography (CR) soft-copy interpretation**

T. Sugimoto[1], Y. Okamoto[2], R. Irimajiri[2], Y. Nakauchi[2], F. Suehiro[2], K. Nakanishi[2], T. Motoki[2], M. Ogawa[1], T. Oki[1], K. Dabanaka[1], K. Hanazaki[1]. *[1]Kochi Medical School, Department of Surgery, Kochi, Japan; [2]Kochi Kenshin Clinic, Department of Screening, Kochi, Japan*

**Background:** We recently reported the usefulness of soft-copy interpretation of computed radiography (CR) mammography for several times because the majority of mammography machines were CR in Japan. However, Flat Panel Ditector (FPD) mammmography increased up to one-thirdsand we also introduced FPD into our tele-mammographic screening in 2012. The purpose of this retrospective study is to elucidate the differences between CR and FDP through our ten years' experience.

**Materials and Methods:** We took CR mammograms of 44,058 screenees with PCM system (Konica Minolta) and digitized them with Regius Model 190 (Konica Minolta) at Kochi Kenshin Clinic and transferred them to Kochi Medical School via optic fiber (provided by NTT and STNet) between July 2005 and Aug. 2012. We interpreted them using two kinds of mammography viewing system: SenoAdvantage (GEYM) and a viewer produced by Carestream Health Care Inc. with a couple of 5M-pixel monitors and reported the results of interpretations through the same network. We introduced digital mammography systems using FPD (Amulet, FUJI) into our tele-mammographic screening program. We interpreted mammograms of 18,762 screenees between Sep. 2012 and Mar. 2015 using mammary 2, mammography viewing system produced by Crime Medical Inc. We compared the process indexes and the usability between CR and FPD.

**Results:** The recall rate of CR and FPD was 5.3% and 2.3%, cancer detection rate was 0.27% and 0.19% and positive predictive value (PPV) was 5.1% and 8.3% respectively (table). As the pixel size is 25 microns in PCM, the average data size of one image is 135M in CR. Otherwise, pixel size 50 microns, data size 33M in FPD. This difference of data sizes cause the difference of speeds for demonstrating images on the monitor. So, interpretations comparing the previous images using FPD were easier than CR. Moreover, we can utilize computer-aided diagnosis (CAD) in FPD. The reason why cancer detection rate by FPD is lower than CR is that the rate of repeated screenees in screening with FPD (83.2%) is much more than that in CR (64.2%). However, the usefulness of FDP i.e., comparative interpretation and CAD, reduced recall rate and remarkably increased PPV.

Table: Deferences of process indexes according to modalities

| | CR | FPD |
|---|---|---|
| No. of screenees | 44,058 | 18,762 |
| No. of repeaters | 28,293 (64.2%) | 15,615 (83.2%) |
| No. of recall | 2,329 (5.3%) | 433 (2.3%) |
| No. of detected cancer | 119 (0.27%) | 31 (0.19%) |
| Positive predictive value | 5.1% | 8.3% |

**Conclusions:** Soft-copy interpretation using CR mammography was useful in mammographic screening. However, FPD was superior to CR especially in our tele-mammographic screening.

**No conflicts of interest**

**128** Poster

**Nipple aspirate fluid (NAF) cytology supports prediction of breast cancer risk using the IBIS model**

J. Kylstra[1]. *[1]Atossa Genetics, Clinical Research and Development, Seattle- Washington, USA*

**Aims:** Ductal Hyperplasia is part of most breast cancer (BCa) predictive algorithms including IBIS, conferring a 1.9−4.2 fold risk increase for resp. benign- and atypical hyperplasia. However, absent of prior biopsy, ductal pathology information is usually absent, leading to underestimation of BCa risk. We explored the contribution of ductal pathology information to IBIS' ability to classify women to risk groups.

**Methods:** IBIS risk factors were recorded from women w/o prior history of BCa during routine annual exams. Cytology was graded per King Classification. IBIS risk was calculated with and w/o hyperplasia information in the model, and each woman classified to 1 of 3 groups: high (⩾8%), medium (>5⩽8%), and low (<5%) 10-year risk, and analysis stratified by age (<45 vs ⩾45).

**Results:** Information on IBIS factors incl. hyperplasia was available for 832 women Age ⩾45 and 509 Age <45. Absent hyperplasia information, IBIS classified 3.7% (19/509) of women Age <45 and 20.6% (171/832) Age ⩾45 as having >5⩽8% 10-year risk; 1.4% (7/509) Age <45 and 4.2% (35/832) women Age ⩾45 were classified to ⩾8% 10-year risk. Low risk were 483 women Age <45 and 626 women Age ⩾45. With hyperplasia present in 72/626 (15%), IBIS reclassified 16 of 72 (22%) low-risk women Age <45 to high or intermediate risk. Among 626 women Age ⩾45, 59 (9%) had hyperplasia and IBIS reclassified 39 of 59 (66%) from low- to intermediate/high risk. 11 women Age <45 (2.3%) and 15 women Age ⩾45 (2.4%) moved from low (<5%) to medium (>5⩽8%) 10-year risk.

**Conclusions:** Availability of ductal pathology information aids the IBIS model in identifying more women at increased risk for BCa. Among various factors in BCa predictive algorithms, hyperplasia is the most actionable, as it presents a target for therapeutic intervention.

**Conflict of interest:** Ownership: Atossa Genetics − employee.

## Wednesday, 9 March 2016

**POSTER SESSION**

# Nursing

**129** Poster

**Implementing inter-professional practice model improves palliative care in terminal breast cancer woman**

S.Y. Huang[1]. [1]*Chi Mei Medical Center, Nursing, Tainan, Taiwan*

**Background:** This article described a terminal breast cancer patient with brain and bone metastasis, pneumonia and urinary tract infection problems. The author used observation, listening, interview, physical assessment, medical records and other methods to assess patient's physical, family and social aspects. Identify several major health problems, including risk for aspiration, imbalanced nutrition, impaired skin integrity, and home care health maintenance.

**Material and Methods:** This paper shows that the process involved authors organized an inter-professional case conference as a communicative platform and, in accordance to the patient's issues, the team reached a consensus on the strategies with the patient and the patient's family on nursing care and nutrition treatment strategy. We provided a patient-centered nursing plan, which included individualized nutrition intervention, direct nursing care by home care nurse, phone reminders and utilizing community resources.

**Results:** The nursing care method included assessment, planning and practice. Eventually, the patient's hospice palliative nursing care improved under the inter-professional practice model.

**Conclusion:** The paper findings illustrate that the inter-professional practice model for taking care of a terminal breast cancer woman with brain and bone metastasis, pneumonia and urinary tract infection problems. Improved the terminal breast cancer patient's hospice palliative nursing care quality.

**No conflicts of interest**

**130** Poster

**Breast cancer survivorship in the Arab world: A phenomenological study of Arab experiences post diagnosis**

J. Sprakel[1]. [1]*RCSI Bahrain, Community Engagement, Manama, Bahrain*

**Background:** The aim of this research was to explore the lived experience of seven Arab women diagnosed and treated for breast cancer in Bahrain. Many of the guidelines used in the Arab world are not contextualized to the culture, and do not fit with Islamic values and traditions, where taboos and myths exist around the disease and play a significant role in the interpretation and understanding of knowledge. An integration of Islamic values and beliefs are essential for this specific patient population.

**Material and Methods:** This study explored seven Arab women's experiences with breast cancer in Bahrain. The methodology used was Interpretative Phenomenology. Data was generated through seven semi-structured interviews. All participants had completed clinical treatments six month prior to interview. Smith's (2009) IPA framework of analysis was used. Ethical approval was given by the author's institutional ethics committee and all participants signed an informed consent form.

**Results:** Three major themes emerged: Bodily Awareness, Coping Mechanisms and a Need to be Heard. The findings illustrated the unique needs of Arab women and showed how culture shaped their cancer experience. The women described how they depended on immediate family members for emotional support and how they drew on religious beliefs to give them hope, direction and courage. This distinct set of coping mechanisms and strategies evidence the need for protocols that are culturally sensitive and tailored to the specific needs of Arab women in the region.

**Conclusion:** A knowledge and understanding of the lived experiences of women who survive a cancer diagnosis can facilitate positive change in healthcare practices. Healthcare professionals need to be aware of cultural factors, coping mechanisms and strategies that shape Arab women's responses to care and develop culturally sensitive protocols and guidelines to best support women in the region.

**Conflict of interest:** Corporate-sponsored Research: As a staff member of RCSI Bahrain, after two years, part funding is given for professional development. My research was part of my MSc for which the University paid for part of this tuition.

**131** Poster/Poster Spotlight

**Results of scalp cooling during chemotherapy with anthracyclines depend on scalp skin temperature**

M. Komen[1], C. Smorenburg[2], H. Nortier[3], T. Van der Ploeg[4], C. Van den Hurk[5], K. Van der Hoeven[3]. [1]*Medisch Centrum Alkmaar, Department of Internal Medicine and Medical Oncology, Alkmaar, Netherlands;* [2]*Antoni van Leeuwenhoek, Department of Medical Oncology, Amsterdam, Netherlands;* [3]*Leiden University Medical Centre, Department of Medical Oncology, Leiden, Netherlands;* [4]*Medical Centre Alkmaar, Science Department, Alkmaar, Netherlands;* [5]*Comprehensive Cancer Organisation the Netherlands, Research Department, Eindhoven, Netherlands*

**Background:** The success of scalp cooling in preventing or reducing chemotherapy induced alopecia (CIA) is highly variable between patients undergoing similar chemotherapy regimens. Scalp skin temperature seems to be an important factor, but data on the optimum temperature of scalp cooling to prevent CIA are lacking. This study investigated the relation between scalp skin temperature and the efficacy of scalp cooling.

**Material and Methods:** In this explorative study, scalp skin temperature was measured during scalp cooling in 62 breast cancer patients undergoing up to six cycles of anthracycline containing chemotherapy. Temperature was measured by using two thermocouples at both temporal sides of the head. The efficacy of scalp cooling was defined by not requiring a wig or additional head covering to mask hair loss of the scalp.

**Results:** Maximal cooling was reached after 45 minutes and was continued for 90 minutes after chemotherapy infusion. The scalp skin temperature after 45 minutes cooling varied from 10ºC to 31ºC, resulting in a mean scalp skin temperature of 19ºC (SEM: 0.4). Intrapersonal scalp skin temperatures during cooling were consistent for each chemotherapy cycle (ANOVA: $p = 0.855$). Thirteen out of 62 patients (21%) did not require a wig or other head covering and showed satisfactory hair preservation. They appeared to have a significantly lower mean scalp skin temperature during all scalp cooling cycles (17.7ºC; SEM: 0.7) than patients with alopecia (19.9ºC; SEM: 0.5) ($p = 0.01$).

**Conclusions:** The efficacy of scalp cooling during chemotherapy is temperature dependent. A precise cut-off point could not be detected, but the best results seem to be obtained when the scalp temperature lies below 18ºC.

(Trialregister.nl NTR number 3082)

**No conflicts of interest**

**132** Poster

**Results of 20 versus 45 minutes post-infusion scalp cooling time in the prevention of docetaxel-induced alopecia**

M. Komen[1], W. Breed[2], C. Smorenburg[3], T. Van der Ploeg[4], S.H. Goey[5], K. Van der Hoeven[6], H. Nortier[6], C. Van den Hurk[7]. [1]*Medisch Centrum Alkmaar, Department of Internal Medicine and Medical Oncology, Alkmaar, Netherlands;* [2]*Foundation Give Hair a Chance- Knowledge Institute Scalp Cooling, Research Department, Eindhoven, Netherlands;* [3]*Antoni van Leeuwenhoek, Department of Medical Oncology, Amsterdam, Netherlands;* [4]*Medical Centre Alkmaar, Science Department, Alkmaar, Netherlands;* [5]*Twee Steden ziekenhuis, Department of Internal Medicine, Tilburg, Netherlands;* [6]*Leiden University Medical Centre, Department of Medical Oncology, Leiden, Netherlands;* [7]*Comprehensive Cancer Organisation the Netherlands, Research Department, Eindhoven, Netherlands*

**Background:** For patients, chemotherapy-induced alopecia (CIA) is one of the most distressing side-effects of treatment. Scalp cooling can prevent or minimise CIA; the results may depend on the duration of cooling. Since a previous study on post-infusion cooling time in patients treated with docetaxel chemotherapy found no difference between 90 and 45 minutes, we investigated whether hair-preserving results could be maintained with a shorter post-infusion cooling time.

**Material and Methods:** In this multi-centre randomised study, 134 patients who started treatment with docetaxel 75–100 mg/m$^2$ in a 3-weekly schedule were randomly assigned in a 1:1 ratio to a post-infusion cooling time of 45 minutes or 20 minutes. The primary end-point was the need for a wig or other head covering as assessed by the patient. A visual analogue scale (VAS) with a range from 0 (not tolerable) to 10 (very tolerable) was used to measure tolerance.

**Results:** Scalp-cooling results were similar for 45 minute and 20 minute post-infusion cooling times. Thirty-three out of 45 patients (73%) treated with 20 minutes of post-infusion cooling did not need a form of head covering, compared with 41 out of 52 patients (79%) treated with 45 minutes of post-infusion cooling ($p = 0.5$). The procedure was well tolerated (mean Visual Analogue Score 8.3). Six patients stopped due to intolerance during the first treatment cycle.

**Conclusion:** A 20 minutes post-infusion cooling time is effective and tolerable for patients treated with scalp cooling to prevent docetaxel-induced alopecia.

(Trialregister.nl Identifier, NTR 1856)

The study was supported by Sanofi Aventis. Sanofi Aventis did not contribute to the study design, data collection, analyses and interpretation of data or to the writing of the report. The decision to submit the results for publication was made by the authors.

**No conflicts of interest**

**133** Poster

**What reactions and needs have children of different age groups when mum is newly diagnosed with breast cancer?**

E. Vaaben[1]. [1]*Copenhagen University Hospital, Department of Breast Surgery, Copenhagen, Denmark*

**Background:** Every year around 4000 children experience that one of their parents is diagnosed with cancer. These children are known to experience increased psychosocial stress. At the Department for Breast Surgery at Copenhagen University Hospital 148 women under the age of 50 years underwent surgery for breast cancer in 2013. Many of these women ask for information on the reactions of their children.

At the Department of Breast Surgery the staff have had professional discussions on the issue and have concluded that they need information on how children experience being a relative when mum gets diagnosed with breast cancer.

**Purpose of the study:** What reactions and needs have children according of different age groups when mum is newly diagnosed with breast cancer?

**Method:** Systematic literature review using PubMed, CINAHL and Psykinfo. Years 2000–2014. 15 studies were found, 5 of which covered the issue raised. The studies were reviewed for quality and have been summarized in a structured manner.

**Results:** Children seem to protect their parents, try to be brave, feel guilt and attempt to find a meaning in events. Children have thoughts about death and waits for the parents to invite conversation on the subject. Generally children need honest information about illness and treatment encouragement from the parents to talk to be able to talk about difficult thoughts a normal everyday life where the school is an active part professionals that help parents and children to talk the parents to be able to unravel the grief of the child.

**Conclusion:** The literature shows that children need to talk to their parents about the illness. Children try to protect their parents and can experience guilt in relationship to the mother's illness and they wait for their parents to initiate talk about the illness. Children need somebody to share their grief with. They need a normal everyday life and they need their school to be involved.

**Changes to praxis:** At the Department of Breast Surgery children as relatives have become a subject which is in focus and guidelines have been set up. The staff have been taught about the subject from a leading expert in this field, Preben Engelbrekt.

It has been agreed that this is an area of the highest priority and both surgeons, secretaries and nurses have to take the children into consideration when planning the pathway for the mothers. Two of the surgeons have volunteered as resource persons in case some of the older children wish to talk to a professional. The clinic's oral guidance is supplemented by written handouts, describing the reactions and needs of children in specific age groups. An official guide on how to best help children as relatives is in the pipeline.

**No conflicts of interest**

**134** Poster

**Adjuvant endocrine therapy for breast cancer: Giving postmenopausal women a voice**

L. Vandezande[1], M. Reymen[1], B. Raeymaekers[1], I. Heedfeld[2], D. Biebuyck[1], M.R. Christiaens[3], P. Neven[4]. [1]*UZ Leuven, KU Leuven- Department of Public Health and Primary Care- University Hospitals Nursing Center of Excellence- Multidisciplinary Breast Center UZ Leuven, Leuven, Belgium;* [2]*Jessa Hospital, Jessa Hospital Departement of Pneumology, Hasselt, Belgium;* [3]*UZ Leuven, KU Leuven- KU Leuven Department of Oncology- University Hospitals Multidisciplinary Breast Center, Leuven, Belgium;* [4]*UZ Leuven, KU Leuven Department of Gynecology- University Hospitals Multidisciplinary Breast Center, Leuven, Belgium*

**Background:** Breast cancer is the most common cancer in women. In Europe, 75% of patients are postmenopausal at the time of diagnosis. Of these postmenopausal women (PMW), 80−85% has an hormone-sensitive (ER+) tumor. Adjuvant endocrine therapy (AET) significantly reduces the risk of recurrence. However, this treatment induces many side-effects which lead to low adherence rates. Therefore, research on women's experiences and restraints continuing AET is of great importance.

**Materials and Methods:** First, in-depth interviews with PMW treated in the University Hospital of Leuven (UZ Leuven) were performed to explore their experiences and needs. Next, focus groups of the target group and their partners were completed to further develop a strategy to meet the informational and supportive needs. Permission of the Ethical Committee was obtained.

**Results:** We started with 10 in-depth interviews followed by 4 focus groups with a total of 18 PMW and 1 focus group with 4 partners of PMW. Although PMW have individual needs that are influenced by patient-related factors, 2 common themes arose. PMW need information on and counseling for their AET. Throughout the interviews PMW stipulate the perceived lack of information on working mechanism, benefits and (management of) side-effects. Furthermore, women need support in self-management considering AET, preferably by a nurse. The participants of the focus groups further focused on a patient decision aid (PDA) and an information session developed with the data received from the interviews. They clearly pointed out the importance of this tool becoming an equal partner in medical decision making on AET. Moreover, PMW indicate additional important themes in the focus groups. PMW experience that their environment is unfamiliar with AET and thereby do not acknowledge the consequences and impairments of AET on patients daily living. Analyzing the data, also led to the conclusion that usually a rather paternalistic communication model is handled in their treatment. Patients seek to be more involved in decision making, so they can learn more about their own illness. Finally, PMW feel that their side-effects are not taken seriously enough by healthcare workers. Therefore, they feel isolated during this therapy. Saturation of data was not obtained within this sample.

**Conclusions:** Women need more information on all aspects of AET and want nurse-led counseling to better manage their side-effects. They stipulate that the UZ Leuven PDA in combination with information sessions and individual counseling by their track companion will be beneficial in the care for PMW. In further research our PDA needs to be reviewed by a panel of experts and the efficacy must be investigated. Accordingly it will meet the International Patient Decision Aids Standards.

**No conflicts of interest**

**135** Poster

**Breast units: nurses' functions and organization**

B. Merck[1], C. Torres[2], V. Escribà[3]. [1]*Universidad Cardenal Herrera CEU, Surgery, Alfara del Patriarca. Valencia, Spain;* [2]*Universidad Cardenal Herrera CEU, Biomedical Science, Castellón de la Plana, Spain;* [3]*Instituto Superior de Salud Pública, Salud Pública, Valencia, Spain*

**Background:** The breast unit or breast center, is the clinical structure needed for the multidisciplinary approach to breast cancer. This implies the creation of new clinical teams consisting of physicians, nurses and other health related workers. These groups will provide high-quality management to all the aspects related to breast malignancies. Specific training is required for each member of the team. Nurses are part of the core team of the breast unit, and responsible for care management. Their work in a breast unit includes different tasks.

**Material and Methods:** The results of a transverse descriptive study are presented. A survey about specific training and nurses functions was sent to 234 Spanish hospitals.

**Results:** Total participation rate was 62%. Breast units were available in 147 (63%) Spanish hospitals. A nurse was a member of the breast unit's core team in 90.5%. Postgraduate training of nurses had been available for only one third of the nurses working in breast unit. The different functions of the breast unit nurses are shown in Table 1.

Table 1.

| Function | Yes, n (%) | No, n (%) |
|---|---|---|
| Healthcare process coordination | 79 (54.5) | 66 (45.5) |
| Responsible for case management | 67 (46.2) | 78 (53.8) |
| Patient's education | 95 (65.5) | 50 (34.5) |
| Surgical assistant | 7 (4.8) | 138 (95.2) |
| Scar follow up | 110 (75.9) | 35 (24.1) |
| Control of surgical drains | 111 (76.6) | 34 (23.4) |
| Seroma evacuation | 72 (49.6) | 73 (50.4) |
| Health promotion & Coaching | 131 (90.3) | 14 (9.7) |
| Participation in patient's advocacy groups | 43 (29.6) | 102 (70.4) |

**Conclusions:** Breast units are available in two thirds of the Spanish hospitals. The high involvement of nurses (90.5%) in breast units is shown

up in our survey. Nurses tasks at the breast unit include care-specific functions like scar follow up and control of surgical drains, as well as management and coordination functions. Our study points out the role of breast unit nurses (90.3%) in health promotion and coaching. The results of there survey should guide the content of the new training programs.

**No conflicts of interest**

**136** Poster

**Shared decision making in daily practice in early stage breast cancer care; how to make it work**

W. Savelberg[1], M. Smidt[1], L. Boersma[2], D. Ubbink[3], M. Bessems[4], S. Van der Meij[3], A. Moser[5], C. Haekens[1], T. Van der Weijden[6]. *[1]Maastricht University Medical Centre, Oncology, Maastricht, Netherlands; [2]Maastricht University Medical Centre, Radiotherapy, Maastricht, Netherlands; [3]Academisch Medisch Centrum Universiteit van Amsterdam, Surgery, Amsterdam, Netherlands; [4]Jeroen Bosch Ziekenhuis, Surgery, Den Bosch, Netherlands; [5]Zuyd University of applied sciences, Health care, Heerlen, Netherlands; [6]Maastricht University, School for public health and primary care, Maastricht, Netherlands*

**Background:** Breast conserving therapy and mastectomy have been shown equally effective in early stage breast cancer, indicating that the patient's preference may dominate the decision. At the time of diagnosis, each patient has her own values, concerns and knowledge, which influence her treatment preferences. Shared decision making (SDM) is regarded as a promising model to achieve a personalised treatment plan. Nevertheless, SDM has not yet been implemented widely. Evidence shows that physicians feel that they already apply SDM, or that patients prefer to rely on the doctor's advice instead of being involved or that they feel they lack time or skills to offer a balanced presentation of medical options including all pros and cons. There is evidence that a patient decision aid may support SDM, by facilitating neutral discussion and deliberation about treatment options.

The aim of the study, with pre and post intervention measurements, was to evaluate SDM in clinical practice.

**Method:** We developed an implementation strategy for SDM, including a patient decision aid. We piloted the implementation in dedicated breast cancer teams in four hospitals, by measuring performance indicators and experiences of both professionals and patients. We invited each hospital to include 10 patients in the pre-implementation as well as in the post-implementation phase. We collected qualitative data by interviewing professionals about barriers and facilitators for change, quantitative data of patient involvement in decision making by audiotaping consultations using the OPTION 5-item instrument on objective scoring and questioning patients after the treatment decision was made using a 18-item patient knowledge test, the 16-item decisional conflict scale, and the patients' perception of SDM using the 9-item SDM-Q9 scale.

**Results:** Qualitative data: Professionals reported insufficient awareness of what SDM is and stated that integration of SDM within the entire breast cancer team is needed to normalize SDM in the routine setting. Quantitative data: Table gives preliminary results. SDM, patients' knowledge and decisional conflict tend to slightly improve.

**Conclusion:** Compared with global data from other studies the breast cancer professionals show relatively good performance, but there is still ample room for improving SDM. Integrating SDM into the daily routines of the multidisciplinary tumor board and in clinical practice calls for thoughtful, mainly organizational, changes.

**No conflicts of interest**

**137** Poster

**Patients' experience with track companionship in the course of treatment for breast cancer in the Leuven Multidisciplinary Breast Centre**

L. Van Eldere[1], M. Reymen[1], L. Vandezande[1], B. Raeymaekers[1], M.R. Christiaens[2]. *[1]University Hospital Leuven, KU Leuven- Department of Public Health and Primary Care- University Hospitals Nursing Center of Excellence- Multidisciplinary Breast Center, Leuven, Belgium; [2]University Hospital Leuven, KU Leuven- Department of Oncology- Multidisciplinary Breast Center, Leuven, Belgium*

**Background:** Breast cancer patients have high informational and psychosocial needs. At the Multidisciplinary Breast Center (MBC) of the University Hospitals Leuven (UZ leuven), track companions (TC) are actively involved in counseling patients. The TC are a group of oncology nurses (including two Advanced Practice Nurses (APN)) and social workers. They accompany the patients throughout the disease process, from the diagnosis until the end of adjuvant treatment, based on predefined successive contacts. This study examined how women experience a nurse TC.

**Materials and Methods:** Only patients of nurse TC were included to achieve homogeneity. The experiences of these patients were studied through a qualitative approach, Grounded Theory. An APN and a nurse conducted 10 in-depth interviews, using a topic guide, from April, 2014 until April, 2015. All patients received information about the research and signed an informed consent. Moreover, approval was obtained by an Ethical Committee. All interviews were recorded, and verbatim transcribed. The transcripts were analyzed by using the Qualitative Analysis Guide of Leuven (QUAGOL).

**Results:** Within the ten performed interviews, the first concept is that TC are experienced as a "thread" throughout the treatment. Patients experience involvement and accessibility of the TC as authentic. Patients also indicate that having a familiar person is essential during the treatment. Secondly, the experiences around track companionship are determined by "patient centeredness". The empathy of the counselors is repeatedly cited by the surveyed patients. Patients felt understood and heard because the TC adapt an honest accepting and non-judgmental attitude. In third place, the TC is seen as an expert. In other words, there is "skilled companionship". TC has both the experience as well as the knowledge and professional skills to help the patients. Fourth, "advocacy" is an important concept in this research. When patients have problems or ambiguities, the TC is the first person they will contact. The TC therefore acts as a moderator. Patients feel supported and protected. Lastly, the "authenticity" of the TC, a personality trait and a key condition in health services, determines the therapeutic relationship between patient and a TC. Moreover, the experiences of patient counseling depended strongly on the therapeutic relationship, in which authenticity is an important concept. Saturation was not obtained.

**Conclusions:** Authenticity is seen as the basis for the experiences of patients with their TC. Additional research is needed, in which theoretical saturation of the data is reached. This can also focus on other breast centers and non-university hospitals. In addition, it is necessary to examine the whole group of TC in UZ Leuven, thus also the social workers, in order to get a full insight in the patient experiences with their TC.

**No conflicts of interest**

**138** Poster

**The Trastuzumab Café − a place for the exchange of experiences and networking while getting treatment**

E. Gejsing[1], R.L. Østergaard[1], K. Axelsen[1]. *[1]Oncology D7, Department of Oncology- Aarhus University Hospital, Aarhus, Denmark*

**Background:** Trastuzumab is a monoclonal antibody for adjuvant treatment of HER-2 positive breast cancer. Previously Trastuzumab was administered as an intravenous infusion lasting approximately 2 hours. Now it is administered as a subcutaneous injection, duration 2 to 5 minutes.

Table (abstract 136).

| Variable | Pre-intervention | | Post-intervention | |
|---|---|---|---|---|
| | Respondents | Result | Respondents | Result |
| SDM score on OPTION scale 0–100 | N = 14 | 37 (SD 16, min 0, max 50) | N = 11 | 45 (SD 12, min 20, max 55) |
| Knowledge test | N = 10 | 9 (SD 3) correct answers | N = 19 | 11 (SD 5) correct answers |
| SDM-Q9 scale 0–100 | N = 10 | 82 (SD 14, min 51, max 100) | N = 19 | 83 (SD 12, min 56, max 100) |
| Decisional Conflict scale 0–100 | N = 13 | score 42 (SD 9, min 31, max 66) | N = 14 | score 37 (SD 5, min 30, max 45) |

We have discovered, that during the 2 hour treatment the patients benefited from the possibility of each others company, and therefore we would like to continue this. We would like to retain the possibility for the patients to exchange their experiences despite the short treatment time. Contact to others in the same situation had a rehabilitating effect on many of the patients, making the transition back to a normal daily life easier.

**Purpose:** To create the environment for exchanging experiences, networking, and rehabilitation for breast cancer patients undergoing outpatient subcutaneous Trastuzumab treatment.

**Method:**

- Treatment was given in a different building and under different circumstances, than where the patients received their chemotherapy.
- Tea and coffee were served in the waiting room before treatment.
- A small team of four nurses took it in turns to give the treatment. This was to maintain continuity.
- Patients with the same type of breast cancer, and whose situation were similar, were grouped together.
- Evaluation by the participants by means of written answers to the open question: "Name up to 3 advantages or disadvantages of visiting the Trastuzumab Café." 22 out of 24 patients participated in the evaluation.

**Results:** Summary of the patients answers:

- They appreciate the good conversations with like minded people.
- It is good to get away from the department, where they received their chemotherapy.
- Cosy surroundings.
- Speedy and efficient treatment.
- It is nice that one sees the same nurse each time.
- Some had commented, that it could be difficult listening to the other patients experiences.

**Conclusion:** Based on the principles of primary nursing, we experience a greater openness, and a more pronounced closeness, between patient and nurse. We have discovered, that the women benefit from each other, and use the possibilities for exchanging experiences. Some patients also build a network through the café. Patients describe how they get a lot of benefit from this method of treatment, and we feel that this should be integrated more in future treatment.

**No conflicts of interest**

**139** Poster

**Investigation at the breast unit from a process viewpoint**

P. Landberg[1], A. Carlsson[1], E. Vikhe-Patil[1], C. Hedin[1], A. Rzepecka[2], A.B. Larsson[2], M. Borras Sastre[2], E. Hiertonn[2], B. Andersson[3], L. Malmström Sandvall[1]. *[1]University Hospital, Kirurgiska Kliniken, Linköping, Sweden; [2]University Hospital Mammografienheten, Linköping, Sweden; [3]University Hospital Onkologiska Kliniken, Linköping, Sweden*

**Background:** Long waiting lists and examination times are worrisome for the Swedish health care system. In order to reduce the lead time from first medical contact to surgery to no more than 3 weeks for patients with malignancies of the breast, planning for a breast clinic for patients with symptoms in the breast started in 2010. The mandate came from the Director of Östergötland County Council Sweden.

**Method:** The appointed project team suggested to start breast clinic for patients with breast symptoms to increase accessibility to the County Council's breast unit. In addition to the new way in seeking advice and mammography screening, the possibility would also remain to go via a health center or other health care provider. People in Östergötland with symptoms of breast now have the option to call directly to the breast clinic. They then talk to a nurse with expertise in breast cancer care (30hp). If further investigation is required an appointment is scheduled within a week for a clinical examination by the breast nurse with the possibility of mammography at the same time. The clinic is located in the mammography unit at Linköping university hospital.

**Results:** The open patient department started on 1st September 2014 and from 1st October 2014 up until 30th September 2015 we have had 2000 people contact the clinic and 1237 visits have been booked. 88 patients (7%) were diagnosed with a cancer diagnosis. Investigation times for patients have been shortened considerably. Patients feel safe and know where to go. An interview study shows that patients are very satisfied in terms of service and information.

**Discussion:** The open patient department has meant a more efficient allocation of various staff category skills. The improved process is expected to lead to increased quality for the patient and better use of healthcare resources.

**No conflicts of interest**

**140** Poster

**Analyzing satisfaction and quality of life of patienst after a breast reconstruction**

C. Cereijo[1], B. Acea[2], S. Pita[3], R. Rey[1]. *[1]Nurse, Breast Unit, A Coruña, Spain; [2]Breast surgeon, Breast Unit, A Coruña, Spain; [3]Coordinator, Departament of Epidemiology, A Coruña, Spain*

**Background:** It is necessary to know the quality of life of the woman undergoing breast reconstruction if we want provide patient-centered care.

**Material and Methods:** Retrospective evaluation of 92 patients undergoing mastectomy and immediate breast reconstruction performed from 2004 to 2014. After interview with the breast cancer nurse to obtain demographic data, the patients completed a validated self-reporter questionnaire, the BREAST-Q© (post-reconstruction module). Domains were scored on a 0 to 100 point scale.

**Results:** n = 92 patients completed the surveys. The satisfaction scores for appearance of the breast were 59.4, satisfaction with outcomes 74 and satisfaction with information 72.3. Satisfaction with surgeon 94.3 and satisfaction with clinical nurses 96.3. Quality of life scores were, psychosocial well-being 75.2, sexual well-being 58.1 and physical well-being 70.1.

**Conclusions:** The satisfaction scores for appearance fo the breast and outcomes were comparable to other published studies, but were better for satisfaction with surgeons and clinical nurses. We need to have more attention to the worst scores to quality of life in the nurses care plan, especially with sexual well-being.

**No conflicts of interest**

## Wednesday, 9 March 2016

**POSTER SESSION**

# Risk Factors

**142** Poster

**Ductal carcinoma in situ diagnosed by breast needle biopsy: Novel predictors of invasion in the excision specimen**

C. Doebar[1], C. De Monyé[2], H. Stoop[1], J. Rothbarth[3], S.P. Willemsen[4], C.H.M. Van Deurzen[1]. *[1]Erasmus MC Cancer Institute- Rotterdam- the Netherlands, Pathology, Rotterdam, Netherlands; [2]Erasmus MC Cancer Institute- Rotterdam- the Netherlands, Radiology, Rotterdam, Netherlands; [3]Erasmus MC Cancer Institute- Rotterdam- the Netherlands, Surgical Oncology, Rotterdam, Netherlands; [4]Erasmus MC Cancer Institute- Rotterdam- the Netherlands, Biostatistics, Rotterdam, Netherlands*

**Background:** A substantial proportion of women with a pre-operative diagnosis of pure ductal carcinoma in situ (DCIS) has a final diagnosis of invasive breast cancer (IBC) after surgical excision and, consequently, a potential indication for lymph node staging. The aim of our study was to identify novel predictors of invasion in patients with a needle-biopsy diagnosis of DCIS that would help us to select patients that may benefit from a sentinel node biopsy (SNB).

**Patients and Methods:** We included 155 patients with a needle-biopsy diagnosis of DCIS between 2000 and 2014, which was followed by surgical excision. Several pre-operative clinical, radiological and pathological features were assessed and correlated with the presence of invasion in the excision specimen. Features that were significantly associated with upstaging in the univariable analysis were combined to calculate upstaging risks.

**Results:** Overall, 22% (34/155) of the patients were upstaged to IBC. The following risk factors were significantly associated with upstaging: palpability, age $\leqslant$40 years, mammographic mass lesion, moderate to severe periductal inflammation and periductal loss of decorin expression. The upstaging-risk strongly correlated with the number of risk factors present: e.g. 9% for patients without risk factors, 29% for patients with 1 risk factor, 37% for patients with 2 risk factors and 54% for patients with $\geqslant$3 risk factors.

**Conclusion:** The identified risk factors may be helpful to predict the upstaging-risk for patients with a needle-biopsy diagnosis of pure DCIS, which facilitates the performance of a selective SNB for high-risk patients and avoid this procedure in low-risk patients.

**No conflicts of interest**

**143** Poster

**Underestimation rates and upgrading in patients with a needle biopsy diagnosis of DCIS in the Netherlands**

C. Meurs[1], M. Menke-Pluijmers[2], R. Bretveld[3], L. Overbeek[4], P. Westenend[5,6]. [1]*CMAnalyzing, Zevenaar, Netherlands;* [2]*Albert Schweitzer Hospital, Surgery, Dordrecht, Netherlands;* [3]*Comprehensive Cancer Centre the Netherlands, Research, Nijmegen, Netherlands;* [4]*PALGA: Dutch Pathology Registry, Research, Houten, Netherlands;* [5]*Laboratory of Pathology, Dordrecht, Netherlands;* [6]*Regional screening organization South West, Rotterdam, Netherlands*

**Background:** Initial treatment of ductal carcinoma in situ (DCIS) is based on diagnosis at core needle biopsy. Extensive histological evaluation is performed on resection specimens as more tumour material is available. Then, a considerable number of patients will turn out to have invasive breast cancer, as well as DCIS. This is defined as underestimate. The aim of this study is to explore the quality of care for patients with a biopsy diagnosis DCIS. We analysed the hospital variation in underestimate rate and defined determinants for underestimation. We also compared the DCIS grade at biopsy and excision.

**Materials and Methods:** Patients with a final biopsy diagnosis DCIS were selected from the nationwide network and registry of histopathology and cytopathology in the Netherlands (PALGA). All PALGA records were assessed to extract DCIS grade, suspected invasive component at biopsy etc. The PALGA data were merged with the National Cancer Registry (NCR) data, thereby adding information about being screen-detected, palpable, BI-RAD score, hospital of treatment etc. In this study no information was available about the size of the mammographic lesion. Population based data from incidence years 2011 and 2012 were available for analysis. Multivariate analysis was conducted to define determinants of quality of care. Variation in care between hospitals were shown in plots and analysed in multilevel analysis.

**Results:** 2331 patients with a biopsy diagnosis DCIS were analysed. The underestimate rate was 21%. For the biopsy DCIS grades low, intermediate and high the underestimate rates were respectively 14%, 21% and 23%. Determinants for underestimation were intermediate grade (OR 1.5, 95% CI 1.0−2.1), high grade (OR 1.5, 95% CI 1.1−2.1), synchronous contralateral tumour (OR 1.8, 95% CI 1.0−3.0), a palpable tumour (OR 2.2, 95% CI 1.7−2.8), a BI-RAD score 5 (OR 2.7, 95% CI 1.8−4.0), and a suspected invasive component at biopsy (OR 3.7, 95% CI 2.5−5.5). 6% of the variance in underestimate rate was due to the hospital. 29% of the patients with a low grade DCIS at biopsy had an intermediate or high grade DCIS at surgery. 27% of the intermediate grade DCIS at biopsy had a high grade DCIS at excision.

**Conclusions:** We conclude that variation between hospitals in underestimate rate was mostly due to case mix variation. When treatment options for patients with biopsy diagnosis DCIS are considered, the possibility of both underestimate and upgrading of the DCIS grade has to be taken into account.

**Conflict of interest:** Other Substantive Relationships: This study is supported by a grant from the Dutch Cancer Foundation (KWF), project number 2013–6495.

**144** Poster

**Clinical significance of adiponectin receptor 1 (AdipoR1) expression in invasive breast cancer**

L.S. Kim[1], Y. Lee[1], J.W. Bae[2]. [1]*Hallym University Medical Center, Division of Breast & Endocrine Surgery, Anyang, Korea;* [2]*Korea University Anam Hospital, Department of Surgery, Seoul, Korea*

**Background:** Recent studies have demonstrated that obesity is associated with an increased risk of breast cancer, but the mechanisms underlying this relationship remain to be fully elucidated. Adiponectin is one of major adipokines secreted from adipose tissue. This protein is believed to act through AdipoR1 and has been suggested to play an important role in cancer development. The purpose of this study was to quantitatively evaluate the expression of AdipoR1 in invasive breast cancer tissue compared to normal breast tissue. And then, we analyzed clinical significance of AdipoR1 in invasive breast cancer.

**Material and Methods:** Tissues were obtained from 269 patients who were underwent curative surgery with no prior treatment for invasive ductal carcinoma from Jan. 2003 to Dec. 2008 in Hallym Sacred Heart Hospital. A tissue microarray (TMA) containing 269 invasive ductal carcinomas as well as 269 adjacent normal breast tissues was established from paraffin-embedded tissue. AdipoR1 expression was investigated in epithelium and stroma by immunohistochemistry and correlated with clinical and pathologic tumor parameters. In 269 patients, median follow-up period was 57 months.

**Results:** AdipoR1 was detected in epithelial and stromal component of both normal breast and invasive ductal carcinoma tissues. In epithelium, immunoreactivity for AdioR1 was much lower in cancer tissue than normal one (24.5% versus 72%). This trend was quite similar in stroma, although the gap between cancer and normal was a bit narrow (48.7% versus 77.6%). AdipoR1 was more expressed in stroma than in epithelium among invasive breast cancer (48.7% versus 24.5%). In clinicopathologic features, mean age at diagnosis of AdipoR1 expression group in both epithelium and stroma was older than negative group. Furthermore, in epithelial component, HER-2/neu overexpression rate was slightly higher in AdipoR1 negative group than in positive one (27.8% versus 15%, $p < 0.059$). And, Ki67 was more expressed in AdipoR1 negative group than in positive one (49.5% versus 34.5%, $p < 0.051$). However, in stroma component, there was no other difference between AdipoR1 expression and clinicopathologic parameters. In survival analysis, AdipoR1 expression group in stroma showed significantly better disease free survival (DFS) than negative group ($p < 0.02$). DFS curve according to AdipoR1 expression in epithelium showed a quite similar trend with ones in stroma ($p = 0.06$).

**Conclusion:** This study showed that AdipoR1 expression was suppressed in both epithelium and stroma of invasive breast cancer tissue, compared to normal breast tissue. Even though there was no significant difference between AdipoR1 expression and many well-known prognostic factors, AdipoR1 expression in stroma as well as epithelium appears to play a role of good prognostic factor to predict disease progression somehow.

**No conflicts of interest**

**145** Poster

**A meta-analysis on impact of parity, age at first pregnancy and breastfeeding on the risk of developing breast cancer according to subtype**

M. Lambertini[1], L. Santoro[2], L. Del Mastro[3], B. Nguyen[4], L. Livraghi[5], D. Ugolini[6], F.A. Peccatori[7], H.A.J. Azim[8]. [1]*IRCCS AOU San Martino − IST, Department of Medical Oncology − U.O. Oncologia Medica 2, Genova, Italy;* [2]*European Institute of Oncology, Division of Epidemiology and Biostatistics, Milan, Italy;* [3]*IRCCS AOU San Martino − IST, Department of Medical Oncology − U.O. Sviluppo Terapie Innovative, Genova, Italy;* [4]*Institut Jules Bordet, Breast Cancer Translational Research Laboratory, Brussels, Belgium;* [5]*Azienda Ospedaliera "Papa Giovanni XXIII", USC Oncologia Medica, Bergamo, Italy;* [6]*IRCCS AOU San Martino − IST, Department of Internal Medicine- University of Genoa- Unit of Clinical Epidemiology, Genova, Italy;* [7]*European Institute of Oncology, Fertility and Procreation Unit- Division of Gynecologic Oncology, Milan, Italy;* [8]*Institut Jules Bordet, BrEAST Data Centre- Department of Medicine, Brussels, Belgium*

**Background:** Breast cancer (BC) is a heterogeneous disease with at least three subtypes defined on the expression of hormone receptors (HR) and HER2. Previously, it was shown that nulliparity, late age at first pregnancy (AFP), and lack or short lifetime duration of breastfeeding are associated with an increased risk of developing BC. However, it remains unclear whether the effect of these reproductive factors is more relevant in one specific subtype. The aim of our meta-analysis is to better elucidate the association of parity, AFP and breastfeeding with the risk of developing BC according to subtype.

**Material and Methods:** Epidemiologic studies (case–control studies [CCS] and cohort studies [CS]) were identified by searching PUBMED and EMBASE databases with no date restriction up to October 2014. Eligible studies were those that evaluated the impact of parity and/or AFP and/or breastfeeding on BC risk with available information on HR and HER2. Tumor subtypes were defined as: Luminal (HR+/HER2− and HR+/HER2+), HER2+ (HR−/HER2+) and triple negative (TNBC: HR−/HER2−).

The summary risk estimates (pooled odds ratio [OR]) and 95% confidence intervals (CI) were calculated using random effects models (DerSimonian-Laird method) for the association between parity, AFP and breastfeeding and risk of BC by tumor subtype.

**Results:** A total of 15 eligible studies (10 CCS, 3 CS and 2 pooled analyses [one from 2 CS and 2 CCS, the other from 2 CCS]) were identified, including 21,941 BC patients (17,307 luminal, 1,073 HER2+ and 3,561 TNBC) and 864,177 controls (i.e. women who did not develop BC). For parity, women were divided in "ever" parous ($\geqslant$1 pregnancy) or "nulliparous" (0 pregnancies). For AFP, most studies defined "young" AFP as $\leqslant$24 years and "old" AFP as >24 years. For breastfeeding, women were divided between those who ever breastfed ("yes") and those who never breastfed ("no"). Study results are summarized in the table.

**Conclusions:** The association between BC risk and parity, AFP and breastfeeding varies according to BC subtype suggesting possible etiologic differences. Parity and AFP only impacts the risk of developing luminal BC, while breastfeeding impacts the risk of developing both luminal BC and TNBC. This information would be helpful to better counsel women on their risk to develop BC and could have relevant implications on preventive strategy.

**No conflicts of interest**

Table (abstract 145).

| | Luminal BC | HER2+ BC | TNBC |
|---|---|---|---|
| Parity (ever vs nulliparous) | OR = 0.75 (95% CI 0.70–0.81); p < 0.0001; $I^2$ = 46.2% | OR = 0.90 (95% CI 0.69–1.16); p = 0.36; $I^2$ = 33.2% | OR = 1.01 (95% CI 0.87–1.17); p = 0.89; $I^2$ = 30.3% |
| Age at first pregnancy (old vs young) | OR = 1.15 (95% CI 1.00–1.32); p = 0.05; $I^2$ = 83.9% | OR = 0.91 (95% CI 0.72–1.16); p = 0.41; $I^2$ = 64.3% | OR = 0.94 (95% CI 0.80–1.11); p = 0.45; $I^2$ = 64.5% |
| Breastfeeding (yes vs no) | OR = 0.77 (95% CI 0.66–0.88); p = 0.003; $I^2$ = 79.1% | OR = 0.78 (95% CI 0.59–1.03); p = 0.07; $I^2$ = 45.6% | OR = 0.79 (95% CI 0.66–0.94); p = 0.01; $I^2$ = 65.1% |

**146** Poster

**Prognostic influence of primary tumor site in breast cancer: A study based on nation-wide Korean breast cancer registry database**

K.T. Hwang[1], S. Oh[2], J. Kim[3], J.H. Park[4]. *[1]Seoul National University Boramae Medical Center, Departments of Surgery, Seoul, Korea; [2]Seoul National University Boramae Medical Center, Department of Biostatistics, Seoul, Korea; [3]Seoul National University Boramae Medical Center, Department of Surgery, Seoul, Korea; [4]Seoul National University Boramae Medical Center, Department of Internal Medicine, Seoul, Korea*

**Background:** Although several papers have occasionally reported the influence of primary tumor site on the survival rate of breast cancer, the results are not consistent but still controversial. We investigated the prognostic influence of primary tumor site on the survival of breast cancer patients.

**Material and Methods:** Data of 63,388 primary breast cancer patients from the Korean Breast Cancer Registry from The Korean Breast Cancer Society was analyzed. Primary tumor sites were classified into 5 groups according to the site codes of the International Classification of Diseases for Oncology; upper-outer quadrant, lower-outer quadrant, upper-inner quadrant, lower-inner quadrant (LIQ), and central lesion.

**Results:** LIQ and central lesion showed lower survival rates than those of other primary tumor sites in overall survival (hazard ratio [HR], 1.215 and 1.251; 95% confidence interval [CI], 1.097 to 1.345 and 1.166 to 1.342; P < 0.001 and P < 0.001, respectively) and in breast cancer specific survival (hazard ratio [HR], 1.213 and 1.235; 95% confidence interval [CI], 1.067 to 1.380 and 1.129 to 1.350; P = 0.003 and P < 0.001, respectively), but there was no statistically significant difference between LIQ and central lesion. LIQ and central lesion were statistically significant independent factors at multivariate analyses in overall survival (hazard ratio [HR], 1.555 and 1.315; 95% confidence interval [CI], 1.270 to 1.904 and 1.149 to 1.504; P < 0.001 and P < 0.001, respectively) and in breast cancer specific survival (hazard ratio [HR], 1.588 and 1.313; 95% confidence interval [CI], 1.228 to 2.054 and 1.109 to 1.555; P < 0.001 and P = 0.002, respectively). LIQ showed favorable clinicopathologic features as compared with the other primary tumor sites, but central lesion showed poorer clinicopathologic features than the other 4 primary tumor sites in terms of body mass index, tumor size, nodal positivity, and stage.

**Conclusions:** LIQ showed a lower survival rate despite favorable clinicopathologic features, and internal mammary node was suggested to play a key role in this condition. Central lesion also showed lower survival rates than those of the other 4 primary tumor sites, and unfavorable clinicopathologic features could explain the causality in major part. Consideration of primary tumor n as a prognostic factor in breast cancer could be helpful for appropriate staging, treatment, and prognostication in clinical setting.

**No conflicts of interest**

**147** Poster

**False-positive results according with the mammographic features and risk of breast cancer**

X. Castells[1], I. Torà-Rocamora[1], M. Posso[2], M. Román[3], M. Vernet[4], A. Rodríguez-Arana[5], L. Domingo[1], C. Vidal[6], M. Baré[7], J. Ferrer[8], M.J. Quintana[9], M. Sánchez[10], C. Natal[11], J.A. Espinàs[12], F. Saladié[13], M. Sala[1]. *[1]IMIM − Hospital del Mar Medical Research Institute − Research Network on Health Services in Chronic Diseases REDISSEC, Epidemiology and Evaluation, Barcelona, Spain; [2]IMIM − Hospital del Mar Medical Research Institute, Epidemiology and Evaluation, Barcelona, Spain; [3]Cancer Registry of Norway, Research, Oslo, Norway; [4]IMIM − Hospital del Mar Medical Research Institute, Obstetrics and Gynecology, Barcelona, Spain; [5]IMIM − Hospital del Mar Medical Research Institute, Image Diagnostics, Barcelona, Spain; [6]Catalan Institute of Oncology, Cancer Prevention and Monitoring Program, Barcelona, Spain; [7]Parc Taulí Univerity Hospital, Clinical Epidemiology and Cancer Screening, Sabadell, Spain; [8]Hospital de Santa Caterina, Radiology Department, Girona, Spain; [9]Hospital de la Santa Creu i Sant Pau, Epidemiology, Barcelona, Spain; [10]Direction General of Public Health − Government of Cantabria, Department of Health, Santander, Spain; [1]Principality of Asturias, Breast Cancer Screening Program, Oviedo, Spain; [12]Department of Health- Catalonia − Spanish Cancer Research Network RTICC- Carlos III Health Institute, Catalan Cancer Plan, Barcelona, Spain; [13]The Foundation League for the Research and Prevention of Cancer, Breast Cancer Screening Program of Tarragona, Tarragona, Spain*

**Background:** False-positive result is associated with an increased risk for detecting breast cancer within subsequent mammographic examinations in the context of population screening. The aim of this study was to evaluate the risk of breast cancer in women with false-positive results according to the radiological classification of the mammographic features.

**Material and Methods:** Retrospective cohort of 536,261 women (50−69 years) screened in the Spanish Breast Cancer Screening Programs between 1994 and 2011 and followed up until December 2012. The mammographic features in the false-positive result were classified as mass (circumscribed or not), distortion, asymmetric density, and calcifications with and without associated mass. Screening and interval cancers were included. Age-adjusted hazard ratios (aHR) of breast cancer and 95% confidence intervals (95% CI) among women with false-positive results compared with women with negative mammograms were estimated using Cox proportional-hazard regression analysis. Time to breast diagnosis was plotted using Kaplan–Meier curves.

**Results:** The overall aHR of cancer among women with false-positive result compared with women with negative mammograms was 1.84 (95% CI=1.73–1.94). The most prevalent mammographic features were mass (n = 41,595, 52%), but the risk of breast cancer was lower than calcifications (aHR=1.61, 95% CI=1.48–1.74; aHR=2.26, 95% CI=2.05–2.51; respectively). The lowest breast cancer risk was found for asymmetric density (aHR=1.56, 95% CI=1.34–1.81). Time to cancer detection was similar in all mammographic features except for asymmetric density that

Table 1 (abstract 147). Age-adjusted risk of breast cancer in women with false-positive results according to the mammographic features

| Mammograms | | | Overall breast cancers | | |
|---|---|---|---|---|---|
| Result | Number | % | Time at risk (mo), median (P25−P75) | No. of breast cancers | Adjusted HR (95% CI) |
| Negative mammograms | 456,347 | | 72 (40–111) | 5,004 | 1.00 (Referent) |
| False-positive mammograms | 79,914 | 100.0 | 61 (24−98) | 1,443 | 1.83 (1.73–1.94) |
| Mass | 41,595 | 52.0 | 66 (24–101) | 675 | 1.61 (1.48–1.74) |
| Calcification | 16,302 | 20.4 | 73 (36–108) | 408 | 2.26 (2.05–2.51) |
| Asymmetric density | 14,783 | 18.5 | 48 (24−80) | 183 | 1.56 (1.34–1.81) |
| Calcification associated with mass | 4,036 | 5.1 | 70 (24–108) | 120 | 2.74 (2.28–3.28) |
| Distortion | 3,198 | 4.0 | 48 (24−76) | 57 | 2.11 (1.62–2.74) |

showed the shortest interval time from mammographic features to breast cancer (Median time=35, 25th and 75th percentiles=23−51, months).

**Conclusion:** Women with false-positive results had an increased risk of breast cancer, particularly women who showed calcifications at mammographic reading. Previous mammographic features might provide useful information for further risk prediction models in these women and personalized follow-up screening protocols.

**No conflicts of interest**

**148** Poster

**Risk factors of invasive ductal breast carcinoma in elderly (⩾65 years) women. Retrospective study in a cohort of 299 postmenopausal patients who underwent curative surgery**

F. Lumachi[1], G.B. Chiara[2], D.A. Santeufemia[3], S.M.M. Basso[2].
*[1]University of Padova, School of Medicine Department of Surgery-Oncology & Gastroenterology, Padova, Italy; [2]S. Maria degli Angeli Hospital, Surgery 1, 33170 Pordenone, Italy; [3]City Hospital, Medical Oncology, 07041 Alghero SS, Italy*

**Background:** In patients with breast cancer (BC) a number of risk factors (RF) have been studied. Unfortunately, many RFs associated with BC cannot be changed. However, several observational trials showed that the use of oral contraceptive (OC) and hormone replacement therapy (HRT), together with familial and reproductive RFs, can be useful in active or passive prevention of BC. The aim of this retrospective study was to evaluate the weight of the main data obtained from patients' medical history (MH) in a population of elderly (⩾65 years) women with confirmed invasive BC.

**Materials and Methods:** We retrospectively reviewed data regarding a series of 299 consecutive postmenopausal women (mean age, 62.3±9.1 years), who underwent curative surgery for pT1−2, N0−1 (stage I and IIA) invasive ductal breast carcinoma. Two Groups of patients were considered: elderly (⩾64 years) patients (Group 1, N = 93, median age 73, range 65−86 years), and younger (<65 years) patients (Group 2, N = 206, median age 57, range 45−64 years). Odds ratio (OR) estimates and the associated 95% confidence interval (95% CI) were obtained. Ninety-eight (47.6%) and 64 (68.8%) patients, respectively, underwent dual-energy X-ray absorptiometry for studying bone density.

**Results:** At univariate analysis, HRT (OR=5.62, 95% CI=3.21–9.87, p < 0.001), OC use (OR=2.58, 95% CI=1.31–5.10, p = 0.005), first child-bearing >30 years (OR=3.00, 95% CI=1.13–8.00, p = 0.02) were strong RFs in younger patients (Group 2), while BMI >25 (OR=1.81, 95% CI=1.02–3.20, p = 0.04) was a weak RF in elderly patients (Group 1). As expected, the presence of osteopenia or osteoporosis (OR=0.46, 95% CI=0.24–0.88, p = 0.02) represented a protective factor in Group 1. Other data obtained from patients' MH, including family history of BC (p = 0.79), no pregnancies (p = 0.58) or breast-feeding (p = 0.09), and history of benign breast diseases (p = 0.43) did not differ significantly between Groups. At multivariate analysis, only HRT was an independent RF, and the area under the curve (ROC) was 0.68.

**Conclusions:** In older (⩾65 years) patients, most of whom (62.1% vs. 22.6%, $\chi^2$=31.1, p < 0.001) had taken HRT, such as MH represents a significant RF for BC, and should be more carefully considered in the prevention campaigns.

**No conflicts of interest**

**149** Poster

**Active smoking and breast cancer risk in Danish nurse cohort study**

Z. Andersen[1], K.K. Andersen[2], R. Grøn[1], E. Brauner[3], E. Lynge[1].
*[1]University of Copenhagen- Public Health, Department of Public Health-Center for Epidemiology and Screening, Copenhagen K, Denmark; [2]Danish Cancer Society, Danish Cancer Research Centre, Copenhagen, Denmark; [3]University of Copenhagen, Research Center for Prevention and Health-Capitol Region of Denmark- Rigshospitalet − Glostrup, Glostrup, Denmark*

**Background:** Active smoking has been recently linked to increased risk of breast cancer. However, in Denmark, with some of the highest smoking rates in women and highest breast cancer rates, association between smoking and breast cancer has not been yet reproduced. Notably, no association between smoking and breast cancer was detected in Danish data contributing to large EPIC (European Prospective Investigation into Cancer and Nutrition) study [1], despite association being detected overall, mainly driven by other EPIC cohorts. Aim of this study is to examine association between active smoking and breast cancer risk in a Danish Nurse Cohort.

**Material and Methods:** We used the data from Danish Nurse Cohort on 19,582 female nurses (age >44 years) who at recruitment in 1993 or 1999 reported information on smoking status, onset, duration, and intensity, as well as breast cancer risk factors. We obtained data on incidence of breast cancer from Danish Cancer Registry until 2013, and data on vital status (date of death, immigration) at Central Person Registry. We used Cox regression model to analyze association between smoking and breast cancer, adjusted for body mass index, physical activity, alcohol use, parity, menopausal status, age at first birth, hormone therapy, nigh shift work, and birth cohort.

**Results:** Of 19,582 women (mean age at baseline 54 years) 1,078 developed breast cancer during 16 years (311,913 person-years) with incidence rate of 3.4 per 1,000 person-years. 39% of nurses were current, and 34% former smokers at cohort baseline. Compared to women that never smoked, we found statistically significant increased risk of breast cancer of 19% in ever smokers (hazard ratio and 95% confidence interval: 1.19; 1.04–1.38) and 28% in current smokers (1.28; 1.10–1.50). We found a dose-response association of increasing breast cancer risk with increasing smoking duration and intensity. Women smoking more than 20 lifetime pack-years had 32% increased risk of breast cancer (1.32; 1.11–1.57) compared to never smokers. Highest risk, of 46% increase in breast cancer risk (1.46; 1.11–1.92) was observed in parous women with early smoking initiation (more than 10 years before first birth) compared to parous women smoking after first birth.

**Conclusions:** Active smoking is a riskfactor for breast cancer, and early smoking seems to be most relevant exposure window.

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**No conflicts of interest**

**150** Poster

**Prevalence and risk factors of nonalcoholic fatty liver disease in breast cancer patients**

Y.L. Jung[1], S.W. Lee[1]. *[1]Pusan National University Hostpital, Surgery, Busan, Korea*

**Background:** We aimed to evaluate the prevalence of non-alcoholic fatty liver disease (NAFLD) in breast cancer patients using liver magnetic resonance imaging (MRI), and to investigate factors associated with NAFLD.

**Material and Methods:** We evaluated 104 patients surgically treated for breast cancer at our hospital between September and November 2013. None of the patients had received prior neoadjuvant treatment (i.e., chemotherapy, endocrine therapy or targeted therapy), and none had any of the following conditions: clinical symptoms and signs of inborn metabolic disorder, elevated liver enzymes, a history of drug use associated with liver steatosis, or consumption of >20 g of alcohol per day. We also ascertained patients' demographic characteristics and preoperative laboratory test results, Hepatic fat accumulation was measured using liver MRI in all patients before surgical treatment. We chose an fat signal percentage (FSP) cutoff of 5.5% to denote steatosis, as determined by MRI, which is a value commonly attributed to the likelihood of NAFLD. Therefore, the cohort was divided into two groups: control (FSP ⩽5.5%) and NAFLD (FSP >5.5%).

**Results:** Using FSP from liver MRIs, 19 of 104 patients were diagnosed with NAFLD. As a result, the prevalence of NAFLD in breast cancer patients was 18.3%. To identify risk factors associated with NAFLD, we performed univariate and multivariate analyses. In univariate analysis, factors associated with NAFLD were older age (odds ratio [OR]: 1.087; 95% confidence interval [CI]: 1.028–1.149; P = 0.003); high body mass index (BMI, kg/m$^2$) (OR: 1.295; 95% CI: 1.126–1.490; P < 0.001), diabetes mellitus (DM) (OR: 4.702; 95% CI: 1.261–17.531; P = 0.021); hypertension (OR: 12.000; 95% CI: 3.863–37.274; P < 0.001); and abnormal aspartate aminotransferase (OR: 5.400; 95% CI: 1.215–23.994; P = 0.027), abnormal alanine aminotransferase (OR: 9.333; 95% CI: 2.548–34.184; P = 0.001), and abnormal triglyceride (TG) levels (OR: 4.028; 95% CI: 1.360–11.926; P = 0.012). In multivariate analysis, factors associated with NAFLD were a high BMI (OR: 1.403; 95% CI: 1.111–1.771; P = 0.005), DM (OR: 11.872; 95% CI: 1.065–132.373; P = 0.044), and an abnormal TG level (OR: 50.267; 95% CI: 4.409–573.030; P = 0.002).

**Conclusions:** Breast cancer patients with risk factors such as DM, a high BMI, and elevated serum TG levels need more careful observation, a preventative strategy, and treatment for NAFLD.

**No conflicts of interest**

**151** Poster

**The clinical significance of lymphovascular invasion as a prognostic predictor in patients with lymph node-positive breast cancer**

M.H. Park[1], J.H. Yoon[1], Y.J. Ryu[1], J.S. Cho[1]. *[1]Chonnam National University Hwasun Hospital, Surgery, Jeollanam-do, South Korea*

**Background:** Lymphovascular invasion (LVI) is an important prognostic factor in patients with lymph node-negative breast cancer. However, the role

of LVI is unclear and controversial about its prognostic value in patients with lymph node-positive breast cancer. So, we report the long-term analysis of the prognostic significance of LVI in a large cohort study of lymph node-positive patients with invasive breast cancer.

**Material and Methods:** We retrospectively reviewed 967 patients with invasive breast cancer that had undergone surgical treatment at our Hospital, from January 2004 to December 2007. Among these patients, 349 lymph node-positive breast cancer patients were included in this study. We evaluated clinical and pathologic data in these patients, we compared with 5-year Overall survival and Disease-free survival between an LVI-present group and an LVI-absent group.

**Results:** The median follow-up was 48 months (range, 12−78 months) and the mean age of the patients was 48 years (range, 23−78 years). LVI was present in 192 patients (55%) of with tumors and was associated with age $\leqslant$40 years ($p = 0.009$), high histologic grade ($p = 0.007$), estrogen receptor status ($p = 0.001$), tumor size $\geqslant$2 cm ($p < 0.001$), number of involved lymph nodes ($p < 0.001$), but not with progesterone receptor status, HER2 status, p53 status, or tumor multiplicity. LVI was a significant independent prognostic factor for disease-free survival ($p < 0.001$) and overall survival ($p = 0.006$). By multivariate analysis revealed that LVI ($p = 0.003$), number of involved lymph node ($\geqslant$4; $p = 0.005$), and high histologic grade (II and III; $p = 0.02$) were an independent significant predictors of disease-free survival and overall survival in the whole group of patients.

**Conclusions:** In this study, we demonstrated that LVI is a significant predictor of poor prognosis in patients with lymph node-positive invasive breast cancer. So, LVI should be considered in the therapeutic strategy as a decision making tool in the adjuvant chemotherapy setting.

**No conflicts of interest**

**152** Poster

**Implementation of BRCA1/2 recurrent mutation genotyping panel in Chinese HBOC patients**

A. Kwong[1,2,3], J.C.W. Ho[1], V.Y. Shin[1], T.L. Chan[3,4], E.S.K. Ma[3,4], J.M. Ford[5]. *[1]The University of Hong Kong, Department of Surgery, Hong Kong, Hong Kong; [2]Hong Kong Sanatorium & Hospital, Department of Surgery, Hong Kong, Hong Kong; [3]Hong Kong Hereditary Breast Cancer Family Registry, Hong Kong, Hong Kong; [4]Hong Kong Sanatorium & Hospital, Department of Pathology, Hong Kong, Hong Kong; [5]Stanford University School of Medicine, Department of Medicine Oncology, Stanford, USA*

**Background:** Pathogenic germline mutations in breast cancer susceptibility genes, BRCA1 and BRCA2, are associated with elevated lifetime risks of developing breast, ovarian and other cancers. It was estimated that mutations in BRCA1/2 and other less penetrant genes account for 10−15% of all breast cancer cases and 20−25% of ovarian cancers. Specific recurring mutations were more commonly found in some ethnic groups due to the founder's effect, such as BRCA1 c.68_69delAG, c.5266dupC and BRCA2 c.5946delT in Ashkenazi Jewish, and BRCA2 c.771_775delTCAAA in Icelandic and Finnish. Targeted screening of these recurrent mutations provides more cost-effective and timely diagnostic options for identifying mutation carriers, however, screening of BRCA1/2 recurrent mutations in Chinese populations remain largely under-developed.

**Materials and Methods:** High-risk patients meeting the selection criteria for hereditary breast and ovarian cancer syndrome (HBOC) genetic testing were recruited in Hong Kong and USA. Based on the BRCA1/2 pathogenic mutation spectrum previously identified from Hong Kong and overseas collaborating groups, a Chinese-specific genotyping panel has been developed, covering 25 distinct BRCA1/2 recurrent mutations (mutations that were seen $\geqslant$2 in the cohort). Amplicons of mutation loci were PCR amplified from patients genomic DNA extracted from blood specimens, and were genotyped for these 25 mutations by single-base extensions of designed oligonucleotide primers. Fluorescent labels were analyzed in DNA sequencer, and detected mutations were verified with Sanger sequencing.

**Results:** A local (Hong Kong) cohort of 428 HBOC patients was screened for BRCA1/2 recurrent mutations prior to full-gene sequencing. 14 mutation probands (5 BRCA1 and 9 BRCA2) were identified with the genotyping panel, in which the most common mutation was BRCA2 c.3109C>T (one of the six Southern Chinese founder mutations). 20 additional sporadic or novel mutations were identified from full-gene sequencing with NGS. Taken together, recurrent mutations identified from the genotyping panel represented 3.3% of the local HBOC cases and 41.2% of the overall BRCA1/2 mutations found. In an overseas cohort of 56 Chinese American patients, 2 BRCA1/2 recurrent mutations were identified with the panel, representing 3.6% of the tested cohort.

**Conclusions:** Our results of a targeted genotyping panel for BRCA1/2 recurrent mutations in Chinese populations demonstrated a cost-wise, up-front screening strategy for diagnostic mutation detection for Chinese HBOC patients, which implicated the clinical application to overseas Chinese. An investigation of more Chinese patients residing in Europe or North America is warranted to verify the effectiveness of this screening strategy.

**No conflicts of interest**

**153** Poster

**RECQL as a novel breast cancer susceptibility gene in Chinese breast cancer patients**

A. Kwong[1,2,3], J. Chen[1], I.W.Y. Cheuk[1], M.T. Siu[1], C.H. Au[4], F.B.F. Law[4], D.N. Ho[4], B.K. Ip[4], A.T.C. Wong[4], V.Y. Shin[1], T.L. Chan[3,4], E.S.K. Ma[3,4], S.A. Narod[5]. *[1]The University of Hong Kong, Department of Surgery, Hong Kong, Hong Kong; [2]Hong Kong Sanatorium & Hospital, Department of Surgery, Hong Kong, Hong Kong; [3]Hong Kong Hereditary Breast Cancer Family Registry, Hong Kong, Hong Kong; [4]Hong Kong Sanatorium & Hospital, Department of Pathology, Hong Kong, Hong Kong; [5]Women's College Research Institute, Familial Breast Cancer Research Unit, Toronto, Canada*

**Background:** Breast cancer is the most common cancer in women worldwide and in Asia. High penetrance breast cancer susceptibility genes, BRCA1 and BRCA2, attributed to 10−15% of familial breast cancer. Other high penetrance genes, for example, TP53, PTEN and CDH1, also showed to be bona fide breast cancer susceptibility genes. Several moderate- and low-penetrance genes including ATM, CHEK2, PALB2, RAD50 have also been found to be associated with breast cancer risk and account for 5% of familial breast cancer. Recently, RECQL germline mutation has been identified to be associated with increased risk of breast cancer. However, the genetic contribution in the Chinese population remains undetermined.

**Methods:** A total of 1114 patients with breast cancer patients (BRCA, TP53 and PTEN negative) were selected from the Hong Kong Hereditary Breast Cancer Family Registry and underwent genetic testing for RECQL mutation. 88 normal controls were also included in the study. DNA was extracted from peripheral blood samples from patients and controls. RECQL full gene sequencing using targeted next generation sequencing was carried out by MiSeq (Illumina) and further validated by Sanger sequencing. Sequencing data were analyzed by our in-house developed fully automatic bioinformatics pipeline including BWA-MEM and variant callers, SAMtools and GATL.

**Results:** We have identified six germline RECQL mutations in this cohort. Interestingly, among these mutations, RECQL c.796C>T was identified in two unrelated families. 3 out of 6 mutations (50%) affect the splice donor consensus sequence. And one mutation (c.974_977delAAGA) is a small deletion. The mean age of diagnosis is 49.3 year old. Interestingly, more than one type of cancers, including hepatocellular carcinoma, colorectal cancer, lung cancer and prostate cancer, were reported in each family. Notably, there seemed to have an association with cardiovascular disease in 3 of the families.

**Conclusions:** RECQL germline mutations have been found in 0.5% of familial breast cancer patients who do not have detectable germline mutation of BRCA1, BRCA2, TP53 and PTEN in the Chinese population. Further studies are warranted to delineate the clinical application of including RECQL in the genetic testing panel, and its association with different cancers or cardiovascular disease.

**No conflicts of interest**

**154** Poster

**Tumour subtype and age-specific breast cancer risk estimates for CHEK2*1100delC carriers**

M.K. Schmidt[1], F. Hogervorst[2], S. Cornelissen[3], L. Van der Kolk[4], M. Adank[5], H. Nevanlinna[6], S. Bojesen[7], T. Dörk[8], D.F. Easton[9]. *[1]Netherlands Cancer Institute- Antoni van Leeuwenhoek Hospital, Division of Molecular Pathology- Division of Psychosocial Research and Epidemiology, Amsterdam, Netherlands; [2]Netherlands Cancer Institute- Antoni van Leeuwenhoek Hospital, Molecular Diagnostic Laboratory, Amsterdam, Netherlands; [3]Netherlands Cancer Institute-Antoni van Leeuwenhoek Hospital, Division of Molecular Pathology, Amsterdam, Netherlands; [4]Netherlands Cancer Institute- Antoni van Leeuwenhoek Hospital, Department of Clinical Genetics, Amsterdam, Netherlands; [5]VU University Medical Center, Department of Clinical Genetics, Amsterdam, Netherlands; [6]Helsinki University Central Hospital, Department of Obstetrics and Gynecology, Helsinki, Finland; [7]University of Copenhagen, Faculty of Health and Medical Sciences, Copenhagen, Denmark; [8]Hannover Medical School, Gynaecology Research Unit, Hannover, Germany; [9]University of Cambridge, Centre for Cancer Genetic Epidemiology, Cambridge, United Kingdom*

**Background:** CHEK2*1100delC is a well-established breast cancer risk variant, mostly prevalent in European populations. However, there are

limited data on risk of breast cancer by age and subtype, limiting its usefulness in breast cancer risk prediction. We aimed to generate tumour subtype and age-specific risk estimates using data from the Breast Cancer Association Consortium, including 44,777 breast cancer cases and 42,997 controls from 33 studies genotyped for CHEK2*1100delC.

**Materials and Methods:** Data were extracted from the Breast Cancer Association Consortium database. CHEK2*1100delC genotyping had mostly been done by a custom Taqman assay. Breast cancer relative risks (odds ratios: OR) for CHEK2*1100delC carriers versus non-carriers were estimated using logistic regression. Analyses were adjusted for study (categorical) and age; the main analyses presented here only included invasive breast tumours from population- and hospital-based studies.

**Results:** The proportions of CHEK2*1100delC carriership in controls, breast cancer patients from population- and hospital-based studies, and breast cancer patients from familial or clinical genetics centre-based studies were 0.5%, 1.3%, and 3.0%, respectively. The estimated OR for invasive breast cancer was 2.26 (95% CI: 1.90–2.69; $p = 0.23 \times 10^{-19}$). The OR was higher for Oestrogen Receptors (ER)-positive tumours 2.55 (2.10–3.10; $p = 0.49 \times 10^{-20}$) than ER-negative tumours 1.32 (0.93–1.88; $p = 0.12$) (p interaction = $0.01 \times 10^{-3}$).

The OR declined with age for ER-positive tumours, from 3.26 (1.05–10.18; $p = 0.04$) for women aged <35 years, 3.12 (2.13–4.58; $p = 0.05 \times 10^{-7}$) for 35−50 years, 2.73 (2.02–3.70; $p = 0.07 \times 10^{-9}$) for 50−65 years, to 1.58 (1.01–2.49; $p = 0.05$) for women aged 65 and older. This interaction with age was to a lesser extent, and not statistically significant, seen for ER-negative tumours.

**Conclusion:** These CHEK2*1100delC breast cancer risk estimates provide a basis for incorporating CHEK2*1100delC into breast cancer risk prediction models. Our findings will be discussed in the light of the recent introduction of routine CHEK2*1100delC diagnostic screening in the Netherlands.

**No conflicts of interest**

**155** Poster

**Inequalities in health: The era of austerity impacts on breast cancer patients in southeast Wales**

K. Gomez[1], K. Boyce[1], P. Hunt[1], T. Micic[1]. [1]*Nevill Hall Hospital, Oncoplastic Surgical Breast Unit, Abergavenny, United Kingdom*

**Background:** Aneurin Bevan, the founder of the National Health Service in the United Kingdom (UK) was acutely aware of the implied association between poor health and social deprivation. Breast cancer, the commonest female cancer in the UK typically affects women from higher socioeconomic groups but with evidence suggesting that prognosis is worse for those from more deprived social classes. The aim of this study was to assess if any differences in presentation, treatment and prognostic factors existed between various socioeconomic groups within a single geographical area, over an 8-year period, in light of the austerity measures affecting government spending on health.

**Materials and Methods:** Data was collected using the Welsh national Cancer Network Information System Cymru (CaNISC), for an 8-year period from 2007 to 2014. Patients' postcodes were used to calculate their Welsh Index of Multiple Deprivation (WIMD) score, which is the Welsh Government's official measure of relative deprivation for geographical areas in Wales. Continuous data were summarised as a mean (plus range), and tested using t-tests. Categorical data were cross-tabulated, and differences in proportions were tested using chi-squared. Where appropriate, 95% confidence interval (95% CI) were calculated. RStudio v2.1 (R Foundation for Statistical Computing) was used for statistical analyses and $p < 0.05$ was considered to be statistically significant.

**Results:** 1075 patients, from 938 different postcode areas, were registered on CaNISC undergoing breast cancer treatment in southeast Wales between 1st Jan 2007 and 1st Jan 2014. Postcodes and WIMD scores were available for 1062 patients. There were 2 male patients within the series. There were 5 categories of WIMD, with 93/1075 (8.7%) being in the most deprived group and 526/1075 (48.9%) in the least deprived. 11 surgeons were involved in care of the patients. Lower WIMD scores showed significant association with increased age at diagnosis (95% CI 832.1–894.6), time to diagnosis (95% CI 900.1–964.74), larger invasive size (95% CI 880.8–945.5), larger overall tumour size (95% CI 877.1–941.8), number of operations (95% CI 899.2–963.9) and a worse Nottingham Prognostic Index (95% CI 896.2–960.9). No association was found with variables associated with the biology of breast cancer or access to adjuvant treatment.

**Conclusions:** Breast cancer is in the main a disease of more affluent women. Prognostic indicators such as, Nottingham Prognostic index are shown to be worse in those from lower socioeconomic groups. The reasons for this are multifactorial and include poorer uptake of screening, larger tumour and invasive size at diagnosis in those patients. Further study is warranted into the factors affecting disparity between breast cancer patients from different socioeconomic groups, but the findings included inform the planning of a larger study.

**No conflicts of interest**

**156** Poster

**Risk of locoregional recurrence after breast conserving surgery for ductal carcinoma in situ**

C. Drukker[1], M. Menke-Pluijmers[1], P. Plaisier[1], P. Westenend[2,3]. [1]*Albert Schweitzer Hospital, Surgery, Dordrecht, Netherlands;* [2]*PAL Dordrecht, Pathology, Dordrecht, Netherlands;* [3]*Regional Screening Organization South West, Breast Cancer Screening, Rotterdam, Netherlands*

**Background:** Over the past decade, breast conserving surgery for ductal carcinoma in situ (DCIS) has become common practice. Along with this development came the need to improve risk-assessment for locoregional recurrence in the individual patient with DCIS. To date, proper risk prediction tools are not available. Also, only limited studies evaluated the additional value of traditional immunohistochemistry (IHC) including Estrogen Receptor (ER), Progestrone Receptor (PR), Human Epidermal growth factor Receptor 2 (HER2) and Ki67 for risk estimation in patients with DCIS.

**Methods:** Follow-up was updated for 208 patients with DCIS diagnosed and treated with breast conserving surgery at the Albert Schweitzer Hospital between 2000 and 2013. Original tumor samples were collected and used for IHC staining. We report here preliminary data, final results will be available at EBCC-10.

**Results:** Through a median of 59 months of follow-up 13 events of locoregional recurrence occurred of which 6 were ispilateral DCIS and 7 ipsilateral invasive breast cancer. The risk of locoregional recurrence is 5.9% at 5 years and 16.8% at 10 years at diagnosis. Age at diagnosis, grade and administration of radiotherapy were not significant prognostic factors for locoregional recurrence in our population. For all patients tumor samples are available. Analyses are currently being performed.

**Conclusion:** The risk of locoregional recurrence after breast conserving surgery for DCIS is 5.9% at 5 years. When analyzing the results from IHC staining, we expect to find prognostic value especially for ER and HER2.

**No conflicts of interest**

**157** Poster

**Targeting breast cancer outcomes − What about the primary relatives?**

A. Johnston[1], M. Sugrue[1]. [1]*Letterkenny University Hospital, Breast Centre North West and Donegal Clinical Research Academy, Co Donegal, Ireland*

**Introduction:** A recently published study identified that 65% of newly diagnosed breast cancer patients had not been screened correctly before diagnosis, resulting in increased stage of cancer at presentation[1]. This study assessed whether newly diagnosed breast cancer patients' primary relatives are, in turn, assessed appropriately.

**Methods:** An ethically approved prospective study, involving primary relatives of 280 women diagnosed with breast cancer between 2009–2012 at Letterkenny University Hospital, was undertaken. Telephone interview established: demographics, menstrual history, family history verification and breast screening history. Personal risk level was calculated using IBIS risk calculator[2] and NICE CG164[3] This was followed by an evaluation as to whether current screening met screening guidelines. Participants were enrolled into appropriate screening programmes if currently not in one and results were analysed.

**Results:** 215 of the 280 (76.8%) newly diagnosed patients responded giving details of their 274 primary relatives which made up the study cohort. Mean age 50±10 (35−75). 32% were low risk, 64% moderate and 4% high. 190/274 (69%) were being screened appropriately. 75/84 who had not been screened but met criteria were then assessed with: mammography alone in 55 or with ultrasound in 16. Four underwent a biopsy and to date none had cancer. Surveillance was: annual screening in 48%; Breast screening and GP in 33%; GP only in over 65s in 13%; undecided as yet 6%.

**Conclusions:** This study identified that only 69% of primary relatives are being screened according to international guidelines. Care to 31% was improved and facilitated by this study. New proactive health promotion measures for breast cancer are required.

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**No conflicts of interest**

**158** Poster/Poster Spotlight

**Diabetes, diabetes treatment and mammographic density in Danish diet, cancer, and health cohort**

Z. Andersen[1], K. Buschard[2], K. Thomassen[1], E. Lynge[1], I. Vejborg[3], M. Von Euler-Chelpin[1], A. Tjønneland[4]. *[1]University of Copenhagen-Public Health, Department of Public Health- Center for Epidemiology and Screening, Copenhagen K, Denmark; [2]Bartholin Institute, Rigshospitalet, Copenhagen, Denmark; [3]Diagnostic Imaging Centre, Copenhagen University Hospital- Rigshospitalet, Copenhagen, Denmark; [4]Danish Cancer Society, Danish Cancer Research Center, Copenhagend, Denmark*

**Background:** Diabetes is associated with increased risk of breast cancer, but exact mechanisms are unknown. The role of insulin has been debated. High mammographic density (MD) is one of the strongest predictors and a biomarker of breast cancer risk. Few studies have linked diabetes to MD, finding none or weak inverse associations, but none had data on diabetes treatment. We examined whether diabetes and diabetes treatment are associated with MD in a prospective cohort study of Danish women above age of 50 years.

**Materials and Methods:** Study cohort consisted of 5,703 women (4,501 postmenopausal) who participated in the Danish Diet, Cancer and Health cohort (1993–1997) and subsequently attended mammographic screening in Copenhagen (1993–2001). We used MD assessed at the first screening after the cohort entry. MD was defined as mixed/dense or fatty. Diabetes diagnoses, and diabetes treatments (diet, insulin, pills) were self-reported at recruitment (1993–1997). The association between MD and diabetes was analyzed by logistic regression adjusted for potential confounders. Effect modification by menopausal status and body mass index (BMI) was performed by introducing an interaction term into the model and tested by Wald test.

**Results:** Of 5,703 women with mean age of 56 years, 137 (2.4%) had diabetes and 3,212 (56.3%) had mixed/dense breasts. Having diabetes was significantly inversely associated with having mixed/dense breasts, in both, the crude model (odds ratio; 95% confidence interval: 0.33; 0.23–0.48), and after adjustment for adiposity and other risk factors (0.61; 0.40–0.92). Similar inverse associations were observed for 44 women who controlled diabetes by diet only and didn't receive any medication (0.63; 0.29–1.36), and 62 who took pills only for diabetes (0.59; 0.32–1.09), while diabetic women taking insulin seemed to have increased odds of mixed/dense breasts (2.08; 0.68–6.35). There was no effect modification of these associations by menopause or BMI.

**Conclusions:** Having diabetes controlled by diet or pills decreases MD, whereas taking insulin may increase MD.

**No conflicts of interest**

**159** Poster

**Clinico-pathological characteristics and mutation profile of breast cancer in women with neurofibromatosis type 1**

Y.S. Yap[1], P. Munusamy[2], J.R. McPherson[3], S. Ng[4], C.H.T. Chan[2], S.Y. Loke[2], A. Prawira[2], E.S.Y. Wong[2], C.K. Ong[5], S.B.C.R.G. SingHealth Breast Cancer Research Group[6], A.S.G. Lee[2]. *[1]National Cancer Centre Singapore, Medical Oncology, Singapore, Singapore; [2]National Cancer Centre Singapore, Molecular Oncology, Singapore, Singapore; [3]Duke-National University of Singapore Graduate Medical School, Division of Neuroscience and Behavioral Disorders, Singapore, Singapore; [4]Institute of Molecular and Cell Biology, Institute of Molecular and Cell Biology, Singapore, Singapore; [5]National Cancer Centre Singapore, Lymphoma Genomic Translational Research Laboratory, Singapore, Singapore; [6]SingHealth Breast Cancer Research Group, SingHealth Breast Cancer Research Group, Singapore, Singapore*

**Background:** Women with neurofibromatosis type 1 (NF1), an autosomal dominant genetic disorder, are at increased risk of getting breast cancer, but there is limited data on the characteristics of NF1-associated breast cancer. This study aims to study the clinicopathological characteristics and mutation profile of breast cancer in women with NF1.

**Material and Methods:** Patients with both NF1 and breast cancer were identified retrospectively from hospital records as well as prospectively when seen at National Cancer Centre Singapore (NCCS) and Singapore General Hospital (SGH). All women had histologically proven breast cancer and fulfilled at least 2 of the 7 criteria developed by the NIH Consensus Conference for clinical diagnosis of NF1. Details on patient demographics, tumour grade, stage, receptor status and clinical outcome were evaluated. Whole exome sequencing and targeted exome sequencing have been performed on breast cancer specimens and matched normal in 3 and 5 patients respectively so far. Customized Agilent SureSelect 283-gene panel was used for 3 fresh frozen tumour specimens while Integrated DNA Technologies (IDT) xGen 127-gene Pan-Cancer panel was used for 2 formalin-fixed paraffin-embedded specimens.

**Results:** We identified 18 women with NF1 and breast cancer seen at our institutions from 2001 to present date. Median age of breast cancer diagnosis was 48.5 years (range 30−74 years). All 18 patients had invasive ductal carcinoma; of which 8 (44.4%) were stage 3 or 4 at diagnosis. To date, 5 out of 17 patients (29.4%) with stage 1−3 breast cancer have relapsed. Grade, estrogen, progesterone and HER2 receptor status were fully available for 17 patients; findings are tabulated in the table. Apart from germline NF1 mutations, recurrent somatic mutations in the breast cancer included TP53 (62.5%), KMT2C (37.5%), and PIK3CA (25%). In addition, second-hit somatic mutation in NF1 was observed in 2 patients (25%).

Table 1. Pathological characteristics of NF1-related breast cancers

| | NF1 cases [a] |
|---|---|
| Stage at diagnosis | |
| 0 | 0 |
| 1 | 2/18 (11.1%) |
| 2 | 8/18 (44.4%) |
| 3 | 7/18 (38.9%) |
| 4 | 1/18 (5.5%) |
| Grade | |
| 1 | 0 |
| 2 | 3/17 (17.6%) |
| 3 | 14/17 (82.4%) |
| Immunohistochemical subtype | |
| ER±PR±HER2+ | 11/17 (64.7%) |
| ER and/or PR+, HER2− | 2/17 (11.8%) |
| Triple negative | 4/17 (23.5%) |

[a] Among patients who had tissue for histological evaluation.

**Conclusion:** Our findings suggest that there is a higher frequency of grade 3 and HER2 positive tumours in NF1-associated breast cancer compared to sporadic breast cancer. Heterozygous germline NF1 mutation may lead to the development of these aggressive features, in cooperation with alterations in other cancer-related genes. Further genomic profiling of these tumours (in progress) may elucidate the role of NF1 in these breast cancers. This may also have implications for sporadic tumours with somatic NF1 mutations in individuals without NF1.

**No conflicts of interest**

**160** Poster

**Clinical and genetic characteristics of young women with breast cancer in Jerusalem, Israel**

T. Hadar[1,2], N. Ozer[1], O. Olsha[1], A. Tomer[2,3], S. Lolas[2,3], R. Abu-Dalo[1], M. Carmon[1], E. Levy-Lahad[2,3]. *[1]Shaare Zedek Medical Center, Unit for Breast Health- General Surgery Department, Jerusalem, Israel; [2]Shaare Zedek Medical Center, Medical Genetics Institute, Jerusalem, Israel; [3]Hebrew University, Faculty of Medicine, Jerusalem, Israel*

**Background:** Our center serves an ethnically diverse population of Ashkenazi Jewish (AJ), non-AJ and Arab origin. AJs trace their origins to European countries. Non-AJs, who originate from Asia and Africa, are genetically more heterogeneous. There is little knowledge of founder mutations in the non-AJ and Arab populations.

**Methods:** Retrospective review of clinical and genetic characteristics of 25−40 year old AJ, non-AJ and Arab women who had surgery for primary BC from January 2000 to May 2014.

**Results:** Characteristics of young breast cancer patients are presented in the table.

According to the patients' grandparents country of origin, 34.5% of non-AJs originated in Africa, 45.8% in Asia and 8.9% in Europe. Common countries of origin were Morocco (23.3%), Iraq (17.2%), Kurdistan (8.3%) and Iran (7.5%). Others originated from countries in North Africa, Syria, Ethiopia, Greece, Turkey, India and more.

98% of the AJs counseled were tested, significantly more than the other groups ($p = 0.017$). 6 BRCA1–185delAG, 3 BRCA1–5382insC, and two non-founder mutations were found. Of the non-AJ patients counseled, 81% were tested for the founder AJ mutations, with or without specific origin mutations. One had BRCA1–185delAG mutation and 3 others − non founder BRCA1 or 2 mutations. 79% of the Arab patients counseled were

Table (abstract 160): Characteristics of young breast cancer patients

| | Non-Ashkenazi Jewish | | Ashkenazi Jewish | | Arab | | Overall | | P value |
|---|---|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | N | % | |
| Number | 87 | 48.3 | 52 | 28.9 | 41 | 22.8 | 180 | 100 | |
| Mean age | 35.9 | | 36.3 | | 35.1 | | 35.8 | | 0.306 |
| Mean number of children | 2.5 | | 2.9 | | 2.7 | | 2.7 | | 0.43 |
| 1st or 2nd degree relative with BC | 30 | 34.5 | 27 | 51.9 | 12 | 29.3 | 69 | 38.3 | **0.049** |
| Genetic counseling | 62 | 71.3 | 47 | 90.4 | 24 | 58.5 | 133 | 73.9 | **0.002** |
| Pathology − IDC | 74 | 85.1 | 42 | 80.8 | 42 | 73.2 | 146 | 81.1 | 0.276 |
| Tumor size T1c or higher | 67 | 77 | 46 | 88.5 | 32 | 78 | 145 | 80.6 | 0.23 |
| Positive nodal status | 45 | 51.7 | 27 | 51.9 | 23 | 56.1 | 95 | 52.8 | 0.889 |
| ER positive | 58 | 66.7 | 36 | 69.2 | 27 | 65.9 | 121 | 67.2 | 0.931 |
| HER2 positive | 22 | 25.3 | 14 | 26.9 | 8 | 19.5 | 44 | 24.4 | 0.688 |
| Mastectomy | 34 | 39.1 | 17 | 32.7 | 22 | 53.7 | 73 | 40.6 | 0.115 |
| Prophylactic contralateral mastectomy | 13 | 14.9 | 3 | 5.8 | 0 | 0 | 16 | 8.9 | **0.014** |
| Reconstruction | 22 | 46.8 | 6 | 30 | 5 | 22.7 | 33 | 37.1 | 0.118 |
| Neoadjuvant chemotherapy | 18 | 20.7 | 7 | 13.5 | 6 | 14.6 | 31 | 17.2 | 0.486 |

tested, 9 for the BROCA gene panel. 2 mutations were found in BRCA1 and one in the ATM gene.

**Conclusions:** Young breast cancer patients have diverse geographic ethnic origins. Ethnic groups were similar in tumor characteristics. Rates of contralateral prophylactic mastectomy were low − 8.9% in all patients, none in Arab group.

AJs had significantly more family history than non-AJ or Arab women, and were more likely to be referred for genetic counseling. Among women referred for genetic counseling, most had genetic testing. Mutation rate was in the expected range.

Further genetic analysis is now possible using new technology and panels. This will allow us to determine if carrier rates differ between the groups, and is likely to change referral patterns and testing uptake in the near future.

**No conflicts of interest**

**161** Poster

**FYI: Breast cancer − the use of mobile technology to deliver accurate and relevant cancer education**

E. Rutherford[1], J. Finn[2], E. Lehane[1], M. Forde[3], P. Waters[1], A. Asharaf[1], S. Tabirca[2], M. Bennett[1], H.P. Redmond[1], M. Corrigan[1]. *[1]Cork Breast Research Centre- Cork University Hospital- Cork- Ireland, Surgery, Cork, Ireland; [2]University College Cork, Computer Science, Cork, Ireland; [3]Cork University Hospital, CUH Charity, Cork, Ireland*

**Background:** We have previously demonstrated that breast cancer is the most searched cancer term on the Internet. However, online medical information is often unreliable, irrelevant or in a form that makes it inaccessible to the majority of people.

As breast cancer treatment options advance and prophylactic treatments become available, the question of how best to inform consent and empower individual patients of varying literacy, to make considered decisions is increasingly important.

We aimed to identify the most frequently searched breast cancer questions and answer them in a way that would be accessible to individuals of all literacy levels. In conjunction with the National Adult Literacy Agency, we developed a freely available app to present this information in a user-friendly format.

**Methods:** Data mining software was utilised to identify the fifty most searched for terms regarding breast cancer in a three-month period (April–June 2014 inclusive). Terms were collated and then extrapolated into questions. Spurious associations, including commercial links, were excluded. The questions were then comprehensively answered and reviewed by a literacy specialist. All content was assessed by the National Adult Literacy Agency to ensure maximum accessibility. Information was also accompanied by diagrams and recorded as audio files for patients with limited literacy. Simple definitions of essential medical terminology were provided, along with tools to help modify personal risk e.g. BMI tracker.

**Results and Conclusions:** This free app (FYI: Breast Cancer) has been downloaded in over 30 countries worldwide with an average user rating of 4.5/5. Given its success, it is intended to expand this approach to include other cancers and chronic conditions.

**No conflicts of interest**

**162** Poster

**CDH1 gene mutation: The need for a multidisciplinary team approach**

A. Fareleira[1], S. Costa[2], L. Garrido[3], L. Ferro[3], R. Guimaraes[3], S. Castedo[4], M. Baptista[5], A. Magalhaes[6], F. Osório[7], J.L. Fougo[2], J. Costa Maia[5]. *[1]Centro Hospitalar S. João- E.P.E., General Surgery, Matosinhos, Portugal; [2]Centro Hospitalar S. João- E.P.E., General Surgery − Breast Center, Porto, Portugal; [3]Centro Hospitalar S. João- E.P.E., Breast Center, Porto, Portugal; [4]Centro Hospitalar S. João- E.P.E., Breast Center, Matosinhos, Portugal; [5]Centro Hospitalar S. João- E.P.E., General Surgery, Porto, Portugal; [6]Centro Hospitalar S. João- E.P.E., General Surgery − Breast Centre, Porto, Portugal; [7]Centro Hospitalar S. João- E.P.E., General Surgery − Bresat Centre, Porto, Portugal*

**Background:** Breast cancer (BC) is a common malignancy, but only 5−10% are hereditary. The main mutations are in BRCA 1, BRCA 2 and TP53 genes. E-cadherin protein gene (CDH1) germline mutations are also associated with increased risk of developing lobular BC as well as highly aggressive diffuse type gastric cancer and colon cancers. Endoscopic screening may miss early gastric lesions which are usually multifocal and intramucosal. The aim of this study is to characterize a cohort of CDH1 gene mutation carriers followed at a Breast Cancer Center.

**Material and Methods:** Retrospective study of three families with an identified germline mutation of CDH1 gene (n = 61).

**Results:** In our Breast Cancer and Digestive Tumors High Risk Consultation we follow three families with identified CDH1 gene deleterious mutation (c.1901C>T (p.Ala634Val) on exon 12). From the 61 members, 28 carry the mutation and 7 are still undergoing genetic investigation. Two index cases were diagnosed with advanced diffuse gastric cancer and died at the age of 39 and 18 years old.

In these families, 3 patients had breast cancer. Two of the three were clinically asymptomatic and the cancer was only diagnosed with MRI screening after the genetic result. One of them had an axillary metastasis with occult primary BC, identified after bilateral mastectomy. The other 2 patients also underwent prophylactic gastrectomy, being diagnosed with diffuse gastric cancer (pT1aN0).

Additionally, six other patients also underwent prophylactic gastric surgery, all of them with evidence of early stage carcinoma (one pT2N0 and five pT1aN0) despite having previous normal endoscopy.

**Conclusion:** Genetic counselling and the identification of CDH1 gene mutation carriers is vital in order to initiate gastric, breast and colo-rectal screening and to consider prophylactic gastrectomy and bilateral mastectomy before the development of the disease or to avoid progression to advanced and incurable cancer stages. A multidisciplinary approach in these families is essential to ensure adequate psychosocial support and to discuss the appropriate management of very young carriers (<18 years old).

**No conflicts of interest**

**163** Poster

**Risk score and factors for breast cancer patients planning to undergo lipofilling after deep inferior epigastric perforator (DIEP)-flap reconstruction**

S. Fertsch[1], D.M. Hagouan[1], D.B. Munder[1], D.P. Richrath[1], D.M. Otte[1], D.P. Stambera[1], D.A. Abu-Ghazaleh[1], P.C. Andree[1], M. Michalak[2]. [1]*SANA Kliniken Dusseldorf GmbH, Department of Plastic and Reconstructive Surgery, Dusseldorf, Germany;* [2]*Poznan University of Medical Sciences, Department of Computer Science and Statistics, Poznan, Poland*

**Background:** The Deep Inferior Epigastric Perforator (DIEP)-flap is nowadays a common approach for breast reconstruction in breast cancer patients after mastectomy. Fat-grafting to optimize the aesthetic outcome often follows the reconstruction. Although lipofilling is widely used in this field, there is still no clear consensus on its oncological safety. Furthermore certain patients have additional personal risk factors (e.g. high grade tumor) that could potentially work in synergy with the lipo-aspirate and increase the risk of cancer recurrence. Therefore it is crucial to improve patient selection for fat grafting procedures.

This study identifies potential risk factors to create a patient risk profile, which enables physicians to perform patient selection for lipofilling procedures by the guidance of a "lipofilling risk score".

**Material and Methods:** Matched cohort study. The survival rate of 100 patients that underwent lipofilling after their DIEP-flap reconstruction was compared retrospectively with 100 matched control patients that did not undergo lipofilling after their flap surgery. Both groups had no recurrence between their mastectomy and lipofilling, the latter labeled as the "startpoint" of the survival follow-up. Further, the lipofilling and control group were subdivided according to their risk factors, which were categorized as patient-dependent and tumor-dependent ones and their survival and hazard rates were compared to each other to identify the potential risk factors that may increase the recurrence risk.

**Results:** Median follow-up was 76.5 months from the mastectomy and 31 months from startpoint to most recent follow-up. 7 and 11 patients had an event in the lipofilling and control group, respectively, presenting with comparable survival rates [P = 0.24; Hazard Ratio Lipo vs Control = 0.57 (95% confidence interval 0.22–1.47)]. The subgroup survival analysis showed that lipofilling increased the risk of recurrence in women that had a breast cancer with a positive HER2/neu receptor status (p = 0.05), a high grade neoplasia (G3) (p = 0.049) or a positive nodal status (N1,N2,N3) (p = 0.035).

**Conclusions:** No general increased recurrence risk was observed between the lipofilling and control group, yet the subgroup analysis allowed us to create a patient risk profile and to generate a "lipofilling risk score" that reflects the survival time. It is composed of the score**1**: lowest risk of recurrence for patients that had a G3 breast cancer, score**2**: intermediate risk for positive lymph node status and score**3**: highest risk for patients with a positive HER2/neu receptor breast cancer. Further studies are required to validate our conclusions, yet patients belonging to the risk profile should be handled with special attention.

**No conflicts of interest**

**164** Poster

**Screen detected breast cancers exhibit good clinicopathological characteristics: Updated results of Turkish Bahcesehir Breast Cancer Screening Project**

N. Cabioglu[1], S. Ozkan-Gurdal[2], A. Kayhan[3], N. Ozaydin[4], B. Ozcinar[1], E. Aribal[5], V. Ozmen[1]. [1]*Istanbul University Faculty of Medicine, Department of Surgery, Istanbul, Turkey;* [2]*Namık Kemal University-Faculty of Medicine, Department of Surgery, Istanbul, Turkey;* [3]*Kanuni Sultan Suleyman Research and Teaching Hospital, Department of Radiology, Istanbul, Turkey;* [4]*Faculty of Medicine- Marmara University Istanbul- Turkey, Department of Public Health, Istanbul, Turkey;* [5]*Marmara University Faculty of Medicine, Department of Radiology, Istanbul, Turkey*

**Background:** Turkish Bahcesehir Breast Cancer Screening Project is a 10-year organized population based screening program carried out in one of the largest counties of Istanbul, Turkey. Our aim is to examine the biological features of screen detected and interval breast cancers for the first 6-year study.

**Methods:** Between 2009 and 2015, mammographies were obtained by 2-year intervals for 7025 women with ages 40−69 years. Clinicopathological and biological tumor characteristics (ER, PR, HER2-neu, Ki-67) were analysed for those diagnosed with breast cancer.

**Results:** Seventy-five breast cancers (1%) were detected. The median age was 51 (40−70). Sixty-three patients (85%) underwent breast conservation, whereas 49 (66%) had sentinel lymph node biopsy only as axillary procedure. There were 14 (18.7%) ductal carcinoma in situ exclusively found among screen detected cancers (n = 60) and 61 (81.3%) invasive cancers. Patients with interval cancers (n = 15) were more likely found to have invasive lobular cancers (OR: 2.17; 95% CI: 0.54–8.67) and less likely found to have minimal cancers (OR: 0.4; 95% CI: 0.1–1.57). Invasive cancers were found to be either luminal A (69%) or luminal B type (21%), whereas non-luminal HER2 (6%) and triple negative cancers (4%)were less likely detected.

**Conclusions:** Our findings suggest that the majority of screen-detected breast cancers exhibit either luminal A or B subtype, and interval cancers were more likely to have invasive lobular histopathology. However, more aggressive subtypes such as non-luminal HER2-neu or triple negative cancers are less likely to be detected by mammographic screening programs, requiring other preventive strategies.

**No conflicts of interest**

**165** Poster

**High-risk breast cancer is less likely to occur in the ductal hyperplasia lesions or low-grade DCIS − Consideration of long-term follow-up observation after surgical biopsy**

K. Takebe[1]. [1]*Takebe Breast Cancer Care Clinic, Surgery, Takematsu, Japan*

**Background:** Even if many ductal hyperplasia lesions and low grade DCIS are detected by breast cancer screening using high-resolution imaging modalities, we have often experienced high-grade breast cancer as an interval cancer. We might consider whether the detection of ductal hyperplasia lesions and low grade DCIS in breast cancer screening really leads to a decrease in breast cancer death. Therefore, we examined the follow-up periods after the removal of lesions.

**Subjects and Methods:** At our facility from 1997 to 2012, we examined 354 cases of ductal hyperplasia lesions which were treated with surgical biopsy and followed up with observations spanning at least three years. The ductal hyperplasia lesions shown here are the usual ductal hyperplasia, flat epithelial atypia, atypical ductal hyperplasia, and intraductal papilloma. The median of the follow-up observation period was 73 months. In addition, we had 153 cases of low-grade DCIS patients who underwent follow-up of more than three years without postoperative irradiation. The median of the follow-up period was 63 months.

**Result:** (1) In ductal hyperplasia lesions, 25 cancers occurred in both breasts. There were 13 cases of DCIS in the histopathological examination (52%) and 12 cases of invasive cancer (46%). In DCIS, low-grade DCIS of Van Nuys1 accounted for 86%. Luminal A was 75% in invasive cancer. Lymph node metastasis was observed in only two cases, with one case having one metastatic lymph node and the other having two. Her2 type and triple-negative type accounted for one case each. Her2 type was microinvasive carcinoma, and Ki67 was 22% in triple negative type. The potential for malignancy in both was not so high.

In low-grade DCIS (non-irradiated), 11 cancers occurred in both breasts. There were 8 cases of DCIS (73%) and three cases of invasive cancer (27%). All of the DCIS cases were VanNuys1. All of the invasive cancer cases were luminal A.

(2) We compared the cancer occurrence in benign lesions and low-grade DCIS (surgery side). The occurrence rate was 2.2% for benign lesions and 3.2% for low-grade DCIS over a five-year period. There was no significant difference found between the two groups.

**Conclusion:** High-risk breast cancer is less likely to occur in ductal hyperplasia lesions or low-grade DCIS. In other words, terminal duct lobular unit (TDLU) in both breast who had been affected with ductal hyperplasia or low grade DCIS lost a potentiality of the occurrence of high grade malignant cancer. Therefore, women with breast ductal hyperplasia lesions or low-grade DCIS should be placed in the low-risk group of future breast cancer deaths. This might indicate the limits of breast cancer screening.

**No conflicts of interest**

**166** Poster

**Impact of selected tumor and patient characteristics on outcome of Egyptian patients with breast carcinoma**

M. Kamal[1], N. Gado[1], M. El-Shaarawi[1], M. Daruish[1], A. Shehata[1], S. Mousa[1]. [1]*Ain Shams University, Clinical Oncology, Cairo, Egypt*

**Background:** Attribution of the adequacy of the provided breast cancer (BC) therapy to the patient's outcome remains anecdotal in developing countries. This study is conducted to estimate the impact of tumor and patient characteristics on the outcome of Egyptian patient's with BC.

**Materials and Methods:** Medical records of 1295 BC patients treated in Ain Shams University, Egypt between January 2007 and December 2012, were analyzed retrospectively. The Kaplan–Meier method and log-rank test were used to estimate and compare the disease free survival (DFS) and the overall survival (OS).

**Results:** Median age was 51 years (SD±11.41, Range 20−88) and 40.5% were premenopausal. About 50.1% and 15.7% of the patients presented in early and advanced stages respectively. Positive axillary lymph nodes (ALN) were seen in 40% of the patients. Positive ER, PR and HER2neu expression was seen in 57.2%, 52.8%, and 11.9% respectively. Adjuvant chemotherapy (CT), neo-adjuvant CT, adjuvant radiotherapy, adjuvant hormonal therapy (HT) and adjuvant targeted therapy have been received in 74.5%, 8.2%, 64.4%, 51.2% and 1.2% respectively. Median DFS was 36.37 months (SD±27.76) and the median OS was 40.79 months (SD ±27.41). About 36.6% of the cases developed progression. About 58.5%, 20.4% and 9.9% of the relapsed patients received 1st, 2nd and 3rd lines of CT respectively. Single agent CT, combined regimes CT and HT included in 1st line metastatic treatment of 25.7%, 19.2% and 31.6% respectively. Single agent CT, combined regimes CT and HT included in 2nd line metastatic treatment of 8.6%, 11.6% and 10.3% respectively. Single agent CT, combined regimes CT and HT included in 3rd line metastatic treatment of 4.6%, 5.3% and 1.7% respectively.

HER2neu negative status was associated with prolonged DFS of 36.3 months (95% CI= 33.6–38.9) versus 26.57 months (95% CI=21.53–31.6) for HER2neu positive (p = 0.00). The group of patients with negative LN was associated with statistically significant prolonged DFS of 40.6 months (95% CI=36.38–44.83) versus 33.04 months (95% CI =30.3–38.78) for patients with positive LN (p = 0.02).

OS was 41.74 months (95% CI=39.17–44.31) in patients with early stages versus 35.73 months (95% CI=31.6–39.86) in patients with advanced stages (p = 0.00). OS in Patients with positive LN was 38.51 months (95% CI =36.04–40.99) but in those with LN negative OS was 45.17 months (95% CI=41.11–49.23) (p = 0.01). OS in patients with HER2neu negative status was associated with prolonged survival of 40.63 months (95% CI= 38.23–43.03) versus 31.46 months (95% CI= 26.8–36.12) for positive HER2neu receptor (p = 0.00).

**Conclusion:** This study highlights the importance of contribution of BC patients from developing countries in clinical trials. The ALN and HER2neu status of patients with BC is still considered as a prognostic value to detect DFS and OS.

**No conflicts of interest**

**167** Poster

**BCL2 as subtype specific prognostic factor in 13th St. Gallen immunohistochemical classification**

Y.H. Eom[1], B.J. Chae[2], B.J. Song[2]. *[1]Seoul St. Mary's Hospital, Surgery, Seoul, South Korea; [2]Seoul St. Mary's Hospital, Surgery, Seoul, South Korea*

B-Cell Lymphoma/Leukemia 2 (BCL2), an antiapoptosis protein, has been recognized as an important clinical prognostic marker in breast cancer. Since the role of BCL2 is dependent on the relations with estrogen receptor status, this effect is different in molecular subtypes. The aim of this study was to evaluate the relationship between prognostic outcome and bcl2 expression in individual molecular subtypes.

We retrieved data from 800 patients with primary breast cancer who underwent surgery and the adjuvant treatment at the breast cancer center of Seoul St. Mary's Hospital between 2006 and 2010. Immunohistochemistry was used to measure Estrogen receptor (ER), Progesterone receptor (PR), human epidermal growth factor receptor 2 (HER2), Ki67 and BCL2. We classified breast cancer into five molecular subtypes, including Luminal A, Luminal B (HER2 negative), Luminal B (HER2 positive), HER2 overexpression, Basal-like. We analyzed the clinicopathologic features and assessed the correlation between BCL2 expression and clinical outcome [relapse free survival (RFS) and overall survival (OS)] according to the five new molecular subtypes.

A total of 352 (56.3%) breast cancers showed BCL2 expression. BCL2 expression was associated with young (<50 years old) (p = 0.036), G1 grade (p = 0.002), low level of Ki-67 (<14%) (p = 0.000), ER positive (p = 0.000), PR positive (p = 0.000), HER2 negative (p = 0.000) breast cancer. BCL2-negative showed a significant association with worse RFS (p = 0.001) in breast cancer. There was no significant difference in OS (p = 0.446).

When breast cancers were divided into five molecular subtypes, BCL2 expression showed a significant association with favorable RFS (p = 0.006) in luminal A breast cancer. In multivariate analyses, BCL2 expression was also an independent favorable prognostic factor for RFS in Luminal A breast cancer [Hazard ratio (HR), 0.633; 95% confidence interval (95% CI), 0.174–2.303; p = 0.015].

Otherwise, BCL2 expression was a poor prognostic marker for RFS in basal-like breast cancer (p = 0.045). There was no significant difference of OS in luminal A and basal-like breast cancer (p = 0.832 and p = 0.748, respectively). Also, BCL2 expression showed no association with RFS and OS in three other molecular subtypes.

While BCL2 expression is an independent favorable prognostic marker for luminal A breast cancer, it is poor prognostic marker for basal-like breast cancer. We should be conscious of the different prognostic role of BCL2 expression according to the molecular subtypes. The analysis of BCL2 in a large prospective studies is needed to assess the clinical utility as an independent prognostic marker.

**No conflicts of interest**

**168** Poster

**Age at diagnosis and breast cancer outcomes after ten years of follow up among postmenopausal women with hormone receptor positive breast cancer**

M.G.M. Derks[1], W. Van de Water[1], E. Bastiaannet[1,2], H. Putter[3], A.J.M. De Craen[2], C. Seynaeve[4], D.W. Rea[5], J.W.R. Nortier[6], G.J. Liefers[1], C.J.H. Van de Velde[1]. *[1]Leiden University Medical Center, Surgical Oncology, Leiden, Netherlands; [2]Leiden University Medical Center, Gerontology and Geriatrics, Leiden, Netherlands; [3]Leiden University Medical Center, Medical statistics, Leiden, Netherlands; [4]Erasmus MC-Daniel Den Hoed Cancer Center, Medical Oncology, Rotterdam, Netherlands; [5]University of Birmingham, Medical Oncology, Birmingham, United Kingdom; [6]Leiden University Medical Center, Medical Oncology, Leiden, Netherlands*

**Background:** To assess the association between age at diagnosis and breast cancer outcomes after ten years of follow up in postmenopausal women with hormone receptor positive breast cancer.

**Material and Methods:** Patients with hormone receptor positive breast cancer who enrolled in the Tamoxifen Exemestane Adjuvant Multinational (TEAM) randomized control trial from countries that completed 10 year follow up were included for analysis. Age at diagnosis was divided into three age categories: younger than 65 years (n = 2389), 65−74 years (n = 1371) and 75 years and older (n = 682). Primary endpoint was disease specific mortality. Secondary endpoints were other-cause mortality and breast cancer relapse. Disease specific mortality as a proportion of all-cause mortality was calculated and compared between age categories using Pearson's $\chi^2$ test. Multivariate cox proportional hazard models were used to evaluate the association between age at diagnosis and breast cancer outcomes.

**Results:** Median follow up was 9.5 years (interquartile range 6.1–10.2). Overall, 465 patients (19.5%) aged younger than 65 years, 383 patients (27.9%) aged 65 to 74 years and 384 (56.3%) patients aged 75 years and older died during follow up. Disease specific mortality as a proportion of all-cause mortality decreased with age (76% <65 years, 56% 65−74 years, 31% ⩾75 years, P < 0.001). However, in adjusted regression analysis, disease specific mortality was higher in patients aged 65−74 years (hazard ratio (HR) 1.25, 95% CI, 1.02–1.53) and patients aged 75 years and older (HR 1.66 95% CI, 1.28–2.16) compared to patients younger than 65 years (reference), P = 0.001. Other cause mortality increased with age in patients aged 65−74 years (HR 2.17, 95 CI%, 1.65–2.84) and patients aged 75 years and older (HR 7.88, 95% CI 5.99–10.36) compared to younger patients (reference), P < 0.001. Breast cancer relapse was not associated with age (<65 years, reference; 65−74 years, HR 1.04, 95 CI%, 0.88–1.24; ⩾75 years, HR 1.18, 95% CI 0.94–1.47; P = 0.377). However, in patients who experienced a relapse, the proportion of patients who died due to breast cancer increased with age (66% <65 years, 74% 65−74 years, 81% ⩾75 years, P < 0.001).

**Conclusion:** In older patients, breast cancer mortality as a proportion of all-cause mortality was lower compared to younger patients with hormone receptor positive breast cancer. However, a higher breast cancer mortality rate was observed in older patients. Although breast cancer relapse rate was comparable across different age groups, the proportion of patients that died due to relapse was higher among older patients.

**No conflicts of interest**

**169** Poster

**Recurrence risk in T1mic/a/b, node-negative, early breast cancer by breast cancer subtype**

R. Nagaoka[1], D. Takata[1], A. Sato[1], T. Fujii[1], H. Tokiniwa[1], R. Yajima[1], H. Toru[1], S. Uchida[1], M. Tsuboi[1], T. Oyama[2], Y. Iino[3], J. Horiguchi[1]. *[1]Gunma University, Breast and Endcrine Surgery, Gunma, Japan; [2]Gunma University, Diagnostic Pathology, Gunma, Japan; [3]Kusunoki Hospital, Breast and Endcrine Surgery, Gunma, Japan*

**Purpose:** As recurrences and deaths less frequently occur in small, node-negative breast cancer patients, decision on adjuvant treatments remains controversial. In this study, we evaluate recurrence risk in patients with pT1mic/T1a/T1b, node-negative, breast cancer, accordingly with some prognostic factors.

**Patients and Methods:** We retrospectively evaluated 173 pT1mic/T1a/T1b, pN0 patients treated between 2004 and 2010 in our institution. Patients treated by neoadjuvant chemotherapy were excluded. We defined 4 different cohorts: ER positive/HER2 negative (ER+HER2−), ER positive/HER2 positive (ER+HER2+), ER negative/HER2 positive (ER−HER2+), and triple negative (TN).

**Results:** pT1mic was seen in 11% of patients, 29% pT1a, 60% T1b. Concerning the 4 different cohorts, 82% were ER+HER2−, 2.3% were ER+HER2+, 4.7% were ER−HER2+, 10.9% were TN. Adjuvant therapy was given to 86.7% of patients (83% hormone therapy, 6.4% chemotherapy, 4.6% trastuzumab). At a median follow-up of 69 months, 5-year DFS and OS was 98.3% and 100%, without differences among pT1mic,a,b, or among the 4 cohorts. All recurrence patients were without adjuvant therapy. For HER2+ cohorts, patients treated by trastuzumab had a good prognosis.

**Conclusions:** 5-year DFS and OS was very favorable in this series of small, node-negative cancers, but patients without adjuvant therapy have a worse outcome. Effective adjuvant treatment should be considered in these favorable subgroups.

**No conflicts of interest**

**170** Poster

**Exome sequencing and gene expression analysis of a matched case–control study generates novel indicators for metastatic progression in breast cancer**

K. Govindasamy Muralidharan[1]. [1]*Karolinska Institutet, Oncology pathology, Stockholm, Sweden*

The metastatic potential of newly diagnosed primary breast cancers can only partly be determined by evaluating classical biomarkers, grade and stage. Hence, it is currently not possible to properly predict the systemic metastatic potential for breast cancer using the present markers for prognostication and prediction. To identify that, a cohort consisting of fresh-frozen primary tumors from a matched case control study including 92 patients gaining metastatic relapse (cases) and 98 not gaining metastatic relapse (controls) within 5 years from diagnosis of the primary breast cancer was designed. The cases and controls were matched according to treatment, age and age at diagnosis. Using these samples whole exome sequencing, microarray and SNP arrays were performed. A total of 21,497 variants were detected in 190 samples (92 cases and 98 controls) with 113 mutations per sample in average (min: 3, max: 1109). TP53 (Mutation frequency of 23% both in cases and controls) and PIK3CA (Mutation frequency of 20% in cases and 34% in controls) were the only genes mutated at higher frequency (<20%) and all the remaining genes harbored mutations at lower frequencies. GATA3 was mutated with higher frequency in cases (8%) than in controls (2%). GATA3 and SLC3A1 were the only two genes having frequency >5% in the cases but not in the controls using MutsigCV analysis to identify putative driver genes. The set of genes showing highest contrast in mutation frequency between cases and controls were found to be significantly enriched with pathways and GO terms related to metastasis mechanisms such as focal adhesion, angiogenesis and cell-cell communication. Interestingly, some of the genes implicated in these mechanisms were predominantly mutated in cases (TEK, FLT4, APOB, LAMA1, FLNC and TJP1). We analyzed SNP array data for 162 samples (68 cases and 94 controls) with ASCAT. The highest contrast between cases and controls with predominance in cases at the copy number level was observed in chromosomes 11 and 17, more specifically, amplifications in 11q13 (CCND1, PPFIA1) and 17q12 (ERBB2) as well as deletions in 17q21 (BRCA1) and 11q25 (OPCML). Further, microarray-based gene expression for 181 samples (89 cases and 92 controls) identified 411 genes (corrected p-value <0.05 and absolute $\log_2$ fold change $\geqslant$0.3) differential expressed. The set of differentially expressed genes was significantly (q-value <0.05) enriched with GO terms related to metastasis such as angiogenesis, cell motility, cell adhesion and cell migration. DNA predictors for risk to develop systemic metastatic disease have so far not been characterized. Identification of such genetic markers would be highly valuable to identify high-risk patients and to further personalize cancer care.

**No conflicts of interest**

**171** Poster

**Clinical factors associated with discordance in hormone receptor status between primary and recurrent breast cancer**

S. Shiino[1], T. Kinoshita[1], M. Yoshida[2], K. Jimbo[1], S. Asaga[1], S. Takayama[1]. [1]*National Cancer Center Hospital, Department of Breast Surgery, Tokyo, Japan;* [2]*National Cancer Center Hospital, Department of Pathology and Clinical Laboratories, Tokyo, Japan*

**Background:** The immunohistochemical expression status of hormone receptor [HR, i.e. estrogen receptor (ER) and progesterone receptor (PR)] and HER2 status in the primary tumor are the most important markers for the treatment decisions of the patients with recurrent breast cancer. However, recent retrospective studies have reported discordance in these statuses between primary and recurrent tumors. Notably, discordance in hormone receptor status is more frequently than discordance in HER2 status. The aim of this study is to assess the discordance rates and the clinical factors associated with discordance in hormone receptor status.

**Material and Methods:** We retrospectively reviewed the records of 7,248 patients who underwent surgery for primary breast cancer between 1991 and 2013 at the National Cancer Center Hospital, Tokyo. There were 153 patients that underwent either core needle biopsy or surgical excision for recurrent breast cancer. We re-performed immunohistochemistry (IHC) for all tumor specimens using standardized methods with an autostainer. Two experienced pathologists diagnosed all these specimens in a blinded fashion. HR status was judged as positive if more than 10% of tumor cells were stained. HER2 positivity was assessed by IHC (score 3+) or FISH amplification (HER2/CEP 17 ratio $\geqslant$2.0). We evaluated the association between clinical characteristics and discordance in hormone receptor status by using multivariate logistic regression analysis.

**Results:** Among 153 patients, 104 patients had local recurrences and 49 patients had distant metastasis. The discordance rates in ER, PR and HER2 were 18%, 26%, and 7%. The proportions of positive-to-negative changes were 14%, 20%, and 3%. Distant metastasis (lung, liver, or brain) and early recurrence (within 2 years) were significantly associated with discordance in hormone receptor status: Distant metastasis (Odds ratios (OR) = 3.51 [95% CI: 1.05–11.7]), early recurrence (OR = 23.4 [95% CI: 5.55–98.4]).

**Conclusions:** Discordance in hormone receptor status and HER2 status often occurred between primary and recurrent breast cancer. Discordance in hormone receptor status were significantly associated with early recurrence within 2 years and distant metastasis.

**No conflicts of interest**

**172** Poster

**Predictors of early cancer related mortality for T1/T2 node negative breast cancer: A single institute experience**

T. Mehmood[1]. [1]*Shaukat Khanum Memorial Cancer Hospital and Research Centre, Radiation Oncology, Lahore, Pakistan*

**Background:** Early-stage breast cancer is generally treated successfully with surgery, adjuvant chemotherapy, radiation therapy, and hormonal therapy, and this cancer typically has a favorable prognosis, with 5-year survival rate over 95%. Early recurrence and mortality infrequently occurs but is confusing in many clinicians. Identifying risk factors for early cancer-related mortality in early stage breast cancer may help to guide treatment and follow-up.

**Methods:** We retrospectively analyzed 621 pathologically confirmed T1/T2 node negative breast cancer patients. Patient demographics, clinical, and pathologic variables were analyzed. We then defined 'early cancer-related mortality' group confirmed death within 5 years of their date of operation.

**Results:** The median follow-up period was 87.0 (58–144) months. Overall 1.6% died from breast cancer during a median follow-up of 87 months. The median age at diagnosis was 40 years. Clinical predictors of early cancer-related mortality within 5 years by multivariate analysis included Age >50 years (HR 1.721; CI 1.046–2.831), Estrogen receptor negative (HR 2.808; CI 0.111–3.734), No hormonal treatment (HR 1.881; CI 1.058–3.344). Operation type, body mass index, tumor size, progesterone receptor status, HER2 status were not associated with early cancer-related mortality.

**Conclusion:** In patients with T1 to T2 node-negative breast cancer, age and estrogen receptor status may be independent predicting factors for early cancer-related mortality.

**No conflicts of interest**

**173** Poster

**Local-regional recurrences after mastectomy and adjuvant radiotherapy for breast cancer**

T. Mehmood[1]. [1]*Shaukat Khanum Memorial Cancer Hospital and Research Centre, Radiation Oncology, Lahore, Pakistan*

**Objective:** To determine risk factors for local-regional recurrences (LRR) after mastectomy and adjuvant radiotherapy for breast cancer (BC) patients.

**Materials and Methods:** We retrospectively analyzed 651 BC women treated with mastectomy, axillary dissection and adjuvant radiotherapy from January 1995 till December 2009. Neoadjuvant and/or adjuvant chemotherapy was given in 57.5% of the patients and 77% also received endocrine therapy. 15% of the patients received radiotherapy of the chest wall alone, 60% to the chest wall and supraclavicular nodes and 25% to the

chest wall, supraclavicular and axillary nodes. All clinical and pathological data were reviewed retrospectively. The association between categorical variables and the risk to relapse is tested by means of the log-rank test.

**Results:** At a median follow-up of 9 years, 3.5% developed LRR. 5 and 10 years local-regional control rates were 97.6% and 96.0%. Predictive factors to develop LRR are grade III tumors ($p = 0.009$), pT4 ($p < 0.001$), pN3 ($p = 0.03$), estrogen receptor negative BC ($p < 0.001$), progesterone receptor negative BC ($p = 0.006$), Her-2 receptor positive BC ($p = 0.03$) and triple negative BC ($p = 0.02$). There was no association between LRR and tumor type ($p = 0.3$), extensive intraductal component ($p = 0.7$) and positive surgical margins ($p = 0.06$). We also found no correlation between age and LRR ($p = 0.2$).

**Conclusions:** In breast cancer patients treated with mastectomy and adjuvant radiotherapy with or without systemic treatment the LRR at our institution are very low at 10 years. Notwithstanding few LRR, grade III tumors, pT4, pN3, ER negative, PR negative, Her-2 positive and triple negative BC are clear risk factors to develop LRR.

**No conflicts of interest**

**175** Poster

**Caspase 3 expression in remnant disease after neo-adjuvant chemotherapy may predict outcomes of breast cancer patients**

T. Himuro[1], Y. Horimoto[1], A. Arakawa[2], E. Tokuda[1], M. Tanabe[1], M. Saito[1]. [1]*Juntendo University, Departments of Breast Oncology, Japan;* [2]*Juntendo University, Departments of Human Pathology, Japan*

**Background:** It is well known that patients obtaining a pathological complete response (pCR) from neoadjuvant chemotherapy (NAC) have a good prognosis. However, prognostic factors for non-pCR patients are not yet well established. Therefore, we sought to identify a new marker predicting patient outcomes, by examining remnant disease in non-pCR patients.

Cleaved Caspase 3 (Casp3) is an apoptotic marker, which has central roles in the apoptotic cascade. Despite several studies of the relationship t between Casp3 expression and patient prognosis, this putative relationship remains unclear.

We immunohistochemically examined the Casp3 expression in remnant invasive nests of breast carcinoma to determine whether there is a relationship with patient outcomes.

**Material and Methods:** We investigated 218 patients with invasive breast cancer who received NAC and underwent surgery during the 2006 through 2008 period at our institution. The basic NAC regimen was CEF (cyclopfosphamide:500 mg/m$^2$, 5-FU:500 mg/m$^2$, epirubicine: 75–100 mg/m$^2$, 4 cycles) followed by taxane (paclitaxel: 80 mg/m$^2$, weekly, 12 treatments; or docetaxel: 75 mg/m$^2$, tri-weekly, 4 cycles). Following surgery, standard adjuvant endocrine therapy and/or Trastuzumab was administered. Casp3 was evaluated based on numbers of positive cells in five high-power fields.

**Results:** pCR was obtained in 49 patients (22%), only one of whom developed recurrent disease, during the median 82-months observation period. Fifty (30%) of the 169 non-pCR patients developed recurrences.

We investigated factors related to recurrences in the 169 non-pCR cases. Employing univariate analysis, we found large tumour size, lymph node involvement, lymph vessel invasion and high Ki67 expression to be factors related to tumour recurrence ($p < 0.01$). Also, patients with estrogen receptor (ER)-negative, progesterone receptor (PgR)-negative/high Caspase-3 tumours significantly more often developed recurrent breast cancer ($p < 0.05$).

Next, we performed a multivariate statistical analysis employing a logistic regression model and found lymph node involvement, negative PgR status ($p < 0.01$) and high Casp3 ($p < 0.05$) to be factors independently predicting recurrence, while lymph vessel invasion, negative PgR status and high Ki67 expression were found to be related to breast cancer mortality.

**Conclusions:** Patients with remnant disease showing high Casp3 expression had poor outcomes. Casp3 is a potential predictive marker for non-pCR patients, as are classical factors such as PgR.

**No conflicts of interest**

**176** Poster

**Combining cancer stem cell markers might predict patient outcomes and treatment effects in breast cancer patients with recurrences**

Y. Horimoto[1], A. Arakawa[2], N. Sasahara[2], T. Himuro[1], M. Tanabe[1], M. Saito[1]. [1]*Juntendo University, Breast Oncology, Bunkyo-ku- Tokyo, Japan;* [2]*Juntendo University, Human Pathology, Bunkyo-ku- Tokyo, Japan*

**Background:** CD44, 24 and aldehyde dehydrogenase 1 (ALDH1) have been established as cancer stem cell (CSC) markers in breast cancer. However, CSC populations recognized as positive for these markers do not always correspond to each other and how their expressions relate to patient outcomes remains unknown. Employing a double-staining method, we immunohistochemically investigated relationships between CSC marker expressions and patient outcomes.

**Material and Methods:** Primary invasive breast cancer samples from 61 patients who eventually developed recurrences after curative surgery were immunohistochemically examined. All patients were free of metastatic disease at the time of surgery and received standard adjuvant systemic treatments. Subtypes of primary tumours were; luminal type 65%, HER2 type 10% and triple negative 25%. The median disease free survival (DFS) and overall survival (OS) were 30 and 60 months, respectively. CD44(+) tumour was defined as more than 5% of cancer cells showing a CD44-positive and CD24-negative staining pattern on the cell membrane by the double-staining method. ALDH1 was also defined as positive when more than 5% of cancer cells showed cytoplasmic staining.

**Results:** Basically, the expression patterns of CD44 and ALDH1 in single tumours were completely different.

In oestrogen receptor (ER)-positive cases, CD44(+) tumours tended to be associated with longer DFS during the median 60-month observation period (69 vs 36 months). On the other hand, CD44(+) tumours were associated with shorter OS in ER(−) patients (23 vs 47 months). These results indicate that CD44 expression might reflect characteristics of luminal tumours to be effective to endocrine therapy and resistant to chemotherapy given after development of recurrent disease.

In ER(−) cases, ALDH1(+) tumours were associated with longer DFS (23 vs 10 months). Therefore, patients with CD44(−) and ALDH1(+) tumours were expected to have the best outcomes in our dataset. Indeed, median DFS and OS of CD44(−)ALDH1(+) tumours were longer than those in other triple negative patients (65 and 116 vs 30 and 60 months, respectively).

**Conclusions:** Populations of CD44(+)24(−) and ALDH1(+) cells in primary tumours were each related to the outcomes of patients who developed recurrences, but differently according to ER status. Combining several CSC markers might be useful for predicting patient outcomes and treatment effects.

**No conflicts of interest**

**177** Poster

**Analysis of clinicopathological features and the p53 expression in breast cancer**

M. Kikuyama[1], M. Sagawa[1], H. Kunimata[2], T. Oka[3], A. Tachibana[1]. [1]*Kanto Central Hospital of the Mutual Aid Association of Public School Teachers, Department of Breast Surgery, Tokyo, Japan;* [2]*Kanto Central Hospital of the Mutual Aid Association of Public School Teachers, Department of Radiology, Tokyo, Japan;* [3]*Kanto Central Hospital of the Mutual Aid Association of Public School Teachers, Department of Clinical Laboratory, Tokyo, Japan*

**Background:** The p53 alteration is known to be one of the prognostic factors in breast cancer. Immunohistochemistry (IHC) cannot detect all p53 mutations and the criteria hasn't been established. However, we considered that IHC was useful in clinical practice and confirmed the association between the p53 status by IHC and clinicopathological characteristics*. In this study, our goal was to perform independent validation study.

**Material and Methods:** We selected 129 patients who underwent breast cancer surgery between January 2006 and December 2008. The p53 expression status was measured using IHC and the cutoff value was determined as 45% based on our previous study.

**Results:** Out of the 129 patients, 20 patients (15.5%) were in the p53-high group (p53 expression $\geqslant$45%) and 109 patients (84.5%) were in the p53-low group (p53 expression <45%). The nuclear grade in the p53-high group was higher than that of the p53-low group ($p = 0.019$). The estrogen receptor was positive in 8 patients (40.0%) of the p53-high group and in 98 patients (89.9%) of the p53-low group ($p < 0.0001$). The progesteron receptor was positive in 6 patients (30.0%) of the p53-high group and in 76 patients (69.7%) of the p53-low group ($p = 0.0007$). The ki 67 was $\geqslant$14% in 20 patients (100.0%) of the p53-high group and in 46 patients (42.2%) of the p53-low group ($p < 0.0001$). The high expression of p53 was associated with poor disease-free survival ($p \leqslant 0.0001$). Overall survival in the p53-high group was shorter than in the p53-low group but there was no statistical significance ($p = 0.059$). Eight patients (40.0%) out of the 20 patients in the p53-high expression group relapsed and 7 of the 8 patients demonstrated a very high expression of p53 which was over 90%.

**Conclusions:** This study validated that the high expression of p53 by IHC was associated with poor prognoses, however other prognostic factors, not only p53 expression, impacted patients' outcomes. Further investigations are needed to implicate the p53 expression by IHC as a clinically meaningful biomarker.

*Discussion of the p53 research findings was submitted and presented at the 14th St. Gallen International Breast Conference.

**No conflicts of interest**

## Wednesday, 9 March 2016

POSTER SESSION

# Supportive and Palliative Care Including End of Life Treatment

**178** Poster

### Assessing quality indicators in breast cancer psychological support: is it feasible?

N. Beauloye[1], M. Aimont[1], I. Liebens[1], B. Carly[1], F. Liebens[1]. [1]*CHU Saint-Pierre, Isala Breast Unit, Brussels, Belgium*

**Background:** It has been recommended that all cancer patients be evaluated for symptoms of depression and anxiety throughout their trajectory of care. However data are scarce what concerns quality measurement in psychological counseling and support. To identify quality indicators (QI) that could be routinely used as tools to continuously monitor improvement of psychological care in women at the time of breast cancer (BC) surgery.

**Material and Methods:** From December 2014 to April 2015, all consecutive BC patients admitted for surgery were included. Anxiety and depression were assessed using HADS questionnaire. We collected three process QI: (1) the percentage of BC patients seen by the psycho-oncologists (minimal target: 85%); (2) the percentage of patients who received HADS questionnaire and, (3) the percentage of questionnaire returned. We also collected two outcome QI: (1) the percentage of respondents with significant emotional distress (minimal target: 35−50%) and (2) the percentage of distressed patients accepting "follow up" psychological services.

**Results:** The mean age of the studied population (n:70) was 56 years (range from 30 to 89). Fifteen patients were classified as Stage 0 BC, 33 as Stage I, 16 as Stage II, five as Stage III and one as Stage IV. Sixty-three (90%) patients were seen by the psycho-oncologists during their hospital stay (target: $\geqslant$85%). HADS questionnaire were delivered to 55 (78.5%) women only (target: >95%) and amongst them, 37 (67.3%) returned it (target: >90%). Fifteen patients (42%) were diagnosed with significant emotional distress and nine out of these (60%) attended the psychological consultation for further support (target: >90%).

**Conclusions:** This pilot study indicates that process and outcome QI can be measured easily and reliably. These QI measurements provide a tool for regular self-examination that can promote continuous quality improvement in BC psychological support.

**No conflicts of interest**

**179** Poster

### Ultrasound-guided intervention in management of locoregional neuropathic pain after breast cancer surgery

P. Steyerova[1], E. Blazkova[1], J. Kopecka[1], J. Danes[1]. [1]*General University Hospital Prague, Clinic of Radiology, Prague, Czech Republic*

**Background:** Locoregional neuropathic pain is one of the factors affecting quality of life of breast cancer survivors. Two nerves are mainly affected in the region of breast cancer surgery: intercostobrachial nerve and long thoracic nerve. High-resolution ultrasound can visualize both nerves and identify their lesions responsible for the clinical symptoms. The lesions are usually seen as nerve oedema or entrapment within a scar. Ultrasound-guided intervention is very precise and can help alleviate the painful symptoms with significant duration of time. The intervention carries minimum risk for the patient and is fast and cheap.

**Materials and Methods:** We evaluated interventions performed from February 2014 to September 2015. The included patients previously underwent breast and axillary surgery for breast cancer and complained of intermittent acute piercing pain with irradiation to axilla and proximal arm or along the lateral chest wall which has arisen after the treatment. The nerves and their lesions were identified using high-resolution ultrasound. Under ultrasound guidance mixture of local anaesthetic and corticoid was applied to the vicinity of the nerve lesion, with boost of anaesthetic to the scarring tissue. During follow-ups the patients were asked to provide information about the effect (with subjective quantification) and the period of its duration.

**Results:** We performed 10 interventions in 8 patients (aged 47−78 years) with history of mastectomy and axillary dissection (6 patients) or breast conserving surgery with sentinel node biopsy (2 patients). The affected nerve was intercostobrachial nerve in 7 cases, long thoracic nerve in 2 cases and both nerves in 1 case. The lesion was seen as nerve oedema in 6 cases and scarring with nerve entrapment in 4 patients.

Eight patients underwent single ultrasound-guided intervention; two patients had a repeated procedure with interval of 2 and 3 months. 4 interventions were done in the region of chest wall, 6 in the axilla.

The effect of the procedure ranged from 30 to 100% in 9 out of 10 patients. 2 patients were pain free following single intervention, one with on-going duration of 18 months, the second with duration of 9 months. 2 interventions were followed by a long-term (and still on-going) relief of 50 and 80% after 12 and 18 months. 5 procedures induced a period of 30−50% relief with duration of 1−2 months. Two patients also reported additional effects − improved mobility of the arm and softening of the scar. One patient had no effect of the procedure. We observed no complications.

**Conclusion:** Our experience suggests that identification of nerve lesions in patients after breast cancer surgery followed by ultrasound-guided intervention can be helpful in relieving locoregional neuropathic pain and improving quality of life of breast cancer survivors.

**No conflicts of interest**

**180** Poster

### A phase II prospective, randomized, double-blind, placebo-controlled multi-centre clinical trial to assess the safety of 0.005% estriol vaginal gel in hormone receptor-positive postmenopausal women with early stage breast cancer in treatment with aromatase inhibitors (AIs) in the adjuvant setting − Initial safety results

P. Sanchez Rovira[1], M. Gil Gil[2], J. Presa Lorita[1], J. Suárez Almarza[3], C. Nieto Magro[3]. [1]*Complejo hospitalario de Jaén, Medical oncology, Jaén, Spain;* [2]*L'Institut Català D'Oncologia I.C.O., Medical oncology, Barcelona, Spain;* [3]*ITF Research Pharma S.L.U., Medical, Madrid, Spain*

**Background:** 0.005% Estriol vaginal gel is a new formulation for local treatment of postmenopausal vaginal atrophy which delivers an ultra-low dose of estriol (50 μg) per application. A study is proposed with the hypothesis that 0.005% Estriol vaginal gel is a safe therapeutic option to treat symptoms of vaginal atrophy caused by AIs in women with breast cancer, without producing a significant decline in gonadotropins or increase in systemic estrogens. The Initial Safety Phase of the Study aims to preliminarily evaluate the influence of 0.005% estriol vaginal gel on hormonal levels and obtain safety data in an initial subset of women.

**Methods:** 70 women with breast cancer in treatment with AIs suffering from moderate/severe symptoms of vaginal atrophy are randomized to receive 1 g of either estriol gel or placebo gel (4:1) daily for 3 weeks and twice weekly up to 12 weeks. The initial safety phase comprised 10 women receiving estriol gel or placebo gel daily for 3 weeks. Serum FSH and LH were analyzed at screening, baseline and after 21 days. Estriol (E3), estradiol (E2) and estrone (E1) were determined at baseline and after 21 days by a newly developed and validated ultrasensitive LC-MS/MS assay (limit of quantification − LOQ: 1 pg/ml, 3 pg/ml and 5 pg/ml for E3, E2 and E1, respectively). Adverse events were also collected. Changes in hormonal levels were assessed to decide the study continuation to the second study phase. FSH changes from postmenopausal to premenopausal levels were primarily evaluated.

**Results:** 13 women were recruited and 10 were finally randomized. 2 of them were discontinued as they met one exclusion criteria. Mean (SD) FSH levels (mIU/ml) in women receiving estriol were 71.2 (15.7), 67.5 (23.9) and 68.1 (12.0) at screening, baseline and week 3 respectively, while were 70.3 (28.3), 66.9 (27.3) and 63.8 (20.4) in the 2 patients receiving placebo. No statistical differences between week 3 vs baseline were shown, and none of these women presented with changes in FSH from post- to pre-menopausal levels. Mean (SD) LH (mUI/ml) in women receiving estriol were 23.4 (7.9), 22.5 (9.1) and 24.3 (6.8) at screening, baseline and week 3 respectively, while they were 18.0 (3.5), 16.7 (2.5) and 17.5 (4.3) in placebo patients. No significant changes between pre and post-treatment values were observed. Levels of E3, E2 and E1 were below LOQ in all women at baseline, and remained below LOQ after treatment in all of them (except one in which the post-treatment sample was not collected). No relevant adverse events were shown.

**Conclusions:** These preliminary data suggest that 0.005% Estriol vaginal gel does not have an influence on hypophyseal axis or estrogen levels. These results must be confirmed in a larger group of women in the second phase of the study, where the safety and efficacy of estriol will be further evaluated.

**No conflicts of interest**

**181** Poster

**Treatment of bone metastatic breast cancer patients with denosumab in real life**

A. Irelli[1], V. Cocciolone[1], K. Cannita[2], L. Zugaro[3], M. Di Staso[4], P. Lanfiuti Baldi[2], S. Paradisi[1], T. Sidoni[2], C. Ficorella[1], E. Ricevuto[1]. *[1]Medical Oncology- S. Salvatore Hospital, Department of Biotechnological and Applied Clinical Sciences- University of L'Aquila, L'Aquila, Italy; [2]Medical Oncology- S. Salvatore Hospital, University of L'Aquila, L'Aquila, Italy; [3]Radiology- S. Salvatore Hospital, University of L'Aquila, L'Aquila, Italy; [4]Radiation Oncology- S. Salvatore Hospital, University of L'Aquila, L'Aquila, Italy*

**Background:** Efficacy of denosumab to delay or prevent skeletal-related events (SREs) has been significantly demonstrated in bone metastatic breast cancer (BMBC) patients. Real life data are useful to verify its proper indication.

**Material and Methods:** From July 2012 to April 2015 (33 months), 50 consecutive BMBC patients were treated with denosumab, 120 mg subcutaneously every 28 days, at Medical Oncology, San Salvatore Hospital, University of L'Aquila. Median age at diagnosis of metastatic disease was 61 years. ECOG PS was: 0, 29 patients (58%); 1, 15 (30%); 2, 6 (12%). Cumulative Illness Rating Scale (CIRS): primary, 19 (38%); intermediate, 17 (34%); secondary, 14 (28%). BM disease was: synchronous in 7 patients (14%), metachronous in 43 (86%); multiple sites 47 (94%), single site 3 (6%). Metastatic bone lesions: lytic, 19 (38%); blastic, 19 (38%); mixed, 12 (24%). Involved bone sites: column, 41 (82%); pelvis, 35 (70%); long bones, 27 (54%); others, 43 (86%). Involved visceral sites: liver, 14 (28%); lung, 9 (18%); brain, 5 (10%); others, 26 (52%). The extension of metastatic disease was: bone-only, 25 patients (50%); bone and visceral, 25 patients (50%). According to hormone receptor (HR)/Her2 status: HR positive/Her2 negative, 39 patients (78%); Her2 positive, 7 (14%); triple-negative, 4 (8%). Prior bisphosphonate treatment was administered in 22 patients (44%). Median number of denosumab cycles was 12 (range 1−33). Concomitant chemotherapy or hormonal therapy, and daily supplementation with calcium and vitamin D were administered. A baseline mouth assessment with orthopantomography of the jaws and dental visit was performed in all patients.

**Results:** Median time to skeletal metastases was 52 months. At median follow-up 36 months, median overall survival (OS) after diagnosis of BM was 94 months, with 14 events. At median follow-up 14 months after onset of denosumab, median OS was 32 months. Median number of SREs during denosumab treatment was 1; 4 patients (8%) had one SRE: radiation therapy (100%). Prior bisphosphonate treatment was administered in 3 out of these 4 patients (75%). Median time to first SRE after diagnosis of bone metastases was 72 months (range 28–157). Median time to first SRE after the start of denosumab was 12 months (2−19). Median OS after first SRE was not reached. Adverse events overall were: G3 hypocalcemia, 2%; G2 hypocalcemia, 4%; G2 dyspnoea, 8%; G2 diarrhea, 10%; toothache, 4%; dental infection, 4%. In the subgroup of patients not treated with bisphosphonates (28 patients), the toxicity profile was: G3 hypocalcemia, 4%; G2 hypocalcemia, 4%; G2 dyspnoea, 4%; G2 diarrhea, 11%; no toothache and dental infection occurred.

**Conclusions:** Our experience confirms efficacy of denosumab to control SREs with acceptable toxicity profile.

**No conflicts of interest**

**182** Poster

**Taste, smell and food preferences during chemotherapy in breast cancer patients**

Y. De Vries[1,2], R. Winkels[1], S. Boesveldt[1], M. Van den Berg[1], A. De Kruif[3], H. Van Laarhoven[4], E. Kampman[1], K. De Graaf[1]. *[1]Wageningen University, Division of Human Nutrition, Wageningen, Netherlands; [2]Top Institute Food and Nutrition, N/A, Wageningen, Netherlands; [3]VU University, Department of Health Sciences, Amsterdam, Netherlands; [4]Academic Medical Center, Department of Oncology, Amsterdam, Netherlands*

**Background:** Changes in taste and smell perception are an important and burdensome side effect of chemotherapy in cancer patients with a prevalence of 8% to 85% for taste and smell changes. However, literature is inconsistent in reporting the nature and prevalence of these changes due to differences in study design, tumour type and treatment. Since sensory characteristics are main drivers of food choice and intake, this may be affected as a result of olfactory and gustatory changes during chemotherapy. However, to what extent and in which direction sensory changes may affect food preferences is largely unknown. The aim of the current study is to follow and characterize sensory changes and food preferences in breast cancer patients treated with chemotherapy.

**Materials and Methods:** 30 women with incident newly-diagnosed breast cancer treated with chemotherapy and 30 age-matched women without breast cancer (age 52.0 years versus 52.2 years respectively) were followed in the course of time. Patients were measured before start of chemotherapy, halfway and 1−3 weeks after the end of treatment. A similar time frame was used for the control group. Gustatory and olfactory function was assessed with Taste Strips and the Sniffin' Sticks test battery (Burghart Wedel, Germany) respectively. Food preferences were assessed using a computer based task with food pictures from four macronutrient categories (high fat, high carbohydrate, high protein and low energy) including both sweet and savoury food products.

**Results:** Preliminary results show a decrease in gustatory function during chemotherapy compared to the control group, results on olfactory function show no clear change during chemotherapy. Follow-up measurements and analyses are currently ongoing, updated results of gustatory and olfactory functioning including results of food preferences will be presented at the conference.

**Conclusion:** Results from the current study will give more insight in the effect of chemotherapy on sensory perception and food preferences and may be an underlying factor for weight changes seen in breast cancer during chemotherapy. Eventually these results may help creating for better nutritional advices for breast cancer patients during chemotherapy treatment.

**No conflicts of interest**

**183** Poster

**Scalp cooling: Perceptions and experiences of Australian and Dutch health professionals**

F. Boyle[1], J. Shaw[2], B. Baylock[2], L. Pugliano[1], K. Andrews[1], C. Van den Hurk[3]. *[1]Mater Hospital, Patricia Ritchie Centre for Cancer Care and Research, Sydney, Australia; [2]University of Sydney, Psycho-oncology Co-operative Research Group, Sydney, Australia; [3]Netherlands Comprehensive Cancer Organisation, Research, Utrecht, Netherlands*

**Background:** Chemotherapy-induced alopecia (CIA) is a common and distressing side effect for patients. Scalp cooling with coolant based devices to reduce CIA has been available in Europe for more than a decade, but has only recently been introduced in Australia. It is mainly used by breast cancer patients. We explored health professionals' knowledge of and attitudes to scalp cooling to identify barriers and facilitators to the implementation and use of scalp cooling in both countries.

**Material and Methods:** In Australia a qualitative study was conducted with 21 cancer care professionals in 5 oncology departments (4 with and 1 without scalp cooling). In the Netherlands a quantitative study was conducted with 100 Medical Doctors (MDs) and 49 nurses (half of them in hospitals with scalp cooling).

**Results:** Although there have been different lengths of exposure to scalp cooling in both countries, outcomes were overall comparable. 1) CIA was considered an important side effect worthy of intervention. (2) Professionals were overall satisfied with the results of scalp cooling. (3) There is need for empirically derived information to address current scalp cooling knowledge-gaps, mainly for patient selection. Over one-third of the Dutch professionals perceived their knowledge about efficacy and scalp skin metastases insufficient to inform their patients well. (4) About one third of MDs expected scalp cooling to be too burdensome for patients. (5) Scalp cooling was not offered to all eligible patients. (6) Previous scalp cooling experiences, including experience with non-coolant based systems influenced professional attitudes to scalp cooling. (7) Integration of the technology requires adjustments to nursing practice to manage the increased time, workload and change in patient flow.(8) Information for patients on hair care during treatment is vital.

**Conclusions:** Compilation of up to date knowledge of efficacy, safety and tolerability is required for implementation of scalp cooling in routine care in both countries. The results highlight that professional attitudes drive the introduction of scalp cooling and strategies to manage the change in nursing practice are essential for patients to have better access to this valued supportive care strategy. International collaborations to improve information for professionals and patients are underway.

**No conflicts of interest**

**184** Poster

**Fatigue among breast cancer patients who underwent radiotherapy at the National Center for Radiotherapy and Nuclear Medicine, Accra, Ghana**

S. Opoku[1]. *[1]University of Ghana, Department of Radiography, Accra, Ghana*

**Background:** Fatigue is one of the symptoms most frequently reported by breast cancer patients during and after treatment which impacts upon

their quality of life. The condition is caused by the cancer and its treatment and often interferes with daily activities. However the prevalence of fatigue in breast cancer patients and its associated factors in Ghana is unknown. Therefore a study to determine the prevalence of fatigue among these patients and also to identify the coping mechanisms and interventional strategies to help improve breast cancer care was undertaken.

**Material and Methods:** This was a qualitative cross sectional survey carried out at the National Centre for Radiotherapy and Nuclear Medicine, Korle Bu Teaching Hospital, Accra Ghana involving 40 patients. Data was collected using a structured questionnaire in the form of a modified 'Fatigue Symptom inventory scale'.

**Results:** Various degrees of fatigue ranging from mild to extreme were observed two weeks into radiotherapy. Mild fatigue accounted for 12.5%, of the patients whilst 37.5% experienced extreme fatigue. Majority of the patients representing 42.5% experienced moderate fatigue but 7.5% reported no occurrence of fatigue. Various coping mechanisms and strategies in dealing with fatigue were reported by the participants. These include sleeping, self medication and seeking medical help among others.

**Conclusion:** This study identified high prevalence rates of fatigue among the breast cancer patients who participated in the study.

**No conflicts of interest**

## Thursday, 10 March 2016

**POSTER SESSION**

# Local Regional Treatment − Radiotherapy

**185** Poster

### Comparison of acute and late toxicity with hypofractionated to conventional radiation therapy (RT) for early breast cancer

T. Mehmood[1]. [1]*Shaukat Khanum Memorial Cancer Hospital and Research Centre, Radiation Oncology, Lahore, Pakistan*

**Objective:** The purpose of the present study is to evaluate toxicity and cosmetic outcome in breast cancer survivors treated with hypo-fractionated adjuvant radiotherapy (HFRT) and to identify risk factors for toxicity, with special focus on the impact of age, co morbidities and chemotherapy.

**Materials and Methods:** From January 2012 and December 2013, 169 women with early breast cancer were treated with HFRT, after conserving surgery. The patients received 40.05 Gy in 15 fractions. The boost to the tumor bed was administered with a total dose of 9 Gy in 3 consecutive fractions in 50 women due to young age (<50 years) or to positive margins. Physician-rated toxicity and cosmetic outcomes were prospectively assessed during 6 monthly follow-up after radiotherapy. For comparison, a group of 65 patients with similar characteristics and consecutively treated with conventional fractionation was retrospectively selected.

**Results:** In the HFRT group, the mean age was 64 years. Pathological tumor stage; pTis = 17%, pT1a = 6%, pT1b = 23%, pT1c = 41% and pT2 = 13%; 12% had estrogen-receptor-negative disease and 32% had high-grade disease. Pre-operative chemotherapy was administered in 5% of patients; adjuvant systemic therapy and hormone therapy were given in 8% patients, while 15% and 73% patients received chemotherapy or hormone therapy alone, respectively. The mean follow-up duration was 19.2 months (range 6−32 months). The median time from surgery was 31 days, with overall median treatment duration of 24 days. At last follow up, all patients were alive without local recurrence. By the end of RT, 19% of the patients treated with HFRT developed no toxicity, while 54.7% showed grade I and 13.3% grade II acute skin toxicity. Only one patient experienced grade III acute skin toxicity. In the control group, early grade I reactions were observed in 42%; 19% of patients showed grade II acute toxicity and only one patient developed grade III acute reaction. Neither grade IV skin ulceration nor soft tissue necrosis was observed. Late toxicity was assessed after 6 months from RT completion in 109/169 patients in the hypofractionation group and in 53/65 patients in the standard RT group. Late toxicity according to the RTOG criteria was observed in 7.5% in the HFRT group and in 8% in the conventional fractionated radiation group. The difference was not statistically significant ($p = 0.09$). Cosmetic result was assessed and scored at the RT end and 6 months later: at last follow up, 73% of women in the control-group as compared with 69% of the women in the HFRT group had a good or excellent cosmetic outcome.

**Conclusions:** Our results confirm the feasibility of the HFRT with acceptable late toxicity and cosmetic outcome as compared with conventional RT group. This further needs to be evaluated in large scale clinical trials.

**No conflicts of interest**

**186** Poster

### Accelerated partial-breast irradiation for early breast cancer using proton radiation therapy (Initial clinical experience: Phase I/II study)

E. Ogo[1], U. Toh[2], N. Iwakuma[2], M. Mishima[2], K. Arimura[3], T. Ogino[3], Y. Hishikawa[3], M. Kubo[4], R. Nishimura[5], S. Mitsuyama[6]. [1]*Kurume University Hospital, Radiation Therapy Center, Kurume, Japan;* [2]*Kurume University Hospital, Surgery, Kurume, Japan;* [3]*Medipolis Proton Therapy and Research Center, Radiation Oncology, Ibusuki, Japan;* [4]*Kyushu University, Surgery, Fukuoka, Japan;* [5]*Kumamotoshinto General Hospital, Surgery, Kumamoto, Japan;* [6]*Kitakyushu Municipal Medical Center, Surgery, Kutakyushu, Japan*

**Purpose:** Proton therapy allows for radiation delivery to targeted areas using decreased radiation dose to healthy surrounding tissues when compared with standard radiation (photon). The accelerated partial-breast irradiation (ABPI) is given to the low risk early breast cancer patient after partial operation as a clinical trial. We present our initial clinical experience with proton beam for early breast without operation.

**Material and Methods:** We treated early breast cancer patients without operation in a phase I/II clinical trial. The indications are (1) T1N0 (UICC); single tumor size is less than 1.5 cm by MMG and/or US, (2) no malignant calcification, (3) histology in invasive ductal carcinoma, (4) no high lympatic invasion, (5) ER(+) PgR(+) HER2 negative, (6) age is between 40 and 70 years old, (7) height is less than 175 cm and weight is less than 70 kg, (8) no axillary lymph node and distant metastases, (9) performance scale; 0−1, (10) patients approve of this clinical trial. The proton treatment (phase I study) is delivered 64.4GyE/26 fractions and 70.2GyE/2 fractions. The recommended phase II dose is decided after phase I study. We used by field in field technique. Patients are followed at one, 3, 6, and 12 months, and 6 months thereafter for recurrent disease, cosmetic outcome, toxicity, and patient satisfaction. If the local recurrence occurs, patients will have to undergo recurrent cancer removal. It will be acceptable to do reconstruction after mastectomy.

**Results:** We started this clinical trial in June 2015. We can make a high quality proton dose volume histogram for small breast cancer. The first case had 5 mm single breast cancer, and underwent proton therapy in 64.4GyE/26 fractions. We have very good local control after partial proton therapy. The acute complication, such as dermatitis, is acceptable.

**Conclusion:** There are some preliminary clinical observations and Limitations although proton ABPI without operation anticipates excellent results in the restricted criteria. The biggest challenge is immobilizing the breast tissue adequately to specifically target the breast cancer.

**No conflicts of interest**

**187** Poster

### The management of local advanced breast cancer

A. Rafik[1], N. Bahechar[1], A. Chlihi[1]. [1]*CHU Ibn Rochd, National Center of Burns and Plastic Surgery, Casablanca, Morocco*

**Background:** Locally advanced breast cancer are frequent in our context and a therapeutic problem registering as part of a multidisciplinary support. They are a double problem for the plastic surgeon: the operability and the resultant substance loss cover. This work has aimed to clarify the place of plastic surgery before these tumors locally advanced together with oncologists for the indication of a curative or palliative resection and coverage of the resulting substance losses, and to ask in a palliative resection a thoughtful indication, after neo adjuvant chemotherapy and not from the outset.

**Material and Methods:** Our retrospective study consists of 150 cases of breast cancers locally advanced admitted to the Department of surgery plastic and burned the CHU IBN ROCHD in Casablanca, from January 2011 to January 2015. 120 patients were initially seen with locally advanced tumors, and 30 others were admitted for recurrence after curative resection.

**Results:** The Age of patients is 34 a 65 years (means: 45 years of age), the clinical aspect of tumors: ulcerations 36%, nodule 35%; closet 29%, size >6 cm: 75%. Oncology profiles: standing T3 and T4 (58.8%); EPI II and III (20%); grading SBR: (Grade III 52%, Grade II 21.8%), type histological galactophoric carcinoma 82%; N+ 88%. The treatment was on plan: surgical: wound excision with like terms of coverage: latissimus dorsi flap (120 cases); the pedicled TRAM flap: 30 cases, Adjuvant: curietherapy 35%; Radiotherapy (63%); Chemotherapy 30%. Complications: partial necrosis 06 cases, infection 05 cases, suffering post radiotherapy 02 cases. The closure of first intention of the donor zone was possible in most patients and a supplement by a skin graft was needed in 12 cases. Local recurrence was 23% after a median follow-up of 86 months.

**Conclusion:** Despite progress in screening, locally advanced breast cancer, remain frequent in the Morocco. Support for these cancers is a collaboration between the oncologist and the plastic surgeon. When

possible, preoperative chemotherapy offers more chance by carcinologic satisfactory resection. The methods of cover by shreds pedicules initial (latissimus dorsi and great law) are reliable to cover the large resulting PDS do not increase morbidity and does not delay the adjuvant treatment. However, the best ways remain prevention by a wide public awareness and a generalization of the means of screening.

**No conflicts of interest**

**188** Poster

**The modern approach of combination of breast cancer therapy using the intraoperative radiation therapy**

A. Manikhas[1], I. Grinev[1], R. Babeshkin[1], L. Lee[1], A. Oganesyan[1], V. Skvortsov[1], A. Shemerovsky[1], G. Manikhas[1], I. Avramenko[1]. [1]*City Clinical Oncology Dispensary, Oncomammology, Saint-Petersburg, Russian Federation*

**Objective:** to evaluate the usage of intraoperative radiation therapy device INTRABEAM with in breast cancer patients after neoadjuvant therapy, when conservative surgery is allowed.

**Materials and Methods:** 18 patients are currently taken for the investigation. Sentinel lymph node biopsy has been done for all patients followed by systemic drug therapy depending on the tumor's phenotype and lymph node status signal. When conservative surgery was allowed, lumpectomy with intraoperative radiation therapy with INTRABEAM were performed for patients according to the positive tumor response. This approach is considered to provide the additional tumor bed boost. Thereafter external beam radiotherapy performed and patients received systemic adjuvant treatment. Three patients have triple-negative tumor phenotype, 8 − luminal type A and 7 − luminal type B present.

**Results:** Metastasis in the sentinel lymph nodes were identified in 7 patients among 18 examined patients (US exam identified suspicious metastatic lymph nodes in 3 cases). FAC regimen was assigned to 9 patients, the remaining nine patients received aromatase inhibitors (exemestane). For now, lumpectomy with intraoperative radiation therapy was done for 9 patients. Axillary lymph node dissection was done in 1 case due to the presence of 3 sentinel lymph nodes which had a metastatic change. The full complex of our treatment approach has been already made for 4 patients.

**Conclusion:** The current research is conducted to investigate if a comprehensive approach to the treatment of resect breast cancer can be the alternative way of reconstructing plastic surgery. The usage of intraoperative radiation therapy to the tumor bed may reduce the risk of local recurrence, which was specified in previous studies. Biopsy of sentinel lymph node, performed prior systemic therapy, is justified by research results of SENTINA, and allows some patients with favorable conditions to avoid traumatic intervention by axillary lymph node dissection.

**No conflicts of interest**

**189** Poster

**Accelerated partial breast irradiation versus whole breast radiotherapy: Quality of Life results from a phase 3 randomized trial and focus on patients aged 70 years or older**

I. Meattini[1], C. Saieva[2], I. Desideri[1], C. De Luca Cardillo[1], V. Scotti[1], G. Miccinesi[2], P. Bonomo[1], L. Orzalesi[3], M. Bernini[3], D. Casella[3], L.J. Sanchez[3], J. Nori[4], S. Bianchi[5], L. Livi[1]. [1]*Azienda Ospedaliero-Universitaria Careggi − University of Florence, Radiation Oncology Unit, Florence, Italy;* [2]*ISPO, Istituto per lo Studio e la Prevenzione Oncologica, Florence, Italy;* [3]*Azienda Ospedaliero-Universitaria Careggi − University of Florence, Breast Surgery Unit, Florence, Italy;* [4]*Azienda Ospedaliero-Universitaria Careggi − University of Florence, Radiology Senology Unit, Florence, Italy;* [5]*Azienda Ospedaliero-Universitaria Careggi − University of Florence, Pathology Unit, Florence, Italy*

**Background:** Accelerated partial breast irradiation (APBI) represents a valid option for selected early breast cancer (BC); potential advantages of APBI include shorter treatment time and improved safety profile, assuming an equivalent disease control rate.

We recently published the 5-years median follow-up results of a phase 3 randomized trial (ClinicalTrials.gov, NCT02104895), showing a very low rate of disease failure. We also observed a significant impact on patients compliance in terms of acute and early late toxicity, and a consistent improvement of overall quality of life (QoL) in the whole series.

The aim of the present analysis is to compare the QoL results of the whole series focusing on the subgroup of patients aged 70 years or older, treated with either APBI or whole breast irradiation (WBI).

**Material and Methods:** Eligible patients of the trial were women aged more than 40 years old with early BC suitable for breast conserving surgery. At the end of radiotherapy, patients were asked to compile two specific questionnaires on QoL, the EORTC QLQ-C30, and the BR23 module as a supplementary questionnaire for issues relevant to patients with BC. Overall 205 patients (105 APBI, and 100 WBI) fully completed the given questionnaires. Concerning patients aged 70 years or older, 43 patients fully completed the questionnaires (23 APBI, and 20 WBI).

**Results:** Concerning the whole series, significant differences between the two arms emerged by global health status (GHS; $p = 0.0001$) and most functional and symptom scales, with better outcomes in the APBI arm. Women treated with APBI reported a significantly better QoL in terms of physical, role, emotional and social functioning ($p < 0.01$). Among the functional scales of BR23 module, the body image perception and the future perspective were significantly better in the APBI group ($p = 0.0001$). Significant differences ($p = 0.0001$) emerged also for symptom scales (breast and arm symptoms), with better scores for APBI group.

Focusing on patients aged 70 years or older, evaluation of the functional and symptom scales of EORTC QLQ-C30 module showed no significant differences in terms of GHS and most functional and symptom scales assessment. Conversely, we reported significant differences concerning functional and symptom scales scores of BR23 module. Among the functional scales, the body image perception was significantly better in the APBI group ($p = 0.007$). Significant impact ($p = 0.008$) emerged also for symptom scales (breast symptoms), with better scores for APBI group.

**Conclusions:** Overall, women treated with APBI reported a significant better QoL outcome. Although the small sample size, also in the elderly group of patients we observed a significant positive impact on functional and symptoms features in favor of the APBI arm.

**No conflicts of interest**

**190** Poster

**EORTC breast cancer survivorship project: First analysis of 3 large early breast cancer radiotherapy trials**

C. Vrieling[1], L. Moser[2], L. Collette[3], J. Bogaerts[3], S. Collette[3], S. Litière[3], L. Slaets[3], P. Poortmans[4], E. Rutgers[5], H. Struikmans[6], G. Van Tienhoven[7], H. Bartelink[8], A. Fourquet[9]. [1]*Clinique des Grangettes, Department of Radiation Oncology, Geneva, Switzerland;* [2]*Champalimaud Cancer Centre, Department of Radiation Oncology, Lisbon, Portugal;* [3]*EORTC Headquarters, Department of Statistics, Brussels, Belgium;* [4]*Radboud university medical center, Department of Radiation Oncology, Nijmegen, Netherlands;* [5]*The Netherlands Cancer Institute, Department of Surgery, Amsterdam, Netherlands;* [6]*Medical Center Utrecht, Department of Radiation Oncology, Utrecht, Netherlands;* [7]*Academic Medical Center, Department of Radiation Oncology, Amsterdam, Netherlands;* [8]*The Netherlands Cancer Institute, Department of Radiation Oncology, Amsterdam, Netherlands;* [9]*Institut Curie, Department of Radiation Oncology, Paris, France*

**Background:** The analysis of 3 successive European Organization of Research and Treatment of Cancer (EORTC) trials in early breast cancer (EBC) created a unique opportunity to obtain insight in time-trends in treatment and clinical outcome.

**Material and Methods:** The EORTC boost/no-boost trial (1989–1996; 5318 patients) randomized patients treated with breast-conserving surgery and whole breast irradiation (BCT) between a radiotherapy (RT) boost and no further treatment. The Internal Mammary-Medial Supraclavicular (IM-MS) trial (1996–2004; 4004 patients) randomized patients with positive axillary nodes and/or centrally located tumor between IM-MS RT or not. In the AMAROS trial (2001–2010; 1425 patients randomized) sentinel node positive patients were randomized between axillary lymph node dissection (ALND) and axillary RT (ART). Of the 10,747 patients included, 5,018 patients are still in follow-up (FU). The median FU ranged from 17.2 to 6.1 years. A descriptive analysis is provided.

**Results:** Around 60% of patients were postmenopausal. Most patients had a pT1 tumor: 80% in the boost trial, 61% in the IM-MS trial and 66% in AMAROS. The proportion of patients with nodal involvement increased from 21%, 56%, to 97%, respectively, reflecting studies' entry criteria.

In the boost trial, all patients had BCT, compared to 76% in the IM-MS trial and 82% in AMAROS. ART was given in 5 and 8% of patients in the boost and IM-MS trial, respectively. IM-MS RT was given in 21% and 10% of patients in the boost and AMAROS trial, respectively. Adjuvant systemic therapy was not protocolized. Chemotherapy use increased over time: 12% in the boost trial, 55% in the IM-MS trial and 61% in AMAROS. A similar trend was observed for the use of endocrine therapy: 18%, 60%, and 78% in the 3 trials, respectively.

The 10-year overall survival (OS) was around 80% and the 10-year breast cancer mortality (BCM) around 13% in all trials (Table). The 10-year progression-free survival (PFS) varied between 66% in the boost trial and 75% in AMAROS. The 10-year cumulative local relapse rate (LRR)

Table (abstract 190).

| | Boost | | IM-MS | | AMAROS | |
|---|---|---|---|---|---|---|
| | Boost | No-Boost | RT | No RT | ALND | ART |
| % pN positive | 21 | 21 | 56 | 56 | 93 | 100 |
| % 5-yr OS (95% CI) | 92 (90–93) | 91 (90–92) | 92 (90–93) | 90 (89–92) | 93 (91–95) | 93 (90–94) |
| % 10-yr OS | 81 (79–82) | 81 (79–83) | 82 (80–84) | 81 (79–83) | 83 (77–87) | 75 (65–82) |
| % 10-yr BCM | 13 (11–14) | 13 (12–14) | 13 (11–14) | 14 (13–16) | 12 (8–16) | 20 (12–28) |
| % 10-yr PFS | 68 (66–69) | 66 (65–68) | 72 (70–74) | 69 (67–71) | 75 (68–81) | 70 (63–76) |
| % 10-yr LRR | 6.5 (5.5–7.4) | 10.2 (9.0–11.4) | 4.2 (3.3–5.1) | 4.8 (3.8–5.8) | 1.8 (0.8–2.7) | 1.3 (0.5–2.2) |

decreased from 6% to 1% over time. The main cause of death was related to breast cancer, death related to cardiovascular disease or secondary cancer was 3% or less in all trials.

**Conclusions:** Over time and despite less favorable prognostic factors in the EBC patients included in the more recent trials, local control improved and 10-year OS and BCM remained stable at 80% and 13%, respectively.

**No conflicts of interest**

**191** Poster

### Hydrosorb® versus control (water based spray) in the management of radiodermatitis: Results of multicentre controlled randomized trial

L. Bazire[1], I. Fromantin[2], A. Diallo[3], B. De la Lande[4], V. Pernin[1], R. Dendale[1], A. Fourquet[1], A. Savignoni[3], Y. Kirova[1]. *[1]Institut Curie, Radiotherapy, Paris, France; [2]Institut Curie, Plaies et Cicatrisations, Paris, France; [3]Institut Curie, Recherche Clinique, Paris, France; [4]Institut Curie, Radiotherapie, Saint-cloud, France*

**Purpose:** to report the efficacy of Hydrosorb® versus control (water based spray) as topical treatment of grade 1−2 radiodermatitis in patients (pts) treated for early stage breast cancer (BC) with normo fractionated radiotherapy (RT).

**Patients and Methods:** BC pts were randomised to receive either Hydrosorb® (A) or water based spray (B). The primary endpoint was local treatment failure defined as interruption of RT because of skin radiotoxicity or change of local care because skin alteration. Secondary endpoints were: evaluation of skin colorimetry, pain, quality of life.

**Results:** Two-hundred seventy eight pts were enrolled. There were 186 successfully treated pts. There were 60 "failures" in the Hydrosorb® arm, and 62 in the control arm ($p = 0.72$), but mostly without interruption of the RT. Twenty-four pts stopped RT for local care. The average absolute reduction of colorimetric levels between day 28 and day 0 was 4 in the Hydrosorb®, and 4.2 in the water spray groups, respectively ($p = 0.36$). Forty-eight patients in the Hydrosorb® arm had a VAS >2 versus 51 pts in the placebo arm, i.e. 34% and 38%, resp. ($p = 0.45$). A significant reduction of pain was observed on D7 and D21 in the Hydrosorb® arm.

**Conclusions:** This study showed no significant difference between Hydrosorb® and simple water spray in the treatment of acute radiodermatitis even if there was slight pain improvement at the first weeks. Systematic prevention measures and modern breast RT techniques allow excellent tolerability, but the place of topical treatment to optimize this tolerability has yet to be defined.

**No conflicts of interest**

**192** Poster/Poster Spotlight

### The SUPREMO Trial − Pathology quality assurance of a large phase 3 randomised international clinical trial

J. Thomas[1], A. Hanby[2], G. Van Tienhoven[3], N. Russell[4], K. Riddle[5], D. Cameron[6], J. Bartlett[7], T. Piper[6], C. Cunningham[6], P. Canney[8], I. Kunkler[6]. *[1]Nhs Lothian, Pathology, Edinburgh, United Kingdom; [2]Leeds Institute of Cancer Pathology- University of Leeds, Pathology, Leeds, United Kingdom; [3]Academic Medical Center, Radiation Oncology, Amsterdam, Netherlands; [4]The Netherlands Cancer Institute − Antoni Van Leeuwenhoek Hospital Nki-avl, Department of Radiotherapy, Amsterdam, Netherlands; [5]Scottish Clinical Trials Research Unit- Nhs National Services- Scotland, Scottish Clinical Trials Research Unit, Edinburgh, United Kingdom; [6]University of Edinburgh, Edinburgh Cancer Research Centre, Edinburgh, United Kingdom; [7]Ontario Institute of Cancer Research, Maars, Ontario, Canada; [8]University of Glasgow, Beetson Oncology Centre, Glasgow, United Kingdom*

**Background:** SUPREMO is a phase 3 randomised trial evaluating radiotherapy post-mastectomy for intermediate risk breast cancer accruing 1688 patients from 16 countries between 2006 and 2013. It was coordinated by the Scottish Clinical Trials Unit, Edinburgh. Intermediate risk was defined as either node-positive disease of any grade in tumours $\leqslant 5$ cm diameter (T1 or T2), or T2 node-negative tumours that were either grade 3 and/or showed lymphatic invasion, or T3N0 tumours, independent of pathological features. Central pathology review was carried out for quality assurance. We report the results of this review.

**Methods:** The two reviewing pathologists were sent a single H&E section and were blinded to the original reported pathology and all patient-related data including nodal status. The review comprised tumour type, histological grade and lymphatic invasion. The slides from potentially ineligible patients by central review were scanned and reviewed online together by the two pathologists and a consensus reached. A subset of 25 of these cases was double-reported independently by the pathologists as an additional comparison.

**Results:** The two major contributors to the trial were the UK (75%) and the Netherlands (10%). There were no significant differences in the overall reporting profiles (grading and lymphatic invasion) of different countries. There were 1215 node-positive patients and 414 node-negative patients. 1369 (82.0%) of cases were reviewed and the pathologists reviewed 406 and 963 cases respectively. Of the node-negative cases 104 (25.1%) would have been deemed ineligible by initial central review by virtue of grade and/or lymphatic invasion status. Following online consensus review this figure fell to 70 cases (16.9%). The reviewing pathologists show similar reporting profiles with no evidence of case selection bias. There is a striking difference in lymphatic invasion rates (41.2% v 15.1% (UK); $p \leqslant 0.0001$) and proportions of grade 3 carcinomas (54.6% v 42.4% (UK); $p \leqslant 0.0001$) on comparing local reporting with central review. There was no significant difference in the locally reported lymphatic invasion rate in the node-negative and node-positive groups (38.2% v 39.6%; $p = 0.76$) whereas the reviewing pathologists found significant differences between these groups (10.3% v 16.9%; $p = 0.003$).

**Conclusions:** These data have important implications for the interpretation of outcomes from this clinical trial and the design of future trials and how they are powered. If critical pathology criteria are determinants for trial-entry serious consideration needs to be given to up-front central pathology review. The use of slide scanning technology can facilitate such QA exercises. The lack of difference in pathology reporting profiles in different countries lends encouragement to mounting international trials in the future.

**No conflicts of interest**

**193** Poster

### Can personalized treatment reduce cardiotoxicity in left breast cancer radiotherapy?

S. Cima[1], M.C. Valli[1], M. Frapolli[1], G. Nicolini[2], N. Azinwi[1], S. Presilla[2], A. Richetti[1]. *[1]Centro Di Senologia Della Svizzera Italiana, Radiation Oncology, Bellinzona, Switzerland; [2]Ente Ospedaliero Cantonale, Medical Physics Service, Bellinzona, Switzerland*

**Background:** Radiation treatment to the left breast could be associated with increased cardiac morbidity and mortality. Moreover young women could experience an increased risk of cardiotoxicity due to a longer perspective of life and a wider use of cardiotoxic adjuvant chemo/immunotherapy. Cardiac mortality ratio for left vs right breast radiotherapy treatment was 1.42 at 10−14 years and 1.58 at more than 15 years with old radiotherapy techniques. (Darby SC et al. N Engl J Med 2013; G. Curigliano et al ESMO Clinical Practice Guidelines). Noteworthy advanced radiation techniques and personalized setup are associated with a lower cardiac toxicity. We compared 3 different techniques to perform an adjuvant radiation treatment planning, analyzing the dose given to the heart and Left Anterior Descending coronary artery (LAD).

**Material and Methods:** A 35 year-old woman underwent a virtual Computer Tomography (CT) simulation in three different sets: supine position with free breathing$_1$, supine position with deep inspiration breath hold (DIBH)$_2$ and prone position$_3$. Left breast and organs at risk (lungs, heart, controlateral breast and LAD) were outlined on CT slices. The total dose prescribed to the breast was 50 Gy followed by 16 Gy to the tumoral

bed. Dose volume histograms (DVHs) of left breast and organs at risk were calculated. Maximum dose (Dmax) and mean dose (Dmean) to the heart and LAD in the 3 different scenarios were compared.

**Results:** See the table. The Dmean to the heart was reduced by 74% and 82% with DIBH and prone setup when compared to the supine free breathing one. The Dmean to the LAD was reduced by 79% and 83% with DIBH and prone setup respectively in comparison to the supine position. The heart and LAD Dmax was 44.7 Gy and 29.0 Gy with DIBH; 21.4 Gy and 18.5 Gy in prone setup; 50 Gy and 6.3 Gy in supine free breathing position.

| Technique | Dose (Gy) | | | |
|---|---|---|---|---|
| | LAD | | Heart | |
| | Max | Mean | Max | Mean |
| Free breathing | 49.8 | 29.7 | 50.0 | 6.3 |
| DIBH | 29.0 | 6.2 | 44.7 | 1.6 |
| Prone | 18.5 | 4.9 | 21.4 | 1.1 |

**Conclusions:** There is evidence that any reduction of radiation exposure to the heart will lower the incidence of ischemic heart disease in patients with breast cancer We demonstrate that DIBH increases the distance between the breast target and the heart/LAD, reducing the dose given to these organs. The prone position permits a much better avoidance of the heart and LAD, even if the distance is not improved. Recently reported data demonstrate that more sophisticated RT techniques and setup reduce acute and late cardiotoxicity. Therefore in our department we are treating all the left breast cancer patients with DIBH and we are improving the prone position technique for offering the best personalized treatment.

**No conflicts of interest**

**194** Poster

**IOERT versus external beam APBI after breast conserving surgery: preliminary results of a non-randomized comparative study**

H. Struikmans[1], U. Fisscher[1], M. Mast[1], A. Petoukhova[1], A. Marinelli[2], J. Van der Sijp[2], T. Van der Lans[2], J.H. Franssen[3], J. Merkus[4], I. Jannink[4], G. Speijer[3], F. Gescher[3], E. Roeloffzen[5], L. Zwanenburg[5], P. Koper[1]. *[1]Medisch Centrum Haaglanden/Bronovo, Radiotherapy, The Hague, Netherlands; [2]Medisch Centrum Haaglanden/Bronovo, Surgery, The Hague, Netherlands; [3]HagaZiekenhuis, Radiotherapy, The Hague, Netherlands; [4]HagaZiekenhuis, Surgery, The Hague, Netherlands; [5]Isala ziekenhuis, Radiotherapy, Zwolle, Netherlands*

**Background:** In 2011 we started a non-randomized comparative study about external beam "Accelerated Partial Breast Irradiation" (ABPI) versus IntraOperative Electron RadioTherapy (IOERT) after breast conserving surgery. Endpoints are: efficacy; toxicity; quality of life; frailty scores; cosmetic results.

**Material and Methods:** Written informed consent was obtained in all cases. We included low risk breast cancer patients: age $\geqslant$60 years and a tumour diameter of $\leqslant$3 cm: if the diameter was >2 cm the Her2 receptor status had to be negative and the estrogen receptor status had to be positive. Patients with multicentric disease, lymph node metastasis, irradical resection, contralateral breast cancer and/or history of malignant disease <5 year before diagnosis or recurrent disease was not included. IOERT was administered immediately after the lumpectomy (and sentinel node procedure). A total dose of 23.3 Gy was given with a tube diameter of 5−6 cm and 9−12 MeV. External beam APBI was administered postoperatively: 38.5 Gy in 10 fractions in 2 weeks. Levels of pain and fatigue were registered by the patients according to the EORTC-QLQ-C30 and BR23 questionnaires before surgery, at 1−3 weeks and after 3, 6, and 12 months, thereafter yearly (response rate >90%). For the external APBI cases we also monitored after surgery and before radiotherapy.

| | TLR-first event | TLR-all | N+/M+ | Secondary BC | CBC | NBC |
|---|---|---|---|---|---|---|
| IOERT | 3 [a] (26) | 6 (29) | 6 (29) | 2 (24) | 1 (28) | 10 (17) |
| External APBI | 1 (28) | 1 (28) | 0 | 0 | 0 | 4 (13) |

Number in brackets is mean number of months after surgery.
TLR, True Local Recurrence; N+, Axillary recurrence; M+, Distant metastases; Secondary BC, Second breast cancer ipsilateral; CBC, Contralateral breast cancer; NBC, Non-breast cancer.
[a] 2 port-site metastases.

**Results:** Until 01-10-2015 a total of 238 IOERT and 117 external APBI cases were included. The mean follow-up periods were 20 months and 15 months and >2 year follow-up in 102 and 44 patients, respectively. Acute grade III-IV toxicity was noticed in 8% and 5%, for the IOERT and external APBI cases, respectively. For both groups we noticed moderate increased levels of fatigue and pain around the period of treatment, which thereafter returned to pre-treatment levels in 6−12 months. Liponecrosis was observed in 30−40% of the IOERT cases and disappeared after 6−12 months. For both groups the cosmetic result was good/excellent in the vast majority of cases. In 2 IOERT patients we observed port-site metastases. The 14 non-breast cancers (NBC) had various histology's. Further details of treatment efficacy for both groups are given in the table.

**Conclusions:** The local recurrence rates and toxicity levels were low. We noticed 2 port-site metastases in the IOERT group: a new phenomenon in breast conserving radiotherapy. A high rate of non-breast cancers was diagnosed.

**No conflicts of interest**

**195** Poster

**Ductal carcinoma in situ (DCIS) and adjuvant radiotherapy: does one size fit all? Analysis from two large institutions' experiences**

L. Livi[1], I. Meattini[1], F. Rossi[2], P. Bastiani[2], I. Desideri[1], V. Scotti[1], C. De Luca Cardillo[1], L. Orzalesi[3], D. Casella[3], L.J. Sanchez[3], M. Bernini[3], J. Nori[4], A.H. Smith[5], G. Tinacci[6], S. Bianchi[7]. *[1]Azienda Ospedaliero Universitaria Careggi − University of Florence, Radiation Oncology Unit, Florence, Italy; [2]Azienda Sanitaria Locale 10 Firenze, Radiation Oncology Unit, Florence, Italy; [3]Azienda Ospedaliero Universitaria Careggi − University of Florence, Breast Surgery Unit, Florence, Italy; [4]Azienda Ospedaliero Universitaria Careggi − University of Florence, Senology Radiology Unit, Florence, Italy; [5]Azienda Sanitaria Locale 10 Firenze, Breast Surgery Unit, Florence, Italy; [6]Azienda Sanitaria Locale 10 Firenze, Pathology Unit, Florence, Italy; [7]Azienda Ospedaliero Universitaria Careggi − University of Florence, Pathology Unit, Florence, Italy*

**Background:** Ductal carcinoma in situ (DCIS) represents around 20% of breast cancers (BC). Standard treatment after breast conserving surgery is still adjuvant radiotherapy (RT). Several randomized trials and meta-analysis showed how RT reduces local recurrence (LR) rate of around 50%. The main challenge is to prevent invasive tumors LR. Many predictive tools exist in clinical practice, but conflicting results are available concerning the reproducible power of published nomograms. The aim of our analysis was to explore the LR rate of two institutions series, focusing on possible risk groups identification.

**Material and Methods:** We analyzed 457 patients that underwent conservative surgery and adjuvant RT between 1990 and 2012. Median dose to the whole breast was 50 Gy in 25 fractions; patients with positive/close final surgical margins received a tumor bed boost. Van Nuys Prognostic Index (VNPI) was evaluated for patients risk assessment. Estrogen and progesterone receptors status, nuclear grade, and Ki-67 proliferative index were available for most of the patients.

**Results:** The mean age was 57 years (range 33−80). Hormonal status was positive in 92% of patients, 83 cases (18.2%) received adjuvant endocrine therapy. All patients received postoperative RT, 198 cases (43%) received also a RT boost on tumor bed. At a median follow up time of 12 years (range 3−23), we observed 27 LR (5.9%). The 5-year and 10-year LR rates were 2.6% and 4.9%, respectively. Concerning relapsed patients, mean age was 53.6 years (range 41−77). Hormonal status was positive in 80% of cases, mean size was 13 mm (range 3−36), 18% of patients received RT boost and 15% adjuvant endocrine therapy with tamoxifen. At univariate analysis, main features had not significant impact on LR. VNPI had no significant impact on LR rate.

**Conclusions:** DCIS patients treated with adjuvant RT had a very low incidence of invasive LR. Our experience evidenced the wide heterogeneity of DCIS behavior independently of risk-groups stratification. Waiting for results from ongoing clinical phase 3 trials and genomic studies, postoperative RT still remains a mainstay in adjuvant treatment for DCIS.

**No conflicts of interest**

**196** Poster

**Mid-term results of INTRABEAM intraoperative radiotherapy in an Asian population**

S.Z. Lim[1], V.K.M. Tan[2], W.S. Yong[2], P. Madhukumar[2], B.K.T. Tan[1], E.T. Chua[3], D.Y.H. Tan[3], V.K. Sethi[3], R.M.C. Yeo[3], F.Y. Wong[3], K.W. Ong[2]. *[1]Singapore General Hospital, Department of General Surgery, Singapore, Singapore; [2]National Cancer Centre Singapore, Division of Surgical Oncology, Singapore, Singapore; [3]National Cancer Centre Singapore, Division of Radiation Oncology, Singapore, Singapore*

**Background:** INTRABEAM intraoperative radiotherapy (IORT) is a form of accelerated partial breast irradiation (APBI) which has been used as an adjuvant treatment for early breast cancer following breast conserving

surgery (BCS). It has been shown to be non-inferior to whole breast radiotherapy (WBRT) in the TARGIT-A trial. While IORT has been widely used in the Western countries, there is limited experience with Asian patients. Here, we describe the mid-term results of IORT in an Asian population.

**Methods:** A retrospective review of all patients that were offered IORT from June 2012 to February 2015 at the National Cancer Centre Singapore was performed. Selection criteria for IORT includes tumour size ⩽3 cm, estrogen receptor (ER) positive, N0 disease, margins ⩾2 mm, absence of lymphovascular invasion (LVI) and extensive in situ component (EIC). Patients found to have nodal disease on sentinel lymph node biopsy, inadequate margins or presence of LVI and EIC on histology will be offered WBRT. Patients who had IORT at least 18 months ago were interviewed with regards to their cosmetic outcomes and quality of life (QOL).

**Results:** During this period, 48 patients were offered IORT. Forty-six (96%) were ⩾50 years old, 42 (87%) had tumour size ⩽2 cm, 40 (84%) had grade 1 or 2 tumours, 45 (94%) had pN0 disease, 42 (87%) and 43 (90%) tumours were negative for LVI and EIC respectively.

IORT was delivered in 44 (92%) cases. It was aborted in 4 (8%) cases due to inadequate flap thickness (n = 2, 4%) and excessive cavity size post-wide excision (n = 2, 4%).

The majority of patients (n = 24, 55%) were of small breast size, breast cup B and below. However, all except 1 patient could accommodate a large size applicator (size 4−5).

Nine (20%) cases required further surgery due to involved or close margins. Of these, 7 (16%) patients had wider excision while 2 (4%) patients underwent completion mastectomy. WBRT was recommended after IORT in 13 (30%) cases due to inadequate margins, positive nodal disease and presence of LVI or EIC.

There were no clinically significant complications, including hematoma or abscess requiring open drainage, seroma requiring aspiration more than 3 times or grade 3−4 radiation toxicity.

At a median follow up of 20 (range 2−33) months, there was no ipsilateral breast or systemic recurrence. However, there was 1 (2%) ipsilateral axillary nodal recurrence which occurred at 8 months post-surgery in a patient with T1cN0M0 disease who declined adjuvant chemotherapy and hormonal therapy.

Majority of the patients scored their mid-term cosmetic outcome and QOL as excellent (70% and 79% respectively).

**Conclusions:** IORT can be successfully delivered to Asian women despite their relatively small breast size, with excellent mid-term disease control. The surgical complications and radiation toxicities were mild. Most patients reported good cosmetic outcome and QOL.

**No conflicts of interest**

**197** Poster

**The role of intraoperative ultrasound in improving quality and reducing risk in breast IOERT**

M. Severgnini[1], M. Urbani[2], M. Bortul[2], C. Vidali[3], H. Aslian[4], A. Beorchia[3], M. De Denaro[1]. *[1]A.O.U. "Ospedali Riuniti Di Trieste", Department of Medical Physics, Trieste, Italy; [2]A.O.U. "Ospedali Riuniti Di Trieste", Department of Surgery, Trieste, Italy; [3]A.O.U. "Ospedali Riuniti Di Trieste", Department of Radiation Oncology, Trieste, Italy; [4]International Center For Theoretical Physics and Trieste University, Department of Medical Physics, Trieste, Italy*

**Background:** We started using intraoperative electron radiation therapy (IOERT) as a boost during breast conserving surgery in June 2012. The risk assessment was carried out before starting clinical trials and was integrated with a predictive matrix risk analysis (FMECA). Even after the introduction of corrective actions, the highest score was attributed to the misalignment of the internal shield which was used to protect the underlying normal tissues.

In November 2014, we began using the new HIOB protocol (IOERT 11.1 Gy, WBERT 2.7 Gy in 15 fractions) and at the same time Intraoperative ultrasonography (IOUS) was introduced based on the recommendation of HIOB protocol in order to accurately measure depth of target and accordingly selection of the proper electron energy.

The aim of this study is to evaluate the role of intraoperative ultrasonography in reducing risk and improving quality of breast IOERT.

**Material and Method:** From November 2014 till now 20 patients have been treated using the HIOB protocol. In every treatment after positioning the shield and reconstructing the target, the measurement of target thickness was performed five times by surgeons using both needle and intraoperative ultrasonography. The correct positioning of the shielding disk was also verified by ultrasound probe.

The verification procedure of shield positioning was performed using a protocol developed at our center to also evaluate "in vivo dosimetry" as following: two layers of radiochromic films (Gafchromic® EBT3) with the same size of the shielding disk were prepared and were fixed on both disk's sides by sterile tape. Eventually, all the relevant data related to target and pectoralis muscle dose as well as shield alignment were obtained with the calibrated EBT3.

**Results:** Comparison between the measurement of target thickness obtained with ultrasonography and needle showed a good agreement for all the 20 patients and a negligible mean difference was reported in the order of 0.1 mm (ranged from 0.1−1.2 mm).

The results of in-vivo dosimetry with EBT3 demonstrated that applying intraoperative ultrasonography could reduce misalignment between electron field and shielding disk (in terms of electrons field area outside the shielding disk) from 5.4 $cm^2$ to 3.0 $cm^2$.

Moreover, the percentage of patients in whom the shielding disk was perfectly aligned (when field is totally inside the shield) was improved from 22% to 58%.

**Conclusions:** As a conclusion, intraoperative ultrasonography has improved the accuracy in the measurement of the target depth which leads to the excellent results in terms of delivered target dose. In addition, IOUS can optimize patient safety by reducing alignment error between target and shield with a significant reduction of the undesirable dose.

**No conflicts of interest**

**198** Poster

**Phase II trial of hypofractionated VMAT-based treatment for early stage breast cancer: 2-years toxicity and clinical results**

D. Franceschini[1], F. De Rose[1], A. Fogliata[1], C. Iftode[1], E. Villa[1], A.M. Ascolese[1], P. Navarria[1], C. Franzese[1], T. Comito[1], A. Tozzi[1], E. Clerici[1], R.L.E. Liardo[1], G.R. D'Agostino[1], M. Scorsetti[1]. *[1]Humanitas, Radiotherapy and Radiosurgery, Rozzano Milan, Italy*

**Background:** RT is a standard adjuvant treatment after breast conserving surgery. Conventional RT usually requires 6 weeks. However, there has been a recent shift toward the possibility to deliver adjuvant RT using shorter treatment schedules, with hypofractionation. There are still some open issues about hypofractionated RT, expecially in early stage breast cancer. It is still unclear the benefit of techniques like Intensity Modulated RT (IMRT) and Volumetric Modulated Arc Therapy (VMAT) in this setting. To investigate the role of VMAT hypofractionated RT with simultaneous integrated boost (SIB) as adjuvant treatment after breast-conserving surgery in early stage breast cancer, we conducted this phase II trial. Here we report toxicity and early clinical outcomes in patients with at least two years of follow up.

**Methods and Materials:** Patients presenting early-stage breast cancer were enrolled in a phase II trial. Eligibility criteria were: age >18 years, invasive cancer or DCIS, Stage I−II (T <3 cm and N ⩽3), breast-conserving surgery without oncoplastic reconstruction, any systemic therapy was allowed in neoadjuvant or adjuvant setting. All patients underwent VMAT-SIB technique to irradiate the whole breast and the tumor bed. Doses to whole breast and surgical bed were 40.5 Gy and 48 Gy, respectively, delivered in 15 fractions over 3 weeks. Acute and late skin toxicities were recorded based on RTOG scoring criteria and CTCAE v. 4.0, respectively. Cosmetic outcome was assessed as excellent/good or fair/poor, according to the Harvard scale.

**Results:** In this study we report the long-term results of a cohort of 144 patients with a minimum follow-up of 24 months (median 37, range 24−55 months). Median age was 62 y.o. (range 30−88). At one year, the highest reported skin toxicity was G1, in 14% of the patients; this data dropped to 4% at the last follow-up, after more than 2 years. Breast pain was recorded in 21.6% of the patients 6 months after treatment, while it was present in 3.5% of the patients at the last follow-up, showing a significant improvement with time. No correlation with liponecrosis as recorded from ultrasound exam, nor with dosimetric data. Skin toxicity was correlated with breast volume. No pulmonary or cardiological toxicities were recorded. After an early evaluation of clinical outcomes, only one case presented disease relapse, as liver metastases.

**Conclusions:** The hypofractionated VMAT-SIB course as adjuvant treatment after breast-conserving surgery showed to be safe and effective with optimal local control. This approach requires validation with long-term follow-up data.

**No conflicts of interest**

**199** Poster

**Combination of radiotherapy and double blockade HER2 with pertuzumab and trastuzumab in HER2 positive metastatic or locally recurrent unresectable breast cancer: assessment of toxicity**

Z. Ajgal[1], S. De Percin[1], D. Loirat[2], J.Y. Pierga[2], F. Campana[1], A. Fourquet[1], Y. Kirova[1]. *[1]Institut Curie, Radiotherapy, Paris cedex 05, France; [2]Institut Curie, Medical Oncology, Paris cedex 05, France*

**Background:** The tolerance of the concurrent use of radiotherapy (RT), pertuzumab (P) and trastuzumab (T) is unknown. This combination can

become frequently used in a metastatic and/or in an adjuvant setting. The aim of this study is to evaluate the early toxicity of this association in patients (pts) treated for HER2 positive metastatic and/or locally recurrent unresectable breast cancer.

**Material and Methods:** A retrospective study was performed in a population of 23 pts treated outside clinical trials in a single institution between 2013 and 2015. RT was performed while pertuzumab and trastuzumab were administrated as a maintenance treatment at the dose of 420 mg (total dose) and 6 mg/kg respectively every 3 weeks. Toxicity was assessed according National Cancer Institute Common Terminology Criteria for Adverse Events version 4.0. Left ventricular ejection fraction (LVEF) was measured at baseline and then every 3 to 4 months.

**Results:** Median age was 47 years old (range:33−85). 15 pts were diagnosed at metastatic stage and 9 pts had relapsing disease. All pts were treated in first metastatic line and they received 6 cycles of P-T (P=420 mg, T=6 mg/kg) and docetaxel including one loading dose of antibodies (P=840 mg, T=8 mg/kg). For 5 pts, docetaxel was replaced during treatment by paclitaxel to reduce toxicity. All pts presented a good partial or complete response according to RECIST criteria allowing maintenance treatment with P-T. Median total doses administrated of P and T were 6720 mg and 6308 mg respectively. Before and during radiation, median total doses were 4200 mg and 3808 mg respectively. Irradiation volumes were whole breast (8 pts) and chest wall (9 pts) at a dose of 50 Gy with a median duration of 39 days. Radiotherapy of the draining lymph nodes was performed in 16 patients with RT of the supraclavicular nodes in 16pts, the axillary area in 9 pts and the internal mammary nodes in 9pts. For 5 pts RT was palliative: bone irradiation (4 pts), whole-brain RT (1 patient). Since the start of RT, median follow up was 7.3 months (1.2–18.9), from the date of diagnosis it was 13.8 months (6.3–23.4). Two pts presented an asymptomatic grade II decrease of LVEF requiring no treatment discontinuation and one presented a grade III requiring a 3 months discontinuation of P and T. Two pts presented asymptomatic radiation pneumonitis: one grade I and one grade II. Acute skin toxicity was grade III (one patient with inflammatory tumor), grade II (6 pts), grade I (5pts).

**Conclusion:** In this exploratory study, the toxicities are expected, manageable and similar to these encountered with trastuzumab alone. Results of randomized trials in locally recurrent and metastatic tumors are needed with longer follow up and prospective design to confirm our results.

**No conflicts of interest**

**200** Poster

**Breast conserving therapy in elderly breast cancer patients: Low risk on recurrences**

F. Van der Leij[1], E. Van Werkhoven[2], S. Bosma[1], S. Linn[3], E. Rutgers[4], M. Van de Vijver[5], H. Bartelink[1], P. Elkhuizen[1], A. Scholten[1]. *[1]The Netherlands Cancer Institute Antoni van Leeuwenhoek Hospital, Radiation Oncology, Amsterdam, Netherlands; [2]The Netherlands Cancer Institute Antoni van Leeuwenhoek Hospital, Statistics, Amsterdam, Netherlands; [3]The Netherlands Cancer Institute Antoni van Leeuwenhoek Hospital, Medical Oncology, Amsterdam, Netherlands; [4]The Netherlands Cancer Institute Antoni van Leeuwenhoek Hospital, Surgery, Amsterdam, Netherlands; [5]Academical Medical Center, Pathology, Amsterdam, Netherlands*

**Background:** Early stage breast cancer incidence rate in elderly patients is increasing. The challenge is to find the right balance between avoiding over- and under treatment in this patient population. Because both non-cancer related mortality as well as disease-specific mortality has been reported to be increased with age, good patient selection is important. We analyzed prognostic factors and the risk of recurrence and death in a large consecutive series of patients ⩾65 years old with breast cancer treated at our institute.

**Patients and Methods:** Using the tumor registry at our institute, patients ⩾65 years old with breast cancer (T1−2/N0−2) treated with breast conserving therapy (BCT) at the Netherlands Cancer Institute − Antoni van Leeuwenhoek (NKI-AVL) between 1980–2008 were identified. Endpoints were locoregional recurrence (LRR), distant metastases (DM) and overall survival (OS). To define subgroups with low or high risk of recurrence we compared a pre-defined patient subgroup with low risk tumors (T-stage 1, estrogen receptor positive, node negative and histologic grade 1 or grade 2) to a patient group with higher risk tumors (histologic grade 3 and/or node positive).

**Results:** 1922 patients with a median age of 70 years were analyzed. All patients underwent breast conserving surgery and radiotherapy (RT) of the whole breast. In addition 63% received a RT boost dose and 38% received adjuvant hormonal therapy. Only 1.4% of all patients received chemotherapy. The 5- and 10-years LRR rates were 2% and 3% respectively. In multivariate analysis there was no significant factor (including RT boost and hormonal therapy) influencing LRR risk. The 5- and 10-years DM-rates were 10% and 16% respectively. 673 patients had died at time of analysis. Death was breast cancer related in 22% (150 patients). Patients with low risk tumors had lower risk on DM (HR 0.26) and better OS (HR 0.65) compared to higher risk tumors.

**Conclusions:** In elderly breast cancer patients the risk of LRR and DM is low. In patients with higher risk tumors (defined as histologic grade 3 and/or node positive) the risk on LRR is not higher, but there is a higher risk to develop DM and the OS is worse compared to patients with low risk tumors (defined as T1, estrogen receptor positive, node negative and histologic grade 1 or 2). For this higher risk group the added value of more intensified adjuvant systemic treatment should be investigated while treatment in the low risk group should be minimized, e.g. by omitting adjuvant RT, hormonal therapy or both. With a growing number of elderly breast cancer patients individualized adjuvant treatment strategies are of great importance for this group.

**No conflicts of interest**

**201** Poster

**Initial experience with respiratory gated radiotherapy using deep inspiration breath hold technique for left-sided breast cancer**

M.S. Raghunathan[1], S. Ramachandran[1], A. Vaz[1], S.K. Natarajan[1]. *[1]Kovai Medical Centre and Hospital Ltd., Department of Radiation Oncology, Coimbatore- Tamilnadu, India*

**Background:** Patients receiving adjuvant radiotherapy for left-sided breast cancer are at late risk of cardiac and pulmonary toxicity. It is documented that a clear dose-response relationship exists between cardiac morbidity and radiation dose to cardiac volumes. We present our initial experience in utilizing deep inspiration breath hold (DIBH) technique to achieve cardiac dose reduction.

**Material and Methods:** 17 patients with stages I-III left-sided breast cancer with good breath-hold capacity underwent CT-simulation in free breathing (FB) and DIBH on Varian Real-time Position Management (RPM) respiratory gating system. Treatment plans were generated using conformal tangential fields on both CT sets with adequate coverage of PTV. Dose-volume histograms were calculated and dosimetric comparison was made between the two techniques for doses to heart, left anterior descending coronary artery (LAD) and left lung.

**Results:** As compared to FB, DIBH plans resulted in a significantly reduced mean dose to heart (14.4 Gy to 7.8 Gy, −46%, $p = 0.000035$), heart V30 (27.1% to 10.6%, −61%, $p < 0.00001$) and mean dose to LAD (46.5 Gy to 30.4 Gy, −35%, $p = 0.000061$). A non-significant reduction in the left lung V20 (29.4% to 26.9%, $p = 0.214$) was observed. Radiation treatment delivery was executed using DIBH plans for 15 out of 17 patients. Two patients were unable to reproduce the same breathing pattern.

**Conclusions:** DIBH technique significantly reduces radiation doses to heart and LAD compared to FB technique in left-sided breast cancers. Delivery of DIBH is feasible in regular clinical setting with appropriate patient selection and training.

**No conflicts of interest**

**202** Poster

**Patient's willingness-to-pay for post-mastectomy radiotherapy: Experience from a single institute in India**

R.V. Kumar[1], C. Satyan[1], D.M. Gangaiah[2], A. Mandava[1], L.N. Kashyap[1], D.S. Nihanthy[1]. *[1]Kidwai Memorial Institute of Oncology, Radiation Oncology, Bangalore, India; [2]Kidwai Memorial Institute of Oncology, Surgical Oncology, Bangalore, India*

**Background:** Breast cancer patients need radiotherapy as part of their multi-disciplinary management. Radiotherapy technique range from conventional body-contouring guided cobalt-60 based tele-therapy through intensity modulated radiotherapy (IMRT) with or without respiratory gating/ active breath control (active breath co-ordination). Newer technologies are both capital- and labor-intensive and mostly inaccessible, un-affordable or impractical in developing countries. IMRT is widely available, however is expensive considering the earning capacity of the local population. Public insurance scheme pays for 3-dimensional radiotherapy (3-D CRT). However waiting time can be another important factor in deciding the technique of post-mastectomy radiotherapy (PMRT) by patients and their care-givers. Patients not covered by public health insurance have to bear the cost of radiotherapy from their pocket. We interviewed patients regarding their willingness to pay for radiotherapy and acceptability of the current cost of PMRt.

**Material and Methods:** Forty-one breast cancer patients were treated in the department of radiotherapy, Kidwai Memorial Institute of Oncology, Bangalore between January 2015 and October 2015. Patients were

explained about the cost and outcome of each of available radiotherapy technology and were asked about their willingness-to-pay. Thirty five patients has public or employers insurance and were excluded from the study. Six patients had to bear cost out of pocket for PMRT were included in the study and analysis.

**Results:** Five out of six patients paying out-of-their pocket opted for PMRT by conventional body-contouring based cobalt-60 tele-therapy due to its lowest cost compared to other techniques and immediate start of radiotherapy within three days as against the long waiting time for 3-D CRT and IMRT due to multiple steps in planning and implementation.

**Conclusions:** Almost all patients were reluctant to pay the user fee for radiotherapy in public sector hospital. They chose radiotherapy technique based on the rate for the same and we were not able to ascertain cost/level of their willingness-to-pay as they chose technique that cost least when explained about the non-inferiority of the conventional technique over advanced techniques with respect to oncologic outcome. They chose technique based on equi-control and survival over inferior adverse events rate of conventional technique over probable better toxicity profile of IMRT. Immediate start of PMRT with conventional technique was another factor that could favor conventional technique over IMRT.

**No conflicts of interest**

**203** Poster

**Adjuvant radiotherapy versus observation following lumpectomy in ductal carcinoma in-situ: A meta-analysis of randomized controlled trials**

P.K. Garg[1]. [1]*University College of Medical Sciences and Guru Teg Bahadur Hospital- University of Delhi, Surgery, Delhi, India*

**Background:** The role of adjuvant radiotherapy (RT) following lumpectomy for ductal carcinoma in-situ (DCIS) was addressed in four major randomized controlled trials (RCTs) which were conducted two to three decades ago. Initial results of these trials suggested the protective role of RT in reducing the ipsilateral breast recurrences. Long-term results of all these four trials, based on more than 15-years follow-up data, have recently been published.

**Methods:** A meta-analysis of four published RCTs which have addressed the role of adjuvant RT following lumpectomy for DCIS was conducted. Review manager (Cochrane Collaboration's software) version RevMan 5.2 was used for analysis. Evaluated events were ipsilateral breast recurrences (both DCIS and invasive), regional recurrences, contralateral breast events, distant recurrences, and overall mortality. The events were entered as dichotomous variable.

**Results:** The present meta-analysis included four RCTs and a total of 3680 patients − 1710 received adjuvant RT following lumpectomy while 1970 patients did not receive any adjuvant treatment. Patients who received RT had almost half of risk of ipsilateral breast recurrence (RR=0.53, 95% CI 0.45–0.62) and regional recurrence (RR=0.54, 95% CI 0.32–0.91) compared to those who did not receive adjuvant treatment − there was absolute risk reduction of 15% (95% CI 12−17%) for ipsilateral breast recurrences in adjuvant RT treated patients. There was no significant difference in distant recurrence (RR=1.06, 95% CI 0.74–1.53), contralateral breast events (RR=1.22, 95% CI 0.98–1.52) and overall mortality (RR=0.93, 95% CI 0.79−1.09).

**Conclusion:** Though addition of post-operative radiotherapy to lumpectomy does not reduce overall mortality, the present meta-analysis confirms that it decreases the ipsilateral breast and regional recurrence by almost half.

**No conflicts of interest**

**204** Poster

**Phase II trial of hypofractionated VMAT for early stage breast cancer: Acute toxicity and cosmetic results in 840 patients**

F. De Rose[1], D. Franceschini[1], A. Fogliata[1], C. Iftode[1], E. Villa[1], A.M. Ascolese[1], P. Navarria[1], G.R. D'Agostino[1], C. Franzese[1], T. Comito[1], A. Tozzi[1], E. Clerici[1], R.L.E. Liardo[1], A. Stravato[1], M. Scorsetti[1]. [1]*Istituto Clinico Humanitas, Radiotherapy, Rozzano MI, Italy*

**Background:** To evaluate acute toxicity and early clinical outcomes of hypofractionated simultaneous integrated boost (SIB) approach with Volumetric Modulated Arc Therapy (VMAT) as adjuvant treatment after breast-conserving surgery.

**Materials and Methods:** Patients presenting early-stage breast cancer were enrolled in a phase II trial. Eligibility criteria were as follow: age >18 years, invasive cancer or DCIS, Stage I to II (T <3 cm and N $\leqslant$3), breast-conserving surgery, any systemic therapy was allowed in neoadjuvant or adjuvant setting. All patients underwent VMAT-SIB technique to irradiate the whole breast with concomitant boost irradiation of the tumor bed. Doses to whole breast and surgical bed were 40.5 Gy and 48 Gy respectively, delivered in 15 fractions over 3 weeks Acute skin toxicities were recorded according to RTOG scoring criteria, and late skin toxicities according to CTCAE v4.0. Cosmetic outcomes were assessed as excellent/good or fair/poor according to the Harvard scale.

**Results:** Between August 2010 and January 2015, 840 consecutive patients were treated. Median age was 60 year (range 19−89 years). The median follow up was 16 months (range 6−55). At the end of RT treatment skin toxicity profile was G1 in 49% of the patients, G2 in 13%, and one patients presented G3 toxicity (0.1%). At six months of follow up skin toxicity was G1 in 27% of patients, G2 in 1%, no G3 cases; cosmetic outcome was good/excellent in 94% of patients. At one year skin toxicity was G1 in 13% of patients, 1 patient G2, 1 patient G3; cosmetic outcome was good/excellent in 93% of patients. After an early evaluation of clinical outcomes we have found 12 cases of progression disease, only one patient had an In-Breast-Recurrence.

**Conclusion:** Hypofractionated VMAT treatment with SIB was safe and well tolerated in terms of acute and early late settings. Cosmetic results were also good or excellent in the most of patients. Long-term follow-up data are needed to assess late toxicity and clinical outcomes.

**No conflicts of interest**

**205** Poster

**Simultaneous-integrated boost 3D conformal radiotherapy vs volumetric modulated arc therapy in synchronous breast cancer**

M. Spałek[1], K. Pawlewicz[1], P. Mężeński[2], P. Kukołowicz[2], A. Zawadzka[2], J. Gałecki[1]. [1]*The Maria Skłodowska-Curie Memorial Cancer Center and Institute of Oncology, Department of Teleradiotherapy, Warsaw, Poland;* [2]*The Maria Skłodowska-Curie Memorial Cancer Center and Institute of Oncology, Medical Physics Department, Warsaw, Poland*

**Background:** The standard treatment of early breast cancer includes breast conserving surgery (BCS) followed by postoperative radiotherapy. Basing on literature data, synchronous breast cancer occurs in approximately 1−2% of patients with operable breast cancer. The concomitant both breasts radiotherapy planning and delivery is challenging because of the size of planned target volume (PTV), inter and intrafraction motion, important organs at risk (heart, lungs) and higher risk of treatment toxicity. Authors present a case study of 4 patients with synchronous breast cancer who were qualified to postoperative radiotherapy after breast conserving surgery.

**Material and Methods:** For 4 synchronous breast cancer patients, computed tomography-based treatment planning were performed. The CTV (Clinical Target Volume) covered the whole both breasts. Boost covering post-lumpectomy tumor bed and important organs at risk (OAR: heart, lungs) were also delineated. The medical physicist prepared treatment plans for each patient in two techniques − volumetric modulated arc therapy (VMAT) and 3D conformal radiotherapy simultaneous-integrated boost (3D-CRT-SIB).

**Results:** After treatment plan assessment by radiation oncologist, the two-isocenter 3D-CRT-SIB was used to irradiate 3 patients and VMAT was chosen in one case. The 3D-CRT-SIB was superior to VMAT in lower mean doses, volume receiving 20 Gy and 30 Gy or more in OAR. Coverage of PTV was similar in both techniques. The VMAT was chosen in one case because of similar dose distribution and decreased single fraction delivery time. The prescribed doses were 50 Gy (2 Gy/fr.) to PTV breast and 60 Gy (2.4 Gy/fr.) to PTV boost. The overall treatment time for both techniques was 5 weeks. The individual verification protocol for these patients were prepared and approved by radiation oncologist. The early treatment tolerance was good − no toxicity higher than Grade 1 skin toxicity according to RTOG Acute Radiation Morbidity Scoring Criteria was observed. The reproducibility of patient's setup was satisfactory.

**Conclusion:** The 3D-CRT-SIB in patients with synchronous breast cancer is a preferred treatment method. In some cases VMAT is also a considerable option.

**No conflicts of interest**

**206** Poster

**Adjuvant hypofractionated radiation therapy for breast cancer in the Algerian west: Preliminary results in a cohort of 163 cases**

A. Boukerche[1], M. Brahmi[1], R. Madouri[1], F. Boudinar[2], A. Dali-Youcef[1]. [1]*Faculty of Medicine- University of Oran 1, Radiation Oncology, Oran, Algeria;* [2]*Faculty of Medicine- University of Oran 1, Madical Oncology, Oran, Algeria*

**Background:** To evaluate the incidence of locoregional recurrence (LRC) and the toxicity results (acute and late) in a group of patients with breast cancer treated with a hypofractionated schedule of adjuvant radiotherapy after surgery.

**Patients and Methods:** From January to December 2014, 163 patients underwent radiotherapy treatment after conservative (7%) and radical (93%) surgery at our department. The dose delivered was 36 Gy (3 Gy daily fraction). The boost dose was 15 Gy (3 Gy daily fraction) in conservative surgery.

**Results:** Mean age was 47.9±0.8 years (Range 28−76). Stage I, II and III were 50, 89 and 24. Commonest adverse effects (NCI-CTC 4.0) were: Grade 1 or 2 dermatisis, dysphagia, oedema and pain occurred in 68 cases (41.7%), 10 cases (6.1%), 25 cases (15.3%) and 12 cases (7.4%) respectively. No Patients developed Grade 3 or 4 toxicities. With median follow-up of 14 months, one patient was presented locoregional recurrence and metastasis. The locoregional control (LRC) and overall survival (OS) rates at one year were: 98.9% (±1.1%) and 99.1% (±0.4%), respectively.

**Conclusion:** This hypofractionated RT scheme is perfectly realizable (acceptable results in terms of local control and toxicity). It permitted a short course of treatment, allowing a larger number of patients to be treated per year, with a reduction in cost to the health system. However, an important number of patients and a longer follow-up are necessary to better appreciate the efficacy and the cosmetic outcome of this scheme.

**No conflicts of interest**

**207** Poster

**Radiotherapy After Primary CHEMotherapy (RAPCHEM): A prospective registration study**

L. Boersma[1], P. Elkhuizen[2], R. Houben[3], E. Van Leeuwen[4], S. Linn[5], L. De Munck[6], R. Pijnappel[7], L. Strobbe[8], T. Van Dalen[9], J. Verloop[6], A. Voogd[10], J. Wesseling[11], P. Poortmans[12]. [1]*Maastricht University Medical Centre MAASTRO Clinic, Radiotherapy, Maastricht, Netherlands;* [2]*Netherlands Cancer Institute, Radiotherapy, Amsterdam, Netherlands;* [3]*MAASTRO Clinic, Radiotherapy, Maastricht, Netherlands;* [4]*BOOG study centre, Board, Amsterdam, Netherlands;* [5]*Netherlands Cancer Institute, Medical Oncology, Amsterdam, Netherlands;* [6]*Netherlands Comprehensive Cancer Organisation, Breast Cancer, Utrecht, Netherlands;* [7]*University Medical Centre Utrecht, Radiology, Utrecht, Netherlands;* [8]*Canisius Wilhelmina Hospital Nijmegen, Surgery, Nijmegen, Netherlands;* [9]*Diakonessen Hospital, Surgery, Utrecht, Netherlands;* [10]*Maastricht University Medical Centre, Epidemiology, Maastricht, Netherlands;* [1]*Netherlands Cancer Institute, Pathology, Amsterdam, Netherlands;* [12]*Radboud University Medical Centre, Radiotherapy, Nijmegen, Netherlands*

**Introduction and Aim:** Indications for post-operative radiotherapy (RT) have traditionally been based on pathologic tumour characteristics observed in primary resected tumour and lymph node specimens. Since the introduction of primary systemic treatment (PST), the indications for RT have become less clear, leading to both over- and undertreatment. Based on the sparse literature available in 2010, we developed guidelines for post-operative RT for patients with relatively early breast cancer treated with PST. A prospective registration study was started [NCT01279304], with the aim to evaluate these guidelines with respect to the 5 and 10 year locoregional recurrence rate, disease-free and overall survival. This first analysis is focussed on the percentage of patients treated according to the recommended guidelines.

**Methods:** From January 2011 until January 2015, the Netherlands Cancer Registry registered the relevant tumour and treatment details of all patients in the Netherlands with cT1−2 disease, and with 1−3 positive axillary nodes as detected by palpation and/or imaging followed by FNA or biopsy, or as detected in the sentinel node (SN), treated with primary chemotherapy. Until half 2013, all patients underwent an axillary lymph node dissection (ALND) after PST. For all patients treated with breast conserving therapy (BCT), whole breast RT with a 16 Gy equivalent boost to the tumour bed was recommended. Guidelines for regional RT and/or RT of the thoracic wall were recommended for three risk groups, largely based on the ypN status: ypN0, no further RT; ypN1 only thoracic wall RT; ypN2, periclavicular RT both after BCT and mastectomy, in combination with thoracic wall RT. In 2013 an amendment was developed taking into account new insights in axillary treatment: in case of a positive SN prior to PST, the ALND could be replaced by axillary RT. We aimed to include 287 patients per group in 5 years.

**Results:** Data acquisition is now complete until Q3 of 2013. In 33 months we registered data of 635 patients, 233 in group 1 (ypN0), 279 in group 2 (ypN1), and 133 in group 3 (ypN2). The majority of patients had ypN0 or ypN1 disease. Preliminary analysis showed that RT guidelines were followed in 2/3 of the patients. In group 1 (ypN0) deviations of guidelines mainly consisted of additional thoracic wall RT, whereas none was recommended. In group 2 (ypN1) deviations of the guidelines consisted either of more RT or less RT, indicating that the largest doubt on post-operative RT is present in patients with ypN1 disease.

**Conclusion:** Treatment guidelines of the RAPCHEM study are being followed in 2/3 of the patients. The largest variation in applied post-operative RT is seen in patients with ypN1 disease. Further analysis will be performed to investigate whether the variation will decrease over time, and to evaluate the outcome of these patients.

**No conflicts of interest**

**208** Poster

**Evaluation of the effect of inverse and field-in-field IMRT plannings on left anterior descending coronary artery (LAD) doses for left breast cancer**

E. Kara[1], M. Akmansu[2], B. Dirican[3], A. Yazici[1]. [1]*ONKO Ankara Oncology Center, Radiation Oncology, Ankara, Turkey;* [2]*Gazi University, Radiation Oncology, Ankara, Turkey;* [3]*GATA, Radiation Oncology, Ankara, Turkey*

**Background:** Radiation therapy (RT) plays an important role in the treatment of breast cancer. Unfortunately, using RT for breast cancer is related to the death secondary to heart disease. Radiation exposure to the left anterior descending coronary artery (LAD) is a major cause of these complications. The aim of the study is to evaluate radiation doses of left anterior descenden coroner artery (LAD) among various radiotherapy treatment planning techniques; field-in-field IMRT, 4 fields inverse and 5 fields inverse IMRT for 45 left breast cancer patients.

**Method:** After definition of the critical organs which are left lung, LAD and opposite breast, three different radiotherapy plans which are field-in-field, 4 fields and 5 fields inverse IMRT, were performed. We use 2 opposed tangential beams which were special for each patient and the other two were obtained by 10º refraction for 4 fields inverse IMRT plannings. Finally, for 5 fields inverse IMRT plans we have chosen 300º, 330º, 30º, 120º and 150º beam angles for optimization. In this study LAD doses are dosimetrically evaluated for 45 left breast cancer patients by using three IMRT techniques. After obtaining IMRT plans, we dosimetrically compared the doses of OARs'.

**Results:** After performed first 5 patients' plannings, we have figured out that 5 fields inverse IMRT technique does not useful for decreasing $LAD_{max}$ dose. $LAD_{max}$, ipsilateral lung and heart's doses are significantly increased by using 5 fields inverse IMRT technique. Therefore, we decided to not use this technique for the rest of our study. There were significant change on $LAD_{max}$, ipsilateral lung (25%) and heart (5%) with 4 fields inverse IMRT (p value <0.05). Secondly, we figure out from our study that there is a significant relation between the distance from chest wall to LAD and the dose of $LAD_{max}$. In our study, 18 of our 45 patients had $LAD_{max}$ value greater than 10 Gy. Finally, our results indicate that ipsilateral lung and heart doses were significantly decreased ($p < 0.05$) by inverse IMRT for 18 patients while contralateral breast dose significantly increased ($p < 0.05$).

**Conclusion:** The previous studies have figured out that in the event of LAD doses which are greater than 10 Gy, is increased the probability of CAD. In our study, we have tried to figure out radiation doses of LAD among various radiotherapy treatment planning techniques for 45 left breast cancer patients. There is not a significant difference between inverse IMRT and FiF. However, if the LAD is located closer than 2.5 cm, the dose of $LAD_{max}$ could increase and could be decreased under 10 Gy by 4 fields inverse IMRT. We investigate in our study that by using 4 fields inverse IMRT the LAD doses can be reduced for the patients having LAD located closer than 2.5 cm. The lung and heart doses can also be reduced by using 4 fields inverse IMRT technique.

**No conflicts of interest**

**209** Poster

**Do breast cancer patients with many positive axillary lymph nodes really need postmastectomy radiotherapy?**

T. Marinko[1], K. Stanic[1]. [1]*Department for Radiation Oncology, Institute of Oncology Ljubljana, Ljubljana, Slovenia*

**Background:** The aim of postmastectomy radiotherapy (PMRT) is to improve survival by eliminating potential occult lesions in the chest wall and lymphatic drainage area. Meta-analysis has shown that PMRT improves survival of patients with node-positive breast cancer (BC), but is questionable if patients with high number of positive axillary lymph nodes (PALN) really benefit from PMRT. The aim of this study was to analyse the impact of the number of PALN on survival and distant metastasis occurrence in patients treated with PMRT.

**Material and Methods:** Medical records of 129 consecutive BC patients with PALN who were treated with PMRT between January 2003 and December 2004 at Institute of Oncology Ljubljana were reviewed. Patients were grouped according to the number of PALN as follows: group 1 (29 patients) 1−3 PALN; group 2 (70 patients) 4−15 PALN; group 3 (30 patients) more than 15 PALN. All patients received adjuvant systemic therapy according to the clinical guidelines. Data were analysed with respect to

overall survival (OS), progression free survival (PFS), distant metastasis free survival (DMFS) and loco-regional free survival (LRFS).

**Results:** The median follow-up time was 11.5 years. Kaplan Meier survival analysis showed that patients with the higher number of PALN had significantly shorter OS (9.1 years; 9.9 years; 7.6 years; $p = 0.022$), shorter PFS (9.5 years; 8.6 years; 6.2 years; $p = 0.006$) and shorter DMFS (10.5 years; 9.0 years; 6.2 years; $p < 0.001$). The number of loco-regional recurrences (LR) occurred as follows: 5 (17%) in group 1, 4 (5.7%) in group 2 and the lowest number was in the group with the highest number of PALN − group 3; only 1 recurrence (3.3%).

**Conclusions:** In spite of the same LR therapy, patients with higher number of PALN significantly earlier develop distant metastases and have shorter survival. Our results indicate that patients with many PALN maybe do not benefit from PMRT, probably due to already present microscopic metastatic disease at the time of adjuvant LR treatment which leads to clinically evident metastases that are treated with systemic therapy before local recurrence may occur. More studies with higher number of patients included are required to confirm our findings.

**No conflicts of interest**

**210** Poster

**Validating phase 3 trial data on the efficacy of accelerated partial breast irradiation using multicatheter brachytherapy in Japanese breast cancer patients**

K. Sato[1], Y. Mizuno[1], H. Fuchikami[1], N. Takeda[1], M. Kato[2]. *[1]Tokyo-West Tokushukai Hospital, Department of Breast Oncology, Tokyo, Japan; [2]Tokyo-West Tokushukai Hospital, Department of Radiation Oncology, Tokyo, Japan*

**Background:** Breast-conserving therapy consists of lumpectomy followed by whole-breast irradiation (WBI). However, up to 20% of patients do not receive adjuvant radiotherapy because of the inconvenient schedule. The introduction of accelerated partial breast irradiation (APBI) had been considered an ideal alternative option of adjuvant radiotherapy. Recently, a randomized phase 3 trial conducted by the Groupe Européen de Curiethérapie of European Society for Radiotherapy and Oncology (GEC-ESTRO) demonstrated that APBI using multicatheter brachytherapy had an equivalent local control, disease-free survival, and overall survival as compared to WBI in patients with early breast cancer, showing cumulative ipsilateral breast tumor recurrence (IBTR) rate was 1.4%, and 5-year disease-free and overall survival were 95.0% and 97.3%, respectively. We had initiated a prospective observational study on APBI by the same technique since October 2008. Here, we reviewed the experience of APBI to validate the phase 3 data for Japanese breast cancer patients.

**Methods:** Between October 2008 and October 2015, 288 patients received APBI as adjuvant radiotherapy using multicatheter brachytherapy at a dose of 32 Gy in eight fractions. The planned target volume was defined as the estimated tumor volume plus a 20-mm margin. Basically, our inclusion criteria had been the same as the GEC-ESTRO trial. Because of no final pathology report available at the time of surgery and compassionate use of APBI, strict selection criteria could not be achieved. Therefore, 226 patients (78.5%) met the inclusion criteria of GEC-ESTRO trial ($\geqslant$40 years old, t $\leqslant$3 cm, n0-mi, and negative margin). The efficacy of APBI in both cohorts was evaluated and compared with the GEC-ESTRO trial with respect to IBTR, disease-free survival and overall survival.

**Results:** The mean age of entire patients (56.4 years) was much lower than that of GEC-ESTRO patients (62 years), and median follow-up (3.8 year) was also shorter than that of the trial (6.6 year). However, 5 patients (2 were outside the original tumor bed) had an IBTR and the actual rate of IBTR was 1.7% (95% CI 0.22–3.24), showing the equivalence of local control in the trial. The 3.5-year probability of disease-free and overall survival was 97.7% and 99.6%, respectively. Among the patient who met the criteria, there was no IBTR, and disease-free and overall survival was 98.1% and 99.5%, respectively.

**Conclusions:** This study was based on a small number of patients with a relatively short follow-up period and questions still remained with respect to patients' selection. However, local recurrence was equivalent between APBI trial and our cohort. APBI using multicatheter brachytherapy should be consider as an alternative technique of adjuvant radiotherapy for Japanese patients.

**No conflicts of interest**

**211** Poster

**Prostheses irradiation in high risk breast cancer patients: clinical and aesthetic outcomes in retrospective series**

D. Smaniotto[1], V. Masiello[1], F. Beghella Bartoli[1], L. Boldrini[1], G.C. Mattiucci[1], F. Marazzi[1], S. Manfrida[1], A. Di Leone[2], G. Franceschini[2], R. Masetti[2], V. Valentini[1]. *[1]Catholic University, Radiation Oncology − GEMELLI ART, Roma, Italy; [2]Catholic University, UOC Breast Surgery, Roma, Italy*

**Background:** Radiation therapy (RT) represents a standard adjuvant treatment for high risk patients with breast cancer, even in post-mastectomy setting. Mammary expanders and prostheses often do not tolerate RT producing a deterioration of aesthetic profile that can lead to clinical risks (rejection, sepsis) or new surgery. This retrospective series evaluates clinical and aesthetic results in patients who did or did not undergo adjuvant RT after reconstruction for breast cancer surgery.

**Material and Methods:** Patients submitted to mastectomy with immediate mammary reconstruction and with a follow-up (FUP) period of at least six months were recruited for this study. Two subgroups were identified between irradiated or not patients. All the patients had the planned surgical and oncoplastic FUP and for the irradiated ones also a specific RT FUP program was provided. For both groups local infection rate (IR), lipofilling rate (LR), reconstruction with DIEP flap rate (DIEPR), local control (LC) and distant failure rate (DFR) were taken into account. All chi square tests were performed on MedCalc. Acute and late RT toxicities were also recorded according to CTCAE v4.0 scale.

**Results:** From January 2012 to April 2015, 152 patients were submitted to mastectomy with implantation of prostheses or expanders in our Institution. Out of them, 76 pts were selected for standard adjuvant RT due to the presence of clinical high risk factors, according to NCCN guidelines. Mean age was 48 years (range 32−74). Median FUP was 28 months (range 6−44). IR, LR, DIEPR are described in Table 1. 21% of not irradiated pts had a second planned surgery to replace the expander with the prostheses. LC showed to be equal in both groups. High risk pts had higher DFR than low-medium risk ones (5.26% vs 0 with $p < 0.05$). Acute RT skin toxicities G0, G1, G2 and G3 were 38%, 40%, 12% and 9.8% respectively, while late RT skin toxicities rates were described as G0 20%, G1 28%, G2 42% and G3 10%.

Table 1.

| | Adjuvant RT | No adjuvant RT | Chi square test |
|---|---|---|---|
| Lipofilling rate | 10 (13.1%) | 16 (21%) | 1.2 ($p < 0.01$) |
| DIEP flap rate | 15 (19.7%) | 7 (9.2%) | 2.5 ($p < 0.01$) |
| Infection rate | 1 (1.3%) | 1 (1.3%) | 0 |

**Conclusion:** In this preliminary analysis RT after mastectomy with breast reconstruction resulted well tolerated and can ensure to high risk patients local control rates comparable to low-medium risk patients in the early FUP. A longer period of observation and specific Quality of Life questionnaires are needed to better describe the results.

**No conflicts of interest**

**212** Poster

**Analysis of data from three centers in Turkey on intraoperative radiotherapy of breast cancer**

A. Altinok[1], O. Alan[2], N. Dizdar[2], H. Caglar[1], U. Ince[3], C. Uras[4], N. Bese[5]. *[1]Medipol University, Radiation Oncology, Istanbul, Turkey; [2]Okmeydani Educational and Research Hospital, Radiation Oncology, Istanbul, Turkey; [3]Acibadem University, Pathology, Istanbul, Turkey; [4]Acibadem University, Breast Surgeon, Istanbul, Turkey; [5]Acibadem University, Radiation Oncology, Istanbul, Turkey*

**Background:** This study aims to analyze intraoperative breast radiotherapy (IOBRT) data collected from three different treatment centers located in Istanbul, Turkey.

**Materials and Methods:** The data was collected over three years (2012–2015) in these three centers. The data includes demographic, pathological and technical information.

**Results:** Three centers participated in this study and data of 105 IOBRT procedures have been collected. Median age of patients was 52 years (range, 26 to 80 years). Treatment intent was curative in all 105 cases. 74 patients (70.5%) had invasive ductal carcinoma, 20 (19%) had ductal carcinoma in situ, 4 (3.8%) had invasive lobular carcinoma, 4 (3.8%) had tubular carcinoma and 3 (2.9%) had mixed invasive carcinoma. T-stage distribution of the patients that underwent IOBRT is Tis 20 (19%), $T_1$ 55 (52.4) and $T_2$ 30 (28.6%). Beam energy units used for treatment of 17

patients (16.2%) was in kV and for the remaining 88 patients (83.8%) the units were in electron. 56 of the 105 patients (53.4%) received IOBRT as a boost and 49 patients (46.6%) as primary. 20 of the latter 49 were treated for DCIS. Distribution of surgery methods used for the 105 patients was as follows; 80 (76.2%) had breast conserving surgery and 25 (23.8%) had nipple–areola sparing mastectomy. 11 of the latter group were treated for ductal carcinoma in situ, another 11 for invasive ductal carcinoma, 2 for invasive lobular carcinoma and 1 for tubular carcinoma.

**Conclusions:** This report documents the patient profiles, treatment particulars and strategies employed during IOBRT in three major centers in Turkey.

**Note:** The data has been submitted to ISOORT 2016 for integration but has not been accepted yet. The update is pending.

**No conflicts of interest**

**213** Poster

**Does sentinel node biopsy affect the use of supine MRI for regional radiotherapy in breast cancer patients?**

D. Eschbach[1], T.C.F. Van Heijst[1], B. Van Asselen[1], J.J.W. Lagendijk[1], M. Van Vulpen[1], H.M. Verkooijen[1], R.M. Pijnappel[2], A.J. Witkamp[3], M.E.P. Philippens[1], T. Van Dalen[4], H.J.G.D. Van den Bongard[1]. [1]*UMC Utrecht, Radiation Oncology, Utrecht, Netherlands;* [2]*UMC Utrecht, Radiology, Utrecht, Netherlands;* [3]*UMC Utrecht, Surgery, Utrecht, Netherlands;* [4]*Diakonessenhuis, Surgery, Utrecht, Netherlands*

**Background:** Regional radiotherapy (RT) is replacing axillary lymph node (LN) dissection in breast cancer patients with tumor positive sentinel node(s) (SNs). Currently, the RT target volume is delineated on Computed Tomography (CT) using anatomical boundaries. Magnetic resonance imaging (MRI) allows high resolution images for explicit LN visualization in supine RT position. The objective of the MILANO trial (NL 50046.041.14) is to assess effects of sentinel node biopsy (SNB) on LN detection rate (number of LNs identified) on MRI and on patient endurance, and relate LN detection rate on MRI to CT.

**Material and Methods:** 10 breast-cancer patients (cT1−3N0) treated with breast-conserving surgery (BCS) and SNB have been enrolled. Additional to standard planning CT, a 1.5 T MRI (T1-weighted, T2-weighted, diffusion-weighted) in supine RT position was acquired before and after SNB. MRI acquisition was limited to 20 minutes per session. Patient endurance to undergo MRI was monitored qualitatively. A radiation oncologist delineated LN levels according to ESTRO contouring guidelines. Individual LNs were delineated using the complementary MRI-sequences. The detection rate was determined for CT and each MRI session. The pre- and postoperative MRI detection rates were compared to assess influence of SNB, and also compared to CT.

**Results:** For all patients, the number of LNs on postoperative MRI including the number of excised LNs exactly matched the preoperative number (19−42) (Table 1). All SNs were retrospectively identified. In 9 out of 10 patients, spatial correspondence of all other LNs between MRI sessions was established. In one patient, a post-SNB seroma was visible, but detection number was unaffected. The majority of LNs were located in the LN levels, while up to 7 were found close to the borders of the axillary levels (up to 6 mm). LN detection on postoperative CT (7−21) was much lower than on postoperative MRI (18−40). Endurance was excellent and unaffected by BCS/SNB.

Table 1. Numbers of LNs found in each patient, on pre- and postoperative MRI, and postoperative CT [a]

| Patient no. | Preop MRI | Postop MRI | Postop CT | Pre- vs. postop MRI | SNs excised |
|---|---|---|---|---|---|
| 1 | 28 | 27 | 21 | 1 | 1 |
| 2 | 42 | 40 | 21 | 2 | 2 |
| 3 | 35 | 33 | 16 | 2 | 2 |
| 4 | 26 | 25 | 10 | 1 | 1 |
| 5 | 34 | 33 | 7 | 1 | 1 |
| 6 | 30 | 29 | 8 | 1 | 1 |
| 7 | 19 | 18 | 7 | 1 | 1 |
| 8 | 23 | 22 | 10 | 1 | 1 |
| 9 | 26 | 23 | 11 | 3 | 3 |
| 10 | 28 | 26 | 11 | 2 | 2 |

[a] The difference between MRI sessions is denoted, as well as the number of SNs excised during SNB.

**Conclusion:** MRI after SNB is able to identify the exact numbers of LNs as found on pre-SNB MRI. CT detection rate is much lower than MRI. SNB does not affect patient endurance to undergo MRI in RT supine position. All excised SNs were identified on preoperative MRI. MRI in RT planning may lead to better target definition compared to CT. In future studies, we will study personalized RT using MRI guidance.

**No conflicts of interest**

**214** Poster

**Patient reported outcomes following hypofractionated radiotherapy in breast cancer patients over 60 years of age**

K.R. Charaghvandi[1], D.A. Young-Afat[2], C.H. Van Gils[3], M.L. Gregorowitsch[1], B. Van Asselen[1], M. Van Vulpen[1], H.J.G.D. Van den Bongard[1], H.M. Verkooijen[3]. [1]*University Medical Center Utrecht, Radiation Oncology, Utrecht, Netherlands;* [2]*University Medical Center Utrecht, Radiation Oncology/Epidemiology, Utrecht, Netherlands;* [3]*University Medical Center Utrecht, Epidemiology, Utrecht, Netherlands*

**Background:** In breast cancer patients ⩾60 years of age, survival is influenced by age-associated comorbidity. Impact of treatment on short-term functionality is therefore an important outcome. This study describes changes in physical and cognitive functioning and fatigue at 6 months following hypofractionated radiotherapy (RT) for breast cancer patients ⩾60 years.

**Material and Methods:** Breast cancer patients referred to the RT department were invited to enter a prospective cohort. Participants consented to collection of clinical data and patient reported outcome measures (PROMs) before and at intervals after RT. For patients ⩾60 years, changes in physical and cognitive functioning (EORTC QLQ-C30) and fatigue (Multidimensional Fatigue Inventory) between baseline and 6 months follow-up (FU) were assessed with paired sample t-test. Subgroup analysis by age (⩾ or <70 years), presence RT toxicity (yes versus no ⩾ grade 2 CTCAE _v4.0) and comorbidity (Charlson Comorbidity Index ⩽2 versus >2) were performed.

**Results:** Between October 2013 and June 2015, 374 patients ⩾60 years were enrolled. PROMs response rate was 90% at baseline and 87% at FU. A total of 157 patients had 6 months FU. Median age was 67 years (range 60−85, n = 56 ⩾70 years). Additional comorbidity was present in 57 (37%) patients. Breast-conserving surgery was performed in 142 (90%) and 73 (47%) of patients received (neo)adjuvant systemic treatment. Median number of RT fractions was 16 (range 16−23) with 35 (22%) women experiencing grade 2 toxicity. Following RT, a decline in physical and cognitive functioning was observed in the total group (Table 1). Motivational fatigue scores improved over time, while physical fatigue scores remained stable (Table 1). In women with comorbidity, physical ($p = 0.025$) and cognitive functioning ($p = 0.037$) deteriorated significantly from baseline, which was not the case for patients without comorbidity. Women ⩾70 years of age, and women experiencing RT toxicity did not show worse deterioration as compared to younger women and women without RT toxicity.

Table 1. PROMs after hypofractionated RT in women ⩾60 years

| | Baseline | 6 months | Δ | p-value |
|---|---|---|---|---|
| Physical functioning [a] | 84.4 | 81.6 | 2.8 | 0.01* |
| Cognitive functioning [a] | 88.2 | 85.4 | 2.8 | 0.04* |
| Fatigue [b] | | | | |
| general | 11.9 | 11.6 | 0.2 | 0.16 |
| physical | 11.9 | 13.2 | 0.2 | 0.22 |
| activity | 13.0 | 12.5 | 0.1 | 0.67 |
| motivation | 12.4 | 11.9 | 0.5 | 0.03* |
| mental | 11.4 | 11.4 | 0.0 | 0.87 |

[a] Range 0–100, higher score indicating better functioning.
[b] Range 0−20, higher scores indicating worse symptoms.
*Significant.

**Conclusion:** At 6 months following hypofractionated RT, a small decline in physical and cognitive functioning was observed in breast cancer patients ⩾60 years. Comorbidity, but not advanced age or experienced RT toxicity, was associated with stronger deterioration of physical and cognitive functioning.

**No conflicts of interest**

**215** Poster

**Locoregional recurrences after neoadjuvant treatment for inflammatory or locally advanced breast cancer**

C.A. Hvid[1], B.V. Offersen[1], M.S. Thomsen[2], H.M. Nielsen[1]. [1]*Aarhus University Hospital, Dept. of Oncology, Aarhus, Denmark;* [2]*Aarhus University Hospital, Dept. of Medical Physics, Aarhus, Denmark*

**Background:** With advances in diagnostics, surgery, medical oncology and radiotherapy locoregional recurrence (LRR) of early breast cancer in

Denmark is historically low with a 5 year risk of 1.6% for local and 0.8% for regional recurrence (DBCG-IMN study). We investigated the frequency and characteristics of LRR after treatment for inflammatory (IBC) or locally advanced breast cancer (LABC) at a single institution, and reviewed the localization compared to the radiotherapy (RT) treatment plan.

**Materials and Methods:** Records for 149 patients consecutively treated for IBC or LABC between September 2006 and December 2014 at the dept. of oncology were reviewed, including pathological reports, imaging, clinical photography and RT treatment plan. Patients had neoadjuvant chemotherapy followed by a mastectomy and axillary node dissection and adjuvant RT including regional nodes, at a dose of 48−50 Gy in 24−25 fractions. A 3 mm bolus was applied 3 cm cranially and caudally to the scar. Patients with LRR as first and only site of relapse were identified. Recurrences were mapped and compared with RT treatment plan.

Various risk factors were tested by chi square tests and risks for local and regional recurrence were compared to DBCG-IMN data by test for exact inference.

**Results:** Median follow-up was 28 months. Median time from surgery to LRR was 8 months, range 2−15 months.

Ten patients developed LRR, 9 were local and 8 of these were located within one cm from the mastectomy scar, mostly in the medial end of the scar. Two patients developed LRR before RT could be delivered and another had recurrence outside the field of prior RT. One was regional (supraclavicular) and also within the RT fields.

Risk of local recurrence was 6% [95% CI 2.8 to 11.2], significantly higher than the early breast cancer population ($p < 0.005$). Risk of regional recurrence was 0.7% [95% CI 0.1 to 3.7] ($p = 0.7$).

In the entire cohort 27 patients had triple negative tumors. For these patients risk ratio of local recurrence was significantly higher at 6.8 [95% CI 2.1 to 22.4] ($p < 0.005$). There was a non-significant trend towards higher risk ratio for inflammatory cancers at 3.0 [95% CI 0.9 to 9.9] ($p = 0.057$).

Nine patients with LRR subsequently developed distant metastases (DM). In the entire IBC/LABC group 35% (N = 52) developed DM.

Twelve patients achieved pathological complete response after neoadjuvant chemotherapy, 3 were triple negative, 2 ER+ and 7 HER-2+. None of these developed LRR.

**Conclusion:** Risk of chest wall recurrence was 3 times higher in the IBC/LABC group compared with a recent historical cohort, however we found no increased risk of regional recurrences. Recurrences were frequently located at the medial end of the scar. In the IBC/LABC group triple negative receptor status was associated with significantly increased risk of local recurrence and might be offered supplementary boost towards the mastectomy scar.

**No conflicts of interest**

**216** Poster

**Variation in the use of boost irradiation in breast conserving therapy in the Netherlands**

K. Schreuder[1,2], P. Spronk[3], J.H. Maduro[4], P.M. Poortmans[5], N. Bijker[6], H. Struikmans[7,8], S. Siesling[1,2]. *[1]Netherlands Comprehensive Cancer Organisation, Department of research, Utrecht, Netherlands; [2]University of Twente, Department of Health Technology and Services Research-MIRA Institute for Biomedical Technology and Technical Medicine, Enschede, Netherlands; [3]Leiden University Medical Centre, Department of surgery, Leiden, Netherlands; [4]University of Groningen- University Medical Centre Groningen, Department of radiation oncology, Groningen, Netherlands; [5]Radboud university medical centre, Department of radiation oncology, Nijmegen, Netherlands; [6]Academic Medical Centre, Department of radiation oncology, Amsterdam, Netherlands; [7]Medical Centre Haaglanden, Department of radiation oncology, Den Haag, Netherlands; [8]Leiden University Medical Centre, Department of radiation oncology, Leiden, Netherlands*

**Background:** A boost dose is applied after breast conserving surgery (BCS) and whole breast irradiation to further reduce the risk of local recurrences in breast cancer. In the NABON Breast Cancer Audit (NBCA) variation in the use of the boost was seen. Identification of factors explaining this variation can be useful to reduce possible undesirable variance in clinical practice. Aims of the current study were to determine the variation of the use of boost irradiation over time and between radiation oncology departments. We also investigated which patient and tumour factors were associated with the use of a boost.

**Material and Methods:** From the NBCA cohort, all patients with primary DCIS or invasive breast cancer without distant metastatic disease diagnosed between January 1, 2011 and December 31, 2014 were selected. Funnel plots were used to evaluate the variation in the use of a boost between departments and over time. Logistic regression was performed to determine factors influencing the variation. Analyses were performed in STATA (version 13.1 2013, Texas).

**Results:** During the study period, 33,902 female patients were treated with radiation for DCIS or invasive breast cancer after BCS. In total 51% of the patients received a boost (45% DCIS, 54% invasive, Table 1). Variation between the 23 departments of radiation oncology was seen for both DCIS and invasive tumours. For DCIS patients, the use of the boost slightly increases over time while for invasive tumours a decrease was seen. Multivariable logistic regression (Table 2) demonstrates that lower age (<50 years), larger tumours (>2 cm diameter), grade 3 and irradical surgery increased boost application for both DCIS and invasive breast cancers. Positive lymph nodes significantly influences boost prescription for invasive breast cancers. Variation could not completely be explained by patient and tumour characteristics.

Table 1.

| | DCIS (n = 4,568) | Invasive (n = 29,334) |
|---|---|---|
| % Boost | 45% | 54% |
| Variation between institutions (n = 23) | 5−92% | 21−80% |
| % boost in 2011 (range) | 45% (5–100%) | 61% (14–100%) |
| % boost in 2014 (range) | 46% (5−86%) | 44% (25−59%) |

Table 2. Multivariable logistic regression boost vs no boost

| | DCIS (n = 4,568) | | Invasive (n = 29,334) | |
|---|---|---|---|---|
| | OR | 95% CI | OR | 95% CI |
| Age <50 vs >50 years | 1.8 | 1.6−2.0 | 8.0 | 7.4−8.7 |
| Larger (>2 cm) vs smaller (<2 cm) tumours | 1.6 | 1.2−2.1 | 1.1 | 1.0−1.2 |
| Grade 3 vs grade 1 | 2.5 | 2.1−3.1 | 7.0 | 6.4−7.6 |
| Irradicality | 14.0 | 9.3–21.2 | 9.5 | 8.0–11.3 |
| Positive lymph nodes | | | 1.4 | 1.3−1.5 |

**Conclusion:** In the Netherlands, a large variation between departments was found for the use of a boost for breast conserving treatment in both invasive breast cancer and DCIS, which could not be explained completely by patient and tumour characteristics. Other factors such as involvement in clinical decision making of the patient for balancing the recurrence risk versus the expected cosmetic result could explain variation and have to be studied in future.

**No conflicts of interest**

**217** Poster

**Inflammatory breast cancer compared to non-inflammatory breast cancer: A Dutch nationwide population-based study**

D. Van Uden[1], R. Bretveld[2], S. Siesling[3], H. De Wilt[4], C. Blanken-Peeters[5]. *[1]Canisius Wilhelmina Ziekenhuis, Surgery, Nijmegen, Netherlands; [2]Comprehensive Cancer Organisation The Netherlands IKNL, Department of Research, Utrecht, Netherlands; [3]MIRA Institute for Biomedical Technology and Technical Medicine, Dept. Health Technology and Services Research, Enschede, Netherlands; [4]Radboud University Medical Centre, Surgical Oncology, Nijmegen, Netherlands; [5]Rijnstate Hospital, Surgery, Arnhem, Netherlands*

**Background:** Inflammatory breast cancer (IBC) is a rare type of locally advanced breast cancer (LABC). The aim of this study was to evaluate patients with IBC (T4D-breast cancer) and compare tumour characteristics, treatment and survival of IBC with T1−3 breast cancer and non-inflammatory LABC (T4A−C breast cancer) in the Netherlands.

**Material and Methods:** Breast cancer patients were selected from the nationwide Netherlands Cancer Registry from the period 1989–2013 (N = 236,502). Data on patient characteristics (i.e. age at diagnosis), pathologic tumour features, treatment and outcome were gathered directly from the patient files by specially trained registrars. Patients were divided in three groups: T1−3 breast cancer, T4A−C breast cancer and IBC (T4D). For analysis of trends in 5-year overall survival, time periods of year of diagnosis were grouped by three periods: 1989–1996, 1997–2004, 2005–2013. Kaplan–Meier survival analysis was performed.

**Results:** 1.3% (3,105/236,502 patients) of the breast cancer patients had IBC. Mean age at diagnosis was highest in the T4A−C group (table). IBC tumours were in one fifth of the tumours triple negative, which was twice as much as the other two groups. IBC patients had more often nodal metastasis with a higher number of positive lymph nodes. Moreover, IBC patients presented themselves more often with distant metastases at time of diagnosis.

Over time an increase in trimodality therapy (neoadjuvant chemotherapy, surgery and radiation therapy) was observed in IBC. In IBC, patients without

distant metastases who received trimodality therapy had the best survival rates when compared to less comprehensive treatment regimens.

The 5-year overall survival (OS) for the whole cohort was 77.2%. Five-year OS significantly increased over time in IBC towards 41% in 2005–2013, which was comparable to the survival in the T4A−C group but lower than the T1−3 group (86%).

| | T1−3 | T4A−C | IBC (T4D) |
|---|---|---|---|
| Number | 236,505 | 13,508 | 3,105 |
| Mean age at diagnosis (yrs) | 60.7 | 68.7 | 61.1 |
| Percentage triple negative (%) | 10.7 | 10.9 | 20.2 |
| M1 at diagnosis (%) | 3.3 | 29.3 | 35 |
| Nodal metastasis at time of diagnosis (%) | 39.6 | 61.6 | 71 |
| Number of involved lymph nodes | | | |
| 0 positive nodes | 59.1 | 28.1 | 17.9 |
| 1−3 positive nodes | 37.5 | 51.8 | 52.1 |
| 4−9 positive nodes | 1.1 | 8.8 | 17.1 |
| ⩾10 positive nodes | 1.0 | 1.0 | 1.9 |
| Overall 5-year survival (%) | 80.1 | 38.1 | 30.5 |
| 1989–1996 (%) | 72.3 | 36.5 | 14.6 |
| 1997–2004 (%) | 77.5 | 34.5 | 24.6 |
| 2005–2013 (%) | 85.7 | 44.4 | 41.0 |

**Conclusions:** IBC is an aggressive and heterogeneous subtype of locally advanced breast cancer, with various factors affecting survival. There has been significant improvement in survival in patients diagnosed with IBC in the last decades in this population-based study. However, there is still an unmet need to improve prognosis since prognosis remain poor.

**No conflicts of interest**

**218** Poster

**Use of adjuvant radiotherapy and endocrine therapy following surgery for DCIS in the ICICLE study**

E. Sawyer[1], G. McCormick[2], R. Roylance[3]. *[1]Kings College London, Oncology, London, United Kingdom; [2]Guys & St Thomas Hospital, Oncology, London, United Kingdom; [3]UCL, Oncology, London, United Kingdom*

**Background:** Ductal carcinoma in situ (DCIS) is a precursor of invasive breast cancer. With the advent of screening mammography, diagnosis of DCIS has become more common. However there is concern regarding over-treatment of DCIS which can lead to variation in treatment. In this study, we analyse the use of postoperative radiotherapy and endocrine therapy in relationship to clinico-pathological features in 2957 cases of DCIS from the ICICLE study.

**Material and Methods:** The ICICLE study (MREC 08/H0502/4), a UK study of DCIS aimed at identifying genetic predisposition to DCIS, recruited cases from 97 centres throughout the UK from 2008–2012. Patients aged under 60 at time of diagnosis, with a current or past history of DCIS (without invasive disease of any histological subtype) were eligible. Pathological and treatment data were collected from local pathology reports and questionnaire.

**Results:** Of a total of 2957 women recruited, 33% underwent mastectomy and 77% BCS, of which 59% underwent postoperative radiotherapy (see Table). Post-operative radiotherapy was strongly associated with grade ($p < 0.00001$).

| | Cases that underwent Mastectomy (980 cases) | Cases that underwent BCS +/− RT (1977 cases) | Cases that underwent BCS + RT (1161 cases) |
|---|---|---|---|
| Median age (yrs) | 50.7 | 52.8 | 52.8 |
| Mean tumour size (mm) | 48 | 17.8 | 20.25 |
| Number of cases | | | |
| High grade / Int grade / Low grade / Unknown | 694 / 224 / 62 / 0 | 1125 / 573 / 247 / 43 | 838 / 264 / 49 / 10 |
| ER+ / ER− / ER unknown | 509 / 205 / 266 | 1126 / 238 / 613 | 659 / 159 / 343 |
| Patients receiving endocrine therapy | 166 | 414 | 267 |

70% of cases had ER status measured and of these 79% were ER positive. 35% of the ER positive patient received endocrine therapy. 166 patients post mastectomy were treated with endocrine therapy and 147 patients who had BCS but no radiotherapy received endocrine therapy.

Of the 1719 cases who had BCS with >6 months follow up, (median 43 months) 103 cases developed ipsilateral recurrence (53% DCIS, 47% invasive), with median time to recurrence 55.5 months.

There was no difference in the frequency of radiotherapy between those that recurred as invasive disease or DCIS or (50% vs 52%) or in the distribution of grade (56% vs 52% high grade). Cases that recurred as invasive disease were originally larger (mean 27.6 mm) compared to those that recurred as DCIS (mean 18.5 mm).

**Conclusions:** Treatment variation demonstrated here reflects that despite trials showing consistent benefit for postoperative radiotherapy and endocrine therapy, clinicians are reluctant to over treat patients. Although the majority of patients had ER status assessed, endocrine therapy was not widely prescribed. In addition 50% of recurrences occurred in patients who had received radiotherapy. It is therefore important to identify more accurate methods for predicting which patients benefit most from radiotherapy and which patients are likely to relapse despite radiotherapy.

**No conflicts of interest**

# Thursday, 10 March 2016

**POSTER SESSION**

## Local Regional Treatment − Surgery

**219** Poster

**Perspectives of cosmesis following breast conservation for multifocal and multicentric breast cancers**

M.P. Tan[1], N. Sitoh[2], Y.Y. Sitoh[2]. *[1]MammoCare, Surgical Oncology, Singapore, Singapore; [2]National University of Singapore, Yong Loo Lin School of Medicine, Singapore, Singapore*

Contemporary data suggest that Breast Conservation Treatment (BCT) for multifocal and multicentric breast cancer (MFMCBC) may be appropriate with non-inferior local control rates. However, there is a paucity of data to evaluate patient's satisfaction with cosmetic outcomes after BCT for MFMCBC. This study was performed to bridge this information gap.

**Materials and Methods:** All patients treated at the author's healthcare facility were included in the study. Patients with MFMCBC who were assessed to be eligible for BCT underwent tumour resection using standard surgical techniques with direct parenchymal closure through a single incision. After at least three years of follow-up, they were invited to participate in a survey regarding their cosmetic outcomes.

**Results:** Of a total of 160 patients, 40 had MFMCBC, of whom 34(85%) underwent successful BCT. Five-year cancer specific survival and disease-free survival was 95.7%. Twenty-one of the 34 patients responded to the survey. No patient rated her cosmetic outcome as 'poor'. Analysis indicated low agreement between patients' self-assessment and clinician-directed evaluation of aesthetic results.

Table 1. Patients' self-assessment and clinician's evaluation of cosmetic outcome

| | Patient's assessment | | | Clinician's assessment | | |
|---|---|---|---|---|---|---|
| | Multifocal | Multicentric | Combined (%) | Multifocal | Multicentric | Combined (%) |
| Excellent − 5 | 5 | 7 | (57.2) | 3 | 6 | (42.9) |
| Good − 4 | 4 | 1 | (23.8) | 7 | 1 | (38.1) |
| Satisfactory − 3 | 4 | 0 | (19.0) | 1 | 1 | (9.5) |
| Fair − 2 | 0 | 0 | | 2 | 0 | (9.5) |
| Poor − 1 | 0 | 0 | | 0 | 0 | |
| Total | 13 | 8 | | 13 | 8 | |
| | | | p = 0.05 | | | p = 0.13 |

Kappa value = 0.11.

**Conclusion:** BCT for MFMCBC is feasible with acceptable survival and cosmetic outcomes. However, there appears to be a disparity between patient and clinician directed evaluation of cosmetic results which warrant further research.

**No conflicts of interest**

**220** Poster

**Feasibility of breast conservation treatment for multifocal and multicentric breast cancer within guideline constraints**

M. Tan[1], N.Y. Sitoh[2], Y.Y. Sitoh[2]. *[1]MammoCare, Surgical Oncology, Singapore, Singapore; [2]National University of Singapore, Yong Loo Lin School of Medicine, Singapore, Singapore*

**Background:** Breast conservation treatment (BCT) is an accepted treatment modality for early unifocal breast cancer provided fundamental oncologic principles are fulfilled. Widespread disease which cannot be incorporated by local excision through a single incision that achieves negative margins with a satisfactory cosmetic result is considered an absolute contraindication to BCT in certain guidelines. Hence, BCT would be contraindicated for multifocal and multicentric breast cancer (MFMCBC) where two or more incisions are required. This study was therefore

performed to evaluate the feasibility of BCT for MFMCBC through a single incision. A secondary objective was to compare BCT rates in MFMCBC and unifocal tumours and their respective outcomes.

**Material and Methods:** A retrospective analysis was performed for patients with breast malignancies who underwent operative treatment between 2009 and 2011. A diagnosis of MFMCBC was made through a combination of clinical findings, standard imaging studies and pathology. Routine MRI of the breasts was not performed. MFMCBC was defined as separate foci of cancer detected either preoperatively or through surgical biopsy. Successful BCT was defined as the ability to obtain clear margins for all tumour foci through a single incision with acceptable resultant cosmesis.

**Results:** A total of 160 patients were analysed, of which 40 (25%) were MFMCBC. Thirty-four of the 40 patients with MFMCBC underwent BCT (85%). After a mean follow up period of 55 months, there were no local recurrences in patients with MFMCBC.

Table 1. Summary of clinicopathologic data for study population

| Clinicopathologic characteristic | All (n = 160) | Unifocal (n = 120) | MFMCBC (n = 40) | p value |
|---|---|---|---|---|
| Age in years | | | | **0.04** |
| Median (range) | 48 (28−78) | | | |
| Mean (SD) | 48.8 (9.8) | 49.7 (9.8) | 46.13 (9.6) | |
| Tumour size in mm | | | | 0.37 |
| Median (Range) | 19.0 (4−97) | 19.0 | 20.0 | |
| Mean (SD) | 21.6 (15.7) | 22.2 (16.2) | 19.6 (14) [a] | |
| Neoadjuvant medical therapy | | | | **0.006** |
| Yes | 23 | 12 | 29 | |
| No | 137 | 108 | 11 | |
| Surgical procedure | | | | 0.99 |
| BCT | 137 (85.7%) | 103 (85.8%) | 34 (85%) | |
| Mastectomy by need | 15 (9.3%) | 11 (9.2%) | 4 (10%) | |
| Mastectomy by choice | 8 (5.0%) | 6 (5%) | 2 (5%) | |
| Re-operations | 4(2.5%) | 0 | 4 | **0.01** |
| Recurrence | | | | 0.42 |
| Local recurrence | 3 (1.9%) | 3 | 0 | |
| Distant disease/Death | 4 (2.5%) | 2 | 2 | |
| 5-yr survival | 96.7% | 97.1% | 95.8% | Log rank test: 0.32 |

[a] Dimension of largest lesion.

**Conclusion:** Within the constraints of guidelines, BCT was achieved in 85% of the patients with MFMCBC in this cohort without evidence of poorer survival when compared with unifocal breast cancer. As there is now emerging evidence suggesting higher survival and improved local control with BCT for unifocal breast cancers, further investigation is needed to confirm if there is a similar trend for MFMCBC.

**No conflicts of interest**

**221** Poster

**Immediate breast reconstruction in locally advanced breast cancer patients treated with neoadjuvant chemotherapy (NAC) or patients with ipsilateral breast tumor recurrence (IBTR)**

T. Shien[1], S. Watanabe[1], Y. Itano[1], K. Kawada[1], Y. Katayama[1], M. Saiga[1], T. Nogami[1], T. Mizoo[1], T. Iwamoto[1], T. Motoki[1], N. Taira[1], Y. Kimata[1], H. Doihara[1]. *[1]Okayama university hospital, Breast Cancer Treatment and Reconstruction Center, Okayama, Japan*

**Background:** Neoadjuvant chemotherapy (NAC) for locally advanced breast cancer patients (LAB) is selected to undergo breast conserving therapy (BCS). The preoperative diagnosis of extent of residual tumor is very difficult depending on the cases and unnatural BCSs are performed for them. Meanwhile the cosmetic outcome of the surgery for the ipsilateral breast tumor recurrence (IBTR) diagnosed after adjuvant radiation and drug therapy is insufficiently. Immediately reconstruction is very useful for early breast cancer patients to keep both curability and cosmetic outcome. However there are not enough evidences of immediately reconstruction for these advanced cases concerning about safety and methods.

**Methods:** We retrospectively analyzed the clinicopathological features, operative methods, perioperative complication, cosmetic outcome and prognosis of immediately reconstruction for LAB with NAC and IBTR.

**Results:** From April 2009 to May 2015, 240 patients underwent breast surgery with immediately reconstruction in Okayama University Hospital and there were 35 (15%) LAB and 10 (4%) IBTR. All LAB were received NAC containing anthracycline and/or taxane and the response of 10 (29%) patients were pCR. The median disease free survival of IBTR was 56 months (26−99). 7 patients underwent adjuvant radiation therapy and 7 patients were treating by TAM. Nipple sparing mastectomy was performed for 26 (74%) of LAB and 7 (70%) of IBTR. DIEP, LD and tissue expander were selected for 15, 10 and 10 LAB and 4, 4 and 2 IBTR as reconstruction surgery. The major skin incision was antero-axillar for 21 LAB and the same as primary surgery for 5 IBTR. Median hospitalization periods of LAB and IBTR were 9 (5−40) and 8 (7−20) days respectively. There were one seroma in LAB and one cholangitis in IBTR. After reconstruction surgery, radiation therapy was performed for 14 LAB patients. There were 4 (11%) and 3 (30%) recurrences after surgery in LAB and IBTR respectively.

**Conclusion:** Immediately reconstruction surgery for LAB and IBTR were preformed safety without complication. It is the very important to prevent the recurrence that the adjuvant therapy was conducted according to plan for these advanced cases.

**No conflicts of interest**

**222** Poster

**Shutting the gate on chronic post-mastectomy pain**

K. Gomez[1], O. Buffin[1], L. Price[1]. *[1]Nevill Hall Hospital, Oncoplastic Breast Unit, Abergavenny, United Kingdom*

**Background:** The risk of developing persistent post-surgical pain varies from 5% after minor surgery to up to 50% for phantom limb or post-mastectomy pain. Chronic pain is defined as pain that persists past the normal time of healing, usually 3-months in the case of non-malignant pain. We hypothesise that preventing the onset of pain transmission prior to commencing surgery reduces the risk of persistent post-mastectomy pain.

**Methods:** This was a retrospective cohort analysis on the prevalence of chronic post-mastectomy pain within one District General Hospital over a 5-year period from 2009–2013. Specifically designed postal questionnaires were sent out to all eligible patients. If no response was received within a set time frame, one follow-up telephone call was made. Pain intensity was measured on a validated 11-point pain intensity numerical rating scale (PI-NRS). All patients were operated on by 2 groups of surgeons − one group always instilled a local anaesthetic (LA) mixture into the mastectomy skin flaps pre-surgery and the other did not. Data was also collected on patient demographics, histology, postoperative complications and length of follow up. The primary end-point was a lack of persistent clinically significant pain 3-months post mastectomy. Appropriate statistical analysis was performed on the data obtained with a p value of $<0.05$ being deemed significant.

**Results:** 221 mastectomies were carried out during this 5-year period with a 71% questionnaire response rate. 100% were female, with a median age of 66 years (Range 35−91 years). The median length of follow-up was 37 months (Range 3−87 months). Only 4.7% of patients who received pre-surgery LA complained of clinically symptomatic chronic post-mastectomy pain (cf. 16.4% who did not receive pre-surgery LA) $p = 0.03$. There was no difference in tumour grade, type of axillary surgery or post-op complication rates between the two groups. The median chronic pain score in patients who had received LA pre-surgery was 3.2 (cf. 3.8 for those that did not) Range 0.0−7.0, $p = 0.44$.

**Discussion:** Pain pathways, and hence the perception of pain can be modulated, sensitised and altered as a result of neuronal plasticity. The role of local anaesthetics is to interfere with the conduction of pain impulses from the site of injury to the central nervous system, thus preventing the sensitisation as described above. The results from our study reveal that instilling local anaesthetic into the mastectomy skin flaps pre-surgery can significantly reduce the incidence of chronic post-mastectomy pain. However, the lack of variance in chronic pain scores between the two groups implies that neuronal sensitisation can be triggered by other factors.

**No conflicts of interest**

**223** Poster

**Clinical impact of breast MRI with regard to axillary reverse mapping in clinically node positive breast cancer patients following neo-adjuvant chemotherapy**

M. Beek[1], E. Tetteroo[2], E. Luiten[1], P. Gobardhan[1], H. Rutten[3], J. Heijns[4], A. Voogd[5], E. Klompenhouwer[6]. *[1]Amphia Hospital, Surgery, Breda, Netherlands; [2]Amphia Hospital, Radiology, Breda, Netherlands; [3]Catharina Hospital, Surgery, Eindhoven, Netherlands; [4]Amphia Hospital, Oncology, Breda, Netherlands; [5]Maastricht University, Epidemiology, Maastricht, Netherlands; [6]Catharina Hospital, Radiology, Eindhoven, Netherlands*

**Background:** Axillary reverse mapping (ARM) is a technique that discerns axillary lymphatic drainage of the arm from the breast. In the current study we retrospectively evaluated the incidence of metastatic axillary lymph node involvement, including ARM lymph nodes, in clinically node positive breast cancer patients (cN+ patients) in whom neo-adjuvant chemotherapy (NAC) was administered followed by primary ALND using breast MRI.

**Patients and Methods:** Data from 98 cN+ breast cancer patients were analysed retrospectively. Patients without residual axillary disease at breast MRI following NAC (RAD−, n = 64) were compared with patients with residual axillary disease (RAD+, n = 34). Presence of suspect axillary lymph nodes on pre-NAC and post-NAC breast MRI was determined by

experienced breast radiologists and was correlated to histopathological findings.

**Results:** In the RAD− group residual axillary disease on pathological analysis following NAC was found in 25 patients (39.1%), as compared to 24 patients (70.6%) in the RAD+ group (p = 0.003). Metastatic involvement of ARM lymph nodes following NAC was demonstrated in 5 patients (7.8%) in the RAD− group as compared to 10 patients (29.4%) in the RAD+ group (p = 0.005).

**Conclusion:** Breast MRI following NAC is not suitable to detect residual metastatic disease of the axilla. However, breast MRI post-NAC may be of use to identify cN+ patients with a low risk of ARM lymph node metastases. This may help to select a subgroup of cN+ patients in whom sparing of ARM lymph nodes during axillary lymph node dissection can be considered.

**No conflicts of interest**

**224** Poster

**Outcome of 529 cases of sling-assisted implant-based breast reconstruction**

M. Barber[1]. [1]*Western General Hospital, Edinburgh Breast Unit, Edinburgh, United Kingdom*

**Background:** The use of extrinsic slings to assist implant-based breast reconstruction has revolutionised this technique. It offers the possibility of a one-stage procedure and is felt to have benefits on cosmetic result, however, there are concerns over outcome.

**Materials and Methods:** All cases where an extrinsic sling was used in a breast reconstructive procedure in Edinburgh, Scotland, UK from initial use on 7/7/2008 to 31/6/2015 were reviewed. Statistical analysis was performed using chi square and t tests.

**Results:** Median follow up was 759 days (range 16–2197). 529 sheets of sling material (220 Strattice®, 184 Veritas®, 72 Permacol®, 34 TiLoop® and 18 with 3 other materials) were used in 505 breasts of 338 patients. The sling material used has changed over time. 41.6% of mastectomies were performed for primary cancer, 13.2% for DCIS, 4.3% for recurrence and 40.8% for risk reduction. 87% of procedures were primary reconstructions, 10.4% were salvage procedures following previous reconstruction and 2.6% were delayed reconstructions. 65.4% used a fixed volume implant at first procedure. 9 patients have had locoregional recurrence, 12 metastatic recurrence and 6 have died.

Ninety-six reconstructions were lost (18.1%). Loss rate was 9.2% at 3 months and 13.8% at 6 months. 18 of 74 patients (24.3%) requiring adjuvant therapy had this delayed due to reconstructive problems. 59 of 182 patients (32.4%) having unilateral surgery have undergone contralateral symmetrisation. Patients underwent a mean of 1.4 further operations (0−9) on the affected breast. Implant loss varied significantly with smoking (34.1% loss in smokers vs 11.8% in non-smokers, p < 0.0001) and with use of radiotherapy (27.3% loss with radiotherapy vs 15.1% without, p = 0.0021). There was no statistically significant variation with operating surgeon, type of sling used, breast weight, patient weight, nipple preservation, associated axillary surgery or chemotherapy use. Long term loss rate in non-smokers who did not receive radiotherapy was 9.7%. There was no evidence of an improvement in results over time.

**Conclusions:** While offering potential cosmetic and financial benefits, sling-assisted implant breast reconstruction has a significant rate of reconstruction loss, need for further surgery and delay in adjuvant therapy. These should be important considerations for patient selection and consent.

**No conflicts of interest**

**225** Poster

**Oncological safety of skin sparing mastectomy with immediate breast reconstruction in locally advanced breast carcinoma**

H. Khalifa[1], M. Sakkary[1], O. Nassar[1], R. Oreaba[1]. [1]*National Cancer Institute- Cairo University, Surgical Oncology, Cairo, Egypt*

**Introduction:** The safety and efficacy of skin-sparing mastectomy (SSM) in patients with high-risk breast cancer have not been well studied.

**Materials and Methods:** Prospective, non-randomised study on 70 patients with stage IIIA breast carcinoma, enrolled from 2008–2012, who received anthracycline based neoadjuvant chemotherapy with good response, were allocated to either SSM and immediate reconstruction or CM. The choice between SSM or CM was based on a joint decision by the patients and physicians. There was no attempt to randomize patients.

**Results:** The seventy patients who showed good response to neoadjuvant anthracycline based chemotherapy were divided to two groups: Group (A) underwent skin sparing mastectomy followed by immediate reconstruction either by latissimus dorsi flap or TRAM flap, while Group (B) underwent modified radical mastectomy. The duration of operation and blood loss were more longer in group (A) than group (B). During follow up for two years for patients in both group, local recurrence in group (A) was observed in 3 cases while it was 4 cases in group (B) and the difference was insignificant. Metastasis observed in 12 cases (34.3%) in group (A) and 11 cases 31.4% in group (B) and the difference was insignificant. Overall survival was similar in both groups (A&B), this was 94.3% and 97.1% respectively.

**Conclusion:** In our study the feasibility of skin sparing mastectomy in down staged selected locally advanced breast cancer after neoadjuvant chemotherapy suggested that it is oncologically safe.

**No conflicts of interest**

**226** Poster

**Short term safety of oncoplastic breast conserving surgery for larger tumors**

J. Wijgman[1], B. Ten Wolde[1], K. Van Groesen[1], M. Keemers-Gels[1], F. Van den Wildenberg[1], L. Strobbe[1]. [1]*Canisius-Wilhelmina Hospital, Department of Surgical Oncology, Nijmegen, Netherlands*

**Background:** Oncoplastic surgery (OPS) is becoming state of the art, replacing lumpectomy as standard technique in breast conserving surgery (BCS). OPS has shown to give good cosmetic results, but is it as safe as standard lumpectomy? We conducted a retrospective cohort study to determine postoperative complications, resection margins and re-excision rates for OPS compared to standard lumpectomy.

**Methods:** Based on data from the 'Dutch Cancer Registry' and medical records we scored patient, treatment and follow-up related variables. All consecutive patients, with an initially breast conserving operation, performed between January 2010 and December 2014 in a dedicated breast center were eligible. Breast surgeons performed the operations. Invasive and in situ tumors were included. Primary mastectomy, diagnostic microdochectomy and benign histology were excluded. Postoperative complications had to appear within 30 days after surgery. Major complications included hematoma or bleeding, infection and seroma.

**Results:** We found 828 women with 842 breast cancers, who had a lumpectomy (62.7%) or oncoplastic resection (37.3%). OPS was performed more often for larger tumors (17.5 mm vs 13.6 mm, p = 0.002) and for tumors in the caudal half of the breast (33.1% vs 16.9%, p < 0.001). There was no significant difference in major postoperative complications. Pain as a complication was borderline significantly higher for patients in the OPS group (4.4% vs 1.9%, p = 0.054). Eventually OPS resulted in slightly more positive surgical margins (22.6% vs 18.2% p = 0.119), but did not result in higher re-excision rates. More patients in the lumpectomy group with positive surgical margins had secondary surgery (64.6% vs 53.5%, p = 0.149). Unfortunately the follow-up is too short to have a look at survival rates.

**Conclusion:** Oncoplastic breast surgery can be safely applied in larger tumors, resulting in comparable complication and re-excision rates compared to standard lumpectomy.

**No conflicts of interest**

**227** Poster/Poster Spotlight

**Study of axillary lymph node staging based on a combined use of histology and one-step nucleic acid amplification method for breast cancer patients without axillary lymph node dissection**

T. Kinoshita[1], K. Jimbo[1], S. Shiino[1], S. Asaga[1], S. Takayma[1], M. Toshida[2]. [1]*National Cancer Center Hospital, Division of Breast Surgery, Tokyo, Japan;* [2]*National Cancer Center Hospital, Division of Pathology, Tokyo, Japan*

**Background:** We developed the NCS score based on detailed evaluation of SLNs in breast cancer patients by a combined use of histology and OSNA, to determine breast cancer patients in whom ALND can be omitted. ACOSOG Z0011 study revealed that ALND can be omitted in selected breast cancer patients even when they are positive for SLN metastasis. However, determining the total number of axillary lymph nodes, or staging, is still important when deciding postoperative treatment strategy.

**Material and Methods:** There were 1176 cTis-3 N0 patients who were operated in our institution and diagnosed by a combined use of histology and OSNA for SLNs. Of these, 323 patients who underwent additional ALND for positive SLN metastases were included in this study. SLNs evaluated as MAC, MIC, and ITC in histology and evaluated as 2+, 1+, and +I in OSNA and they were assigned with 3, 2, and 1 points, respectively. In each patient, the total sum of histology and OSNA points of all SLNs was defined as a NCS score point. We compared the performances of NCS score and other clinical factors on predicting the total number of lymph node metastases (N2 staging) and RFS rates.

**Results:** Performances of NSC score on predicting non-SLN metastases and N2 staging (AUC=0.912 and 0.920, respectively) were better than

those of other individual factors. Our data suggested that semiquantitative OSNA was a prognostic factor independent of pathology for N2 staging (OR=4.90, $p < 0.0001$). NSC score and OSNA copy number were both significantly correlated with RFS.

**Conclusion:** NCS score is a good independent prognostic factor for predicting not only non-SLN metastases but also the number of lymph node metastases.

**No conflicts of interest**

**228** Poster

**The iBRA (implant Breast Reconstruction evAluation study) – a prospective multicentre cohort study to inform the feasibility, design and conduct of a pragmatic randomised clinical trial comparing new techniques of implant-based breast reconstruction**

S. Potter[1], on behalf of the Breast Reconstruction Collaborative[2].
[1]*University of Bristol, Bristol, United Kingdom;* [2]*Nationwide, Breast and Plastic Surgery, United Kingdom*

**Introduction:** Implant-based breast reconstruction (IBBR) is the most commonly-performed reconstructive procedure in the UK. New techniques to augment the subpectoral pocket with biological or synthetic mesh have revolutionised the procedure, but there is a lack of high-quality outcome data to support the safety or efficacy of these techniques. RCTs are the best way of comparing treatments but there is currently insufficient data to suggest whether a trial would be appropriate and premature progression to an RCT may alienate potential participants. Feasibility work is therefore essential before a pragmatic trial can be considered.

The iBRA (implant Breast Reconstruction evAluation) study aims to use the trainee research collaborative model with expert methodological support from the Bristol Surgical Trials Centre and the University of Liverpool to determine the feasibility, design and conduct of a pragmatic RCT comparing novel approaches to IBBR.

**Methods:** The iBRA study has four phases. Firstly, a national practice questionnaire (NPQ) will describe current practice including the number of centres and surgeons performing each procedure to inform the selection of potential comparators in a future trial. The survey will also explore variability in patient selection for different techniques and the use of concommittant interventions such as antibiotics to inform the design of the main trial.

Phase 2 will involve a 12-month prospective cohort study of consecutive patients undergoing IBBR. This will generate high-quality data regarding the clinical and patient-reported outcomes of surgery, determining the comparative safety of each technique and informing a future sample size calculation. Candidate outcome measures, including the sensitivity of the BREAST-Q questionnaire to differences between treatment groups will also be explored in this phase as will the feasibility of using the trainee collaborative model to recruit patients to the study and collect robust, complete, longitudinal data.

The results of phases 1 and 2 will be used to design phase 3, an IBBR-RCT acceptability survey to explore patients' and surgeons' views of proposed trial designs, outcome measures and their willingness to participate in a future RCT. Qualitative interviews will build on the questionnaire findings to determine the feasibility of undertaking phase 4, the design of a definitive, pragmatic RCT comparing novel approaches to IBBR.

**Results:** Since May 2014, 85 units have contributed to the NPQ. 1178 patients have been recruited from 61 centres; data completeness is over 90% and the study is 9 months ahead of schedule.

**Conclusions:** The iBRA study has demonstrated that trainee collaboratives are a time and cost-effective method for the delivery of a high-quality, multicentre feasibility studies in reconstructive surgery.

**No conflicts of interest**

**229** Poster

**The use of superparamagnetic iron oxide (SPIO) as sole method for the detection of sentinel node (SN) in breast cancer. The MONOS study**

A. Karakatsanis[1], K. Daskalakis[1], Y. Andersson[2], S. Andersson[2], F. Wärnberg[1]. [1]*University Hospital Uppsala, Dept. For Surgical Sciences- Section For Breast and Endocrine Surgery, Uppsala, Sweden;* [2]*Vastmanlands Hospital- Vasteras, Department of Surgery- Section For Breast Surgery., Vasteras, Sweden*

**Background:** SPIO is a novel method for the detection of SN in breast cancer patients. Comparative studies have verified non-inferiority to the standard use of $^{99}$Tc with or without the addition of ink. The aim of the current study was to evaluate SPIO without the use of $^{99}$Tc.

**Material and Methods:** Patients were recruited from Uppsala University Hospital and Västmanlands Hospital, Västerås. Totally, 342 SN biopsies in 337 consecutive patients were performed. In Västerås, $^{99}$Tc (n = 155) was injected the day before or, on the day of surgery and ink was routinely used. In Uppsala, SPIO (Sienna+) (n = 182) was injected at the outpatient visit several days prior to surgery or on the day of surgery 20−40 minutes start of operation (2 ml+3 ml local anesthetic). At surgery transcutaneous counts were taken and if dubious, ink was injected in standard fashion.

**Results:** Detection rate for SPIO (+/− ink) was 95.6 vs. 96.1% for $^{99}$Tc (+/− ink) ($p = 0.55$). No difference was noted in malignancy rates (21.9 vs. 25.8%, $p = 0.39$). BMI was higher in the $^{99}$Tc (+/− ink) group (25.8 vs. 27.2, $p = 0.006$). Significantly fewer nodes were removed using SPIO, regardless of the use of ink ($p < 0.001$). Additionally, all magnetic nodes were colored gray, facilitating the procedure. No serious adverse effects were noted. In the SPIO group, 62.7% of patients were injected 2−27 days before surgery. No difference was found in the detection rate compared to those who had their injection at the day of surgery.

Discoloration after SPIO was associated ($p < 0.001$) with breast conserving surgery (BCS) and was present in 56.7% of those with BCS. After 9 months staining was paler but 53.4% still had a discoloration. A deeper injection was related to discoloration in 33.3% after BCS in a subset of patients.

| TH COLSPAN=2>Technique | Total SIENNA+ | p-value $^{99}$Tc | | |
|---|---|---|---|---|
| Patients | 182 | 155 | 337 | n.a. |
| Procedures | 183 | 159 | 342 | n.a. |
| Age (m, 95% CI) | 63.4 (61.8, 65.1) | 66.0 (64.0, 68.0) | – | 0.053 |
| BMI (kg/m$^2$) (m, 95% CI) | 25.8 (25.1, 26.4) | 27.2 (26.4, 28.0) | – | **0.006** |
| Operation | | | | |
| Mx | 56 (30.6%) | 52 (32.7%) | 108 | 0.67 |
| BCS | 126 (68.8%) | 105 (66.0%) | 230 | 0.58 |
| SNB | 1 (0.5%) | 2 (1.23%) | 3 | 0.48 |
| Additional ink | 93 (50.8%) | 155 (97.5%) | 248 | **<0.001** |
| Detection rate (%) | 95.6 (91.6–97.8) | 96.1 (93.1–99.2) | – | 0.55 |
| Malignancy rate (%) | 21.9 (16.2, 28.7) | 25.8 (19.3, 33.4) | – | 0.39 |
| SN numbers (95% CI) | 1.4 (1.2, 1.5) | 1.9 (1.7, 2.0) | – | **<0.001** |
| tracer-only detected SN (numbers, 95% CI) | 1.3 (1.2, 1.4) | 1.7 (1.6, 1.8) | – | **<0.001** |

**Conclusions:** SPIO is a safe and effective method for SN biopsy. It does not have the known drawbacks of the dual standard. It simplifies the logistics and can effectively be used instead of $^{99}$Tc. Using SPIO is cheaper per patient, especially when ink is not used.

**No conflicts of interest**

**230** Poster

**Our novel endoscopy-hybrid breast conservation surgery: The pursuit of cosmetic improvement with minimal skin incision**

H. Tanaka[1], S. Umeda[1], S. Murakami[1], M. Ishikawa[1], A. Uchiyama[1].
[1]*JCHO Kyushu Hospital, Surgery, Kitakyushu, Japan*

Background and Objective: We developed our novel Endoscopy-Hybrid breast conservation surgery since 2007 for primary breast cancer at Kyushu University Hospital. This time, we improved this operative procedure by applying new and inexpensive endoscopic breast surgery devices (Light guided Breast-Retractor, Four Medics, Japan, and 5 mm rigid scope, Karl Storz, Germany) and newly introduced to my current institution. Our indication of this surgery is restricted to T1 cases without extensive intraductal spreading. Our goal is to determine the safeness, general versatility, curability, and cosmetic improvement of Endoscopy-Hybrid breast conservation surgery, compared with conventional breast conservation surgery.

**Methods:** We assessed 102 patients with primary breast cancer who underwent breast conservation surgery (BCS) in our department from September 2014 to October 2015. We performed Endoscopy-Hybrid BCS for 20 cases and conventional BCS for 82 cases, combined with sentinel lymph node biopsy or level I + II axillary dissection carried out under direct vision. We reviewed and weighed operative duration, amount of bleeding and positive surgical margin rate between two groups, and follow up local recurrence and overall survival rate.

**Result:** In conventional BCS group, median operative duration was 112 min, mean amount of bleeding was 32GM, and positive surgical margin rate was 2.4% (2 cases). In Endoscopy-Hybrid BCS group, median operative duration was 168min, mean amount of bleeding was 21GM and positive surgical margin rate was 0%. Endoscopy-Hybrid BCS required more operative duration, but the amount of bleeding decreased significantly. Positive surgical margin rates showed no significant differences in both groups. These results (operative duration, blood loss, positive margin rate) also showed no significant differences in each operator (four operators in our department), thus, this new procedure considered easy to learn relatively. About the curability, no significant differences of local recurrence and overall survival rates were observed between two groups after a follow-up period of 6.5 month, though very short duration. For cosmetic

improvement, we could perform more extensive skin flap formation and dissection of mammary gland from pectoral major muscle by employing Endoscopy-Hybrid method. As a result, we could achieve more mobilization of breast tissue and appropriate mammoplasty after BCS.

**Conclusion:** Our improved Endoscopy-Hybrid BCS can minimize skin incision, reduce blood loss, and improve reconstructive outcome. This technique is easy to learn and well introduced to many institutions because requisite new surgical instruments are at low cost. Also, it would be accepted by many patients desiring better esthetic preference.

**No conflicts of interest**

**231** Poster

**Pregnancy associated breast cancer: A tertiary care cancer centre experience from India**

J.R. Vishnoi[1], V. Kumar[1], S. Gupta[1], N. Akhtar[1], S. Misra[2], S. Rajan[1], P.K. Dontula[1], J. Paryani[1], P. Suryavanshi[1]. *[1]King George Medical University, Surgical Oncology, Lucknow, India; [2]All India Institute of Medical Sciences, Director & CEO, Jodhpur, India*

**Background:** Pregnancy-associated breast cancer (PABC) is defined as the development of breast cancer during pregnancy or during the 12 months following delivery or anytime during lactation. It occurs in 1/3000 to1/10,000 pregnancies. It is often diagnosed at an advanced stage and its prognosis is worse compared to non-PABC. PABC data from developing countries like India are scarce. Our objective was to analyze the findings of PABC from a tertiary care cancer centre in India.

**Material and Methods:** A retrospective review of breast cancer patients treated from 2010 to 2015 from departmental computerized database was performed and pregnancy associated breast cancer were identified and data were analyzed.

**Results:** A total 22 patients were identified as PABC. Mean age of patients was 28.6 years (range 19−34 years). Majority of patients (72.7%) were diagnosed during lactation period. Six patients were detected during pregnancy, among them one patient in first trimester who underwent termination of pregnancy, three patients in second trimester and two cases in third trimester. Majority of patients (90.9%) presented with lump in breast and mean duration of symptoms was 4.2 months. Family history of breast or ovarian cancer was seen in 13.6%. High resolution ultrasound was performed in majority of patients. Two patients had bilateral synchronous breast cancer. Inflammatory breast cancer was seen in 9% cases. Stage wise distribution was as stage I (4.5%), II (13.6%), III (63.6%), and IV (18.1%). Among distant metastasis 9% cases had liver and similar number of cases had skeletal metastasis at presentation. Treatment modalities were upfront surgery (18.1%), neo adjuvant chemotherapy (63.6%), palliative chemotherapy (18.1%), and adjuvant radiotherapy (72.7%). Histopathological features were as high grade tumor (54.4%), node positivity (68.1%), estrogen or progesterone receptor negativity (59%) and HER2neu receptor positivity (33.3%). Median follow up was 22 months (range 2 months to 5.2 years). Approximately 44.4% cases had recurrence and most common sites were bone followed by liver. Overall survival and disease free survival at 2 years were as 72.7% and 55.6% respectively.

**Conclusion:** Pregnancy associated breast cancer is very rare occurrence. Majority of patients present in advanced stage with worse outcome. In comparison to non-PABC these patients have more frequent poor prognostic factors like node positivity, higher grade, ER/PR negativity, and Her2neu positivity.

**No conflicts of interest**

**232** Poster

**Recurrence rates after oncoplastic breast surgery in patients aged 60 and over**

W. Ho[1], S. Stallard[2], J. Doughty[2], E. Mallon[3], L. Romics[1]. *[1]New Victoria Hospital, Surgery, Glasgow, United Kingdom; [2]Gartnavel General Hospital, Surgery, Glasgow, United Kingdom; [3]Queen Elizabeth University Hospital, Pathology, Glasgow, United Kingdom*

**Background:** Elderly patients should be offered the same surgical treatment for breast cancer than younger patients if comorbidities and frailty permit. Oncoplastic surgery, however, is less frequently offered to this age group. Recurrence rates after oncoplastic surgery in patients aged 60 and over were analysed.

**Methods:** A retrospective review of breast cancer patients aged 60 and over treated with oncoplastic breast conservation surgery (OBCS) was carried out. Patients were treated in two breast units in Glasgow. While elderly patients are generally regarded as 70 years and above, patients aged 60 and over represent a relatively older subgroup among those treated with OBCS.

**Results:** 55 patients with a mean age of 67 (60−79) were treated with OBCS. 40 patients had invasive ductal, eight patients had invasive lobular, two patients had tubular and one patient had mixed cancer. Another five patients had DICS. Complete pathological regression was noted in one patient after neoadjuvant chemotherapy. Mean tumour size was 22 (3−70) mm. Invasive cancer was G3 in 26 patients, G2 in 18 and G1 in 6 patients. ER receptor was positive in 40 patients, while the same for PR was 32 patients. HER-2 receptor was positive 10 patients. After oncoplastic excision the margins were incomplete in 6 cases (10.9%). Of these, 4 patients underwent completion mastectomy. All pateints who had OBCS received adjuvant radiotherapy. 3 patients received neoadjuvant, 19 patients received adjuvant chemotherapy. 39 patients received adjuvant hormonal therapy. Mean follow-up time was 43 months (17−80). One patient developed local recurrence (1.8%), three patients developed distant recurrence (5.5%).

**Conclusion:** Recurrence rate after oncoplastic surgery in patients aged 60 and above is similar to the published recurrence rates in the younger age groups. Oncoplastic techniques are safe in the relatively older patients, and those should be discussed with the suitable older patients as a possibility to improve the aesthetic outcome of their treatment.

**No conflicts of interest**

**233** Poster

**Does the management of the intercostobrachial nerve influence the postoperatory paresthesia of the upper limb in breast cancer patients?**

R. Georgescu[1], O. Bauer[1], S. Stolnicu[2], D. Podeanu[3], C. Toganel[4], D. Roman[5], D. Moncea[2], H. Hosszu[6], I. Colcer[7], A.M. Filimon[7], M.F. Coros[1]. *[1]University of Medicine and Farmacie Tg Mures, Surgery III, Targu Mures, Romania; [2]University of Medicine and Farmacie Tg Mures, Pathology, Targu Mures, Romania; [3]University of Medicine and Farmacie Tg Mures, Radiology, Targu Muress, Romania; [4]University of Medicine and Farmacie Tg Mures, Oncology, Targu Mures, Romania; [5]Mures County Hospital, Oncology, Oncology, Romania; [6]University of Medicine and Farmacie Tg Mures, Surgery III, Targu Mure, Romania; [7]Mures County Hospital, Surgery I, Targu Mures, Romania*

**Background:** The intercostobrachial nerve (ICBN) is the lateral cutaneous branch of the second intercostal nerve, presenting a significant anatomic variability which means that it has a high risk of being damaged during axillary surgery. As part of the somatic nervous system provides specific sensory information regarding the skin and its damage may be the cause of persistent pain and sensory disturbances of the skin that covers the axilla and the medial face of the arm. The aim of our study is to evaluate how the preservation or the section of the intercostobrachial nerve influences the development of the postoperatory paresthesia. On the other hand our intention was to assess by what means does the paresthesia change the patients life quality in the postoperative period.

**Material and Methods:** We performed a nonrandomized retrospective study including 100 patients who underwent axillary lymph node dissection for breast cancer. Using a questionnaire we studied the patients general life quality in the postoperative period. For the statistical analysis we used GraphPad Prism, Fisher‘s exact test and Pearson‘s correlation test.

**Results:** 100 of cases were identified, with the mean age of 59.76 years. In 47 cases the ICBN was preserved and in 53 cases it was sectioned during the operation. 46% of the cases the patients developed postoperative paresthesia in the axilla or the upper limb. Significantly more patients complained about postoperative paresthesia in which the ICBN was sectioned ($p = 0.026$, RR=0.58, CI=0.3728–0.9218).

In our series the management of the ICBN cannot be significantly correlated with the impairement of the patients daily activity ($p = 0.1$, $r = -0.16$), sleeping cycle ($p = 0.1123$, $r = -0.15$) and general life quality after surgery. ($p = 0.3727$, $r = -0.09$).

**Conclusions:** We can conclude that the ICBN in our series has a great influence on the development of postoperative paresthesia. In our opinion it is important to preserve the ICBN to prevent the postoperative paresthesia, despite de fact that damaging the nerv dose not affect the quality of life.

**No conflicts of interest**

**234** Poster

**Outcome according to immunohistochemical surrogates of the molecular subtypes in early breast cancer**

A. Lombardi[1], S. Maggi[1], G. Stanzani[1], V. Vitale[1], C. Romano[1], I. Gentili[1], L. Bersigotti[1], C. Amanti[1]. *[1]Universita La Sapienza, Unita Di Chirurgia Senologica − Ospedale Sant'andrea, Rome, Italy*

**Background:** Breast cancer heterogeneity is reflected in a wide genomic and phenotypic variability. Both the tumor microenviroment and the neoplastic transformation of different cell subpopulations may contribute

to the development of distinct biological profiles of breast cancer. The improvement of molecular technologies has laid the foundations for a newer taxonomic system based on gene expression profiling. The molecular portraits of human breast tumors painted by Perou allowed to identify several patterns of gene expression that are predictive of biological and clinical behavior: ER+/luminal like, basal-like and normal breast. Despite the microarray-based molecular analysis represents the gold standard method, its application to clinical practice is still limited by high costs and technical complexities. However, a surrogate molecular classification, based on immunohistochemical markers, can be used as a suitable approach for classification purposes.

**Materials and Methods:** The aim of our study is to examine the recurrence pattern of distinct surrogate molecular subtypes in a population of women affected by early breast cancer, taking advantage of a monoinstitutional analysis. The available data comes from 1133 patients who underwent breast surgery and sentinel lymphnode (SLN) biopsy, followed by axillary dissection in case of SLN involvement, from October 2004 to July 2014.

**Results:** Median follow-up was 5.2 years. Breast cancers were immunohistochemically analyzed as follows: 50% as Luminal B, 33% as Luminal A, 9% as Triple negative and 8% as being HER2 positive subtype (with or without hormonal receptor-HR expression). The estimated 10-year Overall Survival (OS) was 92%, whereas the 10-year Disease Free Survival (DFS) was 82%. The LA-like subtype had an higher 10-year OS (95%), compared with LB-like subtype (10-year OS 90%; 10-year DFS 80%) and HER2+HR− subgroup (10-year OS 79%).

**Conclusions:** In our analysis the Luminal B-like subtype is associated with an intermediate long-term prognosis (slightly similar to that of Triple negative breastcancers) and just in these cases molecular profiling could be used to guide therapeutical decisions. An accurate definition of the biological profile of breast carcinomas could be helpful in predicting clinical outcome, in order to personalize therapeutic strategies and design an appropriate follow-up program, assuring the best bioprofiling for the most effective treatment.

**No conflicts of interest**

**235** Poster

**Our experience on sentinel node analysis with O.S.N.A. (one step nucleic acid amplification)**

R. Murgo[1], L. Petito[1], F. Natale[1], A. Marzovillo[1], L. Ciuffreda[1]. *[1]Irccs Hospital "Casa Sollievo Della Sofferenza", Breast Surgery, San Giovanni Rotondo, Italy*

**Background:** The O.S.N.A. (one step nucleic acid amplification) for intraoperative analysis of sentinel node (SN) in patients with breast cancer is a recent molecular technique that allows to search the cancer cells in the first lymph node draining the tumor site, not with a morphological examination but with a molecular approach. Is, in fact, performed the quantitative analysis of mRNA for the cytokeratin 19 (CK19), a specific marker of breast cancer cells.

This method allows, in 35/40 minutes, to detect, with high diagnostic accuracy, the presence or absence of micrometastases (number of copies of CK19 mRNA between 250 and 5000) or macrometastases (number of copies of CK19 mRNA more than 5000) in the SN during breast cancer surgery.

There is, however, a small percentage of breast cancers (1−2%) which does not express this marker, but, recently, it was found that the lack of CK19 expression does not necessarily coincide with the relative gene absence. In addition, the CK19 negative tumors prefer the blood-borne.

In the traditional mode the SN is examined, during the surgery, with microscopic analysis technique, laborious and influenced by the manual and operator subjectivity, or after the surgery (inclusion technique), with need to perform, if positive, the axillary dissection in a second time.

Our guidelines provide the axillary dissection only in case of macrometastases in the SN.

**Material and Methods:** Since October 2012 to May 2015 in our center were performed 573 sentinel node biopsy (SNB) in patients with breast cancer, with O.S.N.A. method to analyze intraoperative sentinel node.

**Results:** The O.S.N.A. method showed the presence of micrometastases in 66 lymph nodes (11.52% of the total), macrometastases in 89 lymph nodes (15.53%) and the absence of metastasis in 418 (72.95%).

**Conclusions:** The O.S.N.A. method, alternative to the traditional microscopic investigation, allows to analyze the SN with automated molecular technique, precise, fast, little influenced by the operator.

Allows the identification of positive lymph nodes, with an optimal discrimination between micro and macro metastasis, removes the false negativity, avoiding, therefore, a second surgery.

Reduces, also, almost half, the analysis running time (from 60/75 to 35/40 minutes), reducing, consequently, the time of anesthesia.

**No conflicts of interest**

**236** Poster

**Our experience on titanium-coated polypropylene mesh in conservative mastectomies**

R. Murgo[1], L. Petito[1], F. Natale[1], A. Marzovillo[1], L. Ciuffreda[1]. *[1]IRCCS Hospital "Casa Sollievo Della Sofferenza", Breast Surgery, San Giovanni Rotondo, Italy*

**Background:** The titanium-coated polypropylene mesh (TCPM) is used in immediate, single or two stage, implant-based breast reconstruction (IIBBR), with the advantage, compared to the traditional technique, of an immediate and natural ptosis thanks to the section of the pectoralis major muscle. The mesh is sutured to the lower muscle border and covers the lower pole of the prosthesis.

**Material and Methods:** Our indications for the use of TCPM in IIBBR were, at first, focused on the nipple areola complex sparing mastectomy (NACSM) and skin sparing mastectomy (SSM) in small/medium volume breasts. From two years we have extended the indications to medium/large size breasts, with distance between the areola and the inframammary fold less than 10 cm, above which is indicated skin reducing mastectomy (SRM).

Contraindications were: previous RT, smoking and diabetes.

The TCPM is fixed to the lower border of the pectoralis major, sectioned on its rib insertions, with a continuous resorbable suture and wrapped around the implant, preserving serratus muscle.

From October 2011 to May 2014, we performed 176 conservative mastectomies with IIBBR:

- 112 NACSM (72 in single stage, 40 in two stage)
- 61 SSM (14 in single stage, 47 in two stage)
- 3 SRM

The mean age of patients was 49 years (range 25−71).

**Results:** In 7 cases of NACSM was removed the nipple areola complex (NAC) for intraoperative detection of tumor on retroareolar tissue.

We recorded 15 major complications (8.5%), followed by surgical revision and, in 13 cases, by removal or replacement of the implant, as detailed below:

Early complications:

- haemorrhage in 2 NACSM with implant preservation;
- infection in 2 NACSM with implant loss;
- exposure on ischemic necrosis with implant loss in 1SSM and in 3 NACSM (2 of which were treated with latissimus dorsi flap (LDF).

Late complications:

- fat necrosis, after 1 month from RT, in 1 NACSM, with implant loss;
- severe capsular fibrosis in 2 NACSM, treated with LDF, and in 4 SSM, treated with implant removal (by will of the patients) in 1 case, and with LDF in 3 cases.

18 minor complications (10.2%) were treated conservatively: temporary ischemia of the NAC in 7 cases, wound dehiscence in 2 cases and infection/lymphangitis in 9 cases.

The mean follow-up was 18 months, during which we had 12 local recurrences (6.8%), in 2 SSM and 10 NACSM, treated with resection and prosthesis removal, in 4 cases (1 SSM 1 and 3 NACSM), or its replacement with an expander in the remaining cases.

**Conclusions:** The TCPM reduces surgical time, extends the indications for a IIBBR also on mastectomies performed in medium/large size breasts, ensures an excellent biocompatibility and lower incidence of capsular fibrosis, even after RT, and, finally, improves the aesthetic outcome, giving a natural ptosis to the reconstructed breast.

**No conflicts of interest**

**237** Poster

**Nipple- and areola-sparing mastectomy for the treatment of breast cancer**

B. Mota[1], J.L. Bevilacqua[2], M.D. Ricci[1], R. Rieira[3], A. Atallah[3], J. Barret[4]. *[1]ICESP, Gynecology and Obstetrician, São Paulo, Brazil; [2]AC Camargo Cancer Center, Breast Cancer surgery, São Paulo, Brazil; [3]Universidade Federal de São Paulo, Medicina Baseada em Evidencia, São Paulo, Brazil; [4]Medical Research Council MRC Biostatistics Unit, Institute of Public Health- University Forvie Site, Cambrige, United Kingdom*

**Background:** The efficacy and effectiveness of nipple sparing mastectomy (NSM) and areola-sparing mastectomy for the treatment of breast cancer are still questionable. We conducted a systematic literature review with meta-analysis with the concrete scientific evidence for NSM in the treatment of breast cancer.

**Material and Methods:** Electronic searches were conducted using the Mesh terms "nipple sparing mastectomy" and "areola-sparing mastectomy" in the following databases: the Cochrane Breast Cancer Group Specialized Register, the Cochrane Center Register of Controlled Trials, MEDLINE by PubMed, EMBASE by Ovid, LILACS and The WHO International Clinical

Trials Registry Platform. Inclusion criteria were randomized or quasi-randomized studies of in situ or invasive breast carcinoma. Data extraction was performed using the RevMan 5.2 software according to the Cochrane Handbook for Systematic Reviews. We performed a descriptive analysis and meta-analyisys of the data. The outcomes evidence was evaluated using the criteria of GRADE working group. The primary endpoint was overall survival (OS). Secondary endpoints were local recurrence rate (LR), surgical side effects.

**Results:** 11 cohort studies were included, evaluating a total of 6502 participants (p) undergoing 7023 procedures: 2259 underwent a NSM, 968 SSM and 3671 MRM. None of them underwent areola sparing mastectomy. For OS non-inferiority was inconclusive was statistically similar between the NSM and SSM because the confidence interval crossed the non-inferiority bound of 1.13 (RR = 0.93, 95% CI 0.73 to 1.18, 4 trials, 1250p) and between NSM and MRM (RR = 1.005; 95% CI = 0.891.01 to 1.140, 5 trials, 2783p). LR was evaluated in eleven studies and was not inferior statistically different with in NSM compared with SSM (RR = 0.71, 95% CI 0.46 to 1.09, 6 studies, 1603p) and MRM (RR = 1.43, 95% CI = 0.96 to 2.14; 6 studies, 4843p) because the confidence intervals were lower than the non-inferiority bound of 2.67. There was no evidence that the overall risk of complications was diferente similar in NSM when compared to other types of mastectomy (RR = 0.21, 95% CI 0.02 to 2.51, 3 trials, 1575p). About skin necrosis, we observed 83% increased risk with NSM when compared with other types of mastectomy (RR = 1.83, 95% CI 1.06 to 3.14, 3studies, 1004p). The quality of evidence was considered low for the most of outcomes as OS, LR, overall complications and moderate for sensitivity analysis of skin necrosis.

**Conclusions:** Based on the evidence from observational studies was inconclusive that five-year survival was similar between the NSM and SSM and MRM treatment for breast cancer. LR was similar, and there was no evidence that the overall risk of complications was different. However, patients undergoing NSM showed an 83% higher risk of developing skin necrosis.

**No conflicts of interest**

**238** Poster

**Tumor location predicts the site of local relapse after NAC sparing mastectomy**

N. Tomasi Cont[1], F. Kubatzki[1], F. Maggiorotto[1], F. Marocco[1], A. Magistris[1], P. Sgandurra[1], A. Rivolin[1], S. Carlucci[1], S. Renditore[1], R. Ponzone[1]. [1]*Institute of Candiolo- FPO − IRCCS, Gynecological Oncology, Candiolo- Turin, Italy*

**Background:** Mastectomy with the preservation of the nipple–areola complex (NAC sparing mastectomy) followed by immediate reconstruction has been recently introduced for the treatment of early-stage breast cancer. Although preliminary reports are reassuring, the safety of NAC sparing mastectomy is under investigation.

**Material and Method:** From January 2010 to September 2015, 590 NAC sparing mastectomies were performed for invasive and in situ breast carcinoma at our Institution. According to breast shape and volume, three different surgical techniques were used (NAC sparing mastectomy, NAC sparing mastectomy with periareolar pexy and skin reducing mastectomy), followed by immediate placement of either tissue expander or definitive prosthesis. Patients were followed at regular 6 months intervals with clinical examination and additional imaging and/or diagnostic biopsy when required.

**Results:** After a mean follow up of 35 months, 10 patients developed a local relapse. The median time interval between surgery and recurrence was 39 months. None of the relapsed patients had received postmastectomy radiotherapy to the chest wall or regional nodes. Surgical margins of the mastectomy specimen were widely negative ($\geqslant$10 mm) in 6 cases, close (1−5 mm) in 3 cases and very close (<1 mm) in 1 case. Young age, close surgical margins, high tumor grade and high proliferative index measured by ki-67 were all correlated with the risk of local recurrence. All relapses occurred in the quadrant where the bulk of original tumor was located, whereas no relapse was detected in the NAC.

**Conclusions:** This study confirms that local recurrences after NAC sparing mastectomy are rare (1.7%) and do not preferentially occur in the preserved NAC area. Conversely, local relapses always developed in the original quadrant where the tumor was located, similarly to what occurs after breast conserving surgery. This observation may suggest that additional treatments, such as partial chest wall radiotherapy directed to the original tumor location and not to the NAC, could be explored in selected high risk patients submitted to NAC sparing mastectomy.

**No conflicts of interest**

**239** Poster

**Topography of superficial lymphatics of the breast and arm in axilla − functional lymphatic anatomy for axilla surgery in breast cancer patient**

D. Pavlista[1]. [1]*Oncogynecologic Center, Clinic of Obstetric and Gynecology of 1st Medical Faculty of Charles University and General Hospital in Prague, Prague, Czech Republic*

**Background:** To simplify and improve the technique of targeted dissection of the axila with aim to spare lymphatics passing from arm, based on the functional anatomy of the breast. To acquire a basic orientation and to map the lymphatics of arm running through the axilla and to reduce occurrence of lymphedema of the upper arm after breast cancer surgery.

**Material and Methods:** A post mortem study was performed on 31 female cadavers. After slow intradermal and subcutaneus administration of blue dye into the medial upper part of the arm, the lympahtics were visualized. A map of the lymphatic vessels running through axilla was based on summation of all patterns.

**Results:** After intradermal and subcutaneous administration of patent blue, the lymphatics of the upper extremity demonstrated great variability which is demonstrated on figures. Most often were two main lymphatic collectors visualized. One run along axillary vein up to clavicle. Second run caudal from the axillary vein and usually led to the nodes in central axillary region and than to the apex of the axilla. Despite great variability in the lymphatic drainage of the arm, there was one collecting lymphatics which lead to the central axillary nodes. On the basis of summation was the schema constructed. (See Figures).

**Conclusion:** From the course of the supperficial lymphatic vessels of the medial side of the arm we can assume, that is highly unlikely to spare all lymphatics running from arm when axilla dissection is perfomed. Reliable prevention of the occurence of lymphedema remains still dubious. There is need to perform subsequent study to prove result of this study.

**No conflicts of interest**

**240** Poster

**Oncologic safety of immediate reconstruction after skin-sparing mastectomy with conservation of the nipple–areola complex in breast cancer**

B.S. Kwak[1], O.C. Kwon[1]. [1]*Dongguk University Ilsan Hospital, Surgery, Goyang-si Gyeonggi-do, Korea*

**Background:** Skin-sparing mastectomy (SSM) with conservation of the nipple–areola complex (NAC) has become popular with patients undergoing total mastectomy. The risk of tumor involvement of NAC and local recurrence are issued, but there are lack of long-term results.

**Material and Methods:** We reviewed clinicopathologic characteristics of 79 cases of breast cancer patients who planned SSM with conservation of the NAC between July 1999 and January 2005 retrospectively and analyzed risk factors of tumor involvement to NAC and local recurrence. A mean follow-up period was 136 months (124.9–192.5).

**Results:** The median age was 37.4 years (22−57), mean tumor size was 2.2 cm (0.1–13.5), and mean distance from nipple to tumor was 2.1 cm (0−6.0). According to AJCC staging, 18 cases (22.8%) were stage 0; 27 cases (34.2%), stage I; 27 cases (34.2%), stage II; 5 cases (6.3%), stage III; and 2 cases (2.5%) were malignant phyllodes tumors. According to reconstruction methods, 51 cases (64.6%) were TRAM; 24 cases (30.4%), direct implant; and 4 cases (5.1%), tissue expander. Intraoperative frozen section biopsy for NAC involvement of tumor was performed in all cases, and NAC was resected in 12 cases (15.2%) due to DCIS involvement. A permanent pathologic report showed focal DCIS in the resected margin of NAC in only one case (1.3%) of preserved NAC. Diffuse malignant microcalcifications ($p = 0.029$) and multifocal lesions ($p = 0.050$) were statistically significant factors of tumor involvement to NAC. During a follow-up period, 2 locoregional and 2 systemic recurrences were detected but, there was no local recurrence of NAC. Partial necrosis of NAC occurred in 11 cases (13.9%) and mean time of spontaneous recovery was 8.9 weeks (3−12).

**Conclusions:** In candidates for total mastectomy and immediate reconstruction, SSM with intraoperative frozen section biopsy of the NAC offers the opportunity of NAC conservation. We conclude this procedure is oncologically safe and achieves satisfactory aesthetic results.

**No conflicts of interest**

**241** Poster

**Impact of neoadjuvant therapy on breast conservation rates in patients with HER2-positive breast cancer: Preliminary results of Ki-67 index guided selection trial of preoperative chemotherapy**

Y. Hozumi[1], M. Takahashi[2], K. Yoneyama[3], T. Fujisawa[4], S. Osumi[5], H. Akabane[6], R. Nishimura[7], T. Takashima[8], A. Matsukata[9], S. Imoto[10], T. Yamashita[11], M. Mieno[12], H. Mukai[13]. *[1]University of Tsukuba Hospital, Breast and Endocrine Surgery, Tsukuba, Japan; [2]Hokkaido Cancer Center, Breast Surgery, Sapporo, Japan; [3]National Cancer Center East Hospital, Breast Surgery, Kashiwa, Japan; [4]Gunma Cancer Center, Breast Oncology, Ota, Japan; [5]Shikoku Cancer Center, Breast Surgery, Matsuyama, Japan; [6]Asahikawa Kosei Hospital, Breast Surgery, Asahikawa, Japan; [7]Kumamoto Morito General Hospital, Breast Surgery, Kumamoto, Japan; [8]Osaka City University, Surgical Oncology, Osaka, Japan; [9]Sagara Hospital, Breast Surgery, Kagoshima, Japan; [10]Kyorin University, Breast Surgery, Mitaka, Japan; [1]Nagoya City University Hospital, Breast and Endocrine Surgery, Nagoya, Japan; [12]Jichi Medical University, Medical Informatics- Center for Information, Shimotsuke, Japan; [13]National Cancer Center East Hospital, Breast and Medical Oncolog, Kashiwa, Japan*

**Background:** Neoadjuvant therapy (NAT) improves breast conserving therapy (BCT) rates, but the extent according to tumor subtype is unknown. To quantify this effect for HER2-positive breast cancer (HER2+ BC), we reviewed surgical outcomes from a randomized phase II trial of Ki-67 index guided selection of preoperative chemotherapy.

**Methods:** This trial compare standard preoperative chemotherapy comprising paclitaxel and trastuzumab (arm C) with Ki-67 index guided preoperative chemotherapy. In Ki-67 index guided therapy, paclitaxel and trastuzumab were administered initially and the Ki-67 index evaluated from biopsy performed two weeks after begining therapy. The subsequent chemotherapy regimen is modified based on changes in the Ki-67 from the start of therapy. If the Ki-67 index is reduced as expected, paclitaxel and trastuzumab are continued (arm E-1). If the Ki-67 index is not reduced as expected, the chemotherapy regimen is changed to epiubicin, cyclophosphamide and trastuzumab. (arm E-2). Patients with Stage II−III HER2+ BC (n = 205) were entered in this trial. The treating surgeon assessed BCT candidacy based on clinical and radiographic criteria before and after NAT. Subsequent surgical management was at the discretion of the surgeon and patient. We evaluated the conversion rate from BCT-ineligible to BCT-eligible and rate of successful BCT, as defined by tumor-free surgical margins.

**Results:** Pre- and post-treatment surgical assessments were received for 97% of 205 patients treated. Of 200 evaluable patients, 77 (39%) were considered BCT candidates prior to NAT; with 41% in arm C, 39% in arm E-1 and 34% in arm E-2, respectively. There were 135 (68%) BCT-eligible patients overall after NAT was, with 69%, 66% and 67% in each arm, respectively. The rates were similar across the three arms. Of 135 patients judged BCT-eligible, post NAT, 21 (16%) overall, and 12%, 28% and 15% respectively, in each arm, chose mastectomy with no attempt at BCT. There was no significance difference among treatment arms. The rate of successful BCT was over 98% in each arm.

**Conclusions:** This trial shows a BCT-ineligible to BCT-eligible conversion rate of 29% in the HER2+ BC subtype. BCT was successful in approximately 98% of patients who chose this approach; however, a substantial fraction of BCT-eligible patients opted for mastectomy.

Clinical trial information: UMIN 000007074

**No conflicts of interest**

**242** Poster

**Accuracy of ultrasound before surgery to predict axillary neoplastic burden**

P. Nicolau[1], M. Vernet-Tomás[1], D. Sabadell[1], M. Vidal[1], A. Rodríguez-Arana[2], F. Plancarte[2], R. Alcantara[2], J. Jimeno[3], V. Juncà[3], M. Segura[3], L. Serrano[4], J. Corominas[4], R. Carreras[1]. *[1]Hospital del Mar, Gynecology and Obstetrics, Barcelona, Spain; [2]Hospital del Mar, Radiology, Barcelona, Spain; [3]Hospital del Mar, General Surgery, Barcelona, Spain; [4]Hospital del Mar, Pathology, Barcelona, Spain*

**Background:** The standard treatment for patients diagnosed of a breast cancer with infiltrated axillary lymph nodes (ALN) includes axillary lymph node dissection (ALND). The objective of our study was to investigate if the items described in the axillary ultrasound (AUS) report performed previous to the surgery, together with the pathology features of the tumor, would help identifying patients with a low axillary tumor burden. These patients could benefit from the Z0011 study criteria sparing ALND.

**Material and Methods:** We did a retrospective cohort study approved by the Ethical Committee for Clinical Research of our institution. We retrieved from our database all the lymphadenectomies performed in our Breast Unit from July 2011 to December 2014. Patients with neoadjuvant treatment were excluded.

Data were obtained from the clinical records, the AUS report and the pathology report. The following data were collected: age, suspected infiltration of axillary lymph nodes by AUS, number of nodes suspected to be infiltrated by AUS, suspicious lymph node description in the AUS (cortical thickening >3 mm, lymph node structure loss and suspicion of extracapsular extension), tumor histological subtype, size of the invasive tumor, number of tumor foci, number of ALN excised, number of ALN infiltrated and expression of estrogen receptor, progesterone receptor, ki67, p53 and Her2Neu. We compared two groups of patients: group with low axillary tumor burden (LATB) if <2 ALN were eventually infiltrated and group with high axillary tumor burden (HATB) if >2 ALN were infiltrated.

**Results:** 244 lymphadenectomies were performed during the study period; 138 patients who received neoadjuvant treatment were excluded, leaving 60 in the LATB group and 46 in the HATB group.

There were no differences between the two groups regarding age and number of nodes retrieved in the ALND. The AUS report described lymph node structure loss and >2 ALN infiltrated more frequently in the HATB group (75% vs 45.1%, Chi2 p = 0.05; and 78.6% vs 43.6% Chi2 p = 0.020, respectively). Of note, when the AUS described <2 ALN infiltrated, 43.65% of these patients had HATB. Regarding pathology features, only positive p53 tumor expression significantly correlated with LATB (78.6% vs 46.2%, Chi2 p = 0.02).

**Conclusions:** AUS is useful detecting HATB but it performs much worse identifying patients with LATB. P53 expression was associated with LATB; this finding is consistent with the findings of a previous research of our group on sentinel node[1]. Further studies should be done to establish if p53 positivity added to the information given by AUS could help identifying patients in who ALND could be spared.

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**No conflicts of interest**

**243** Poster

**Prediction of nodal metastases by St. Gallen molecular subtypes and clinicopathological characteristics in a prospective cohort**

L. Dihge[1,2], D. Aamand Grabau[3,4], P.O. Bendahl[3], L. Rydén[1,5]. *[1]Institution of Clinical Sciences- Lund University, Department of Surgery, Lund, Sweden; [2]Hallands Hospital, Department of Surgery, Halmstad, Sweden; [3]Institution of Clinical Sciences- Lund University, Department of Oncology and Pathology, Lund, Sweden; [4]Laboratory Medicine Skåne- Skåne University Hospital, Department of Clinical Pathology, Lund, Sweden; [5]Skåne University Hospital, Department of Surgery and Urology, Malmö, Sweden*

**Background:** Axillary lymph node stage remains the single most significant prognostic factor for patients with primary breast cancer. St. Gallen molecular subtypes provide prognostic and treatment predictive information for individual patients whereas the association with axillary nodal involvement is incompletely understood. The aim of this study was to assess the relation of St. Gallen molecular subtypes and clinicopathological features to nodal metastatic disease in a population-based prospective cohort.

**Material and Method:** Patients who underwent axillary nodal staging for primary breast cancer between January 2009 and December 2012, were identified in a prospectively maintained pathology-based registry at Skåne University Hospital, Lund, Sweden. The exclusion criteria were bilateral disease, a history of previous ipsilateral axillary surgery and neoadjuvant chemotherapy regimens. Patients with complete data on oestrogen (ER) and progesterone receptor (PR) status, human epidermal growth factor 2 (Her2) status and Ki67 status were included. The cohort was categorized into five breast cancer subtypes according to the St. Gallen consensus criteria 2013. The primary end-point was nodal metastases defined as macro- and micrometastases. Chi-square test was used to assess the associations between subtypes and clinicopathological characteristics. Univariate and multivariate logistic regression analyses were conducted to evaluate nodal involvement.

**Results:** The cohort consisted of 692 patients, classified into Luminal A 54% (n = 372), Luminal B/Her2− 29% (n = 198), Luminal B/Her2+ 9% (n = 64), Her2+ 2% (n = 17) and Triple-negative breast cancer (TNBC) 6% (n = 41). The mode of detection (mammography screening vs. symptomatic presentation) differed by subtypes (p = 0.001). There were significant

associations between subtypes and histological type (p = 0.021), histological grade (p < 0.001), tumour size (p = 0.001) and the presence of lymphovascular invasion (LVI), p < 0.001. Metastatic axillary involvement was detected in 36% of the study population (n = 248); node positivity varied across the subtypes (p = 0.027).

In univariate analysis, the rate of nodal metastasis was significantly related to LuminalB/Her2− subtype relative to Luminal A (OR 1.44; 95% CI 1.01–2.06; p = 0.043). On multivariate analysis, the presence of metastatic node was found to be negatively related to TNBC relative to Luminal A (OR 0.196; 95% CI 0.07–0.53; p = 0.001); and significantly associated to each mm of increase in primary tumour size (OR 1.06; 95% CI 1.04–1.09; p < 0.001), age (p = 0.013), mode of detection (p = 0.007), multifocality (p = 0.015) and LVI (<0.001).

**Conclusions:** The results suggest that there are independent associations between St. Gallen molecular subtypes, clinicopathological prognostic factors and nodal metastases. Additional studies are warranted to clarify the role of predictors for nodal involvement.

**No conflicts of interest**

**244** Poster

**Complications in primary versus secondary deep inferior epigastric artery perforator flap breast reconstructions: A multicentre study**

J. Beugels[1], L. Hoekstra[1], S. Tuinder[1], L. Smit[2], K. Keymeulen[2], R. Van der Hulst[1], A. Piatkowski de Grzymala[1], E. Heuts[2]. *[1]MUMC, Plastic Surgery, Maastricht, Netherlands; [2]MUMC, General Surgery, Maastricht, Netherlands*

**Background:** There is general agreement that immediate breast reconstruction after mastectomy is an integral part of the complete management of breast cancer. However, the number of primary autologous breast reconstructions performed − with the deep inferior epigastric perforator (DIEP) flap as first choice − is still limited in the Netherlands. A possible reason for this could be that the complication rate of primary autologous breast reconstruction is higher as compared to delayed reconstruction. This multicentre study compares the complication rate in primary versus secondary DIEP flap breast reconstructions.

**Materials and Methods:** Between January 2010 and December 2014 a total of 490 free DIEP flap breast reconstructions were performed in 406 patients in one university hospital (n = 278) and two community hospitals (n = 112 and n = 100) in the Netherlands. All DIEP flap breast reconstructions were performed by the same group of plastic surgeons. Medical records were searched retrospectively, documenting patient characteristics, risk factors and the occurrence of major or minor complications at the recipient site. Major complications were total or partial flap loss and venous congestion requiring re-exploration of the flap. Minor complications were infection, hematoma, seroma, fat necrosis, and wound problems (dehiscence, superficial skin necrosis, and/or delayed wound healing). Post-operative flap re-explorations and reanastomoses were also examined.

**Results:** A total of 197 primary (40.2%) and 293 secondary (59.8%) DIEP flap breast reconstructions were performed in 145, and 261 patients respectively. Major complications occurred in 10.2% primary versus 8.5% secondary DIEP flap breast reconstructions (p = 0.543). Patients suffered significantly more frequent from wound problems (primary 5.1% versus secondary 13.7%; p = 0.002) in secondary reconstructions. Minor recipient site complications, the amount of re-explorations of the flap (12 in primary reconstructions versus 16 in secondary reconstructions; p = 0.768), and reanastomoses (9 primary versus 9 secondary; p = 0.388) were not significantly different in both groups. Also, the result in terms of flap viability after re-exploration of the flap was not significantly different (66.7% vital flaps after re-exploration in primary reconstructions versus 50.0% in secondary reconstructions; p = 0.378).

**Conclusion:** Primary autologous DIEP flap breast reconstructions can be safely performed without an increase in complication rate as compared to secondary reconstructions. In secondary reconstructions wound problems at the recipient site occur more frequent. This study shows that the complication rate is no justification to perform a delayed autologous breast reconstruction rather than primary.

**No conflicts of interest**

**245** Poster

**Impact of surgical factors on re-operation and resection ratio for patients treated with primary breast conserving surgery: A retrospective cohort study**

N. Vaithilingam[1], A. Modi[2]. *[1]United Lincolnshire Hospitals NHS Trust, Breast Surgery, Grantham, United Kingdom; [2]Rotorua Hospital, General and Breast Surgery, Rotorua, New Zealand*

**Background:** Despite attempts to minimise revision wide local excision (WLE) rates, these are stubbornly stuck between 15−30%. Larger excisions have a theoretical advantage of reducing re-operation rates at the cost of cosmesis. Literature review states that ensuring 1 cm macroscopic margin reduces re-operation by 70%. A good macroscopic margin compensates for a larger than assessed tumour and for additional foci. The scanty literature on total resection volume quotes a figure of 2.8−3.8 times the optimal resection volume.

**Methods:** 333 (Firm 1: 255 and Firm 2, less experienced: 78) eligible patients were identified between 2008–2012. Patients who had neo-adjuvant therapy and therapeutic mammoplasty were excluded. Pathology and imaging reports were reviewed. Descriptive assessment was carried out for re-operation and successful WLE patients. A logistic regression model was used to determine factors associated with re-operation. Mann–Whitney test was used to analyse CRR (calculated resection ratio) values.

**Results:** 78 patients, 23.4% (Firm 1: 64/255=25% and Firm 2: 14/78=18%) required re-operation. A higher rate of macroscopic margin failure (89% vs 62.5%) was seen in successful WLE than in the re-operation group, but the incidence of positive/close macroscopic margins and multiple macroscopic margin failure was higher in re-operation group (29.2% vs 15.5% and 55% vs 35.3%). We noted a greater impact of tumour factors (particularly in adequate macroscopic margin group) and imaging factors in re-operation patients compared to successful WLE. Multifocality (OR 10.4 [3.05, 35.7] with P-value of 0.001), size, age and close macroscopic margin (OR 10.1 [1.58, 65.43] with P-value of 0.014) were found to be statistically significant risk factors for re-operation. The CRR was found to be relatively lower with associated higher incidence of close macroscopic margins in re-operation patients. CRR was generally high in Firm 2 ($\geq$4) patients and low in Firm 1 re-operation patients (1.74). Wire-guided WLE carried a higher risk of excessive resection in all WLE and probably led to more macroscopic margin failure.

**Conclusion:** This study underpins the relevance and importance of looking at clear microscopic margins from the angle of adequate macroscopic margins without excess resection. The Surgeon's strategy and technique is vital. This concept is new and if validated by a large sample size would be practice-changing. This approach would be helpful in comparing practices of different Breast Units/Breast Surgeons in a more meaningful way. When macroscopic margin failure is the main cause of re-operation, there is scope for improving re-excision rate and completion mastectomy with cavity shaving even for multiple positive/close microscopic margins.

**No conflicts of interest**

**246** Poster

**Breast conserving surgery after neoadjuvant chemotherapy: Where do we stand?**

J.H. Volders[1], M.H. Haloua[2], N.M. Krekel[2], C. Sietses[1], E. Barbé[3], S. Meijer[2], M.P. Van den Tol[2]. *[1]Gelderse Vallei Hospital, Surgery, Ede, Netherlands; [2]VU Medical Centre, Surgery, Amsterdam, Netherlands; [3]VU Medical Centre, Pathology, Amsterdam, Netherlands*

**Background:** Neoadjuvant chemotherapy (NACT) is increasingly used in patients with operable disease due to the potential of converting patients requiring mastectomy to breast conserving surgery (BCS) or lowering resection volumes in patients already suitable for BCS to improve cosmetic outcome. Information about margins and volumes resected after NACT are scarce. This nationwide study aims to determine margin status and specimen volume in patients with invasive breast cancer who underwent BCS after NACT.

**Methods:** All patients who underwent BCS in 2012–2013 for invasive breast cancer were selected from PALGA (nationwide network and registry of histology and cytopathology in the Netherlands).

**Results:** Of the 9902 patients, 626 (6.3%) received NACT. Overall 1101 (11.1%) patients had tumour-involved margins. After NACT, 152 (24.3%) patients had tumour-involved margins; close margins ($\leqslant$1 mm) were seen in another 105 (23.1%) patients. The adjusted odds ratio for involved margins after NACT was 2.94, meaning a three times higher risk of involved margins compared with primary surgery. In patients with lobular carcinoma (54.9%), no response after NACT (42.1%) and positive hormonal (26.7%) or negative Her2neu receptor status (26.2%) higher tumour-involved margins were seen. Median lumpectomy volume in patients with no response to NACT was lower (50 cc) compared with patients with complete response (55 cc, p = 0.018) Volumes >60 cc were observed in 36% of patients after NACT.

**Conclusion:** The primary goal of the surgeon performing BCS after NACT, reaching tumour-free margins, is not accomplished in one out of four patients. High risk patients are patients with ILC and no tumour response; in these patients NACT should not be administered to convert from mastectomy to BCS.

**No conflicts of interest**

Table 1. Patient and tumour characteristics of BCS after NACT considering margins status of invasive carcinoma

| | Tumour-free margins | Tumour-involved margins | p-value |
|---|---|---|---|
| Total | 474 (75.7%) | 152 (24.3%) | |
| Age in years (median) | 53 (24−94) | 52(27−92) | 0.903 [a] |
| Histopathological type | | | <0.001 [b] |
| Invasive ductal carcinoma | 423 (79.5%) | 109 (20.5%) | |
| Invasive lobular carcinoma | 32 (45.1%) | 39 (54.9%) | |
| Other | 19 (82.6%) | 4 (17.4%) | |
| Excision method | | | 0.418 [c] |
| Without localization | 128 (78.0%) | 36 (22.0%) | |
| With localization | 346 (74.9%) | 116 (25.1%) | |
| Response | | | <0.001 [d] |
| (near) Complete response (1+2i) | 81 (88.0%) | 11 (12.0%) | |
| Partial response (2ii+2iii) | 305 (74.4%) | 105 (25.6%) | |
| No response (3) | 22 (57.9%) | 16 (42.1%) | |
| Hormonal status | | | 0.001 [c] |
| Positive | 272 (73.3%) | 99 (26.7%) | |
| Negative | 65 (91.5%) | 6 (8.5%) | |
| Her2neu status | | | 0.011 [c] |
| Positive | 55 (88.7%) | 7 (11.3%) | |
| Negative | 273 (73.8%) | 97 (26.2%) | |
| Triple negative | | | <0.001 [c] |
| Yes | 49 (96.1%) | 2 (3.9%) | |
| No | 277 (73.1%) | 102 (26.9%) | |
| Lumpectomy volume in cc (median) | 52 (5–679) | 39 (6–250) | <0.001 [a] |

[a] Mann–Whitney; [b] Fisher exact test; [c] Chi Square test; [d] Linear by linear test.

**247** Poster

**Intraoperative ultrasound guidance in breast-conserving surgery: Final results of the COBALT trial**

J.H. Volders[1], M.H. Haloua[2], N.M.A. Krekel[2], A.M.F. Lopes Cardozo[3], A.M. Bosch[1], L.M. De Widt-Levert[4], H. Van der Veen[5], H. Rijna[6], E. Bergers[7], K. Jóźwiak[8], S. Meijer[2], M.P. Van den Tol[2]. *[1]Gelderse Vallei Ziekenhuis, Surgery, Ede, Netherlands; [2]VU Medical Center, Surgery, Amsterdam, Netherlands; [3]Medical Center Alklmaar, Surgery, Alkmaar, Netherlands; [4]Waterland Hospital, Surgery, Purmerend, Netherlands; [5]Red Cross Hospital, Surgery, Beverwijk, Netherlands; [6]Kennemer Gasthuis, Surgery, Haarlem, Netherlands; [7]VU medical center, Radiology, Amsterdam, Netherlands; [8]NKI-AVL, Department of Epidemiology and Biostatistics, Amsterdam, Netherlands*

**Background:** The COBALT trial showed that ultrasound-guided breast-conserving surgery (USS) results in a significant reduction in margin involvement, excision volumes and as a consequence, a reduction in additional therapies compared to palpation-guided surgery (PGS). The aim of the present study was to determine long-term cosmetic outcome, patient satisfaction and quality of life (QoL).

**Methods:** A total of 134 patients with T1-T2 invasive breast cancer were included in the COBALT trial (NTR2579) and randomized to either USS (65 patients) or PGS (69 patients). Cosmetic outcomes were assessed by a three-member panel, by computerized software (BCCT.core) and by patient self-evaluation, including patient satisfaction. QoL questionnaire were performed using the EORTC-QLQ-C30 and QLQ-BR23. Time points for follow-up were 3, 6, 12 and 36 months after surgery. Overall cosmetic outcome and patient satisfaction were scored on a 4-point Likert scale (excellent, good, fair or poor). Outcomes were analyzed using a multilevel mixed effect proportional odds model for ordinal responses.

Table 1. Patient satisfaction after 3 years of follow-up

| | Surgery | |
|---|---|---|
| | Palpation-guided (PGS) | Ultrasound-guided (USS) |
| Excellent | 23% | 43% |
| Good | 53% | 43% |
| Fair | 11% | 12% |
| Poor | 13% | 2% |

**Results:** USS achieved better overall cosmetic outcomes with 25% rated as excellent and only 8% as poor, whereas 21% of PGS outcomes were rated excellent and 15% as poor. Overall, USS had lower odds for worse cosmetic outcome compared to PGS (OR 0.53, p = 0.048). Excision volumes >40 cc resulted in 2.54 higher odds of having worse outcome when compared to volumes ⩽40 cc (p = 0.003). No difference in cosmetic outcome between 1 and 3 years were seen. USS resulted in a higher patient satisfaction compared with PGS. Patient satisfaction was higher after 1 year, with 45% lower chances of being less satisfied after 1 than after 3 years (OR=0.55, p = 0.057). No difference in quality of life between both groups were seen. Poor cosmetic outcome resulted in significant worse quality of life on multiple scales such as global health, body image, breast symptoms and sexual enjoyment.

**Conclusion:** USS achieved better overall cosmetic outcomes and patient satisfaction than PGS in short and long term follow up. Lumpectomy volumes above 40 cc resulted in significantly worse cosmetic outcomes. Poor cosmetic outcome has a negative influence on quality of life.

**No conflicts of interest**

**248** Poster

**Managing the axilla in early breast cancer. Impact of ACOSOG Z00011 trial in changing practices in a low income country**

A. Malik[1], N. Urooj[2]. *[1]Shaukat Khanum Memorial Cancer Hospital & Research Center, Surgical Oncology, Lahore, Pakistan; [2]Shaukat Khanum Memorial Hospital & Research Center, Surgical Oncology, Lahore, Pakistan*

**Introduction:** The ACOSOG Z0011 trial has been described as practice-changing. The new guidelines have been adapted at Shaukat Khanum Hospital, Pakistan since April 2014. The goal of this study was to determine the impact of the trial on surgeon practice patterns at our institution.

**Methods:** A comparison of patients undergoing surgery for early breast cancer before and after the implementation of the new guidelines was done. We adopted the new guidelines in April 2015. Patients meeting Z0011 inclusion criteria were identified. For group A (Pre Z0011) patients operated between Jan to Dec 2013 were studied. And for Group B (Post Z0011) patients operated between Jul 2014 to Jun 2015 were included. Clinicopathologic data, no of sentinel lymph nodes identified and no of ALNDs performed, total operative time and length of hospital stay were compared between the two groups.

**Results:** There were 310 patients with clinical T1−2 tumours planned for breast conservation. 57.5% patients had T1 tumour and 42.5% had T2 tumours. 88% of the patients had IDCa. There were 148 patients in the pre-Z0011 group and 162 in post-Z0011. 72% of the patients in Group A were ER+ve while 76% in group B. 38 (25.7%) patients were sentinel lymph node (SLN) positive in the pre-Z0011 group versus 34 (21%) in post-Z0011 (p = 0.39). Tumour size was comparable in both the groups (19 mm vs. 20 mm p value 0.899). Before Z0011 100% (38/38) of SLN-positive patients underwent axillary node dissection (ALND) versus 18% (6/34) after Z0011 (p < 0.001). Median no of SLNs identified in group A were 2.0 and group B were 2.3 (p value 0.789). There was a significant decrease in median operative times of the two groups (80 vs. 60 min, p < 0.001). There was also a significant decrease in the overall hospital stay of sentinel lymph node positive patients in between the two groups (1.8 days vs 1.3 days p value <0.001).

**Conclusions:** Surgeons at our institution have implemented Z0011 results with a significant short term advantages. Lesser number of axillas are being operated upon and there is significant reduction in hospital stay and operative time. However the real questions concerning Z0011 are recurrence rates and overall survival, a question which requires a longer follow-up to be answered.

**No conflicts of interest**

**249** Poster

**Complication rates after oncoplastic breast surgery in patients aged 60 and over**

W. Ho[1], S. Stallard[2], J. Doughty[2], E. Mallon[3], L. Romics[1]. *[1]New Victoria Hospital, Surgery, Glasgow, United Kingdom; [2]Gartnavel General Hospital, Surgery, Glasgow, United Kingdom; [3]Queen Elizabeth University Hospital, Pathology, Glasgow, United Kingdom*

**Background:** Elderly patients should beoffered the same surgical treatment for breast cancer than younger patients ifcomorbidities and frailty permit. General belief that elderly patients are lessconcerned about aesthetic outcome, hence oncoplastic surgery is less frequentlyoffered to this age group. Complication rates after oncoplastic surgery inpatients aged 60 and over were analysed.

**Methods:** A retrospective review of breastcancer patients aged 60 and over treated with oncoplastic breast conservationsurgery (OBCS) was carried out. Patients were treated in two breast units inGlasgow. While elderly patients are generally regarded as 70 years and above, patientsaged 60 and over represent a relatively older subgroup among those treated withOBCS.

**Results:** 55 patients with a mean age of 67(60−79) were treated with OBCS. 25.4% of patients were smokers and 7.3% werediabetic. The mean BMI was 30 (22−42). 38 patients were treated with reductionmammoplasty (Wise pattern or Le Jour), 5 patients had round block excision, 4patients had matrix rotation, 2 patients were treated with Grisotti flap, batwing excision or tennis racquet excision, respectively, while and one

patienthad thoraco-epigastric flap or melon slice excision each. Altogether 17patients developed some degree of complications (30.1%). Five patients requiredreoperation (9.1%), four for postoperative hematoma, while one for delayedwound healing. Table 1. details postoperative complications.

Table 1. Postoperative complications in patients aged 60 and above having been treated with oncoplastic breast conservation surgery

| Complication | Percentage | Number |
|---|---|---|
| Skin cellulitis/necrosis/delayed wound healing | 6.9% | 4 |
| Haematoma | 10.3% | 6 |
| Fat necrosis | 10.3% | 6 |
| Seroma | 3.4% | 2 |
| Chest wall infection | 1.7% | 1 |

**Conclusion:** Complication rate afteroncoplastic surgery in patients aged 60 and above is slightly higher than it isin younger age groups. However, this slight increase still does not justifythat oncoplastic surgery is less frequently offered to the relatively older patients. Oncoplastic techniques should be discussed with the suitable older patients, too, as a possibility to improve the aesthetic outcome of their treatment.

**No conflicts of interest**

**250** Poster

**Validation of the use of radioactive iodine-125 seed localisation of breast carcinoma in patients undergoing breast conservation surgery in the United Kingdom**

R. Milligan[1], A. Critchley[1], S. Nicholson[1], H. Cain[1]. [1]*Royal Victoria Infirmary, Breast Surgery Unit, Newcastle-Upon-Tyne, United Kingdom*

**Background:** In the UK, radiologically placed guidewires have traditionally been the preferred method for localisation of non-palpable breast lesions in patients undergoing breast conservation surgery (BCS). We are the first breast unit in the UK to introduce radioactive seed localisation (RSL) using iodine-125 seeds as an alternative to guidewire localisation (GWL). The aim of this study was to evaluate and compare the efficacy of RSL and GWL in BCS with wide local excision (WLE).

**Materials and Methods:** Data were collected prospectively on the last 100 patients who underwent GWL WLE prior to the introduction of RSL, and the first 100 patients who underwent RSL WLE. Patients with non-palpable and histologically proven invasive carcinoma of the breast were included. Exclusion criteria were: multiple guidewires, pre-invasive carcinoma without invasion, therapeutic mammoplasty, diagnostic excision biopsy and pathological complete response after chemotherapy. All lesions were localised with ultrasound guidance using a single guidewire or radioactive iodine seed. All guidewires were inserted on the day of surgery; RSL was performed 7−14 days pre-operatively. Each specimen was orientated and sent for specimen X-ray for intra-operative radiological assessment; cavity shaves were taken if the lesion was deemed to be close to a radial margin. Local guidelines considered a 1 mm resection margin satisfactory for invasive carcinoma and a 2 mm margin for pre-invasive carcinoma. Margin re-excision or completion mastectomy was performed on any patient with inadequate surgical excision margins. Data collection included: tumour type, size and grade, total specimen excision weight, margin positivity and any further surgery to improve excision margins. Statistical analysis between the two groups was performed using Unpaired Student T-test.

**Results:** Both groups showed similar tumour characteristics of type, grade and receptor status. Mean total tumour size was similar between groups, measuring 19.44 mm (5−55) in the GWL group compared with 18.61(3.8−59) in the RSL group ($p = 0.29$) Mean total specimen excision weights were significantly lower in the RSL group compared with the GWL group, weighing 31.55 g (4.5–112) and 37.42 g (7.8–157.1) respectively ($p = 0.02$). Median total specimen weight to tumour size ratio was 1.56 in the RSL group compared with 1.93 in the GWL group ($p = 0.36$). 13 patients in the RSL group had positive margins after specimen excision compared with 15 in the GWL group (15% vs 13% respectively, $p = 0.34$). There were no adverse incidents relating to the use of iodine seeds.

**Conclusions:** RSL using iodine-125 seeds is a safe and reliable method of localising non-palpable invasive breast carcinomas in patients undergoing BCS in the UK. Specimen weights were smaller and margin positivity was less in the RSL group compared with the GWL group.

**No conflicts of interest**

**251** Poster

**The role of therapeutic mammoplasty in a breast screening unit in the United Kingdom: A two-year review**

R. Milligan[1], C. Allison[1], H. Cain[1], S. Nicholson[1], A. Critchley[1]. [1]*Royal Victoria Infirmary, Breast Surgery Unit, Newcastle-Upon-Tyne, United Kingdom*

**Introduction:** Therapeutic Mammoplasty (TM) is an accepted oncoplastic technique in breast conservation surgery, which is used to combine breast cancer excision with breast reduction surgery in women with larger breasts. Contralateral Breast Surgery (CBS) is often performed in conjunction with TM, either at the time of surgery or as a delayed procedure, in order to symmetrise the contralateral breast. Here we review our practice over a two-year period at a UK breast screening unit.

**Materials and Methods:** Data were collected retrospectively on all patients who underwent TM between 01/01/2013 to 31/12/2014. Information obtained included: age of patient, use of wire localisation, axillary procedure performed, tumour characteristics, Nottingham Prognostic Index (NPI) score, whether and when CBS was performed and histology findings in the CBS specimen. All procedures were performed at the same breast screening unit under the care of four consultant breast surgeons.

**Results:** All patients were female, mean age 58 years (37−73). 89 TM procedures were performed on 87 patients (two had bilateral procedures). 57 (64.0%) patients had Sentinel Lymph Node Biopsy (SLNB), 12 (13.5%) underwent Axillary Lymph Node Dissection and 20 (22.5%) patients had no axillary procedure. A single wire was used to localise the carcinoma in 59 (66.3%) patients and two wires used in 6 (6.7%) patients. Invasive ductal carcinoma was found in 54 patients, lobular in 7 and other invasive tumour types in 6 patients. Patients without invasive disease included: High Grade Ductal Carcinoma In Situ (DCIS) in 13 patients, Low/Intermediate Grade DCIS in 7. “Other” diagnoses were found in 3 patients and complete pathological response to neoadjuvant chemotherapy in 2 patients. NPI scores were as follows: (2−2.4) 12 patients, (>2.4−3.4) 18 patients, (>3.4−5.4) 25 patients, (>5.4) 12 patients. Median total tumour size was 58 mm (35–120). 63/85 (74.1%) patients had CBS at the time of TM (62 reductions, 1 mastopexy); 1/85(1.2%) patient had subsequent revision of CBS (further breast reduction surgery). 9/85 (10.6%) patients had delayed CBS (all breast reduction surgery). 13/85(15.3%) patients underwent unilateral TM without CBS. Specimen histology showed benign findings in all contralateral specimens. TM median weight was 188.4 g (7.8–1242); CBS median weight was 257.2 g (34.4–1600).

**Conclusions:** TM is a suitable procedure for a wide range of patients with large breasts opting for breast conservation surgery for both symptomatic and screen-detected cancers, regardless of NPI or the need for axillary surgery. Most patients undergoing TM in our unit have CBS at the time of surgery, almost exclusively in the form of breast reduction. Smaller numbers of patients either chose delayed CBS or no contralateral surgery at all. It was rare for patients to have surgical revision to their contralateral breast.

**No conflicts of interest**

**252** Poster

**The efficacy of intraoperative frozen section analysis of resection margins during breast conserving surgery for ductal carcinoma in situ**

K. Suhwan[1], C. Jungeun[1], Y. Kyungjun[1], P. Jeongyeong[1], L. Soojung[1]. [1]*Yeungnam University College of Medicine, Department of Surgery, Daegu, Korea*

**Background:** Breast conserving surgery (BCS) is a standard procedure for early breast cancer and resection margin state is the most important risk factor of local recurrence. Re-operation is generally conducted in 20−40% after initial BCS to achieve negative margins, especially in breast cancer with carcinoma in situ components. In this study, we analyzed the long-term follow up results and efficacy of BCS using intraoperative frozen section analysis to access resection margin in ductal carcinoma in situ (DCIS) patients.

**Material and Methods:** Between 2004 and 2006, 1016 patients were diagnosed with primary breast cancer and received breast cancer surgery. Among them, BCS was attempted as an initial operation for 523 patients. Superior, inferior, medial and lateral margin of resected specimen were evaluated according to the intraoperative frozen section analysis. If tumor cells existed less than 2 mm from resected specimen margin, intraoperative further resection was done and if the further resection was impossible, initial BCS was converted to mastectomy. All medical records and pathologic reports were reviewed retrospectively.

**Results:** Out of the 523 patients who had to undergo BCS, 70 patients (13.3%) underwent mastectomy following the results of frozen section analysis during the first surgery. The number of the patients who had either only DCIS or invasive carcinoma with DCIS component was 372

(71.1%, 372/523) and 17.2% (64/372) were converted to mastectomy. One hundred fifty one patients (28.9%) had only invasive carcinoma and 3.97% (6/151) were converted to mastectomy. In this study, we analyzed 94 patients who had to undergo BCS with DCIS. The rate of intraoperative conversion to mastectomy was 13.8% (13/94) and 81 patients had successful BCS with 1−3 times of additional resection. There were no differences between patients who had BCS and final mastectomy in clinicopathologic characteristics such as physical examination of tumor, age of patients, DCIS subtypes, nuclear polymorphism, presence of necrosis, ER/PR, HER2 and Ki67. After permanent biopsy was reported, in 5 patients, resected specimen had tumor cells within less than 2 mm from resected margin, not inked margin. They had no re-operations and no recurrences. Mean follow up period was 76.6 months. One locoregional and 3 local recurrences in BCS patients and 1 local recurrence in mastectomy patients were found. There was no difference in disease free survival between two groups (95.1% vs 92.3%, p = 0.659). In this DCIS patients, re-operation rate was 0%.

**Conclusions:** Intraoperative frozen section analysis during BCS to access resection margin helps to avoid reoperations and increase intraoperative success rate of BCS in DCIS. It also shows oncological safe long term results. Further studies are needed to resolve the problem with cost-effectiveness of intraoperative frozen section analysis.

**No conflicts of interest**

**253** Poster

**Skin-sparing mastectomy for the treatment of breast cancer**

B. Mota[1], J.L. Bevilacqua[2], M. Ricci[1], A. Atallah[3], R. Riera[3]. *[1]ICESP, Gynecology and obstetrician- São Paulo University, São Paulo, Brazil; [2]Ac Camargo cancer center, Breast surgery, São Paulo, Brazil; [3]Universidade Federal de São Paulo, Medicina Baseada em Evidencia, São Paulo, Brazil*

**Background:** The efficacy and effectiveness of skin sparing mastectomy (SSM) for the treatment of breast cancer had not been proved by randomized trials. Based on this We conducted a systematic literature review with meta-analysis with the concrete scientific evidence for SSM in the treatment of breast cancer.

**Material and Methods:** Electronic searches were conducted using the Mesh terms “skin sparing mastectomy” in the following databases: the Cochrane Breast Cancer Group Specialized Register, the Cochrane Center Register of Controlled Trials, MEDLINE by PubMed, EMBASE by Ovid, LILACS and The WHO International Clinical Trials Registry Platform. Inclusion criteria were randomized or quasi-randomized studies of in situ or invasive breast carcinoma. Data extraction was performed using the RevMan 5.2 software according to the Cochrane Handbook for Systematic Reviews 5.2 by two authors. We performed a descriptive analysis and meta-analysis of the data. The primary endpoint was overall survival. Secondary endpoints were local recurrence rate and surgical side effects.

**Results:** 11 studies were included, evaluating a total of 5916 participants undergoing 5936 procedures: 1857 underwent a skin sparing mastectomy (SSM), and 3800 underwent modified radical mastectomy (MRM), and 107 underwent a nipple sparing mastectomy (NSM). For Overall survival non-inferiority was inconclusive between the SSM and MRM because the confidence interval crossed the non-inferiority bound of 1.13 (RR = 0.82, 95% CI 0.39 to 1.75, 9 studies, 3959 participants). Local recurrence was evaluated in eleven studies and was not inferior in SSM compared with MRM (RR = 0.95, 95% CI 0.69 to 1.31, 11 studies, 5458 participants) because the confidence intervals were lower than the non-inferiority bound of 2.67. There was no evidence that the overall risk of complications was different in SSM when compared to MRM (RR = 1.55, 95% CI 0.97 to 2.46, 4 studies, 677 participants). No statistically significant difference among the two techniques with respect to skin necrosis was observed (RR = 0.99, 95% CI 0.67 to 1.46, 4 studies, 677 participants).

**Conclusions:** The evidence from observational studies was that the incidence of local recurrence was similiar between skin sparing mastectomy and radical mastectomy, but the overall survival was inconclusive about non-inferiority between groups. There is no difference about overall risk complication and skin necrosis.

**No conflicts of interest**

**254** Poster

**Pattern of ipsilateral breast recurrence following wide local excision for breast cancer**

Q. Lu[1], B.A. Choo[2], P.M.Y. Chan[1], E.Y. Tan[1]. *[1]Tan Tock Seng Hospital, Department of General Surgery, Singapore, Singapore; [2]National University Hospital, Department of Radiation Oncology, Singapore, Singapore*

**Background:** Local recurrence (LR) is a known concern in breast conserving therapy. Recurrences are either adjacent or close to the previous surgical cavity, in another quadrant of the breast or in the ipsilateral axilla. This study aims to evaluate the pattern of LR and to identify factors that predict for it.

**Material and Methods:** A retrospective review was performed on 579 women who had undergone breast conserving therapy in Tan Tock Seng Hospital between 2004–2009. Those with metastatic cancer at presentation were excluded. All women were followed-up for 5 years or longer.

**Results:** Of the 579 women, 137 (24%) had DCIS, 210 (36%) had Stage I disease, 186 (32%) had Stage II disease and 46 (8%) had Stage III disease. Local recurrence developed in 65 women (11%); with the LR being adjacent to the previous surgical cavity in 40 women (62%), in other quadrants of the breast in 16 (25%) and in the ipsilateral axilla in 14%. LR was more frequent among node positive (P = 0.01), ER negative tumours (P = 0.01), and if the surgical margins were inadequate (P = 0.03). Women who did not received post-operative radiation or who did not complete hormonal therapy were more likely to develop LR (P < 0.05). LR was associated with distant recurrence with a shorter overall survival.

**Conclusion:** The incidence of LR was 11% in our study and majority of these were adjacent to the previous surgical cavity. Inadequate margins, failure to complete radiation and hormonal therapy predicted for LR, as well as unfavourable disease factors such as nodal involvement and ER status.

**No conflicts of interest**

**255** Poster

**Mastectomy skin necrosis with premammary fascial skin flaps: A double blind randomised controlled trial**

S. Patel[1], A. Srivastava[1], A. Dhar[1], S. Hari[2], S. Mathur[3], R.M. Pandey[4], P. Ranjan[1], K. Kataria[1], A. Prem[1]. *[1]AIIMS, Department of Surgical Disciplines, Delhi, India; [2]AIIMS, Department of Radiodiagnosis, Delhi, India; [3]AIIMS, Department of Pathology, Delhi, India; [4]AIIMS, Department of Biostatistics, Delhi, India*

**Background:** In the modern era of breast oncology, the optimum flap thickness supported by robust scientific evidence is yet to be defined. Our study attempts to establish that raising mastectomy flaps at the level of premammary fascia (thick flaps) with cold steel scalpel decreases the incidence of post operative mastectomy skin necrosis (MSN).

**Material and Methods:** We conducted a 2×2 factorial, randomised, double blind trial. 160 ladies with carcinoma breast planned for simple or modified radical mastectomy (without immediate reconstruction) were randomised into four groups with 40 patients each (Table). Flap raising at premammary fascia (thick flap) was compared against the conventional technique of raising flaps between the large and small fat globules (thin flap). Two tools of flap dissection were compared − cold scalpel with electrodiathermy. Patients with previous history of breast surgery/infection/trauma or burn were excluded from the study. Patients were followed for 30 days after surgery for assessment of postoperative outcomes. Our primary outcome measure was the development of MSN.

| Group (group number) | No. of patients | Necrosis, n (%) | Relative risk (95% CI) p = 0.002 |
|---|---|---|---|
| Thick flap & Scalpel (1) | 40 | 1 (2.5) | 1.0 [reference] |
| Thin flap & electrodiathermy (2) | 40 | 4 (10) | 4 (0.5–34.2) |
| Thick flap & Scalpel (3) | 40 | 3 (7.5) | 3 (0.3–27.6) |
| Thin flap & electrodiathermy (4) | 40 | 12 (30) | 12 (1.6–87.9) |

**Results:** The baseline characteristics, i.e. patient profile (age, BMI, breast volume), disease profile (tumour size, location, stage of cancer), treatment received (neoadjuvant chemotherapy, type of mastectomy) were distributed non-significantly across the 4 study groups. Overall incidence of MSN was 12%. MSN was observed in 12 patients in the group with thin flap & electrodiathermy as opposed to 1 seen in the group with thick flap & scalpel (RR of MSN, 12; 95% confidence interval, 1.6–87.9; P = 0.002) (Fisher’s exact test). 14 out of 20 patients with MSN subsequently required surgical intervention. Single factor analysis showed that there is an increased risk of development of MSN with thin flap when compared with thick flap (RR for development of MSN, 4; 95% confidence interval, 1.4–11.4; P = 0.007) (Fisher’s exact test). The secondary outcome measures analysed were Seroma, Surgical site infection, blood loss, time taken, total drain output, number of days with drain.

**Conclusion:** There is an increased risk of development of MSN when raising skin flaps using conventional technique i.e.between the large and small fat globules (thin flaps). Long term patient follow up is needed to observe the loco regional cancer control after raising flaps at premammary fascia (thick flaps).

**No conflicts of interest**

**256** Poster

**When should sentinel lymph node biopsy be recommended in ductal carcinoma in situ?**

V. González-Vidal[1], C. Ferrer Albiach[2], A. Conde[2], D. Martínez Ramos[3], M. Alcalde[3], B. Merck[4]. *[1]Hospital Virgen del Consuelo, Radiation Oncology, Valencia, Spain; [2]Universidad Cardenal Herrera CEU, Medicine, Castellón de la Plana, Spain; [3]Hospital General de Castellón, Surgery, Castellón de la Plana, Spain; [4]Universidad Cardenal Herrera CEU, Surgery, Alfara del Patriarca. Valencia, Spain*

**Background:** Due to the low incidence of axillary lymph node involvement in ductal carcinoma in situ (DCIS) patients, sentinel lymph node biopsy is not a standard procedure for regional staging. There are still situations where this technique should be perform, in order to avoid a possible lymphadenectomy, if an invasive tumor should be present in the final pathological report.

**Material and Methods:** Between October 2007 and November 2014, 109 patients with pathological confirmation of unilateral breast DCIS were included in this study. All the patients were surgically treated (lumpectomy 86.2% or mastectomy 13.8%).

Variables related to clinical presentation, imaging, pathological features and sentinel node biopsy were recorded. Both, descriptive and inferential statistical analyses were performed. We have also analysed the relationship between the variables set at the last Spanish Consensus Meeting for SLNB (tumor size >3 cm, presence of comedonecrosis, high tumor grade, mastectomy or palpable mass at diagnosis) and our results.

**Results:** The presence of a positive sentinel lymph node (SLN) was associated ($p = 0.001$) to existence of comedonecrosis on pathology report and to women treated with mastectomy. High histological grade tumors obtained a partnership at the limit of statistical significance ($p = 0.051$) to positive SLN. Tumor size over 3 cm ($p = 0.187$) and a palpable mass at diagnosis ($p = 0.107$) did not reach statistical significance.

**Conclusions:** These results show a concordance with the Spanish clinical practice guidelines. In our study, tumor size greater than 3 cm did not obtain statistical significance probably related to the small number of patients with this size. The presence of a palpable mass at diagnosis did not correlate significantly with the result of the node, because this clinical presentation was infrequent in our patients, most of them derived from the screening program. Our results support the recommendation of the Spanish guidelines to perform SLNB in case of comedonecrosis or in case of mastectomy.

**No conflicts of interest**

**257** Poster

**Breast conserving therapy versus mastectomy in T1−2N2 stage breast cancer: A population based study on 10-year overall, relative and distant metastasis-free survival in 3,071 patients**

M.C. Van Maaren[1], L. De Munck[1], J.J. Jobsen[2], P. Poortmans[3], G.H. De Bock[4], S. Siesling[1,5], L.J.A. Strobbe[6]. *[1]Netherlands Comprehensive Cancer Organisation, Department of Research, Utrecht, Netherlands; [2]Medical Spectrum Twente, Department of Radiation Oncology, Enschede, Netherlands; [3]Radboud university medical center, Department of Radiation Oncology, Nijmegen, Netherlands; [4]University Medical Center Groningen, Department of Epidemiology, Groningen, Netherlands; [5]MIRA Institute for Biomedical Technology and Technical Medicine- University of Twente, Department of Health Technology & Services Research, Enschede, Netherlands; [6]Canisius Wilhelmina Hospital, Department of Surgical Oncology, Nijmegen, Netherlands*

**Background:** Recent observational studies showed improved survival after breast conserving therapy (surgery with radiation therapy, BCT) compared to mastectomy (MAST) in T1−2N0−2 stage breast cancer. However, N2 stage is described to affect patients' prognosis dramatically compared to N0−1 stage, and is according to the Dutch guidelines an indication for post-mastectomy radiation therapy (RT). We aimed to determine 10-year overall survival (OS), relative survival (RS) and distant metastasis-free survival (DMFS) in T1−2N2 breast cancer after BCT or MAST with RT, stratified for T stage.

**Material and Methods:** All women diagnosed with primary invasive T1−2N2 breast cancer between 1 January 2000 and 31 December 2004, treated with either BCT or MAST with RT, were selected from the Netherlands Cancer Registry. Multivariable Cox regression was performed to estimate 10-year OS, overall and stratified for T stage. Ten-year RS was estimated using general linear models with Poisson distribution, with life tables of the general population. Ten-year DMFS was determined on the 2003 cohort, of which an active follow-up was conducted registering all recurrent events. Multiple imputation was performed to account for missing data.

**Results:** The total population included 3,071 patients, of which 1,055 (34.4%) received BCT and 2,016 (65.7%) received MAST with RT. No difference in 10-year OS and RS between the treatments was observed in T1N2 stage. However, in T2N2 stage, BCT was significantly associated with improved 10-year OS and RS compared to MAST with RT ($HR_{adjusted}$ 0.82 (95% CI: 0.71–0.96) and 0.81 (95% CI: 0.67–0.97), respectively). The 2003 cohort, consisting of 594 patients, presented with similar characteristics as the full cohort. No significant difference between BCT and MAST with RT was found for 10-year DMFS in T1N2 and T2N2 stage ($HR_{adjusted}$ 1.15 (95% CI: 0.69–1.93) and 0.75 (95% CI: 0.51–1.11), respectively) (Table).

Table: Hazard ratios of breast conserving therapy vs. mastectomy with post-operative radiation therapy on 10-year overall, relative and distant metastasis-free survival in T1−2N2 breast cancer

| Cohort | Hazard ratio (95% confidence interval) | | |
|---|---|---|---|
| | 2000–2004 cohort (n = 3,701) | | 2003 cohort (n = 594) |
| | Overall survival | Relative survival | Distant metastasis-free survival |
| Overall cohort | | | |
| MAST + RT | 1 | 1 | 1 |
| BCT | **0.88 (0.77–0.99)** | 0.89 (0.75–1.04) | 0.87 (0.64–1.18) |
| T1N2 | | | |
| MAST + RT | 1 | 1 | 1 |
| BCT | 0.83 (0.68–1.01) | 0.81 (0.62–1.05) | 1.15 (0.69–1.93) |
| T2N2 | | | |
| MAST + RT | 1 | 1 | 1 |
| BCT | **0.82 (0.71–0.96)** | **0.81 (0.67–0.97)** | 0.75 (0.51–1.11) |

Hazard ratios in bold are considered significant ($p < 0.05$). All hazard ratios are corrected for relevant confounders.

**Conclusions:** BCT is associated with at least equal 10-year OS, RS and DMFS compared to MAST with RT in T1−2N2 breast cancer. Therefore, BCT in T1−2N2 breast cancer is preferred if feasible and appropriate.

**No conflicts of interest**

**258** Poster

**A high risk of overestimating ductal carcinoma in situ size exists if microcalcifications mammographic extension is equal or superior to 25 mm**

R. Gamero[1], M. Vernet-Tomas[1], M. Sabadell[1], R. Carreras[1]. *[1]Parc de Salut Mar- Hospital del Mar, Gynaecology and Obstetrics, Barcelona, Spain*

**Background:** Microcalcifications are the most frequent finding to suspect a ductal carcinoma in situ (DCIS) and the standard treatment includes excising the microcalcifications extent. Mammography often under or overestimates DCIS size, leading to re-interventions for incomplete resection or to unnecessary mastectomies. In a former study we found that the accuracy in predicting CDIS size through the extent of mammographic microcalcifications was related to the percentage of estrogen receptor (ER)1 and the size established by mammography (data non published). In that study we defined four groups with different risks of under or overestimation. The aim of this study was to determine if these four groups performed well in a new cohort of DCIS and to define which clinical or pathology features would predict estimation accuracy in this cohort.

**Material and Methods:** Patients treated for DCIS at the Hospital del Mar, Barcelona, between January 2012 and December 2014 were included in a retrospective study approved by our ethics committee, applying the criteria previously defined for each group: Group A, high risk of underestimation including DCIS with ER expression <45%; Group B, high probability of correctly estimated size, DCIS with ER between 46% and 89%; Group C, very high probability of correctly estimated size, DCIS with ER >90% and mammographic extent <25 mm; Group D, high risk of overestimation, DCIS with ER >90% and mammographic extent >25 mm. Data about microcalcifications extent, nuclear grade, ER expression, progesterone receptor expression, p53 expression, Her2Neu expression and DCIS pathology size were recorded. The SPSS Package was used for statistical analysis, applying Chi-square for categorical variables and non-parametric tests for continuous variables.

**Results:** 62 patients were included for the analysis. Statistically significant differences were found between the groups regarding the risk of under or overestimating DCIS size, showing a high risk of overestimation in group D (69.2% vs 5.3% in group C, 33.3% in group B and 44.4% in group A, $p = 0.01$). In this cohort, only mammographic size was related to the risk of overestimation (Kruskal–Wallis $p = 0.00$).

**Conclusion:** this study confirms our previous findings regarding the high risk of overestimating DCIS size when mammographic microcalcifications extent is equal or superior to 25 mm. Our previous findings regarding ER receptor could not be confirmed.

**References**

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predicts the risk of over- or underestimation of the lesion measuring mammographic microcalcifications. EJC 2014;50(suppl 2): 266.

**No conflicts of interest**

**259** Poster

**Postoperative complications in breast cancer patients are independent of age**

B. Ten Wolde[1], M. Kuiper[1], H. De Wilt[2], L. Strobbe[1]. [1]*Canisius Wilhelmina Hospital, Surgery, Nijmegen, Netherlands;* [2]*Radboudumc, Surgery, Nijmegen, Netherlands*

**Background:** Little is known about the optimal surgical treatment for older patients with breast cancer. One element in the discussion regarding treatment choices, is whether fear of increased risk of postoperative complications is valid or whether other variables contribute to the risk of complications. Therefore, the objective of this study is to establish the incidence of postoperative complications in the older breast cancer patients compared to younger patients, and to determine the differences of incidence between breast-conserving treatment and mastectomy.

**Methods:** 1258 female patients (>18 years) who underwent breast cancer surgery for primary diagnosed stage I-III breast cancer in 2010–2014 were included in this retrospective cohort study. Incidence of postoperative complications (POC) were compared between the younger (18−70 year, N = 1008) and older ($\geqslant$71 year, N = 250) patients. Multivariate logistic regression was performed to identify the correlation between age and developing postoperative complications.

**Results:** 38.3% of the younger and 36.4% of the older patients developed a POC (p = 0.317). After lumpectomy the incidence of POC was 26.8% vs 18.4% (p = 0.024) for respectively the younger and the older patient group. After mastectomy, POC occurred in 35.5% of the younger compared to 50.6% in the older group (p = 0.016). Multivariable regression analyses showed increasing age was no predictor for POC (OR 0.592; CI 0.401–0.874, p = 0.008), neither was increasing ASA classification. More extensive surgery, increasing BMI and increasing volume of breast tissue removed did increase the odds of developing a POC. Analyses on the $\geqslant$71 year group separately revealed only type of surgery to be of influence on developing a POC. 9.6% of patients who had a tumor suitable for breast conserving surgery chose mastectomy instead, with increasing age being a predictor for this decision (OR2.624; CI 1.606–4.288, p = 0.000).

**Conclusion:** Fear of increased risk of complications in the older patient is unjustified. Advancing age nor increasing ASA classification are predictors for developing POC. Type of surgery is the most important determinant. Choosing mastectomy while breast conserving surgery is suitable should be discouraged.

**No conflicts of interest**

**260** Poster

**Changing rates of mastectomy and breast conserving surgery in modern breast practice. A single institutional review**

A. Fancellu[1], A. Pinna[1], P. Cottu[1], F. Addis[1], G. Farina[1], A. Porcu[1]. [1]*University of Sassari., Dept. of Clinical and Experimental Medicine. Institute of General Surgery 2. Clinica Chirurgica., Sassari, Italy*

**Background and Aim:** Recent literature suggests that rates of unilateral mastectomy and contralateral prophylactic mastectomy (CPM) are increasing in patients with early breast cancer eligible for breast conserving surgery (BCS). We conducted a single-institutional review of patients operated on for early breast cancer with the aim to evaluate trends of BCS, mastectomy, immediate reconstruction, and CPM.

**Methods:** We searched for patients who underwent surgery for early breast cancer (up to 4 cm) during the period 2005–2014. Patients receiving neoadjuvant chemotherapy and those with sincronous bilateral breast cancer were excluded from the study. In order to evaluate trends of the outcomes of interest, we divided the patients into two groups: Group 1 (patients operated on between 2005 and 2009) and Group 2 (2010–2014). Reasons for unilateral mastectomy as upfront surgery were analyzed, with particular regard to patients' choice. Categorical variables were compared by the $\chi^2$ test or the Fisher exact test as appropriate, and continuous variables were assessed by the t test or the Mann–Whitney test.

**Results:** A total of 1627 patients met the study criteria, 768 in Group 1 and 859 in Group 2. Patients' and tumor characteristics were similar across the 2 groups, with the exception of multicentricity, which was lower in Group 1 (4.7% vs 7.2%, P < 0.05). Rates of BCS as upfront surgery were higher in the Group 1, but the difference missed statistical significance (76.8% vs 74.3%, p = 0.12), as well as rates of total mastectomy rates, including mastectomy as upfront surgery plus mastectomy as reoperation for positive margins after BCS (26.9% vs 28.5%, p = 0.24, respectively in Group 1 and 2). Rates of immediate postmastectomy reconstruction were higher in the Group 2 (72.2% vs 55.8%, p < 0.05). Rates of CPM were also significantly higher in Group 2 (3.5% vs 1.8%, p < 0.05). Interestingly, we observed a significantly higher percentage of patients eligible for BCS who chose a mastectomy plus immediate reconstruction as upfront surgery in the Group 2 (6.3% vs 3.5%, p < 0.05).

**Conclusions:** Our data indicate that BCS remains the treatment of choice in treatment of patients with early breast cancer. However, rates of mastectomy are slowly increasing and will probably continue to grow in the next years. Rates of immediate postmastectomy reconstruction are increasing, as well as rates of CPM. More and more women eligible for BCS will be choosing mastectomy as surgical treatment. These data depict a scenario in which surgical treatment of early breast cancer has becoming quite complex. Each patient should receive appropriate information about risks and real benefits of the different surgical strategies, in order to reach a shared decision making process.

**No conflicts of interest**

**261** Poster

**Patient satisfaction after breast conserving therapy**

H.M.C. Choo[1], V.K. Tan[2], M. Preetha[2], K.T.B. Tan[2], W.S. Yong[2], W.Q. Lee[1], J.W. Ong[1], K. R[1], H.L.S. Khong[2], M.L.M. Tan[2], K.W. Ong[2]. [1]*National University of Singapore, Yong Loo Lin School of Medicine, Singapore, Singapore;* [2]*National Cancer Centre, SingHealth Duke-NUS Breast Centre, Singapore, Singapore*

**Background:** 76% of newly diagnosed Breast Cancer patients in Singapore are early stage. Most would be eligible for breast conserving therapy (BCT). However, rates of BCT are low at 35%. No Patient-Reported Outcome Measures (PROMs) are available at present in Singapore. In this retrospective study, we assessed patient satisfaction among post-BCS patients in terms of cosmetic, body image and psychosocial outcomes and determined the factors influencing them.

**Material and Methods:** The study was conducted in the National Cancer Centre Singapore (NCCS) Specialist Outpatient Clinic from August 2014 to October 2015. Women who had BCT with completion of radiotherapy at least six months before the administration of study were included. An interviewer-administered questionnaire was performed in the form of a validated Hopwood Body Image Scale and a Post-BCS Patient Satisfaction Survey. Tumor parameters were obtained from medical records. The relationships of these variables with patient satisfaction post-BCS were then analysed.

**Results:** 147 patients were recruited, with a median age of 54 years old. The median follow up for this cohort was 45 months (range: 6.5 months to 258 months). 77% had bra size of cups A and B.

Patients were satisfied with their body image based on the Hopwood Body Image Scale. Good patient-reported cosmetic outcomes positively correlated with increased confidence by patients with a significance p value of 0.03. Better patient-reported cosmetic satisfaction was noted in the older age groups and with increased bra size.

**Conclusions:** BCT is the standard of care in managing early stage Breast Cancer. In Singapore, despite a relatively low rate of BCT, good patient-reported satisfaction was demonstrated in this questionnaire survey. A good cosmetic outcome is important in boosting the patient's confidence. Better satisfaction with cosmetic results was noted in older patients and those with larger breast sizes.

**No conflicts of interest**

**262** Poster

**Nipple-sparing mastectomy after neoadjuvant chemotherapy is safe**

T. Pallara[1], E. Manna[1], G. Cortese[2], A. Loreti[3], L. Costarelli[4], M. Mauri[5], M. La Pinta[1], F. Cavaliere[1], E. Santini[6], U. De Paula[7], L. Fortunato[1]. [1]*San Giovanni-Addolorata Hospital, Breast Center − Department of Surgery, Rome, Italy;* [2]*University of Padua, Department of Statistical Sciences, Padova, Italy;* [3]*San Giovanni-Addolorata Hospital, Breast Center − Division of Plastic Surgery, Rome, Italy;* [4]*San Giovanni-Addolorata Hospital, Breast Center − Division of Pathology, Rome, Italy;* [5]*San Giovanni-Addolorata Hospital, Breast Center − Division of Oncology, Rome, Italy;* [6]*San Giovanni-Addolorata Hospital, Breast Center − Division of Radiology, Rome, Italy;* [7]*San Giovanni-Addolorata Hospital, Breast Center − Division of Radiation Oncology, Rome, Italy*

**Background:** Nipple-sparing mastectomy (NSM) with immediate breast reconstruction (IBR) is often considered today for women necessitating radical breast surgery. Survival rates and local control have been suggested to be comparable to those of conventional mastectomy, but little is known regarding NSM for advanced disease or after neoadjuvant

chemotherapy (NCH). We present the outcomes of this approach with a long-term follow-up.

**Materials and Methods:** Patients undergoing NSM for cancer from 2008 and with a minimum follow-up of one year were investigated. All patients necessitating mastectomy, without clinical evidence of nipple–areola complex (NAC) invasion or retraction, and with a minimum of 1 cm clinical-radiological distance of the tumor from the NAC, were considered eligible. Patient demographics, tumor characteristics, stage, and lymph nodes status were prospectively registered on a database and retrospectively reviewed (Table). We compared patients operated after NCH (Group I) with those with early stage disease (Group II).

| | Group I (N = 63) | Group II (N = 152) | p |
|---|---|---|---|
| Median age (y) | 44 | 46 | NS |
| Smoke or Diabetes | 11 (17%) | 34(22%) | NS |
| Average tumor size (mm) (range) | 35 (8−90) | 19 (2−70) | <0.01 |
| Lymph node positivity | 35 (53%) | 42 (28%) | <0.01 |
| Stage II and III | 59 (94%) | 75 (49%) | <0.01 |
| Grade III | 42 (67%) | 52 (34%) | <0.01 |
| Erb-2+/triple negative | 28 (44%) | 16/126 (13%) | <0.01 |
| Positive hormone receptors | 37 (59%) | 107/126 (85%) | <0.01 |

**Results:** Among 319 registered cases, 215 were performed for cancer with a minimum follow-up of one year. Median follow-up for this group was 40 months. Histological positivity of the retro-areolar specimen led to nipple removal in 36 cases (17%), 12 among Group I and 24 among Group II (p = NS). Necrotic NAC and skin flap complications occurred in 8 and 19 patients respectively (Group I 3% and 8%, Group II 4% and 9%; p = NS), necessitating breast implant removal in 17 cases (8%). Minimal necrosis or desquamation were observed in 41 patients (Group I n = 11, 17%; Group II n = 30, 20%; p = NS). Four local relapses (2%) were observed, none of them in the NAC (Group I 1.6%, Group II 2%; p = NS). The same values were observed for contralateral recurrences. Regional relapse occurred in 4 patients (2%) (Group I n = 3, 5%; Group II n = 1, 0.7%; p < 0.05). Systemic recurrences were observed in 21 patients (10%) (Group I n = 10, 12%; Group II n = 11, 7%; p < 0.05). Multivariate analysis showed that only Stage of disease (HR = 12, p = 0.006), and not NCH, was associated with relapse.

**Conclusions:** No statistically significant differences in term of post-operative complications or local relapses were observed between the two Groups. Loco-regional and systemic relapse rates were significantly increased in Group I, but still consistent with traditional mastectomy in the high risk setting. NSM with IBR is safe even for locally advanced cancer and after NCH if the retroareolar margin of resection is free of cancer.

**No conflicts of interest**

**263** Poster

**Patient reported shared decision making regarding breast reconstruction after mastectomy for invasive breast cancer**

K. De Ligt[1], A. Van Bommel[2], M. Mureau[3], K. Schreuder[1], M.J. Vrancken Peeters[4], M. Schrieks[5], J. Maduro[6], S. Siesling[1]. *[1]Comprehensive Cancer Centre The Netherlands IKNL, Department of Research, Utrecht, Netherlands; [2]Leiden University Medical Center, Department of Surgery, Leiden, Netherlands; [3]Erasmus MC Cancer Institute-University Medical Center Rotterdam, Department of Plastic and Reconstructive Surgery, Rotterdam, Netherlands; [4]Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital- Amsterdam, Department of Surgery, Amsterdam, Netherlands; [5]Dutch Breast Cancer Association, Dutch Breast Cancer Association, Utrecht, Netherlands; [6]University of Groningen- University Medical Center Groningen, Department of Radiation Oncology, Groningen, Netherlands*

**Background:** The surgical treatment of breast cancer consists of either a lumpectomy or a mastectomy. Every patient receiving a mastectomy should also be informed about the possibility of an immediate or delayed breast reconstruction, the differences between reconstructive techniques with their advantages and disadvantages. In a nationwide study in the Netherlands the rates of immediate breast reconstruction (IBR) varied significantly between hospitals: on average 41% for DCIS (range 0−85%) and 16% for invasive breast cancer (range 0−63%). It is important to have insight in the shared decision making process and understand whether variation was caused by patient preferences, or that they were simply not informed about the possibility. Therefore, the goal of this study was to gain insight form a patient perspective in the shared-decision making process and information provision regarding breast reconstruction (BR).

**Material and Methods:** A random selection of 24 hospitals in the Netherlands were invited to participate. Patients were selected from the Netherlands Cancer Registry. An online survey asking for patient and treatment characteristics, as well as (shared) decision-making and patient satisfaction with care was distributed among 500 women who had not and 500 women who had received an immediate breast reconstruction following mastectomy between 2013 and 2014.

**Results:** Here we report the results of the first 384 patients that currently completed the survey; 202 without IBR (delayed or no BR), 182 patients with an IBR (Table 1). Of all patients with IBR, 98% received information about IBR and 75% regarding delayed reconstruction; for patients without IBR, this was 76% about IBR and 80% regarding delayed reconstruction. Almost every patient (98%) that underwent IBR and received information about IBR understood this information; for patients without IBR, this was 85%. Eighty percent of the respondents felt they were able to participate in the process of decision making (91% for patients with IBR, 75% without IBR). Almost 90% of all women reported that they were given the opportunity to ask questions about the possibility of a BR.

Table 1.

| | IBR (n = 182) | No IBR (n = 202) (delayed or none) |
|---|---|---|
| Informed about IBR | 179 (98%) | 154 (76%) |
| Informed about delayed BR | 137 (75%) | 162 (80%) |
| Informed about prosthesis | 113 (62%) | 172 (85%) |
| Provided information was understood | 176 (98%) | 155 (85%) |
| Shared decision making | 165 (91%) | 144 (71%) |
| Possibility to ask questions | 182 (100%) | 154 (76%) |

**Conclusions:** This study shows that not every patient is informed about the possibility of IBR. Providing information on BR could improve shared decision making and quality of care.

**No conflicts of interest**

**264** Poster/Poster Spotlight

**Sentinel lymph node biopsy can be omitted in DCIS patients treated with breast conserving therapy**

B. Goorts[1], L. Van Roozendaal[1], M. Klinkert[1], M. Vane[1], B. De Vries[2], L. Strobbe[3], C. Wauters[4], Y. Van Riet[5], E. Degreef[6], E. Rutgers[7], J. Wesseling[8], M. Smidt[1]. *[1]MUMC, Surgery, Maastricht, Netherlands; [2]MUMC, Pathology, Maastricht, Netherlands; [3]Canisius-Wilhelmina Hospital, Surgery, Nijmegen, Netherlands; [4]Canisius-Wilhelmina Hospital, Pathology, Nijmegen, Netherlands; [5]Catharina Hospital, Surgery, Eindhoven, Netherlands; [6]PAMM, pathology, Eindhoven, Netherlands; [7]NKI, Surgery, Amsterdam, Netherlands; [8]NKI, Pathology, Amsterdam, Netherlands*

**Background:** Breast cancer guidelines advise sentinel lymph node biopsy (SLNB) in patients with ductal carcinoma in situ (DCIS) on biopsy when at high risk of invasive breast cancer or in case of mastectomy. The aim of this study was to investigate the incidence of sentinel lymph node (SLN) metastases and relevance of indications in guidelines and literature to perform an SLNB in DCIS patients in current era.

**Materials and Methods:** Patients diagnosed from 2004–2013 with only DCIS on core biopsy without clinically suspicious lymph nodes were included from a national database. The incidence of SLN metastases was calculated. With Fisher exact tests correlation between indications in guidelines and literature for an SLNB and actual presence of SLN metastases was studied. The incidence of DCIS becoming invasive cancer was calculated and correlation with SLN metastases was studied.

**Results:** 910 patients were included. An SLNB was performed in 51.8%, which showed 94.5% pN0, 3.0% pN1mi and 2.5% pN1. Patients undergoing mastectomy had 7% SLN metastases versus 3.5% for BCT (p = 0.107). The only factors correlated to SLN metastases were smaller core needle size (p = 0.01) and upstaging to invasive cancer (p < 0.001). Invasive cancer was detected in 16.7% by histopathology with 15.6% SLN metastases versus only 2% in solely DCIS.

**Conclusions:** SLNB showed metastases in 5.5% of patients; 3.5% in case of BCT and 2% when solely DCIS at definitive histopathology. Consequently, an SLNB should no longer be performed in patients diagnosed with DCIS undergoing BCT. If definitive histopathology shows invasive cancer, it can be performed afterwards.

**No conflicts of interest**

**265** Poster

**Lipofilling of the axilla to reduce secondary lymphedema after axillary lymph node dissection**

L. Vandermeeren[1], J.P. Belgrado[1], S. Vankerckhove[1], J.B. Valsamis[2], V. Feipel[3], M. Rooze[3], J.J. Moraine[3], D. Hertens[4], B. Carly[4], F. Liebens[4]. *[1]CHU St-Pierre, Lymphology clinic, Brussels, Belgium; [2]Université libre de Bruxelles, BEAMS- école polytechnique, Brussels, Belgium; [3]Université libre de Bruxelles, Faculté des Sciendes de la Motricité, Brussels, Belgium; [4]CHU St-Pierre, ISALA Breast clinic, Brussels, Belgium*

**Introduction:** Breast cancer related lymphedema (BCRL) remains a frequent complication (3−60%) of axillary lymph node dissection (ALND). Conventionaly assumed as the expression of the lymph node dissection, lymphedema may also be the consequence of an axillary vein impairment. During surgery, adipose tissue surrounding the axillary vein is partially or completely removed and the axillary sheath can also be damaged. This anatomical disruption reduces the local hemodynamic conditions, with as a consequence an increased microvascular filtration at the distality of the affected limb. This intermittent impairment appears only in orthostatic position. Patients with a venous impairment after ALND are identified by specific clinical signs including pitting edema on the hand and forearm, and by using an innovating imaging technique. Based on these inclusion criteria, we propose an original and simple surgical approach that partially restores the axillary hemodynamic conditions, with as consequence a significant reduction the edema.

**Material and Methods:** BCRL patients with positive clinical signs for axillary hemodynamic changes underwent lipofilling under the axilla vein. Patients remain without any physical treatment nor sleeves during 10 days after surgery. Precise volumetry was performed the day before, the day after and 10 days after surgery (CE AK/13−06−75/4276AD, EudraCT nº 2015–001565−37). After 10 days, patients restart previous physical treatment and we continued to evaluate limb volume by volumetry. Subjective symptoms as numbness, heavy arm, pain and tension of the skin were evaluated.

**Results:** 46 BCRL patients underwent lipofilling surgery. Edema volume reduced significantly in the majority of patients. This reduction was already observed directly after surgery, and was maintained before restart of physical treatment.

Subjective symptoms like heavy arm, numbness, and functional impairment of the upper limb in daily activities started to decrease directly after the operation. Most of the patients continued physical treatment, but felt that compression garments was not essential anymore to maintain edema at low level.

After 24 months of follow up, no complications were recorded.

**Conclusion:** In selected BCRL patients, lipofilling under the axillary vein improves local hemodynamic, reduces distal hyperfiltration and consecutively reduces part of the edema. Results of this pilot study need to be empowered by multicentric studies.

**No conflicts of interest**

**266** Poster/Poster Spotlight

**Can we predict the risk for non-sentinel node metastases? Results from the Swedish Breast Cancer Registry on 23,053 patients**

E. Vikhe-Patil[1], L.G. Arnesson[1], H. Fohlin[2], K. Sandelin[3]. *[1]University hospital, Kirurgkliniken, Linköping, Sweden; [2]RCC, Region Ostergotland, Linkoping, Sweden; [3]Karolinska Institutet, Surgery, Stockholm, Sweden*

**Introduction:** Performing axillary clearance after node positive sentinel node biopsy (SNB) has been challenged. This register study aimed to predict the risk for non sentinel node metastasis after axillary clearance in Swedish patients. The Swedish Breast Cancer Registry has been in use since 2008 with >99% compliance. National guidelines recommend clearance for macro- and micrometastasis in SN but not for isolated tumor cells (ITC). Mammography screening is performed nationwide.

**Materials and Methods:** Data for 33,314 patients, 2008 until May 2012, is evaluated. SNB was performed in 23,053 patients corresponding to 69% of all patients; a stable figure since 2008. This cohort is further investigated. Patients median age was 63 years. Breast conserving surgery (BCT) was performed in 61.5%. SNB detection mode was radiocolloid and blue dye injection in all patients. 41% underwent additional lymphoscintigraphy. Mean tumor size after BCT and mastectomy (ME) was 16 and 27 mm respectively. BCT and ME show SNB positive in 16.7% and 26.8% respectively. Number of excised nodes after axillary clearance was 13 (range 1−50).

**Results:** Median harvested SNBs was 2 (range 1−8). 5382 SNB+ cases were found, giving 15.8% macrometastasis, 5.7% micrometastasis and 1.5% ITC. Altogether non-SN metastasis were found for 31.6% of SNB+ patients.

The risk of non-SNB macrometastasis is: If only 1 macrometastasis in SNB, 38% had further involved nodes. If 2 macrometastasis in SNBs, 52% had non-SNB metastasis and if 3 positive SNBs the figure was 64% positive non-SNB nodes; a significant difference. Evaluating 1010 SNB micrometastatic cases gave figures of freedom of non-SNB metastasis: 1 micrometastatic node 81%, 2 75% free and 3 micrometastasis show 50% non-involved metastasis. These figures are also significant.

Data on lymphovascular invasion (LVI) was available for 18754 cases and showed a significant higher risk for non-SNB metastasis in LVI-positive tumors 48% against 30%. SNB metstasis were more frequent in lobular cancers, 30% against 26% for ductal cancers and significantly more axillas had to be reexplored in lobular cancers, partly due to equivocal frozen section analyses.

**Conclusion:** The SNB diagnostic technique works well in Sweden; 69% of patients had SNB as the primary axillary procedure 2008–2012. 22.1% show SNB-positivity. The risk for non-SNB metastasis is significantly correlated to 2 or more involved SNBs and to positive LVI. Is this the group for axillary surgery? A new national randomized study will investigate the need for completion axillary clearance in a subset of SNB+ patients.

**No conflicts of interest**

**267** Poster

**Robotic nipple sparing mastectomy and immediate breast reconstruction: Future prospectives for breast cancer surgery**

A. Toesca[1], N. Peradze[1], A. Manconi[2], D. Lichosik[3], M. Rietjens[2], P. Veronesi[1]. *[1]European Institute of Oncology, Division of Breast Surgery, Milan, Italy; [2]European Institute of Oncology, Division of Plastic and Reconstructive Surgery, Milan, Italy; [3]European Institute of Oncology, Operating Theatre, Milan, Italy*

**Background:** It goes without saying that the technology is moving forward with unprecedented speed. Robotic surgery made an incredible progress in various disciplines over the past decade. Robotic mastectomy technique was firstly described by Toesca et al. [1] only for risk-reducing surgery. The aim of our study is to evaluate the applicability of robotic surgery also for breast cancer patients.

**Material and Methods:** 10 patients with breast cancer or DCIS candidates for unilateral or bilateral nipple-sparing mastectomy (NSM) and immediate breast reconstruction with implant (IBRI) were selected to perform surgery using Da Vinci Robotic System. A total of 11 robotic mastectomies were performed.

A 2.5-cm-long incision on the mid axillary line was performed; the subcutaneous flap was dissected manually to obtain a working space for the insertion of the single port connected to an insufflator of $CO_2$ and to create a cavity with 7−8 mmHg pressure and introduce robotic arms and camera. The endoscopic view was observed through a 30º 12-mm camera. Dissection was performed with a 5/8 mm monopolar cautery spatula used on the right robotic arm. Traction and counter-traction was performed with an 8 mm Maryland Bipolar Forceps fitted on the left robotic arm. The gland was removed en-bloc through the same incision. The submuscular pocket was prepared maintaining the same axillary access and the same robotic instruments. The implant was placed manually.

**Results:** The learning curve of the total time for the procedure was rapid; from 7 hours for the first case to 3.5 hours for the last cases. High quality 10 fold magnified 3D vision during robotic surgery offered a better view of surgical dissection plane permitting the complete removal of the gland and therefore oncological safety. Intraoperative specimen examination with pathologist confirmed the radicality of the procedure. The use of $CO_2$ enabled the reduction of bleeding. High precision and stability of the instrument movement, sharpness and clarity of the image allowed more accurate preservation of the blood supply and vitality of anatomical structures and nipple areola complex. 2 cases were converted to an open technique. No major complications were observed.

**Conclusions:** Despite superficial organs not being the best target for robotic surgery, we safely performed robotic NSM and IBRI for breast cancer patients. The minimal incision hidden in the axilla improved aesthetic outcome preserving woman body image. The encouraging preliminary results endorse a prospective study aiming evaluation of patient satisfaction, physical function of the upper limb, nipple areola complex sensitivity, pain reduction and cost effectiveness.

**References**

[1] Toesca A, Peradze N et al. Robotic Nipple-sparing Mastectomy and Immediate Breast Reconstruction With Implant: First Report of Surgical Technique. Ann Surg. 2015 Oct 7 [Epub ahead of print].

**No conflicts of interest**

**268** Poster

**Examination of the surgical range diagnosed by contrast-enhanced ultrasonography in breast surgery after preoperative chemotherapy (pilot study)**

K. Futsuhara[1], K. Omoto[2], K. Suzuki[1], A. Yoshizawa[1], N. Kakizawa[1], T. Rikiyama[1]. [1]*Saitama Medical Center- Jichi Medical University, Department of Surgery, Saitama city, Japan;* [2]*Saitama Medical Center-Jichi Medical University, Physiological Laboratory, Saitama city, Japan*

**Background:** A purpose of breast cancer preoperative chemotherapy has the improvement of breast partial resection rate. It is important that cancer cells do not reach the surgical margin in breast partial resection. The determination of surgical range becomes difficult under the influence of chemotherapy by the preoperative chemotherapy. We confirm the range and small nodule of breast cancer by the contrast-enhanced ultrasonography by sonazoid® before breast surgery. An advantage of this method is able to decide a position and the range of the breast cancer on the surgical position. This time, we inspected the effectiveness of contrast-enhanced ultrasonography for the breast surgery after preoperative chemotherapy as pilot study.

**Material and Methods:** We enrolled 27 women who breast cancer was diagnosed from 2007 through 2015, and were treated with the preoperative chemotherapy. Preoperative treatment is the sequential therapy of Anthracyclin and Taxane and HER2 overexpression case was treated by combination therapy with taxmen and trastuzumab.

**Results:** 27 cases were classified into group A (12 cases which had contrast-enhanced ultrasonography) and group B (15 cases which had not). Age of group A is 43−58 years (average 50.5) and group B is 33−57 (average 43.8). ER positive cases of group A is 5, group B is 5 cases. HER2 amplification of group A is 8 cases, group B is 7 cases. Mastectomy was performed for 1 case in group A and 3 cases in group B. Pretreatment tumor size is 13−52 mm (average 28.5) in group A, 13−70 mm (average 32.8) in group B. Post-treatment tumor size is 0−32 mm (average 10.1) in group A, and 4.6−40 mm (average 14.1) in group B. Group A 11 cases and group B 12 cases was examined except mastectomy cases. Surgical area is 22–43.5 $cm^2$ (average 36.1) in group A and 40.5−99 $cm^2$ (average 60.8) in group B. Positive surgical margin is 2 cases in group A and 1 case in group B.

**Conclusions:** The excision area of breast partial resection becomes wider when negative surgical margin is demanded. The wide surgical range influences the esthetic outcome of the breast. The precise surgical range is the important problem in breast partial resection. The contrast-enhanced ultrasonography enabled the smaller surgical area. However, there were few positive surgical margin cases. This method will need more detailed inspection in future.

**No conflicts of interest**

**269** Poster

**Long-term impact of age, intrinsic subtype, and local treatment on 20-year survival among Danish lymph-node-negative breast cancer patients**

T. Laurberg[1], J. Alsner[1], T. Tramm[2], C. Lyngholm[1], P. Christiansen[3], J. Overgaard[1]. [1]*Aarhus University Hospital, Experimental Clinical Oncology, Aarhus, Denmark;* [2]*Aarhus University Hospital, Department of Pathology, Aarhus, Denmark;* [3]*Aarhus University Hospital, Department of Surgery P- Breast and Endocrine Section, Aarhus, Denmark*

**Background:** Optimal local treatment for young women with early-stage breast cancer remains controversial due to the lack of knowledge as to whether local recurrence (LR) is associated with inferior survival.

**Aim:** To evaluate the long-term prognostic impact of age, local treatment, and intrinsic subtypes on the risk of LR and premature death, the hypothesis being that there is no long-term survival difference between breast conserving therapy (BCT) and mastectomy patients in young (⩽45 years) breast cancer patients with a Luminal A (LumA) tumor.

**Material and Methods:** 1077 Danish patients with low risk breast cancer (i.e., lymph-node-negative and tumor size <5 cm) were enrolled between 1989 and 1998 in this population-based cohort study, including all Danish patients below 40 years (N = 305) and 772 patients above 40 years. The patients were treated with mastectomy (N = 712) or BCT (N = 364) and received no systemic treatment. Tumor blocks were successfully collected from 832 (77%) of the patients. Intrinsic subtype approximation was performed by combining information on Estrogen-, Progesterone receptor and Her2 status.

**Results:** After 20 years, the cumulative incidence proportion (CIP) of LR was 18% after BCT (N = 66) and 6.7% after mastectomy (N = 55). Patients treated with mastectomy developed only early LR; older patients within the first 5 years and the younger patients within 10 years. In contrast, patients regardless of age treated with BCT developed LR throughout the 20-year period. LR was significantly associated with young age and BCT treatment, whereas the intrinsic subtypes were neither associated with early LR, nor late LR.

After 10 years, older patients with LumA tumors had a higher breast-cancer-specific survival (BCSS) compared to those with Her2-enriched tumors: 89% vs. 62%, RD = 27% (8−46), and young patients with LumA tumors had a higher BCSS compared to those with Basal like tumors: 89% vs. 71%, RD = 18% (2.6−33). In contrast, after 20 years, there was no association found between intrinsic subtypes and BCSS neither among the older patients nor among the young ones.

Among young patients with LumA tumors and low risk clinicopathological features (i.e., <2 cm, invasive ductal carcinoma grade 1), BCT patients had a higher 20-year breast-cancer-specific mortality [HR = 1.6 (1.0−2.5)] and a higher 20-year all-cause mortality [HR = 1.7 (1.1−2.6)] compared to those receiving mastectomy.

**Conclusion:** Intrinsic suptypes had no prognostic value in terms of LR and BCSS within age- or treatment groups after 20 years. Among young patients those with small LumA tumors, who underwent mastectomy, had a significantly better 20-year survival compared to those who underwent BCT.

**No conflicts of interest**

**270** Poster

**How to measure cosmetic result after breast conserving surgery?**

M. Lagendijk[1], E.L. Vos[1], E.M.L. Corten[2], C. Verhoef[1], L.B. Koppert[1]. [1]*Erasmus MC Cancer Institute, Surgical oncology, Rotterdam, Netherlands;* [2]*Erasmus MC Cancer Institute, Department of plastic and reconstructive surgery, Rotterdam, Netherlands*

**Background:** Overall survival performing breast conserving surgery (BCS) versus a mastectomy for early stage breast cancer is similar. Cosmetic result is thus an important endpoint following BCS for breast cancer. The gold standard for assessing cosmetic results is still under debate. We describe two different techniques and compare them to patient reported outcome measures (PROMs).

**Material and Methods:** Sixty-eight breast cancer patients were included after BCS at a tertiary referral centre between 2007–2012. Cosmetic result following BCS was evaluated by 1) two independent 6-member panels 2) the BCCT.core software used by two observers and 3) PROMs including EORTC-QLQ-C30/B23, EQ-5D-5L and BREAST-Q 'Postoperative-breast conserving module'. Panel scores are calculated as a mean score per patient per panel. When comparing Q-scores for either a 'good' or 'bad' cosmetic evaluation scores of the panel and BCCT.core are dichotomized.

**Results:** Sixty-four patients (94.1%) completed the EORTC-QLQ-C30 and B23 and 58 (85.3%) patients the EQ-5D-5L and BREAST-Q. Absolute agreement between the BCCT.core observers and panel evaluations ranged from 76.1% to 87.3%. Overall agreement between BCCT.core and panel varied from 0.59 to 0.69 interclass correlation coefficient (ICC) (Table 1). Overall agreement between Q-scores and BCCT.core or panel varied from −0.18 to −0.33 (ICC). Inter-observer agreement between both panels and BCCT.core observers was respectively 0.93 and 0.86 (ICC) (Table 1). Q-scores were significantly different for the group with either a 'good' or 'bad' cosmetic evaluation based on both panel and BCCT.core evaluations ($P < 0.05$).

Table 1 (abstract 270). Overall agreement cosmetic evaluation − interclass correlation coefficient [a] (95% CI)

| | Panel [b] 1 | Panel [b] 2 | BCCT.core 1 | BCCT.core 2 | Q-score [c] |
|---|---|---|---|---|---|
| Panel [b] 1 | | 0.93 (0.89−0.96) | 0.69 (0.54−0.79) | 0.61 (0.43−0.73) | −0.2 (−0.27, 0.24) |
| Panel [b] 2 | 0.93 (0.89−0.96) | | 0.66 (0.5−0.77) | 0.59 (0.42−0.72) | −0.18 (−0.27, 0.24) |
| BCCT.core 1 | 0.69 (0.54−0.79) | 0.66 (0.5−0.77) | | 0.86 (0.78−0.91) | −0.3 (−0.28, 0.24) |
| BCCT.core 2 | 0.61 (0.43−0.73) | 0.59 (0.42−0.72) | 0.86 (0.78−0.91) | | −0.33 (−0.28, 0.21) |

[a] 0 indicates 'poor' agreement, 0.01−0.2 'slight', 0.21−0.4 'fair', 0.41−0.6 'moderate' 0.61−08 'substantial' and >0.8 'almost perfect' agreement.
[b] Mean scores per patient per panel.
[c] 'Satisfaction' module.

**Conclusions:** Comparable results were found for BCCT.core and panel in the evaluation of cosmetic outcome. This is the first study to compare the BREAST-Q and EQ-5D-5L to other assessment technique of cosmetic outcome following BCS. Q-scores are sensitive for the differentiation between a 'good' or 'bad' cosmetic outcome. However agreement between PROMs and BCCT.core or panel was limited. Striving for optimal quality of life, a combination of panel evaluation or BCCT.core with PROMs is needed in future trials.

**No conflicts of interest**

**271** Poster

**Level II oncoplastic surgery for craniomedial tumours of the breast: The 12 O'Clock technique**

C. Catsman[1], E. Luiten[2]. [1]*Amphia Hospital, Molengracht, Breda, Netherlands;* [2]*Amphia, Molengracht, Breda, Netherlands*

**Background:** Breast conserving surgery for larger tumours (>2 cm) located in the craniomedial part of the breast (11 to 2 o'clock) may be challenging with regard to obtaining a cosmetic good result. Level I oncoplastic displacement procedures, through batwing or round block incisions, in order to correct the loss of volume may be hampered by the combination of limited breast volume in this region and décolletage visibility. We present a new level II oncoplastic displacement technique to reshape tumour defects craniomedial part.

**Methods:** An observational registration study of a newly introduced technique reporting feasibility, oncologic and cosmetic outcome. The so called 12 O'Clock technique is introduced in patients with larger excisions, >20% of the breast − irrespective of breast tissue quality or age − who were candidates for breast conserving surgery in whom an acceptable cosmetic result with local arrangement of breast tissue following resection was not foreseen. The technique is based on rotation and displacement of a vascularised lateral dermo-glandular breast flap. All patients were asked to score cosmetic result of the operated breast using a 12-point scale. Quality of life was score with the BREAST-Q questionnaire, validated for patients after breast conserving surgery.

**Results:** In this first series of six patients, mean tumour diameter was 43.3 mm (25−60), in two patients re-resection was carried out due to involved margins with re-reconstruction using the 12 O'Clock technique twice. All patients rated the cosmetic result as "good" on a four-point scale. Quality of life was scored for: satisfaction with the breast (100−68%), psychosocial wellbeing (100−68%) and physical wellbeing (63−87%) in comparison with their perceived status before the surgery was high. Sexual wellbeing was moderate (64−69%).

**Conclusion:** The 12 O'Clock level II oncoplastic reconstruction technique may be a valuable addition to intramammary volume displacement techniques for tumours of the upper quadrant of both fatty and glandular breasts. Taken into account patient reported outcome measures good cosmetic results and excellent quality of life can be achieved.

**No conflicts of interest**

**272** Poster

**Flat epithelial atypia on breast core biopsy − to resect or not?**

P. Chan[1], B. Ho[2], S. Lu[1], M. Seah[1], J. Chen[1], E.Y. Tan[1]. [1]*Tan Tock Seng Hospital, Breast Unit, Singapore, Singapore;* [2]*Tan Tock Seng Hospital, Pathology, Singapore, Singapore*

**Background:** Flat epithelial atypia (FEA) is reported in a small proportion of breast core biopsy. It is believed to be associated with atypical hyperplasia and breast cancer and patients are recommended to undergo open surgical excision. The aim of our study is to review our patients with FEA on core biopsy and examine the incidence of upgrade to carcinoma.

**Materials and Methods:** A retrospective review of patients who had undergone percutaneous breast biopsy at our institution from 2012 to 2014 showed 190 patients had FEA in the histological report. 16 patients who also had carcinoma found in the specimen were excluded leaving 174 patients in the analysis. They were divided into two groups − FEA with atypical hyperplasia and 'pure' FEA.

**Results:** Of the 67 patients with FEA with atypical hyperplasia, all underwent surgery and 3 patients had carcinoma after open biopsy (5%) whilst a further 17 patients (25%) had atypical hyperplasia. Of the 110 patients with 'pure' FEA, 87 had open surgical biopsy. The histology of the open biopsy were atypical hyperplasia and FEA in 21 (24%) and 38 (44%) patients respectively. 22% of the patients had no abnormalities found in the open biopsy. There were no patients with upgrade from 'pure' FEA to carcinoma in the final histology.

**Conclusions:** FEA on breast core biopsy is not associated with an upgrade to carcinoma if it is not accompanied with atypical hyperplasia. Factors associated with upgrade of 'pure' FEA to atypical hyperplasia will be discussed.

**No conflicts of interest**

**273** Poster

**Outcome and factors associated with axillary recurrence after negative sentinel node biopsy for breast cancer**

N. Wada[1], K. Yoneyama[2], T. Hojo[2], C. Yamauchi[2]. [1]*Tokyo Dental College Ichikawa General Hospital, General and Breast Surgery, Ichikawa, Japan;* [2]*National Cancer Center Hospital East, Breast Surgery, Kashiwa, Japan*

**Background:** Aim of this study is to determine factors of developing axillary recurrence (AR) and to assess the outcome after AR.

**Patients and Methods:** Between Sep 1999 and Dec 2010, cT1−2N0M0 invasive breast cancer patients who were sentinel node (SN)-negative and did not have axially lymph node dissection (ALND) were included in a prospective cohort. Kaplan–Meier estimates were used to analyze the rates of AR and survival. Multivariate analysis was performed using all available variables, a p-value of <0.05 was considered to be significant.

**Results:** A total of 977 patients were eligible. Median age was 57 years [21−89 years]. Median clinical tumor size was 1.8 cm [0−5.0 cm]. Other background characteristics were as follows, presence of lymphovascular invasion (LVI): 385, histological grade (HG) 3: 228, hormone receptor positive: 737, partial mastectomy: 847, hormone therapy alone: 498, chemo-hormone therapy: 68, chemotherapy alone: 126, radiation treatment: 744. At a median follow-up time of 83 months [0–163month], 81 patients (8.3%) developed a recurrence, and breast cancer specific death occurred in 25 (2.6%) patients and other cause of deaths occurred in 11 (1.1%) patients. During the observation period, a number of the first sites of recurrence were 40 distant metastasis, 28 local recurrences and 18 regional lymph-node recurrences. The 5-year relapse free survival rates was 93% [95% CI 91−94%], and the 5-years overall survival was 98%[97−99%]. Of 40 patients with recurrences, 11 patients were diagnosed with AR. The 5-year estimated AR rate was 1.1% [0.3−1.9%]. Median AR free period was 22 months [3−95manths], median age was 57 years [30−83years], median clinical tumor size was 3.0 cm [1.3−4.3 cm]. Other background characteristics were as follows, HG 3: 7, LVI positive: 9, hormone receptor positive: 6, mastectomy: 6, no adjuvant systemic therapy: 7, no radiation treatment: 7. Nine patients received ALND after AR diagnosis, the median number of metastasis in dissected axially node was 4 [1−26]. In the median observation period 76 months [4–168 months] from AR, breast cancer specific death occurred in 4, and 5-years survival rate from AR was 80% [55–100%]. There was no significant difference in Kaplan–Meier survival curve between recurrence patients with and without AR. Univariate analysis showed that development of AR was significantly more frequent in patients with the following characteristics: large tumor size (T2) ($p = 0.028$), mastectomy ($p = 0.001$), presence of LVI ($p = 0.017$), HG3 ($p = 0.01$), no radiation treatment ($p = 0.006$). Multivariate analysis showed that presence of LVI ($p = 0.022$), HG3 ($p = 0.049$) were independent predictors of AR.

**Conclusions:** Our results confirm that AR is rare in SN-negative patients without ALND. Presence of LVI, HG3 are independent predictors of AR. Survival rate with AR is equal to that with recurrence other than AR.

**No conflicts of interest**

**274** Poster

**Endoscopic transaxillary resection of high risk benign breast tumors**

I. Fyssas[1], G. Trogadas[1]. [1]*Prolipsis, Breast Unit, Athens, Greece*

**Background:** Aim of this method is the avoidance of a surgical scar on visible areas of the chest, in selected women with high risk benign breast lumps, located in peripheral areas of the breast, unreachable through periareolar incisions.

**Material and Method:** The procedure was performed in 28 women from May 2009, till September 2015. All patients gave informed consent prior to the procedure. Selection criteria was the inaccesibility of the lump through periareolar incision and the patient's wish to avoid a visible surgical scar when wearing a decollete dress or a swimwear. All lumps were preoperatively diagnosed as benign with FNA or core biposy. 12 were papillomas, 9 phylloid tumors, 3 epithelial hyperplasias and 4 large fibroadenomas. All lumps were located in the upper inner quadrant of the breast or parasternally. The average size of the lumps was 2.2 cm (1.3−4.8 cm). The average duration of the procedure was 65 minutes (45–100 minutes) under general anesthesia. The ages varied from 17 to 53 years old. We used a 5 mm vessel endoscopy trocar, a 5 mm 30º laparoscopic camera and long bipolar scissors, introduced through a small axillary incision. A normal saline solution with adrenaline was preoperatively injected along the course of the trocar. We did not use $CO_2$ for subcutaneous emphysema.

**Results:** The cosmetic result of the operation was always excellent. There was no breast scar. No serious complications were observed. The disadvantages of the method is the longer duration than the resection through a periareolar or an above the lump incision, a mild bruise along the course of the trocar lasting for less than a week and a small axillary scar, fading after a few months.

**Conclusion:** The endoscopic resection is recommended for every woman, with a high risk benign breast lump unreachable through periareolar incision, who wishes to have an excellent cosmetic result, by avoiding a surgical scar on the front of her chest or parasterna caseslly. Early breast cancer lesions might also be resected, however we have not yet proceeded with this method for invasive or pre-invasive lumps.

**No conflicts of interest**

**275** Poster

**Is it possible to operate breast cancer on an outpatient basis?**

C. Hedin[1], L. Pistioli[1], E. Vikhe-Patil[1], P. Gunnarsson[1], P. Landberg[1], S. Kindstrand[2], C. Wallon[1], M. Vegfors[2]. [1]*Linköping University, Surgery Department, Linköping, Sweden;* [2]*Medicinskt Centrum Linköping, Medicinskt Centrum Linköping, Linköping, Sweden*

**Background:** The Region of Östergötland in Sweden has implemented a time schedule for cancer patient management, with a 17 days interval from diagnosis to surgery. The University Hospital in Linkoping is not always able to provide accommodation and operative facilities with consequential accessibility problem. In 2014 a joined project was launched together with Medicinskt Centrum Linköping (MCL), a private health care provider. The aim of the project was to evaluate breast cancer surgery as day surgery, and giving the patients the scheduled date for surgery at the same time as the patient was informed of the breast cancer diagnosis, while at the same time, maintaining high quality treatment results and patient satisfaction.

**Method:** The project included breast cancer patients, irrespectable of the type of operative procedure. Patients assessed as ASA 4/5 as well as ASA 3 with cardiac arrhythmias, were excluded. The surgeon informed the patient of the diagnosis and at the same time made an assessment of the patient's overall physical status and domestic standing. The anesthesiologist reviewed the patient's file and health declaration form. If more information was needed the patient was contacted. Customized pre-medication, local anesthetics depending on the type of the operation, and anti-emetics were administered to every patient. The operation was carried out under general anesthesia induced with Ultiva/propofol and the airway was managed via a laryngeal mask. In cases of wide excisions, fentanyl was administered before waking the patient up. Even Ropivacain mixed with adrenaline is often instilled in the wound and drainage is clamped for 20 minutes. In the post-operative ward, specialized nursing personnel promptly identified and managed pain and nausea.

**Results:** During the period 2014−10−27 to 2015−10−30 with exception for four weeks of vacation during the summer period, 449 patients were operated at MCL. Three patients stayed over night at MCL. Three patients had to be transported to the University Hospital of Linköping, out of which two had postoperative complications and one due to chest pain. Patient questionnaires regarding the quality of care provided, management of post-operative pain and nausea, and the patients' subjective experience of day-care surgery showed very positive results.

**Conclusions:** Breast cancer surgery can be performed as day-surgery. A well-functioning pre-, peri- and post-operative team approach can ensure patient safety and satisfaction. Day-care surgery renders great efficiency in breast cancer process for both the patient and the health care provider.

**No conflicts of interest**

**276** Poster

**Axillary lymph node recurrence and prognosis of avoiding axillary lymph node dissection by sentinel lymph node biopsy after neoadjuvant chemotherapy**

Y. Kajiwara[1], T. Kin[1], M. Fujihara[1], Y. Yoshimura[1], M. Ito[1], S. Ohtani[1]. [1]*Hiroshima City Hospital, breast surgery, Hiroshima, Japan*

**Background:** Sentinel lymph node biopsy (SNB) in early breast cancer is widely used as a standard treatment. However, SNB after neoadjuvant chemotherapy (NAC) is still investigational. We have studied accuracy and feasibility of SNB after NAC in 275 patients with advanced breast cancer from 2000 to 2009. Our results showed that SNB after NAC can be feasible and predict the axillary nodal status with a high accuracy in patients who are clinically lymph node negative before NAC. (sentinel lymph node identification rate [SNIR]: 92.7%, false negative rate: 0%). We have reported these results at the 13th St Gallen International Breast Cancer Conference. Therefore, we planned to perform SNB (+-axillary lymph node dissection [ALND]) as a treatment for the patients with a clinically negative axillary nodal status before NAC. To our best knowledge, no studies have reported prognosis by SNB after NAC. So we evaluated ALN recurrence rate and prognosis of avoiding ALND by SNB after NAC.

**Material and Methods:** All patients with primary breast cancer diagnosed between January 2011 to December 2013 who received NAC. 164 patients underwent NAC, of which 51 patients with a clinically negative axillary nodal status before NAC were provided SNB without ALND) as a treatment, and events were checked. They were followed for a median of 33 months (3−51 months). The sentinel node was identified by the combined method that used the 99mTc-phytate and Indigocarmine.

**Results:** We provided SNB (+-ALND) for 51 patients. 43 patients (84.3%) were sentinel lymph node negative, 8 patients (15.7%) were sentinel lymph node positive. The median number of sentinel lymph nodes removed was 1 (range 1−5), and SNIR was 100%. All cases responded to NAC in varying degress, however, only one case was progressive disease temporarily by paclitaxel. This case achieved a partial response followed by EC (epirubicin/cyclophosphamide). 3-year Kaplan–Meier estimates for disease-free survival (DFS) were 94.8%. 3-year Kaplan–Meier estimates for overall survival (OS) were 100%. However, there was no ALN recurrence. There were only one Ipsilateral breast recurrence (DFS: 30 months, OS: 38 months) and one brain metastasis (DFS: 13 months, OS: 35 months) in 43 patients avoided ALND. These two cases were Luminal B type.

**Conclusions:** There is no ALN recurrence in the cases avoiding ALND by SNB after NAC in a clinically negative axillary nodal status before NAC, though the surveillance is short term. Therefore, SNB is feasible and accurate after neoadjuvant chemotherapy in a clinically negative axillary nodal status before NAC.

**No conflicts of interest**

**277** Poster

**Three-dimensional breast volume assessment**

P. Gouveia[1], J.P. Monteiro[2], H.P. Oliveira[2], M.J. Cardoso[1], J.S. Cardoso[2]. [1]*Champalimaud Clinical Center, Breast Unit, Lisbon, Portugal;* [2]*INESCTEC, CTM, Porto, Portugal*

**Background:** Breast volume quantification is essential for breast cancer surgery planning. Several methods have been described for breast volume assessment. Breast magnetic resonance imaging (MRI) is considered the gold standard for breast size measurements. However, MRI is not routinely used for breast cancer diagnosis, implying additional costs if used for this purpose. Three-dimensional (3D) imaging of the breast has provided reproducible and clinically valid data for volume evaluation, however, available 3D solutions are still very expensive.

**Objective:** Estimate breast volume using a reconstructed 3D model based on 2.5D images captured with a low cost surface scan device.

**Material and Methods:** 3D reconstructed models of breasts from 2.5D images captured with the Microsoft® Kinect device from 15 patients with early breast cancer before surgery were included. MRI scans were identically performed in all patients before surgery. For each method, breast volumes were computed using a convex hull approach. The agreement between the volumes obtained with both methods was assessed with Spearman, Kendall's tau and Pearson's linear correlation coefficients.

**Results:** Pearson's linear correlation coefficient was 0.90, the Kendall rank correlation coefficient was 0.64, while the Spearman coefficient was 0.81. The average difference between volumes from both methods was 200 cc.

**Discussion:** The direct comparison between breast volumes in each modality is not clear because it is difficult to identify the exact position of the chest wall. Since the Spearman coefficient, Kendall's tau and Pearson's coefficient are high, this indicates that the relationship is monotonic. Although the values obtained by both methodologies still differ, the strong linear correlation coefficient suggests that improvements in the chest wall estimation may bring the results closer. Beyond rear demarcation, breast boundaries delimitation are somehow different when using each method, and variability increases with less anatomically defined landmarks.

**Conclusion:** 3D breast volume measurement using a low cost surface scan device is feasible and can approximate the MRI breast volume with sufficient accuracy. With a more accurate estimation of the chest wall position, it will be possible to have a direct comparison of the volumes obtained with the two modalities.

**No conflicts of interest**

**278** Poster

**Isotope-only localisation of sentinel lymph node biopsy − a safe alternative to dual technique**

A. Parvaiz[1], E. Ball[2], F. MacNeil[3], N. Roche[4], J. Rusby[5]. [1]*Peterborough City Hospital- UK, Oncoplastic Breast Surgery, Peterborough, United Kingdom;* [2]*Royal Marsden Hospital- Sutton, Breast Surgery, Sutton, United Kingdom;* [3]*Royal Marsden Hospital- London, Breast Surgery, London, United Kingdom;* [4]*Royal Marsden Hospital, Breast Surgery, London, United Kingdom;* [5]*Royal Marsden Hospital, Breast Surgery, Sutton, United Kingdom*

**Background:** Isotope and blue dye dual localisation in sentinel lymph node biopsy (SLNB) gives localisation rates of over 98% and is recommended

by the Association of Breast Surgery (ABS) UK guidelines. However blue dye carries a risk of adverse reactions. We stopped routine use of blue dye in 2011 but patients without a clear isotope signal from the axilla do have blue dye injection. We investigated outcome of isotope only SLNB.

**Material and Methods:** All patients intended for isotope only SLNB between July 2010 and April 2012 were included from a prospectively maintained database. Localisation and recurrence data were collected. Potential predictive factors for failure of isotope localisation were assessed using Fisher's exact test. SLN yield and axillary disease burden were also collected.

**Results:** 438 SLNB were performed in 431 patients (2 men and 429 women). Median age was 57 (range 26−91). Isotope-only localisation rate was 97% (425/438). Median SLN yield was 2 (range 0−5). At 40 months median follow up (range 33−54) axillary recurrence rate was 0.6% (never as first site of recurrence). In-breast recurrence was 1.5%, contralateral cancer 2.1%, distant recurrence 4% giving a disease free survival rate of 92.4%. Breast cancer mortality was 2.7%.

Predictive factors for the failure of isotope-only localisation included previous breast or axillary surgery ($p = 0.0001$ and $p = 0.0022$ respectively) and isotope injection on the day before operation ($p = 0.0002$). Factors that did not influence success of isotope only localisation included patient age, BMI, neoadjuvant treatment, type of breast operation and tumour pathology/receptors.

**Conclusions:** Isotope-only SLNB has a high localisation rate and spares the majority of patients the risk of blue dye adverse reactions. The low axillary recurrence rate suggests that clinically relevant nodal disease has not been overlooked, confirming that this is feasible and safe alternative to the dual technique.

**No conflicts of interest**

**279** Poster

**Comparison of 350 consecutive oncoplastic procedures to 350 conventional breast conserving therapies. Oncological, cosmetic and quality of life outcomes**

P. Kelemen[1], D. Pukancsik[1], M. Ujhelyi[1], E. Kovacs[2], N. Udvarhelyi[3], I. Kenessey[4], M. Kasler[5], Z. Matrai[1]. *[1]National Institute of Oncology, Breast and Sarcoma Unit, Budapest, Hungary; [2]National Institute of Oncology, Department of Radiological Diagnostics, Budapest, Hungary; [3]National Institute of Oncology, Department of Surgical and Molecular Pathology, Budapest, Hungary; [4]Semmelweis University, 2nd Department of Pathology, Budapest, Hungary; [5]National Institute of Oncology, Director, Budapest, Hungary*

**Background:** Oncoplastic breast surgery (OPS) is a rapidly evolving, progressive surgical intervention in the treatment of early breast cancers. Progressive surgical strategies, combined with a variety of individualized, aesthetic approaches qualify OPS as a recommended surgical treatment. OPS benefits BCS patients by allowing a maximized resection volume with extended tumor-free margins, resulting in no delay of adjuvant therapy. OPS yields optimized cosmesis, elevated patient satisfaction and enhanced quality of life. Authors conducted this comparison to offer a progressive study of OPS cases, considering oncologic outcomes, complications, patient satisfaction, and to corroborate advantages via the results of a retrospective assessment of conventional BCS meta-datasets.

**Material and Methods:** 350 patients were enrolled in the study, all of whom received OPS, performed by qualified breast surgeons from 2008–2014. A prospectively maintained clinico-pathological database was evaluated and compared with a retrospective assessment of 350, randomized BCS cases. When measuring QoL, the EORTC-QLQ-BR23 survey was distributed. Cosmetics was scored in a patient-assessed 10-point scale.

**Results:** Increased surgical duration, more quadrantectomy, larger excised specimens, extended negative margins, and fewer completion surgeries were recorded in OPS. No difference in time to adjuvant therapy, or complications were summarized. Statistical analytics of QLQ surveys expressed a significant superiority of OPS. This was reinforced by higher cosmetic rates.

**Conclusion:** OPS provides oncologic risk reduction by not delaying adjuvant therapies. Furthermore, the removal of large tumors with wider margins make true quadrantectomy possible. OPS yields fewer re-exscisions, although surgical duration is prolonged. To reassure disease-free survival, longer follow up is required.

**No conflicts of interest**

**280** Poster

**Pre-printed stickers on consent forms: Standardisation at no extra cost**

A. Parvaiz[1], J. Busby[2], B. Isgar[2]. *[1]Peterborough City Hospital, Oncoplastic Breast Surgery, Peterborough, United Kingdom; [2]New Cross Hospital, Breast Surgery, Wolverhampton, United Kingdom*

**Background:** We previously found inconsistencies in benefits/risks written on consent forms by various surgeons. Due to cost issues, we were unable to obtain pre-printed consent forms. Hence we developed our own consent stickers and compare them with hand-written consent forms.

**Materials and Methods:** Consent stickers were generated for 11 commonest operations, including their names, benefits and risks. They were printed on patient identity labels, readily available in hospital. A short questionnaire was given to various staff, involved with theatre WHO checklist, to indicate their preference of sticker/hand-written consent. A patient satisfaction survey was carried out for both types of consent forms.

**Results:** Over 9 months, 167 consent forms were filled with pre-printed stickers (111 general and 56 breast operations). A comparable number of hand-written consent forms were used. 77 staff members and 125 patients were surveyed.

Amongst 77 staff members surveyed, 39 analysed pre-printed stickers consents and 38 looked at hand-written forms. 39/39 (100%) staff considered pre-printed stickers as 'excellent' in terms of ease of reading and ease of understanding. On the other hand, ease of reading for hand-written forms was classified by 38 staff as good (4), satisfactory (11) and poor (23). Ease of understanding for hand-written forms was good (3), satisfactory (27) and poor (8).

125 patients participated in survey; 64 pre-printed stickers and 61 hand written forms. Ease of reading by patients was classified excellent (61) and good (3) in 64 pre-printed stickers consents, whereas it was given good (4), satisfactory (22) and poor (35) in 61 hand-written forms. Similarly ease of understanding by patients was classified excellent (61) and good (3) in 64 pre-printed stickers consents, whereas it was given good (3), satisfactory (27) and poor (31) in 61 hand-written forms.

Overall patient satisfaction with pre-printed stickers: Median 10 (range 9−10). Overall patient satisfaction with hand-written forms: Median 3 (range 2−10).

91% (70/77) staff preferred using pre-printed stickers, 3 preferred hand-written forms and 4 showed no preference. 115/125 (92%) patients preferred pre-printed stickers, 3 preferred hand-written forms and 7 showed no preference.

**Conclusions:** Pre-printed stickers on the consent forms make them standardised, eliminating inconsistencies amongst various surgeons, achieving high satisfaction scores with patients. Majority of the staff as well as patients preferred using them because they are legible, understandable, save time, and they bear no extra cost to the health provider.

**No conflicts of interest**

**281** Poster

**The Specimen Margin Assessment Technique (SMART) trial: A novel 3D method of identifying the most accurate method of breast specimen orientation**

A. Arnaout[1], S. Robertson[2], G. Dostaler[3], S. Saeed[1]. *[1]Ottawa Hospital Research Institute, Surgery, Ottawa- Ontario, Canada; [2]Ottawa Hospital, Pathology, Ottawa, Canada; [3]Ottawa Hospital, Surgery, Ottawa, Canada*

**Background:** Achieving negative margins remains one of the most important determinants for local recurrence following breast-conserving therapy. Re-excision of a positive margin is recommended in order to reduce recurrence. Inaccuracies in margin labeling or orientation during surgery translates into additional unnecessary surgery or wrong margin re-excision. We report the results of the world's first prospective clinical trial that evaluates the accuracy of intra-operative specimen inking versus suturing on the same lumpectomy specimen, in a blinded fashion, using a novel 3 D technique. METHODS: A prospective clinical trial was performed using sham lumpectomies within the prophylactic mastectomy or breast reduction tissue. The specimen was inked using special phospholuminescent inks that dry clear but glow under black light. In addition, specimen suturing using two labeled sutures was performed by the surgeon as per usual. A third "mystery" suture was placed; the location of which is known only to the surgeon but blinded to the pathologist. RESULTS: 73 patients were accrued for the study. There was a 45% discordance between the pathologist and surgeon in identification of the "mystery" suture and a 76% discordance in identification of surface area of each margin. A median of 3 additional "surgeon identified" margins were included in the "pathologist identified" anterior margin. Using 3D imaging, we demonstrated how the specimen center of gravity and volume changes en-route to the pathology department. CONCLUSION: This is the first trial of its kind comparing the two methods of specimen orientation in a

blinded fashion on the same lumpectomy specimen. Discordance between the surgeon and the pathologist in margin orientation would influence the accuracy of margin identification and the subsequent directed re-excisions, as well as subject patients to unnecessary surgeries or prevent them from having re-excisions they need. Intra-operative specimen inking by the surgeon is a more accurate method of margin assessment. Results of this trial can be extended to other cancers in which a negative margin is prognostic.

**No conflicts of interest**

**282** Poster

**A treatment threshold for decision making in breast cancer surgery for optimal quality of life**

E. Vos[1], L. Koppert[1], W. Van Lankeren[2], B. Groot Koerkamp[1], M. Hunink[2]. [1]*Erasmus MC Cancer Institute, Surgery, Rotterdam, Netherlands;* [2]*Erasmus MC, Radiology, Rotterdam, Netherlands*

**Background:** Since survival after breast conserving surgery (BCS) and mastectomy is equivalent, the choice for early stage breast cancer patients may rest upon quality of life (QoL) and cosmetic result considerations. It is believed that BCS entails a QoL benefit over mastectomy if a superior cosmesis is achieved, otherwise mastectomy may be preferred especially when considering breast reconstruction. The preoperative prediction of the cosmetic result after therapy should aid informed treatment decision making. Our aim was to determine the optimal threshold in the preoperative prediction of achieving superior cosmesis after BCS based on tumour volume versus breast volume ratio and location of the tumour in the breast. If the prediction exceeds the threshold, BCS will result in optimal QoL and if below the threshold, mastectomy will result in optimal QoL.

**Methods:** A previously published study population was used of 69 invasive breast cancer women treated with breast conserving therapy and their long-term cosmetic result was evaluated by a panel. A preoperative prediction model was determined by logistic regression analysis to predict superior cosmesis after BCS representing our test with an area under the curve of 0.827 (95% CI 0.71–0.94). A decision tree for our test was built modelling the treatment consequences resulting in health states. To each health state a utility value (QoL weight on a 0−1 scale) was attached derived from the literature (for mastectomy) and our study population (for BCS). The treatment threshold − to perform BCS or not − was defined by the probability of superior cosmetic result after BCS at which the QoL of patients living with BCS and mastectomy is equal, which can be determined by direct comparison of the benefits and harms of BCS. The benefit was defined as the gain in QoL from superior cosmesis after BCS instead of mastectomy (with or without reconstruction) and the harm was defined by the loss in QoL from inferior cosmesis after BCS instead of mastectomy (with or without breast reconstruction).

**Results:** The health states were: BCS with superior cosmesis, BCS with inferior cosmesis, mastectomy only, and mastectomy with breast reconstruction. Their utility values were 0.898, 0.862, 0.891, and 0.859 respectively. The breast reconstruction rate after mastectomy was 41.5% resulting in a utility for mastectomy (with or without reconstruction) of 0.877. The treatment threshold − to treat with BCS or not − was 0.462.

**Conclusions:** The threshold of treatment with BCS versus mastectomy can be used in a preoperative treatment decision aid for breast cancer surgery with QoL as the primary outcome that incorporates the expected cosmetic result after BCS. Further improvement of the decision aid requires the more frequent use of utility values as part of QoL measurements in breast cancer patients.

**No conflicts of interest**

**283** Poster

**Oncoplastic breast surgery: The preferred method to perform breast cancer surgery**

M. Chowhan[1], D. Jha[1], J. Bhatt[1], M. Malhotra[1]. [1]*Artemis Hospital, Surgical Oncology, Gurgaon, India*

**Background:** The Breast cancer profile in India is different. It presents in relatively younger age group and advanced stage. Oncoplasty has emerged rapidly during the last decade. We present our experience of a Comprehensive Breast Oncoplasty Service, comprising of team of surgeons trained in both ablative and reconstructive techniques of Breast Surgery including microsurgical free tissue transfer. The study analyses Oncoplasty in terms of its feasibility, techniques and oncological outcomes in a developing country.

**Material and Methods:** Data for patients undergoing surgery for breast cancer from November 2013 to October 2015, was extracted from a prospectively maintained database of Breast Oncoplasty service. Oncoplastic Neo Breast formation in the study is defined as reconstruction of ablative breast defect post cancer resection either with realignment of residual dermoglandular tissue described as Volume Displacement (VD) or replacement with autologous tissue or prosthetic implant described as Volume Replacement(VR) respectively. Patient undergoing oncoplasty were considered for analysis.

**Result:** Seventy patients (67 ductal cancers and 3 stromal) with mean age of 50.2 years underwent surgery in this period. Fifty two patients (74.2%) opted for Oncoplasty out of which 13 patients were post NACT. 30 patients underwent volume displacement surgeries out of which 29 were early breast cancer(EBC) and only one locally advanced(LABC). And 22 underwent volume replacement surgeries, 15 EBC and 4 LABC (3 were stromal). Six patients developed minor wound complications post-operatively but none had a delay in adjuvant treatment. No patient had margin positive resection and lowest margin was 5 mm. No local recurrence was detected over a median follow up of 11 months (2−23 months) but two patients had distant metastases.

Table 1. Description of oncoplastic surgeries

| Volume displacement | | Volume replacement | |
|---|---|---|---|
| Technique | No. of surgeries | Technique | No. of surgeries |
| Lateral mammoplasty | 8 | Latissimus dorsi flap | 12 |
| Medial mammoplasty | 8 | DIEP/Free TRAM flap | 6 |
| Central techniques | 7 | Thoraco-epigastric adipofascial flap | 2 |
| Wise-pattern/inferior techniques | 7 | Implant | 2 |
| Total | 30 | Total | 22 |

**Conclusion:** Surviving Breast Cancer without Breast is a battle only half won. Our experience of Comprehensive Breast Oncoplasty service depicts higher rates of Neo Breast formation with better oncological resections, better compliance to adjuvant therapy and better disease control.

**No conflicts of interest**

**284** Poster

**Contrast-enhanced ultrasound biopsy of sentinel lymph nodes in patients with breast cancer and implications for axillary conservation: The Tunbridge Wells experience**

K. Cox[1], M. Hashem[1], T. De Silva[1], N. Wakeham[2], S. Kirwan[2], N. Chhaya[2], P. Mills[2], J. Weeks[2], D. Fish[3]. [1]*Maidstone and Tunbridge Wells NHS Trust, Breast Surgery, Maidstone and Tunbridge Wells, United Kingdom;* [2]*Maidstone and Tunbridge Wells NHS Trust, Breast Radiology, Maidstone and Tunbridge Wells, United Kingdom;* [3]*Maidstone and Tunbridge Wells NHS Trust, Breast Pathology, Maidstone and Tunbridge Wells, United Kingdom*

**Background:** There is evidence to suggest that conservative axillary management may be appropriate for some groups of patients with early breast cancer who have sentinel lymph node (SLN) macrometastases. At Maidstone and Tunbridge Wells NHS Trust, all newly diagnosed breast cancer patients with a normal grey-scale axillary ultrasound have a procedure to identify and core biopsy SLN using contrast enhanced ultrasound (CEUS). We have previously published the results from Maidstone Hospital and now present the data from Tunbridge Wells Breast Clinic (TWBC).

**Material and Methods:** Retrospective data was collected on 361 consecutive breast cancer patients who had SLN identified with intradermal microbubbles and CEUS in TWBC between February 2011 and September 2014. Complete data was not available for 15 patients and 5 had an inappropriate test (abnormal grey-scale axillary ultrasound without a benign lymph node biopsy).

**Results:** SLN were clearly visualised in 291 (85%) patients and successfully core biopsied in 270 (79%). In patients with invasive disease who had primary surgical treatment, the test identified 53% of all sentinel node metastases with 98% specificity. The negative predictive value was 85%. The prevalence of axillary lymph node metastases was 27%. Twenty-eight patients had a false negative benign SLN core biopsy but only 7 of these had 2 or more LN macrometastases found at the end of surgical treatment.

**Conclusions:** SLN can be readily identified and biopsied in the breast clinic using intradermal microbubbles and CEUS. These results are similar to those previously published for Maidstone Breast Clinic. The detection and successful biopsy rate was slightly lower at TWBC and these findings could represent the normal fluctuation of the test's performance or be the result of the cumulative 'learning-curves' of newly appointed radiologists. In patients with invasive breast cancer and a normal grey-scale axillary ultrasound, a benign SLN core biopsy result may be highly predictive of either no metastases or low volume metastatic disease in the ipsilateral axilla. This group of patients is therefore likely to benefit from axillary conservation and in certain cases, it may be appropriate to completely omit a surgical SLN excision biopsy.

**No conflicts of interest**

**285** Poster

**The effect of the accordion suturing technique on wound lengths in breast cancer surgery at six weeks**

M. Ita[1], K. Koh[1], S. KaimKhani[1], L. Kelly[1], M.J. O'Sullivan[1], H.P. Redmond[1], M.A. Corrigan[1]. *[1]Cork University Hospital, General Surgery, Cork, Ireland*

**Background:** Cosmetic outcomes and scar lengths remain important considerations in breast cancer surgery. Suturing techniques should decrease scar tissue formation and provide good cosmetic results. The use of an accordion suturing technique may result in decreased surgical wound lengths and better cosmetic outcomes. We compared the outcomes of the accordion suturing technique with the standard suturing technique in breast cancer surgeries.

**Materials and Methods:** We randomly assigned eligible female patients for wide local excision of breast tumours to undergo closure of their surgical wound by either the accordion or the non-accordion (standard) suturing techniques between the months of May and October 2015. Pre-closure and post-closure wound lengths were measured intraoperatively. One primary outcome was a reduction of the surgical wound length at six weeks. The second primary outcome was a composite of the absence of hypertrophic scar tissue formation and optimal cosmesis.

**Results:** Thirty eligible women for wide local excision of breast tumours were randomly assigned to the accordion and non-accordion groups (15 accordion and 15 non-accordion). Seven women were excluded from the study because they underwent re-excision of margins for their breast tumours before the end of six weeks, and one woman was lost to follow up. We therefore compared the outcomes of 12 women who underwent closure of their surgical wound by way of the accordion suturing technique to the outcomes of 10 women who underwent closure with the non-accordion (standard) suturing technique. The percentage reduction of wound length at 6 weeks was significantly greater in the accordion group than in the non-accordion group (M=24.43, SD=10.2 vs. M=8.57, SD=11.5, $p = 0.003$). There was no significant difference in the cosmetic outcome between both groups using the James Quinn's wound evaluation score.

**Conclusion:** The accordion suturing technique was associated with a significant reduction in surgical wound lengths in breast conserving surgery at six weeks with a comparable cosmetic result.

**No conflicts of interest**

**286** Poster

**MRI guided SNOLL after neoadjuvant chemotherapy in breast cancer. Preliminary results**

G. Hernandez Cortes[1], J. Cuesta Louys[1], M. Espada Vaquero[1], S. Fuertes Cabero[2], V. Martinez De Vega[3], J.R. Garcia Flores[1], S. Linares[3], R. Sainz De La Cuesta Abbad[1]. *[1]Quiron Madrid University Hospital, Obstetrics and Gynecology, Pozuelo de Alarcon, Madrid, Spain; [2]Quiron Madrid University Hospital, Nuclear Medicine, Pozuelo de Alarcon, Madrid, Spain; [3]Quiron Madrid University Hospital, Radiology, Pozuelo de Alarcon, Madrid, Spain*

**Background:** The objective of this study is to show the results of our Institution to make conservative surgery after neoadjuvant chemotherapy in breast cancer using MRI guided SNOLL technique.

**Material and Methods:** We study in a retrospective view 35 surgical procedures using MRI guided SNOLL technique. We exclude 11 patients with multicentric disease, previous cosmetic surgery or incomplete record. All patients have a previous pathological study with diagnosis of ductal invasive carcinoma of the breast and a basal MRI before starting chemotherapy. The treatment decission schedule was based always in Breast Cancer Unit Multidisciplinary Committee. We make another MRI in the half of treatment and other one at the end. Then, the day before surgery, the radiologist make MRI guided injection of Tc nanocoloid with gadolinium in residual tumor area or in case of total response, in the original tumor área marked in first MRI, and after they make a gammagraphy to see the breast and sentinel lymph node imaging.

Next day we make the conservative radioguided surgery procedure with gamma probe for lumpectomy and sentinel lymph node biopsy. Our pathologists make intraoperative frozen analysis to perform axillary lymph node disection if sentinel lymph node has metastatic disease.

**Results:** We analyze 24 patients, 7 with Luminal B tumors, 10 with triple negative tumors and 7 with overexpressed Her-2/neu tumors. We have a satisfactory detection of residual disease in the breast and sentinel node detection in all cases, with clear margins and adecuate cosmetic results, with only 5 cases of double marking with isotope and blue dye for better localization of sentinel lymph node.

**Conclusions:** MRI guided SNOLL technique after neoadjuvant chemotherapy in breast cancer is a feasible and safe procedure to make conservative surgery although a higher number of patients, prospective studies and experienced teams are necessary for best evaluation of this way of guiding and practise.

**No conflicts of interest**

**287** Poster

**Impact of surgery on psychological distress in women with breast cancer**

N.A. Jadoon[1], W. Munir[2], M.A. Shahzad[2], Z.S. Chaudhry[2]. *[1]Ittefaq Trust Hospital, Medicine, Lahore, Pakistan; [2]Nishtar Medical College Hospital, Medicine, Multan, Pakistan*

**Background:** The various surgical procedures for early-stage breast cancer are equivalent in terms of survival. In this context other factors, such as the effect of intervention on psychological health, psychosocial adjustment and quality of life assume great importance. The objective of this study was to estimate the prevalence of psychological distress in breast cancer patients who had undergone surgery and compare them with those who had not received surgical intervention.

**Methods:** The study was carried out in outpatient department of Multan Institute of Medicine and Radiotherapy, Multan. The study group comprised of 90 breast cancer patients who were divided into 2 groups on basis surgery for breast cancer. Aga Khan University Anxiety & Depression Scale (AKUADS) was used to assess the prevalence of psychological distress. Data was analyzed using SPSS v.16.

**Results:** Out of 90 patients who were interviewed, 55 were found to have clinically significant levels of anxiety and depression symptoms as measured by AKUADS. Women who had undergone surgery were found to be significantly less depressed than those who had not received such intervention (51.11% vs. 71.11% OR=2.35, 95% CI=1.31–4.22, $p < 0.05$). Although mastectomy patients were more depressed than those who had breast conserving surgery but the difference did not reach significant proportions (OR=1.33, 95% CI=0.76–2.32, $p > 0.05$). Similarly there was no difference between patients who were recently treated and those who received treatment long ago in terms of psychological distress (OR=1.23, 95% CI=0.70–2.15, $p > 0.05$). An intriguing finding was lesser prevalence of depression in women whose surgeons allowed them chose the type of surgery (OR=0.39, 95% CI=0.22–0.69, $p < 0.05$). The factors found to be affecting psychological distress in surgery patients group were living in rural area (OR=1.99, 95% CI=0.96–3.06), having low income (OR=2.66, 95% CI=1.50–4.70), and being physically inactive (OR=2.47, 95% CI=1.39–4.38).

**Conclusions:** Findings from this study show that breast cancer patients have less psychological distress following surgery. The results show the need of psychosocial interventions and patient centered solution for evidence based selection of optimal treatment.

**No conflicts of interest**

**288** Poster

**Is excision biopsy of fibroadenomas based solely on size criteria warranted?**

C.J. O'Neill[1], F. O'Connell[2], M.W. Bennett[2], M. Corrigan[1], L. Feeley[2], T.J. Browne[2]. *[1]Cork University Hospital, Surgery, Cork, Ireland; [2]Cork University Hospital, Histopathology, Cork, Ireland*

**Background:** Fibroadenomas (FA) are the most common benign tumour in the female breast and arise in approximately 25% of asymptomatic women. The majority of FAs have classical clinical and radiologic findings and the diagnosis can be readily confirmed by core needle biospy (CNB). Most FA are managed conservatively provided there is radiologic concordance with the histologic findings. Conversely surgical excision is typically recommended for cellular fibroepithelial lesions to exclude a diagnosis of phylloides tumor. Some studies have suggested surgical excision in all FA >3 cm to reduce CNB sampling errors. The aim of our study was to evaluate if surgical excision was warranted based on size criteria alone.

**Material and Methods:** The pathology data base at a large academic centre with combined screening and symptomatic breast subspeciality service was reviewed for all CNBs with a diagnosis of FA that had a subsequent surgical excision at our institution over a 51/2 year period. Patient demographics including patient age was recorded, CNB diagnosis, excision diagnosis and preoperative radiologic size of FA.

**Results:** 12,109 consecutive radiologically guided CNB were performed January 2010-June 2015. 3438 with a diagnosis of FA were identified. 296 cases went on to have surgical excision at our institution. Average age 34.7 years. Atypical features were reported in 62/296 CNB (20.9%) including lobular neoplasia (n = 24), atypical ductal hyperplasia (n = 4), cellular fibroepithelial lesion (n = 33), fibroadenoma with mucocoele-like lesion (n = 1). The remaining 234 cases were reported as FAs on CNB. Average preoperative radiologic size was 26 cm with 48% of the cases

(n = 142) measuring ⩾3 cm. 4 of the 234 (1.7%) cases with a diagnosis of FA without atypia turned out to be a low grade phylloides tumour on excision. The ages were 25 (n = 2), 46 (n = 1), 56 (n = 1) with the lesions measuring 3.4 cm (n = 3) and 1.6 cm (n = 1).

**Conclusion:** Our study although relatively small suggests that surgical excision based solely on size is not warranted in radiologically concordant cases with a diagnosis of FA on CNB.

**No conflicts of interest**

**289** Poster

**Is specimen radiography still necessary in patients with non-palpable breast cancer undergoing receiving breast-conserving surgery using radioactive seed localization?**

L. Hoevenaars[1], G. Nieuwenhuijzen[1]. [1]*Catharina Hospital Eindhoven, Surgery, Eindhoven, Netherlands*

**Background:** Specimen radiography (SR) is routinely used in women undergoing breast-conserving surgery (BCS), but the diagnostic value and clinical relevance of SR during BCS when radioactive seed localization (RSL) is used, is still unknown.

**Methods:** The clinical, radiographic and histopathological data of women who underwent BCS after pre-operative RSL with intra-operative SR between 2003 and 2011 were analysed. The histological and radiographic outcomes on SR were compared using quantitative and qualitative analyses and receiver-operating characteristic (ROC) curves.

**Results:** A sequential series of 448 women with invasive carcinoma (n = 211), ductal carcinoma in situ (DCIS) (n = 79) and a combination of DCIS and invasive carcinoma (n = 158) were included. The median minimal margins for the radiological masses and microcalcifications measured on SR were 14 mm and 11 mm, respectively. Based on a radiological cut-off SR margin value of 1 mm, the overall sensitivity, specificity, and positive and negative predictive values (PPV and NPV) were 21%, 95%, 26%, and 94%, respectively. A radiological cut-off value of 5 mm resulted in a sensitivity, specificity, PPV, and NPV of 45.5%, 85.3%, 19.7% and 95.2%, respectively. Per-operative re-excisions based on SR were performed in 31 (6.9%) patients, but histopathological examination of the additional excised tissue revealed DCIS or invasive carcinoma in only in 6 (19.4%) patients.

**Conclusion:** SR has a poor diagnostic performance in assessing margin involvement in RSL. SR has no additional value if the I125-seed is placed in the centre of the tumour, and intra-operative monitoring of the location is possible. Routine SR should be abandoned in BCS with RSL.

**No conflicts of interest**

**290** Poster

**An analysis of the necessity to surgically excise fibroadenomas containing LCIS**

C. O'Neill[1], C. Fives[2], M.W. Bennett[2], M. O'Sullivan[2], M. Corrigan[1], R. Murphy[2], L. Feeley[2], F. O'Connell[2], T.J. Browne[2]. [1]*Cork University Hospital, Surgery, Cork, Ireland;* [2]*Cork University Hospital, Histopathology, Cork, Ireland*

**Background:** Lobular carcinoma in situ (LCIS) and atypical lobular hyperplasia (ALH) remain two of the highest risk lesions identified on core needle biopsy. However current data suggests that LCIS and ALH represent an increased global risk of breast cancer rather than specific precursor lesions. A lack of consensus makes the management of these entities challenging, particularly when they are associated with a radiological mass lesion.

The aim of this study was to evaluate whether excision biopsy is warranted in cases of lobular neoplasia associated with fibroadenoma (FA) on Core Needle Biopsy (CNB) when the imaging target is a mass concordant with a FA.

**Material and Methods:** A retrospective case control design was employed at a single large academic centre with a combined screening and symptomatic service. All cases of CNB confirmed FA with ALH or classical LCIS were identified over a three year period. Cases with coexistent DCIS, invasive carcinoma, papilloma, radial scar, atypical ductal hyperplasia or flat epithelial atypia and non classical LCIS were excluded as were cases where the radiologic target was discordant with a FA.

**Results:** A total of 2878 consecutive radiologically guided CNB with a diagnosis of FA were identified. Twenty one cases met the selection criteria of concomitant ALH or classical LCIS. All cases underwent surgical excision. CNB diagnosis was LCIS and FA in 16 cases and ALH and FA in 5 cases. Average size of fibroadenoma was 1.9 cm (range 0.5−2.4 cm). Sixteen cases had residual LCIS or ALH on excision. One of the twenty-one cases (4.8%) was upgraded on excision to invasive ductal carcinoma, Grade 2, 0.2 cm in dimension.

**Conclusion:** This represents the only study to specifically addressing radiologically concordant cases with a diagnosis of classical LCIS/ALH and FA on CNB. We conclude that when strict pathological and radiological correlation is achieved excision biopsy is not necessary.

**No conflicts of interest**

**291** Poster

**The role of surgery to remove the primary tumor in patients with metastatic breast cancer**

A. Sukhotko[1], A. Zikiryahodzhaev[1], L. Bolotina[1]. [1]*Moscow P.A. Gerzen's Cancer Research Institute − The National Medical Research Radiologic Center of the Ministry of Health of the Russian Federation, Department of oncology and reconstructive-plastic surgery of the breast and skin, Moscow, Russian Federation*

**Background:** the problem of the treatment of disseminated breast cancer (DBC) is specially urgent in the present situation, as there is no uniform standard of care for these patients nowadays. There was an opinion for a long time that DBC surgery both cannot improve overall survival due to the presence of distant metastases, and, quite the contrary, can stimulate the progression of the disease. Therefore, this group of patients undergoes surgery only to prevent and/or eliminate local complications (ulceration, tumor lysis syndrome, hemorrhage). However, most of retrospective studies have shown the validity of surgical removal of the primary lesion in the combination treatment of these patients. Analysis of the world literature demonstrates a growing interest in the problem of treatment of patients with stage IV breast cancer.

**Materials and Methods:** this investigation comparatively analyzed the results of complex treatment with or without surgery in patients with metastatic breast cancer. We analyzed retrospectively treatment experience of 196 patients with generalized breast cancer in the department of oncology and breast reconstructive surgery of P.A. Herzen Moscow Cancer Research Institute from 2000 to 2012. Average age was 58±1.1 years. Invasive ductul carcinoma was verified in128 patients (65.3%), invasive lobular carcinoma in 33 (16.8%), complex form in 19 (9.7%). Complex palliative care involving drug and radiation therapies was performed in two patient groups. The first group includes 124 patients who underwent surgical intervention as complex treatment, the second group includes 72 patients with only medical therapy. Standard systemic therapy was given to all patients.

**Results:** overall, 3-and 5-year survival in first group was 43.8% and 21%, in second − 15.1% and 9.3% respectively [p = 0.00002 log-rank]. Median survival in patients with surgical treatment composed 32 month, in patients with only systemic therapy − 21. The factors having influencing an influence on the prognosis and the quality of life outcomes for of patients with generalized breast cancer were are also studied: hormone-dependent tumor, Her2/neu hyper-expression, reproductive function status (age, menopause existence).

**Conclusion:** surgery to remove the primary tumor in generalized breast cancer in a number of patients has been justified and allows in 51.3% of cases improving the 3-year survival rates, and achieving 5-year survival in 34.1% patients. Removing the primary tumor in terms of combination treatment of patients with generalized breast cancer can improve the results of the 5-year survival of patients with solitary or isolated bone metastases compared with multiple 41.1% vs 24.6% and lung metastases 29.2% vs 6.6%. Detection of multiple metastatic lesions within the same organ worsens the prognosis, however, it is not an absolute contraindication to palliative mastectomy.

**No conflicts of interest**

**292** Poster

**A quantitative analysis of tumour characteristics in breast cancer patients with extranodal extension in non-sentinel nodes**

N.A. O'Keeffe[1], C. O'Neill[1], C. Zahere[1], V. Livingstone[2], T.J. Browne[3], H.P. Redmond[1], M.A. Corrigan[1]. [1]*Cork University Hospital, Breast Research Centre, Cork, Ireland;* [2]*University College Cork, Medicine and Health, Cork, Ireland;* [3]*Cork University Hospital, Pathology, Cork, Ireland*

**Background:** The presence of extranodal extension (ENE) is well documented as a predictor of non-sentinel lymph node (NSLN) metastasis. Despite this, the pathophysiology of lymph node spread is poorly understood. The ACOSOG Z0011 trial (2011) concluded that patients who satisfy criteria including the absence of sentinel node (SN) ENE can forgo axillary clearance(AC). Currently there are no studies analysing the rate of ENE in non-sentinel nodes in which the sentinel node was positive but had no ENE. Determining this incidence will help determine if current paradigms are resulting in residual ENE in NSN by forgoing AC based on the Z0011 trial.

**Materials and Methods:** This study determined incidence of ENE at NSN in patients with a positive SN biopsy without ENE in 162 symptomatic

breast cancer patients who underwent axillary clearance (AC) between 2009 and 2014 at Cork University Hospital Breast Cancer Service.

**Results:** Of 965 sentinel node biopsies performed 251 were identified as SLN positive, 162 (64.5%) underwent further AC. Of the 162 patients, 56.8% (92/162) tested positive for ENE at SN, of these 57.6% (53/92) had NSN metastasis versus 17.1% (12/70) in the ENE-negative group ($\chi^2$ test; $P < 0.001$). The incidence of NSN-ENE in patients without SN-ENE was 1/70 (1.4%) compared with 33.7% (31/92) in patients who had no ENE in the SN.

**Conclusions:** Extranodal extension in the sentinel node is a strong predictor of NSN involvement, its absence significantly reduces the likelihood of ENE in the non-sentinel nodes.

Acknowledgments: AID Cancer Research, Cork.

**No conflicts of interest**

**293** Poster

**The maximal removable breast volume percentages in conventional breast conserving surgery. A prospective cohort study. (ClinicalTrials.gov Identifier: NCT01496001)**

D. Pukancsik[1], P. Kelemen[1], M. Ujhelyi[1], E. Kovács[2], N. Udvarhelyi[3], Z. Zaka[4], I. Kenessey[5], Z. Mátrai[1]. *[1]National Institute of Oncology, Breast and Sarcoma Surgery- National Institute of Oncology, Budapest, Hungary; [2]National Institute of Oncology, Department of Radiological Diagnostics, Budapest, Hungary; [3]National Institute of Oncology, Department of Surgical and Molecular Pathology, Budapest, Hungary; [4]National Institute of Oncology, Department of Radiotherapy, Budapest, Hungary; [5]Semmelweis University, 2nd Department of Pathology, Budapest, Hungary*

**Aims:** Breast-conserving therapy (BCT) is considered standard treatment of stage 0−I−II breast cancer. However, fair to poor cosmetic outcomes following conventional BCT are still observed in up to 33% of the patients. The primary aim of the study was to determine the critical tumor-breast volume ratio in each quadrant of the breast − that is the percentage of breast volume excised − above which conventional breast conserving surgery (BCS) can no longer offer adequate cosmetic/functional results or satisfying quality of life.

**Methods:** An analysis of a single-arm prospective cohort study was performed between March 2011 and December 2012, involving patients aged 70 or under with early-stage, 30 mm or smaller unilateral, solitaer breast cancer, who underwent wide local excision and axillary sentinel lymph node dissection, followed by whole breast irradiation (WBI). With the help of internationally validated panels, using ROC-statistical analysis the quality of life, aesthetic and functional parameters, and their changes in correlation to the excised breast volume percentages were determined.

**Results:** Assessing the results of 350 patients, the ideally removable volume percentages throughout conventional BCS not yet resulting in unacceptable aesthetic and functional results or decreased quality of life were 18−19% in the upper-lateral quadrant ($p < 0.0001$), 14−15% in the lower-lateral quadrant ($p < 0.0001$), 8−9% in the upper-medial quadrant ($p < 0.0001$), and 9−10% in the lower-medial quadrant ($p < 0.0001$).

**Conclusion:** In knowledge of the maximal cut-off values for each quadrant of the breast in conventional BCS − taking the tumor size and breast volume into account − an algorithm is provided to help determine the appropriate surgical technique for a breast surgeon. In case of a predictably larger volume loss than the above stated, patients with medium or large breasts might benefit from oncoplastic BCS, whereas patients with small breasts may benefit from mastectomy and reconstruction.

**No conflicts of interest**

**294** Poster

**Patients' satisfaction following oncoplastic surgical procedures for breast cancer**

M. Stathoulopoulou[1], E. Iliopoulos[1], P. Karamanis[1], E. Marousopoulou[1], V. Venizelos[1]. *[1]Metropolitan Hospital, Breast Unit, Athens, Greece*

**Background:** Breast conservation surgery was increased during the last decade and various oncoplastic techniques have been developed in order to improve the asthetic appearance of the breast. The main goal of these procedure is the oncological safety following by an acceptable aesthetic result. The aim of the study is the postoperative outcome and pts satisfaction with oncoplastic procedures after wide local excision (WLE) or partial mastectomy (PM), for breast cancer.

**Material:** This is a retrospective study from January 2014 to December 2014. Pts records were reviewed and all surgical procedures have been performed by the same team of Breast Surgeons.

**Methods:** A questionnaire was sent to the pts regarding satisfaction after the operation and 6 months after the completion of XRT. A modified BREAST-Questionnaire was used.

**Results:** 82 pts underwent WLE and 10 pts PM followed by immediate breast remodeling using oncoplastic techniques. 4 pts underwent a symmetry procedure to the opposite normal breast. 74 pts (90%) very happy with the final outcome. 4 pts (4.87%) were thoroughly unsatisfied and underwent reconstruction with LD flap and implant in one stage procedure. 79/82 pts stated that will undergo the same oncoplastic procedure again and 74/82 had no fear and regrets choosing these surgical operations.

**Conclusions:** Oncoplastic procedures level I&II are feasible in most of the cases for early breast cancer. Very important factors are: The high level of pts satisfaction, better quality of life together with the oncological safety. Another important issue is the achievement of symmetry in both breasts. To obtain satisfaction from the pts these procedures should be performed by a well trained team in an organized Breast Unit.

**No conflicts of interest**

**295** Poster

**Latissimus dorsi reconstruction with a kyte technique: Patient related outcome on functional morbidity and anterior versus dorsal approach comparison**

D. Pinto[1], A. Magalhaes[2], P. Gouveia[1], H. Oliveira[3], D. Carvalho[1], A. Moura[2], J. Martins[1], C. Mavioso[1], J. Correia Anacleto[1], M.J. Cardoso[1]. *[1]Champalimaud Clinical Center, Breast Unit, Lisbon, Portugal; [2]Trindade Hospital, Breast Unit, Porto, Portugal; [3]INESC, INESC, Porto, Portugal*

**Background:** Arm and shoulder dysfunction after Latissimus dorsi (LD) based reconstructions remains a point of concern. LD muscle transfer is a widely accepted choice for breast volume replacing technique after breast conserving technique and for breast reconstruction with an implant or as an autologous reconstruction. Data regarding late functional sequelae remaining more than one year after surgery is lacking, as well as there is little evidence published comparing anterior miniflap harvest technique versus dorsal skin island flap harvest technique regarding scapula disability and arm morbidity. We aim at evaluating functional late sequelae with the kLD harvest technique and comparing anterior versus dorsal approach.

**Material and Methods:** Questionnaires were sent to 45 patients operated by the same oncoplastic team (Level III Oncoplastic Training Unit − EJSO 33 (2007) S1–S23) between April 2012 and June 2014. LD flap was harvested using the kyte technique (kLD), a perforator flap style pedicle dissection, from the muscle, until the external limit of the breast to be reconstructed, leaving no unnecessary bulging under the axilla, with the tendon and nerve sectioned (Pinto D et al. The Kyte LD flap in breast reconstruction: a technique modification attempt to reduce axillary bulging − Poster. European Breast Cancer Conference 9, Glasgow, March 19−21, 2014). Functional impairment was assessed using the self-administered DASH outcome measure questionnaire. Disability scoring from 1 to 100%, with 1−25% being regarded as mild dysfunction, 26−50% as moderate dysfunction, 51−75% as severe dysfunction, and 76–100% as total dysfunction. Statistical analysis was performed using the SPSS v22 and the Chi-square test (statistical significance $p \leqslant 0.005$).

**Results:** Forty-five patients completely answered the disability/symptom section of the DASH questionnaire. Twelve patients were operated with a dorsal skin paddle and 33 with anterior miniflap harvesting technique. Medium DASH score was 18 points, with minimum value 0 and maximum 61.2, with a standard deviation of 14.3 points. Eighty percent of patients have score under 25 points, 13.3% between 25−50 points and 6.7% over 50 points. Ninety-four percent of the patients with an anterior miniflap technique had DASH scores under 50%, comparing with 91.7% of patients with a dorsal approach. No statistically relevant difference has been observed when comparing both harvesting techniques.

**Conclusion:** LD muscle transfer with a kLD technique is well tolerated by the majority of the patients, but can result in functional disability, with symptoms remaining more than 1 year after surgery, with a moderate to severe disfunction in 20% of the patients. Comparing functional late sequelae from anterior partial miniflap harvest technique and dorsal approach did not showed any statistically significant difference.

**No conflicts of interest**

**296** Poster

**Preoperative assessment of axillary lympnodes in clinically negative patients with breast cancer**

M. Sthathoulopoulou[1], E. Iliopoulos[1], K. Sirgiannis[1], S. Lazarou[1], V. Venizelos[1]. *[1]Metropolitan Hospital, Breast Unit, Athens, Greece*

**Background:** One of the most important factors for the management of patients with breast cancer is to know the lympnodes status of the axilla. Accurate documentation of lymph nodes status preop can minimize the need for sentinel node intraoperative frozen section although stil needs to be identified because of Z0011 criteria.

**Material:** The aim of the study was to investigate the efficacy of the combination of axillary U/S and fine needle aspiration (FNA) preop in suspicious LN. A retrospective reanalysis was done in 80 early breast cancer pts with negative clinically axilla. All suspicious nodes seen in the U/S underwent FNA and cytological examination.

**Results:** 25 pts (35%) had suspicious LN in the U/S and 7 (28%) of them were found positive for malignant cells in cytology. 13 pts (52%) were positive in U/S but found negative in FNA. During surgery 3 (23.07%) of them were found with macrometastasis and 4 with micrometastasis (30.7%). Isolated tumour cells have been identified in 1 pts (8%). None of them had extracapsular involvement. In 22/25 (88%) pts, sentinel node was the only suspicious node which was identifed by U/S.

**Conclusions:** The combination of U/S + FNA in suspicious axillary nodes is accurate enought to identify positive for malignancy nodes.

**No conflicts of interest**

**297** Poster

**An audit of breast margin re-excision after wide local excision − the Royal Marsden experience**

K. Greene[1], S. Rokadiya[1], F. MacNeill[1]. [1]*Royal Marsden Foundation Trust, Breast Surgery, London, United Kingdom*

**Background:** Wide local excision (WLE) followed by whole breast radiotherapy (RT) confers equivalent survival and similar local recurrence rates to mastectomy. Breast conserving surgery accounts for over 50% of breast surgery procedures in the UK. The UK NHS sets a 31 day target from cancer diagnosis to each therapeutic intervention in the treatment plan including WLE to RT. However up to 30% of WLE's require re-excision surgery for positive margins.

The aim was to establish if we met the UK 31 day target for time from breast conserving surgery to radiotherapy. The main objective was to assess the impact of margin re-excision surgery on time to radiotherapy. Further objectives were time from wide local excision to margin re-excision, was margin re-excision performed by the original surgeon, how many re-excision specimens revealed further disease and the total specimen weight for WLE and re-excision/WLE surgery.

**Material and Methods:** From November 2014 to June 2015 data was collected retrospectively from the hospital prospectively maintained electronic patient record system on consecutive primary WLE procedures followed by RT. Group A had WLE only, Group B had WLE and re-excision for positive margins.

**Results:** Over 90% were treated within 31days from diagnosis with average time to WLE of 20 days (range 2–161). Of 352 WLE procedures, 51(15%) required margin re-excision either as simple margin shave or as part of a reduction mammoplasty. Further disease was noted on 24 (47%) re-excisions but clear margins were achieved for all procedures.

0.5% and no patients received RT within 31 days of surgery for Group A and B respectively. For Group A average time from surgery to RT was 68 days (28–243) and for Group B 103 days (49–211): time from WLE to re-excision was 39 days (11–184) and from re-excision to RT 84 days. The same surgeon (primary or supervising) was involved for both WLE and margin re-excision in 73% of procedures. The average specimen weight for initial WLE for Group B and the average specimen weights for Group B re-excision.

**Conclusions:** We did not meet the 31day targets for time from surgery to RT for either WLE or WLE with margin re-excision, however, margin re-excision prolongs the patient journey and time to adjuvant therapy to over 12 weeks; this may have an oncological impact. In over half of margin re-excisions no further disease was found: such patients experienced the morbidity and poorer aesthetic outcome of repeat surgery for no benefit. In group B for 27% of procedures the original surgeon was not present: this probably reflects a balance between continuity of care and minimising treatment waits but may limit the accuracy and therefore value of margin re-excision. The average specimen weights for primary excision and re-excision for Group B are presented.

**No conflicts of interest**

**298** Poster

**Management of the axilla for early stage breast cancer with positive sentinel lymph nodes: multicentric retrospective analysis**

E. Marrazzo[1], A. Invento[1], G. Canavese[1], W. Gatzemeier[1], C. Rossetti[1], M. Eboli[1], A. Rubino[1], E. Barbieri[1], A. Sagona[1], C. Tinterri[1]. [1]*Humanitas Research Hospital, Oncological Department, Rozzano (Milan)*

**Background:** The combination of two important factors such as the widespread use of systemic therapies and the use of the biological characteristics of the tumor as a prognostic factor has gradually replaced the value of axillary staging in the choice of adjuvant systemic therapy for early breast cancer. The aim of this study is to evaluate that axillary lymph node status should not be considered the only or the main prognostic parameter to plan the post-surgical treatment for the breast cancer, but to be considered one of the factors in a complex mosaic of data (hormone receptor status, proliferation index, grading, amplification of her 2, LVI).

**Material and Methods:** This analysis was conducted at Cancer Center Humanitas (ICH), Milan, and at IRCCS Azienda Ospedaliera Universitaria San Martino IST, Genoa. From a total of 4669 patients affected by Early breast cancer, we analyzed 1115 consecutive patients with 1 or 2 positive sentinel lymph node (SLN) who received axillary lymph node dissection, unrespectable of primary surgery on the breast (breast conservative surgery or mastectomy). Patients affected by DCIS, those who received neo-adjuvant therapy and those with more than 2 positive SLN were excluded. The presence of micro and macro-metastasis was registered as well as the number of "non sentinel positive lymph nodes".

**Results:** 44.1% of positive with 1 positive macro-metastatic SLN had other positive nodes. For those who had 2 macro-metastatic SLN, the percentage of other positive nodes was 55.6%. The results of this study revealed a significant positive lymph nodes "non-sentinel" in line with the most important studies.

**Conclusions:** The main published studies, ongoing studies and multicenter trials demonstrate that the number axillary recurrence after SLN biopsy is limited compared to the number expected and there is no impact in terms of local regional control, DFS and OS. Due also to the use of adjuvant therapies that lead to an improvement on local control, we expect a favorable result of the ongoing studies, such as SINODAR one study, recently started in Italy. The fact that we considered a population of women who have undergone both conservative surgery and mastectomy, highlights the need to preserve axillary lymph nodes even during mastectomy.

**No conflicts of interest**

**299** Poster

**Tumor infiltrating lymphocytes and their association with pathologic response to neoadjuvant chemotherapy in triple negative breast cancer in National Cancer Institute of Mexico**

M. Robles Estrada[1], C.J. Mejia Gomez[1], J.A. Hidalgo Carrera[1], J.E. Bargallo Rocha[1], F. Vaca Paniagua[1], F.I. Porras[2], V.M. Perez Sanchez[2]. [1]*INCAN, Surgery Oncology, Mexico, Mexico;* [2]*INCAN, Pathology Oncology, Mexico, Mexico*

Triple Negative Breast Cancer (TNBC) is a clinically, pathologically and molecularly heterogeneous disease.

**Objective:** To determine whether the presence of TIL (intratumoral, peritumoral, and stromal) is associated with a pCR in patients treated with conventional NAC (anthracyclines and taxanes) versus platinum based NAC in patients with TNBC.

**Material and Methods:** Retrospective analysis of 104 patients with TNBC in whom TIL has been evaluated twice: (1) pre-NAC biopsy and (2) post-surgical treatment. Correlation with pCR was established in both scenarios.

**Results:** A multiple corresponding analysis (MCA) has been used with the aim of obtaining an association pattern among Average age at diagnosis was 54.8 years. Regarding histological type, 87.5% had ductal cancer, 6.7% lobular, 0.96% metaplastic. Clinical stage, 20.1% had early clinical stage (I−IIB1), 78.8% had advanced clinical stage (IIB2–IIIC) and 0.96% metastatic disease. Scarff–Bloom–Richardson (SBR) G3 in 84.6%. Tumor size at diagnosis, 54.8% had >5 cm, and 43.2% had <5 cm surgical management, 98% had Modified Radical Mastectomy, and 1.9% had conservative surgery. 57.6% had a sentinel lymph node and 42.3% had radical axillary dissection. Surgical margins were negative in 94.2% and in 5.7% were positive. Regarding NAC 52.8% received cisplatin of which 12 had radiotherapy, and 46.1% had conventional NACT based on anthracyclines and taxanes There was no statistically significant difference in 5 year OS among the different groups, nevertheless a TIL rate (peritumoral) of 10−30% with pCR had an OS of 52% versus 27% with pIR. TIL rate (intratumoral) of 1−10% with pCR had an OS of 58% versus 34% with pIR. Pathologic response, 42.3% of patients had pCR, and 57.6% had pIR. No significant differences were found ($p = 0.54$) among the type of pathologic response and the different TIL rates for each evaluated group. However when a correlation was performed between the intratumoral rate of TIL versus peritumoral rate of TIL in patients with pCR: the group with the highest rate of intratumoral pCR was 1−10%, versus 43.1% of pCR for peritumoral TIL 11−30% having a statistically significant difference ($p < 0.001$).

**Conclusions:** There is a strong association between a rate of 11−30% TIL, peritumoral and intratumoral zones, with a pCR. Conventional NAC associated with a rate of 11−30% TIL in the peritumoral zone in addition to a higher rate of pCR. Even though there was not a difference in 5 year OS, a positive impact in OS was seen with an increased rate of TIL peritumoral and intratumoral together with pCR for both groups. Our results represent a platform for future comparative studies between the presence of TIL and its

association with a pathologic response in Mexican population. More studies are required to determine the role of TIL as a biomarker in the pathologic response of patients treated with NAC in TNBC.

**No conflicts of interest**

## Thursday, 10 March 2016

**POSTER SESSION**

# Optimal Diagnosis I

**300** Poster

### Contribution of high-resolution ultrasonography in the diagnosis of non-palpable breast cancer with calcification

T. Arai[1], K. Takebe[1]. [1]*Takebe Breast Cancer Care Clonic, Surgery, Takamatsu, Japan*

**Background:** In diagnosis of non-palpable calcificated breast cancer (NPCBC), stereo-guided mammotome (ST-MMT) serves as the standard. However, ultrasound resolution has improved dramatically recently. We hypothesized that through ultrasonography, it will become possible to diagnose NPCBC by US guided examination such as fine needle aspiration cytology (FNAC) and core needle biopsy (CNB) with much less invasion than ST-MMT.

**Material and Methods:** *Study 1:* The results of ultrasonic detection ability and US guided examination were examined among the benign lesions of 35 cases and 90 NPCBC patients histologically diagnosed in our facilities from 2010 to 2012. Of the 90 histological types, 74 (82%) were DCIS, and 16 (18%) were invasive carcinoma.

*Study 2:* The results of 193 progress observation cases from 2008 to 2012 with Birads Category 3 and 4a calcification were examined.

**Results:** *Study 1:* Using ultrasonography (Toshiba Aprio XG), calcification was detected in 88 of the 90 NPCBC lesions as echogenic foci. Two non-detectable lesions were DCIS of Van Nuys 1 and Van Nuys 2. The results of the FNAC were 80% positive and 20% indeterminate (there were no negative cases). In the 88 cases of possible calcified substance extracted through FNAC, 99% were confirmed under microscopic observation.

*Study 2:* 163 of 193 cases were able to be followed-up every six months for two to four years. An increase in calcification was observed in nine cases. Five of these cases were diagnosed with DCIS: Four were Van Nuys 1; one was Van Nuys 2. All five cases were of low-grade-malignancy.

**Conclusions:** The diagnostic method using FNAC to visualize calcification using high-resolution ultrasonography is an effective method to reduce the non-efficient, invasive breast cancer detecting method of ST-MMT. The diagnostic method is particularly useful in women of small breast of Asian. The few low-grade DCIS cases included were not detected with ultrasound. However, we believe it is not a diagnostic error. As a result, we stopped using the ST-MMT from 2010. In spite of this, in the MMG screening performed in our facilities from 2010 to 2012, the detection rate of only a NPCBC without mass on MMG was 0.17%. This detection rate is excellent in our country.

**No conflicts of interest**

**301** Poster

### Distribution of subclinical lesions in early breast cancer: A histopathological and radiological study

K. Liu[1], J. Chen[2], L. Cao[2]. [1]*Fudan University Shanghai Cancer Center, Department of Radiotherapy, Shanghai, China;* [2]*Rui Jin Hospital Shanghai Jiao Tong Unveristy School of Medicine, Department of Radiotherapy, Shanghai, China*

**Background:** The frequency and pattern of distribution of subclinical lesion of early invasive breast cancer is an issue of interest to guide personalized target volume definition of accelerated partial breast radiation or tumor bed boost after breast-conserving surgery. The current study aims to analyze the distribution characteristics of subclinical lesions in early breast cancer and search for its possible influence factors by pathological-radiological study.

**Material and Methods:** Patients with stage I-II clinically unifocal invasive breast cancer aged 18−80 years were eligible. The enrolled specimens were sectioned into 5-mm-thick subserial slices (all breast tissue of conservation therapy sample and breast tissue within 30 mm of the reference tumor of mastectomy sample). The number and orientation of subclinical lesions were recorded. The 3-dimensional distributions of subclinical lesions around the reference tumor were established according to combination of pathologic information and X-ray radiographic information. The correlation of subclinical lesions in relation to the clinical and histopathological factors including age, tumor diameter, molecular subtypes, tumor grade were analyzed.

**Results:** From January 2011 to August 2015, 63 patients (49 breast conservation and 14 mastectomy) with early invasive breast cancer were enrolled. The median age of these 63 patients was 48 years (34−80 years). The median size of primary invasive tumor was 2 cm (0.7−4 cm). Microscopic disease extension outside the primary invasive tumor was found in44/63 (69.8%) cases. Subclinical lesions were found outside the gross tumor edge of 1 cm, 2 cm and 3 cm in 47.6%, 17.5%, 1.6% of these 63 primary lesions, respectively. Presence of subclinical lesion was significantly influenced by HER2 status ($r = 0.25$, $p = 0.04$) and existence of extensive intraductal carcinoma (EIC) ($r = 0.43$, $p < 0.01$). And presence of EIC in the tumor was the only significant factor which influences the maximum distance of microscopic disease ($r = 0.49$, $p < 0.01$).

The mean resection margin in breast conservation specimen in 6 edges were: $23\pm13$ mm (superior margin); $26\pm14$ mm (inferior margin); $24\pm10$ mm (medial margin); $30\pm13$ mm (lateral margin); $9\pm4$ mm (anterior margin) and $8\pm4$ (deep margin), respectively. The greatest discrepancies between margins was 71 mm in inferior direction.

**Conclusions:** In most of early breast cancer, the distribution of subclinical lesions was within 30 mm from the edge of the gross invasive tumor. It is appropriate to use 30 mm to guide the individualized clinical target volume delineation. HER2 status and EIC affect the presence of subclinical lesions. The presence of EIC is significantly correlated with an extended distance of subclinical lesion. The tumor more often eccentrically locates in the breast-conserving surgical specimen and thus tailored clinical target volume delineation is justified.

**No conflicts of interest**

**302** Poster

### Concordance of preoperative US-guided tattooing of axillary lymph nodes to sentinel lymph nodes and comparison of their pathologic results according to imaging modalities in breast cancer patients

J.H. Jung[1], J. Lee[1], W.W. Kim[1], H. Park[1], J.Y.P. Park[2], H.J. Kim[3]. [1]*Kyungpook National University, Surgery, Daegu, Korea;* [2]*Kyungpook National University, Pathology, Daegu, Korea;* [3]*Kyungpook National University, Radiology, Daegu, Korea*

**Background:** We wanted to know the concordance of preoperative ultrasound (US)-guided tattooing of axillary lymph nodes (ALNs) to sentinel lymph node and to correlate MR and PET-CT findings with the final histologic results.

**Methods:** Axillary US examination was performed for all breast cancer patients before sentinel lymph node biopsy. The detected lymph nodes in US were classified as negative (group I, enlarged but image-benign) or positive (group II, image-suspicious) finding for metastases based on US, MRI and PET-CT findings. US-guided tattooing for ALNs was performed preoperatively by injection of 3 cc of activated charcoal into the cortex of lymph node and the adjacent soft tissue. We evaluated their concordance to sentinel lymph node and correlated the histologic results of US tattooed LN according to each imaging modality.

**Results:** Forty ALNs were tattooed and sentinel nodes corresponded to tattooed nodes in all except one patient with a tattooed non-sentinel node. Ten in group I and 30 in group II on US, 18 in group I and 22 in group II on MR, and 19 in group I and 21 in group II on PET-CT. Eight cases had evidence of metastases in final histology, 2 (20.0%) in group I and 6 (20.0%) in group II on US, 4 (22.2%) in group I and 4 (18.1%) in group II on MR, and 6 (31.6%) in group I and 2 (9.5%) in group II on PET-CT.

**Conclusions:** US-guided tattooing is a feasible method for marking ALNs. In addition, tattooed lymph nodes correlate well with sentinel nodes, which may obviate the need for additional localization for axillary staging.

**No conflicts of interest**

**303** Poster

### A study of the accuracy of core needle biopsy in determining histological grade and receptor status in invasive breast cancer

S.K. Gupta[1], R. Pandey[1], M. Kumar[2]. [1]*Institute of Medical Sciences, Department of General Surgery, Varanasi, India;* [2]*Institute of Medical Sciences, Department of Pathology, Varanasi, India*

**Background:** Core needle biopsy is a key component of "triple assessment" of breast lumps. The histological type, grade and the receptor status as determined by the core biopsy, help in therapeutic decision making in breast cancer patients particularly in the selection of preoperative systemic therapy. The aim of this study was to determine the accuracy of preoperative core biopsy for assessing histological type, grade and receptor status in comparison to the histopathology of the definitive surgical specimen.

**Material and Methods:** After obtaining approval from the Institute Ethical Committee and informed consent, 60 patients with a palpable breast lump which was diagnosed as invasive breast cancer were included in the study. Patients with locally advanced breast cancer who were to receive neoadjuvant chemotherapy or who had biopsy done elsewhere were excluded. The tissue sections of core biopsy and definitive surgical specimen were assessed by one pathologist who was blinded to the core biopsy results during pathologic assessment of surgical specimen. The histological type, grade, estrogen (ER) and progesterone receptors (PR) and human epidermal growth factor receptor 2 (HER 2) were evaluated. Histological grade was classified according to Nottingham's prognostic index. ER, PR and HER-2 status was determined by immunohistochemistry. ER and PR expression was graded in a binary manner (positive at least 5% of tumour cells with nuclear staining). HER-2 expression was also graded in a binary manner (positive, 3+ staining).

**Results:** There was perfect agreement between the core biopsy and the final histopathology regarding the histological type. The concordance for tumour grade was only 63% being better for poorly differentiated cancers. Concordance between core biopsy and surgical specimen histopathology for ER, PR and HER-2 status was 68.9%, 71.3% and 75.8% respectively.

**Conclusions:** The disparity between the assessment of grade and receptor status between core biopsy and definitive surgical specimen necessitates caution in using the results of core needle biopsy for determining therapeutic interventions. It is possible that the high discordance observed in the present study may be due to intra-tumoral heterogeneity.

**No conflicts of interest**

**304** Poster

**Quantitative MTL-HEP test for breast cancer diagnostic and monitoring of advanced patients treatment**

E. Filinova[1], A. Galkin[2], G. Kuznecovs[3], I. Baranova[1]. *[1]Advanced Biomedical Research Laboratory, Cell Biology, Moscow, Russian Federation; [2]Advanced Biomedical Research Laboratory, Molecular Genetics, Moscow, Russian Federation; [3]Advanced Biomedical Research Laboratory, Physics Methods of Analysis, Moscow, Russian Federation*

Antibodies-based immunohistochemistry diagnostics are routinely made test for the determination of hormone receptors and cancer-associated antigens presence. However, it is not quantitative and cannot be applied in advanced patients monitoring and the adjustment of individual aromatase inhibitors/chemo- and radiotherapy regimes.

Quantitative TaqMan single-tube five-primer-pairs RealTime-RT-PCR with fluorimetric RNA concentration measurement test system (MTL-HEP) was developed for measuring the presence of malignant-specific forms of Muc1 antigens (cancer diagnostic, malignancy grade/progression) and levels of expression of estrogen (ER1), progesterone (PR), and HER2-neu (ERBB2) receptors, and for monitoring breast cancer patients' hormone resistance/progression status while they are undergoing hormone- or chemotherapy.

Surgery samples of 97 breast cancer patients were studied using the MTL-HEP test. 80% of all patients showed Muc1 hyperexpression (17 times higher than the background level of healthy donors' blood samples). 90% of them showed the presence of malignant (short) Muc1 isoforms as the difference of expression in Total and Long Muc1. The ratio of Total/Long Muc1 isoforms is significantly higher in high malignancy grade cases (2−3) and in hormone-negative breast cancers. ER1 and PR quantitative results match clinic immunohistochemistry data; however, absolute numbers vary often and can be 10−15 times different from one patient to another. As it is known that ER and PR expressions drop to negative values within 3−4 years of treatment for 75−85% of originally ER−PR-positive patients, the monitoring of individual ER−PR dynamic expression levels is crucial for in-time suppression of node-positive and advanced disease. 30% of patients were ER−PR-negative; one-third of them were also HER2-negative, and 20% were measured as triple-negative breast cancer. More than half (55%) of the triple-negative patients showed hyperexpression of the Muc1 antigen and were eligible for Muc1-targeted treatment. This represents 13.5% of total breast cancer patients whose metastatic stages appeared hopeless with regard to existing treatment.

The MTL-HEP test is quick, quantitative, less expensive and able to fulfill main tasks for biopsy/surgery breast cancer diagnostics. Quantitative measurement of ER1, PR, and HER2-neu expression levels monitors the chances of cancer progression in the individual dynamic and the fastest adjustment in adjuvant treatment for patients' benefit. High levels of Muc1 expression in triple-negative breast tumor as well as ER−PR-negative patients undergoing aromatase inhibitor treatment are suitable for Muc1-specific therapies such as antibodies and immunizing peptides (imMucin). The high ratio of malignant Muc1 isoforms in tumor samples indicates that these patients provide the target for efficient PI3K inhibitor (TOR) neo-adjuvant treatment.

**No conflicts of interest**

**305** Poster

**Invasive cancers presenting as pure mammographic calcification: The radiological flip side of 'over-diagnosis'**

M. Wallis[1], N. Sharma[2]. *[1]Cambridge University Hospitals HNS trust, Cambridge Breast Unit, Cambridge, United Kingdom; [2]LeedsTeaching Hospitals NHS Trust, Leeds Breast Unit, Leeds, United Kingdom*

**Background:** Finding DCIS is considered to be over-diagnosis by much of the lay and some of the medical press. Radiologists detect micro-calcification some of which is invasive disease. We set out to determine the rate and type of invasive disease presenting as calcification.

**Materials and Methods:** Women with a first offer appointment in the 3 years between 01/04/2011 and 31/3/2014 and recalled for pure micro-calcification, requiring stereo guided needle biopsy for diagnosis at 2 English screening programmes were identified using standard reports from the national breast screening computer system. Calcification with an associated mass or mass like lesion were excluded.

**Results:** 86 clients, mean age 59.2 years (range 46−79 yrs), with pure screen detected micro-calcification had a final outcome of invasive disease. 22 (25.6%) were grade 1, 53 (61.8%) grade 2, of which 2 were node positive, and 11 (12.8%) grade 3, of which 4 were node positive. In terms of the Nottingham Prognostic Index (NPI) 18 (20.9%) were in the Excellent Prognostic Group (PG), 51 (59.3%) Good PG, 14 (16.3%) Moderate 1 PG and 3 (3.5%) Moderate 2 PG.

37 of the 86 women were under staged pre operatively. Of the 35 who had a non-invasive core biopsy 28 (80%) were high grade DCIS, 6 (17.1%) were intermediate grade and 1 (2.9%) had pleomorphic LCIS. They had an almost 2.5 fold chance of having a moderate prognosis cancer 11/37 (29.7%) when compared to those with an invasive needle biopsy 6/49 (12.2%).

**Conclusion:** When screen detected micro calcification harbours invasive disease a fifth have moderate prognosis disease. Women under-staged pre operatively have more aggressive disease.

**No conflicts of interest**

Table (abstract 305).

| Nottingham Prognostic Index | | Needle biopsy | | | | |
|---|---|---|---|---|---|---|
| Group | Score | Invasive | Non-invasive | Indeterminate | Non-invasive and indeterminate | Total |
| | | n (%) | n (%) | n (%) | n (%) | n (%) |
| Excellent PG | ⩽2.4 | 13 (26.5%) | 4 (11.4%) | 1 (50%) | 5 (13.5%) | 18 (20.9%) |
| Good PG | 2.41–3.40 | 30 (61.2%) | 20 (57.1%) | 1 (50%) | 21 (56.8%) | 51 (59.3%) |
| Moderate 1 PG | 3.41–4.40 | 5 (10.2%) | 9 (25.7%) | 0 | 9 (24.3%) | 14 (16.3%) |
| Moderate 2 PG | 4.41−5.4 | 1 (2%) | 2 (5.7%) | 0 | 2 (5.4%) | 5 (3.5%) |
| Poor PG | 5.41–6.40 | 0 | 0 | 0 | 0 | 0 |
| Total | | 49 (100%) | 35 (100%) | 2 (100%) | 37 (100%) | 86 (100%) |

**306** Poster

**Clinical management of mucinous carcinoma of the breast with radiologically benign features**

Z.J. Lee[1], P.H. Tan[2], S.L.J. Wong[3], K.M.V. Tan[1], P. Madkumar[1], K.T.B. Tan[1], W.S. Yong[1], C.Y. Wong[1], K.W. Ong[1]. [1]*Singhealth, Duke-nus Breast Center, Singapore, Singapore;* [2]*Singapore General Hospital, Department of Pathology, Singapore, Singapore;* [3]*National Cancer Centre Singapore, Department of Oncologic Imaging, Singapore, Singapore*

**Background:** Mucinous breast carcinomas are rare, representing only 1−7% of all breast cancers. They are known to mimic benign lesions on mammography and ultrasonography, with consequent delay in diagnosis. We analyze the breast imaging-reporting and data system (BIRADS) scores of the imaging assessment done for mucinous breast cancers to determine the proportion initially assessed to be benign. We also report delays in diagnosis, and the clinical features that prompted histological evaluation of these lesions.

**Materials and Methods:** Consecutive patients with histologically proven invasive mucinous breast cancer treated at Singapore General Hospital and National Cancer Centre, Singapore between March 2000 to July 2014 were identified. Patient demographics, imaging data as well as histopathological features were collected. Univariate and multivariate analysis were done on factors that influence the decision to obtain histological diagnosis despite benign imaging studies.

**Results:** A total of 197 patients were identified. 152 (77.2%) were scored as either BIRADS 4 or 5 on initial imaging studies and 45 of 197 (22.8%) were scored BIRADS 3 or lower.

In the group with imaging reports of BIRADS 3 and below, 1 patient (2.2%) was scored as BIRADS 1, 14 (31.1%) as BIRADS 2, and 30 (66.7%) as BIRADS 3. In this group, 41 patients (91.1%) were symptomatic, presenting with a breast lump or abnormal nipple discharge. The 4 asymptomatic cases were called BIRADS 3, and had immediate biopsy, as this is standard practice for screen-detected cases. 26 of the symptomatic patients (63.4%) underwent biopsy after the initial imaging assessment. There was a delay in diagnosis in 15 (36.6%) of the symptomatic cases.. 11 had 1 further imaging while 4 had 2 or more before histological diagnosis were finally obtained. This resulted in a median delay of 21 months (range 2 to 42 months).

On univariate analysis, the presence of a positive family history significantly influences the decision to seek histological diagnosis. 88.2% of patients with positive family history of breast or ovarian cancers had immediate biopsy after the initial imaging, compared to only 57.1% of the patients without ($p = 0.036$). However, this factor was no longer significant on multivariate analysis ($p = 0.202$) There is a trend towards immediate biopsy for women aged 50 or less (76.0% vs 55.0%, $p = 0.138$), the use of hormone replacement therapy (75% vs 69.2%, $p = 0.815$), absent of parity (76.5% vs 64.7%, $p = 0.452$), late menarche (100.0% vs 68%, $p = 0.246$) as well as tumor size larger than 2 cm (72.7% vs 60.0%, $p = 0.716$). These factors however did not reach statistical significance.

**Conclusions:** In this large cohort of mucinous breast cancers, 1 in 5 did not have suspicious imaging features on initial assessment. Delay in diagnosis occurred in 36.6% of the patients. Mucinous breast cancer remains a diagnostic challenge.

**No conflicts of interest**

**307** Poster/Poster Spotlight

**Use of the sentinel node biopsy for patients with a needle biopsy diagnosis DCIS in the Netherlands**

C. Meurs[1], M. Menke-Pluijmers[2], R. Bretveld[3], L. Overbeek[4], P. Westenend[5,6]. [1]*CMAnalyzing, Zevenaar, Netherlands;* [2]*Albert Schweitzer Hospital, Surgery, Dordrecht, Netherlands;* [3]*Comprehensive Cancer Centre the Netherlands, Research, Nijmegen, Netherlands;* [4]*PALGA: Dutch Pathology Registry, Research, Houten, Netherlands;* [5]*Laboratory of Pathology, Dordrecht, Netherlands;* [6]*Regional screening organization South West, Rotterdam, Netherlands*

**Background:** Recommendations in the national guideline for diagnostic work up and treatment in patients with ductal carcinoma in situ (DCIS) at biopsy are ambiguous. A sentinel node (SN) biopsy is considered for patients undergoing mastectomy and for patients at risk for underestimate. Underestimate is defined as patients with a DCIS diagnosis at core needle biopsy for whom also an invasive breast cancer is found at excision. The aim of this study is to explore the quality of care for patients with a biopsy diagnosis DCIS. We analysed the hospital variation in use of the sentinel node biopsy and compared it with the underestimate rates and the SN results.

**Materials and Methods:** Patients with a final biopsy diagnosis DCIS were selected from the nationwide network and registry of histopathology and cytopathology in the Netherlands (PALGA). All PALGA records were assessed to extract DCIS grade, suspected invasive component at biopsy etc. The PALGA data were merged with the National Cancer Registry (NCR) data, thereby adding information about being screen-detected, palpable, BI-RAD score, hospital of treatment etc. In this study no information was available about the size of the mammographic lesion. Population based data from incidence years 2011 and 2012 were available for analysis. Multivariate analysis was conducted to define determinants of quality of care. Variation in care between hospitals were shown in plots and analysed in multilevel analysis.

**Results:** 2331 patients with a biopsy diagnosis DCIS were analysed. A SN biopsy was performed in 88% of patients undergoing mastectomy and in 51% of patients undergoing breast conserving surgery (BCS). The use of the SN biopsy differed significantly between hospitals. For BCS, 44% of the variance in % of SN biopsies was due to the hospital and 10% to the hospital region. Determinants for underestimation and determinants for performing the SN biopsy were DCIS grade and a suspected invasive component. Of patients undergoing BCS, the SN biopsy was performed in 49% of patients with a DCIS diagnosis at excision and in 62% of patients with an invasive cancer at excision. By SN biopsy at BCS, micro metastases were found in <1% and macro metastases in 2% of patients. Of patients undergoing mastectomy, the SN biopsy was performed in 87% of patients with a DCIS diagnosis at excision and in 90% of patients with an invasive cancer at excision. By SN biopsy at mastectomy, micro metastases were found in 3% and macro metastases in 4% of patients.

**Conclusions:** We conclude that there is no uniform policy between hospitals in use of the sentinel node biopsy for patients with a biopsy diagnosis DCIS, reflecting differences in interpretation of the national guideline. The sentinel node biopsy is not used very effectively. We would recommend to reconsider the use of the sentinel node biopsy for patients with a DCIS at biopsy.

**Conflict of interest:** Other Substantive Relationships: This study is supported by a grant from the Dutch Cancer Foundation (KWF), project number 2013–6495.

**308** Poster

**Can 2D or 3D ultrasound (US) with shear wave elastography (SWE) parameters predict re-excision rates in women undergoing breast conserving surgery (BCS) for invasive breast cancer?**

N. Makaram[1], B. Elsberger[2], J. Macaskill[2], Y.T. Sim[1], K. Thomson[1], S. Vinnicombe[2], A. Evans[2]. [1]*Ninewells Hospital and Medical School, Department of Breast Surgery- Dundee Cancer Centre, Dundee, United Kingdom;* [2]*School of Medicine- University of Dundee, Department of Cancer Research, Dundee, United Kingdom*

**Introduction:** It is well known that radiological underestimation of breast tumour size is associated with higher rates of re-excision in BCS. Accurate preoperative prediction of those women at high and low risk of surgical re-excision after breast conserving surgery (BCS) may be helpful when considering surgical planning and suitability for IORT (intraoperative radiotherapy). The size of peri-tumoural stiffness on 2D shearwave elastography (SWE) has previously been shown to enhance the size estimation on breast US in women with small breast cancers. The aim of this study was to assess the ability of 2D US, 3D US and SWE parameters to predict the need for re-excision in women undergoing immediate BCS.

**Methods:** 214 consecutive women, diagnosed with invasive breast cancer between 2011 and 2015, underwent 2D US, 3D US and SWE assessment. All patients subsequently had BCS. Parameters studied were (a) diameter of the lesion on greyscale USS, (b) mean stiffness in kilopascals, (c) greyscale volume of the lesion and (d) volume of tumoural and peritumoural stiffness measured at 3D SWE. The results for each parameter were divided into quartiles and compared to re-excision rates. Statistical significance was assessed with the $\chi^2$ test.

**Results:** The cohort consisted of 214 early stage breast cancer patients, median age 62 years. 85% of cancers were pathologically graded as G2/G3, 192 were ER pos, 23 ER neg. 160 tumours were invasive ductal carcinoma, 23 invasive lobular type, 31 other type. Median whole tumour diameter (WTD) was 18 mm. 19 of 214 (9%) patients underwent re-excision of involved radial margins.

Re-excision rates (%) according to each parameter divided into quartiles, are demonstrated in Table 1. SWE volume measurement in the lowest quartile was associated with only 2% re-excision rate which was statistically significant compared to the rest of the study group ($p < 0.05$).

**Conclusion:** Measuring the stiff volume of invasive cancers (including peri-tumoural stiffness) is able to identify a subgroup of women undergoing BCS, who have a very low rate of surgical re-excision. There is an obvious need for a study randomising patients into groups where the surgeon is or is not informed about 3D volume of the lesion. This may influence surgical planning and potentially reduce re-excision rates.

**No conflicts of interest**

Table 1. Re-excision rates (%) divided by quartile

| Quartile | Re-excision rate (%) | p-value |
|---|---|---|
| Diameter (2D USS) (mm) | | ns |
| <10 | 4 | |
| 10−13 | 9 | |
| 14−17 | 12 | |
| >18 | 11 | |
| Mean stiffness (2D) (kPa) | | ns |
| <77 | 6 | |
| 77–113.99 | 14 | |
| 114–172.99 | 8 | |
| >173 | 10 | |
| Grey scale volume (3D USS) ($cm^3$) | | ns |
| <0.2 | 6 | |
| 0.2–0.5499 | 6 | |
| 0.55–1.2699 | 15 | |
| >1.27 | 10 | |
| SWE volume (3D) ($cm^3$) | | <0.05 |
| <0.77 | 2 | |
| 0.77–1.1869 | 9 | |
| 1.87–3.4699 | 9 | |
| >3.47 | 16 | |

**309** Poster

**A comparative study of breast specific gamma imaging with conventional imaging modality in ductal carcinoma in situ of the breast**

J.H. Yang[1], M.J. Cho[1]. [1]*Konkuk University Hospital, Surgery, Seoul, South Korea*

**Background:** Duct carcinoma in situ (DCIS) of the breast is nowadays increasing but its diagnosis is not simple. The purpose of this study is to evaluate the sensitivity of high resolution breast specific gamma imaging (BSGI) and to compare the sensitivity of BSGI with conventional imaging modality for the detection of DCIS.

**Materials and Methods:** This study enrolled retrospectively 38 women who had been diagnosed with DCIS of the breast. All patients underwent preoperative BSGI, mammography (MMG) and ultrasonography (USG), Magnetic resonace imaging (MRI) was performed on 30 patients. The sensitivity of BSGI, MMG, US and MRI were determined for detection of DCIS.

**Results:** Six patients (15.9%) presented with palpable mass and one patient (2.6%) with unilateral bloody nipple discharge. Remaining thirty-one patients (81.6%) presented with imaging abnormalities only. The sensitivity of detection for DCIS with BSGI was 92.1%. Its sensitivity was 89.5% with MMG, 81.6% with US and 100% with MRI respectively. The pathologic size of DCIS ranged from 4 to 85 mm. There were 3 false positive cases with BSGI which were less than 15 mm in size.

**Conclusion:** BSGI has high diagnostic performance as an excellent adjunct modality for diagnosis of DCIS. It can reliably detect small, even subcentimeter lesions with DCIS of the breast.

**No conflicts of interest**

**311** Poster

**Breast cancer in young women: Correlation of newly identified genetic mutations with estimated individual risk and value of imaging modalities for diagnosis**

P. Steyerova[1], M. Zimovjanova[2], P. Kleiblova[3], J. Zizalova[4], M. Skovajsova[4], J. Danes[1], L. Petruzelka[2]. [1]*General University Hospital Prague, Clinic of Radiology, Prague, Czech Republic;* [2]*General University Hospital Prague, Clinic of Oncology, Prague, Czech Republic;* [3]*General University Hospital Prague, Institute of Biology and Medical Genetics, Prague, Czech Republic;* [4]*Breast Unit Prague, Breast Cancer Screening and Diagnostic Center, Prague, Czech Republic*

**Background:** Breast cancer in young women remains diagnostic and therapeutic challenge. High-risk women undergo intensive surveillance with MRI yet there are numerous young women diagnosed with breast cancer by conventional imaging modalities. Their family history is heterogeneous, some of them are not considered to be of high-risk. Pathogenic gene alterations might be found by subsequent genetic testing. This work evaluates the incidence of newly identified mutations in breast cancer patients diagnosed under the age of 40, their family history and value of imaging methods for the diagnosis.

**Material and Methods:** We evaluated data from women aged 40 years and less diagnosed with breast cancer between January 2012 and September 2015. Data were obtained from medical documentation and patient questionnaires. Genetic testing was offered to all women without previously known genetic predisposition. We evaluated family history of the patients, estimated individual risk, its correlation to the newly found mutations and efficacy of the imaging modalities used.

**Results:** We included 166 patients aged 26−40 years; 159 women with no previously known genetic predisposition, 7 known genetic mutation carriers. 67 patients were tested after the diagnosis. We revealed 19 new genetic mutations (15 BRCA1, 1 BRCA2, 3 CHEK2). 48 patients had negative genetic testing. We analyzed family history of 155 patients to estimate individual risk. 113 (72.9%) patients had no breast or ovarian cancer in the family, 51 of them were tested and 11 genetic mutations were found (21.5%). 42 (27.1%) patients had positive family history, 16 of them were tested and 8 genetic mutations were found (50%). In the non-high risk population the modality of first choice was ultrasound in 127, mammography in 31 women. Mammography reached overall sensitivity 63.2%. Calcifications were seen in 57 (35.6%) cancers including 8 (33.3%) tumors in genetic mutation carriers. The efficacy of mammography and ultrasound combined was 96.2%. 149 patients (93.7%) had clinical symptoms, 49 (30.8%) had lymph node involvement at the time of diagnosis. In the group of mutation carriers (4 BRCA1, 3 BRCA2), 1 cancer was identified by mammography, 4 by ultrasound, 2 were only found by MRI. 6 cancers were asymptomatic and diagnosed by the surveillance protocol, only 1 was palpable, all without lymph involvement.

**Conclusions:** Most breast cancer patients diagnosed at young age have average estimated individual risk. In the group of women with family history of breast/ovarian cancer the probability of finding a genetic alteration is higher. Breast cancer in young women is usually symptomatic and identified by conventional methods with sufficient efficacy. The high-risk surveillance protocol works effectively but conventional imaging methods are also helpful in detecting cancer both in known and previously unknown genetic mutation carriers.

**No conflicts of interest**

**312** Poster

**Logistic regression model based on serum CEA, CA 15-3, IGFBP-3, and IL-2R measurement in predicting the presence of axillary lymph node metastases in patients with breast cancer**

F. Lumachi[1], G.B. Chiara[2], D.A. Santeufemia[3], R. Tozzoli[4], S.M.M. Basso[2]. [1]*University of Padova, School of Medicine Department of Surgery-Oncology & Gastroenterology, 35128 Padova, Italy;* [2]*S. Maria degli Angeli Hospital, Surgery 1, 33170 Pordenone, Italy;* [3]*Alghero City Hospital, Medical Oncology, 07040 Alghero SS, Italy;* [4]*S. Maria degli Angeli Hospital, Department of Laboratory Medicine, 33170 Pordenone, Italy*

**Background:** Approximately 25% of patients with breast cancer (BC) may present with axillary lymph node metastases (NMs) at the time of surgery. Unfortunately, no preoperative imaging studies are available in detecting NMs before sentinel node biopsy, which is considered a routine technique for staging patients. More than 50% of patients had early-stage (stage 0−1) BC, but an early prediction of NMs could be useful in selecting patients scheduled for neoadjuvant chemotherapy and more personalized surgery. A number of serum tumor markers (STMs) have been proposed in the pre- and postoperative management of patients with BC, and the most widely used were carcinoembryonic antigen (CEA), and cancer-specific cancer antigen (CA) 15−3. More recently, relatively new STMs, including insulin-like growth factor binding protein-3 (IGFBP-3) and interleukin-2 receptor (IL-2R), have been suggested. The aim of this study was to evaluate the sensitivity and specificity of serum CEA, CA 15-3, IGFBP-3, and IL-2R in predicting the presence of NMs in patients with pT1−2 BC.

**Patients and Methods:** A group of 34 women with confirmed pN1−2 BC (cases) and 33 age-matched node-negative (pN0) control patients were retrospectively enrolled in the study. All patients underwent serum CEA, CA 15-3, IGFBP-3, and IL-2R measurement using radioimmunoassay (CEA) or chemiluminescent immunoassay, respectively.

**Results:** At univariate analysis, the sensitivity, specificity, and accuracy were the following: 47.1%, 36.4%, 41.8% (CEA); 50%, 48.5%, 49.3% (CA 15-3); 55.9%, 45.4%, 55.2% (IGFBP-3); 52.9%, 48.5%, 50.7% (IL-2R). The IGFBP-3 was the best NMs prediction marker in the univariate analysis, and the area under the curve (AUC) was 0.65. In the multivariate logistic regression analysis, model with IGFBP-3 and IL-2R showed a better predictive value (AUC=0.69), corresponding to a sensitivity and specificity of 70.6% and 66.7%, respectively.

**Conclusion:** In patients with BC, serum IGFBP-3 and IL-2R measurement in combination improves both sensitivity and specificity of STMs in predicting the presence of NMs, and can be useful in selecting patients with elevated risk of having positive sentinel node biopsy.

**No conflicts of interest**

**313** Poster

**Immunohistochemistry and fluorescence in situ hybridization for invasive breast cancer in same-day core needle biopsies with very short fixation time**

A. Halilovic[1], J. Bulte[2], Y. Jacobs[1], H. Braam[1], P. Van Cleef[1], M. Schlooz-Vries[2], A. Werner[2], O. Boelens[3], I. Nagtegaal[1], J. De Wilt[2], P. Bult[1]. *[1]Radboud University Medical Center, Pathology, Nijmegen, Netherlands; [2]Radboud University Medical Center, Surgery, Nijmegen, Netherlands; [3]Hospital Pantein, Surgery, Boxmeer, Netherlands*

**Background:** Pre-operative core needle biopsy (CNB) is commonly used to confirm the diagnosis of breast cancer. For treatment purposes and for determining histological type, especially in case of neo-adjuvant therapy, E-cadherin, estrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor 2 (HER2) status assessment is crucial. Considering the increasing demand for same-day diagnosis of breast lesions an accelerated method of CNB processing was developed, in which the tissue fixation time is radically reduced.

**Material and Methods:** In order to determine whether short fixation time frustrates assessment of ER, PR and E-cadherin immunohistochemistry and HER2 fluorescence in situ hybridisation (FISH), 69 consecutive patients with 70 invasive breast carcinomas were included through the same day diagnostics program of breast lesions of the Radboudumc and the affiliated hospital Pantein. Immunohistochemistry for ER, PR and E-cadherin and HER2 FISH were compared between CNBs fixated for approximately 60−90 min and traditionally fixated resection specimens.

**Results:** Overall agreement between CNBs and resection specimenswas 98.6% for ER ($p < 0.001$; $\kappa = 0.93$), 90.0% for PR ($p < 0.001$; $\kappa = 0.75$), 100% for E-cadherin ($p < 0.001$; $\kappa = 1.00$)and 98.6% ($p < 0.001$; $\kappa = 0.94$) for HER2 FISH. Positive and negative predictive values were respectively 98.4% and 100% for ER, 95.9% and 76.2% for PR, 100% and 100% for E-cadherin and 90% and 100% for HER2 FISH.

**Conclusions:** Hormone receptor and E-cadherin immunohistochemistryand HER2 FISH are highly comparable between briefly fixated CNBs and thecorresponding traditionally fixated resection specimens and can therefore reliablybe used in the daily clinical practice of same day diagnostics of breast cancer.

**No conflicts of interest**

**314** Poster

**Is retraction artifact an implication of poor prognosis in Japanese breast cancer patients?**

H. Hashidate[1], H. Makino[2], S. Hiroyuki[1], M. Keiji[1]. *[1]Niigata city general hospital, Pathology, Niigata, Japan; [2]Niigata city general hospital, Breast surgery, Niigara, Japan*

**Background:** Retraction artifact (RA), a synonym for “periacinar halo” or “retraction clefting”, around cancer cell nests is a characteristic feature of invasive micropapillary carcinoma (IMPC), a special type of breast cancer commonly associated with nodal metastasis. Recently, several reports indicated RA feature in usual invasive ductal carcinoma (IDC) is also a strong predictor of nodal metastasis. We examined whether the presence of RA can be a predictor of nodal metastasis or prognosis in Japanese breast cancer patients.

**Material and Methods:** All 434 primary IDC surgical cases between November 2007 and December 2011, excluding special types and neoadjuvant chemotherapy cases, were provided. RA is histologically defined as clear separating space between tumor nest/cord and surrounding stroma without endothelial lining. The clinicopathological features (including HR, HER2 and Ki-67 beling index), DFS and OS were compared IDC cases with RA to IDC cases without RA.

**Results:** Among 434 IDC cases, 47 (10.8%) IDC cases revealed partial (histologically more than 10% per square) RA feature. Two cases revealed more than 90% RA feature and typical reversed polarity of tumor cells were diagnosed as pure IMPC and excluded from this study. IDCs with RA revealed higher lymphatic permeation rate ($p = 0.001$), higher lymph node metastasis rate ($p = 0.005$) and HER2 positivity ($p = 0.034$), comparing with IDCs without RA. There were no significant differences in patient age, clinical stage, tumor size, histological grade, blood vessel permeation rate, hormone receptor status, Ki-67 labeling index, DFS (log rank test, $p = 0.782$) and OS ($p = 0.872$).

**Conclusions:** The presence of partial RA feature in IDC is not predictive of poor prognosis in Japanese patients, although it indicates significantly higher rate of lymphatic permeation and lymph node metastasis. HER2 positivity may affect the RA feature and polarity of tumor cell nests. HER2 positivity may also affects prognosis due to HER2-targeted treatment. We may need to observe over a longer period of time to evaluate the prognosis of IDC cases with/without RA feature.

**No conflicts of interest**

**315** Poster

**Too young for breast cancer? A dangerous prejudice**

L. Rossi[1], G. Montagna[2], O. Pagani[1]. *[1]Istituto Oncologico della Svizzera Italiana, Centro di Senologia della Svizzera Italiana, Lugano, Switzerland; [2]Ospedale Regionale di Lugano, Department of Obstetrics and Gynecology, Lugano, Switzerland*

**Background:** Locally advanced breast cancer (LABC) is a heterogeneous disease including small tumours with extensive nodal involvement or T4s. LABC accounts for 5−10% of all new primary BC and affects women of all ages, with an increasing trend in very young (<35) women.

BC diagnosis in young or very young women is often delayed because of age-based prejudices. BC in a young woman can be confused with many breast diseases typical of young age (such as cysts, fibroadenomas, phyllodes tumours). In this age group few data exist on risk factors for LABC and causes of diagnostic delay.

**Material and Methods:** Between 2008–2015, at the Breast Unit of Southern Switzerland (CSSI), we treated over 1300 patients with primary BC; 117 patients (9%) had T4 at diagnosis, 14 of them (12%) were under 40. With the aim of understanding the causes of diagnostic delay in this group, we retrospectively investigated the demographic and psychosocial characteristics of these 14 patients. A demographic survey and a semi-structured interview (28 items) was specifically developed and submitted by the treating team (gynaecologist, psychologist, medical oncologist) to all consenting patients.

**Results:** Median age was 38 years (26−40 years). 3 died from metastatic disease, 29% were single, 71% had children. None lived alone. The educational level varied from elementary school to university, all of the patients had a full time job. The majority (86%) were believer. None of the patients regularly visited their GP or had chronic diseases, 20% had psychiatric comorbidities (anxiety and mood disorder) and were taking psychotropic drugs. 20% exclusively used alternative medicine. None of them had previous breast diseases or biopsies. 43% had a family history of BC. All presented with a palpable breast mass and/or breast discomfort. 60% reported anxiety and fear as first reaction and a first delay (time from symptom debut to initial medical examination) of 1−2 months. 40% described indifference and denial as first emotion, and delayed to seek medical care (first delay >12 months), during this period of time they hid symptoms from their partners and beloved relatives.

**Conclusions:** Only 20% of patients had known risk factors for LABC (psychiatric comorbidity or exclusive use of alternative medicine). Delay in diagnosis was either due to patient’s delay in seeking medical advice based on a underlying denial mechanism or doctor’s delay in making the correct diagnosis. Our preliminary data show the importance of awareness among physicians that breast cancer doesn’t discriminate by age.

**No conflicts of interest**

**316** Poster

**Prediction model for extensive ductal carcinoma in situ around early-stage invasive breast cancer**

F. Knuttel[1], B. Van der Velden[2], C. Loo[3], S. Elias[4], J. Wesseling[5], M. Van den Bosch[1], K. Gilhuijs[2]. *[1]UMC Utrecht, Radiology, Utrecht, Netherlands; [2]UMC Utrecht, Image Sciences Institute, Utrecht, Netherlands; [3]Netherlands Cancer Institute, Radiology, Amsterdam, Netherlands; [4]UMC Utrecht, Julius Center for Health Sciences and Primary Care, Utrecht, Netherlands; [5]Netherlands Cancer Institute, Pathology, Amsterdam, Netherlands*

**Background:** Ductal carcinoma in situ (DCIS) is a risk factor for incomplete resection of breast cancer. Especially extensive DCIS (E-DCIS) or extensive intraductal component often results in positive resection margins. Detecting DCIS around breast cancer prior to treatment may therefore alter surgical treatment. The purpose of this study was to develop a prediction model for extensive ductal carcinoma in situ (E-DCIS) around early-stage invasive breast cancer, using clinicohistopathological and dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) features.

**Methods:** DCE-MRI and local excision were performed in 322 patients with 326 ductal carcinomas. Tumors were segmented from DCE-MRI, followed by 3D extension of the margins with 10 mm. Tissue density and enhancement features in these extended margins were automatically extracted from the MR-images. Clinicohistopathological features were also obtained. Principal component analysis (PCA) and multivariable logistic regression were used to develop a prediction model for E-DCIS. Discrimination and calibration were assessed and bootstrapping was applied for internal validation.

**Results:** E-DCIS occurred in 48/326 tumors (14.7%). Incomplete resection occurred in 56.3% of these E-DCIS-positive versus 9.0% of E-DCIS-negative tumors ($p < 0.001$). Five components with eigenvalue exceeding 1 were identified by PCA; two were associated with E-DCIS.

The first, positively associated, component expressed early and overall enhancement in the 10 mm tissue margin surrounding the MRI-visible tumor. The second, positively associated, expressed human epidermal growth factor receptor 2 (HER2) and tissue density around the MRI-visible tumor. The AUC-value was 0.79 (0.76 after bootstrapping).

**Conclusion:** HER2 status, early and overall enhancement in the 10 mm margin around the MR-visible tumor and density in the 10 mm margin around the MR-visible lesion were predictors for E-DCIS.

**No conflicts of interest**

**317** Poster

**Clinical application of color map pattern on shear-wave elastography for invasive breast cancer**

Y.L. Jung[1], S.W. Lee[1]. [1]*Pusan National University Hospital, Surgery, Busan, Korea*

**Background:** The aim of this study was to classify the color map pattern on shear-wave elastography (SWE) and to determine its association with clinicopathological factors for clinical application in invasive breast cancer.

**Material and Methods:** From June to December 2014, 103 invasive breast cancers were imaged by B-mode ultrasonography (US) and SWE before surgery. The color map pattern identified on the SWE could be classified into three main categories: type 1 (diffuse pattern), increased stiffness in the surrounding stroma and the interior lesion itself; type 2 (lateral pattern), marked peri-tumoral stiffness at the anterior and lateral portions with no or minor stiffness at the posterior portion; and type 3 (rim-off pattern), marked peri-tumoral stiffness at the anterior and posterior portion with no or minor stiffness at both lateral portions.

**Results:** High-grade density on mammography (grade 3−4) was more frequent in the type 1 pattern than the other pattern types (80.5% in high-grade density vs. 19.5% in low-grade density). For type 1 tumors, the extent of synchronous non-invasive cancers (pT0), ductal carcinoma in situ (DCIS), was 1.8−2.0 times wider than that measured by US or MRI. For type 2 tumors, the invasive tumor components (pT size) size was 1.3 times greater than measured by MRI ($p = 0.049$). On the other hand, the pT size and pT0 extent of type 3 tumors were almost equal to the preoperative US and MRI measurements. In terms of immunohistochemical (IHC) profiles, type 3 tumors showed a high histologic grade ($p = 0.021$), poor differentiation ($p = 0.009$), presence of necrosis ($p = 0.018$), and high Ki-67 ($p = 0.002$). The percentage of HER2-positive cancers was relatively high within the type 2 group, and the percentage of triple negative breast cancer was relatively high in the type 3 group ($p = 0.011$).

**Conclusions:** We expect that assessments of the SWE color map pattern will prove useful for surgical or therapeutic plan decisions and to predict prognosis in invasive breast cancer patients.

**No conflicts of interest**

**318** Poster

**Histological changes in a high-risk breast cancer screening cohort and their impact on patient management**

K.A. Tendl[1], P. Baltzer[2], M. Bernathova[2], M.A. Marino[2], E.M. Langthaler[1], T. Helbich[2], M. Rudas[1], Z. Bago-Horvath[1]. [1]*Medical University of Vienna, Clinical Institute of Pathology, Vienna, Austria;* [2]*Medical University of Vienna, Dep. of Biomedical Imaging and Image-guided Therapy, Vienna, Austria*

**Background:** BRCA mutation carriers and women with a high familial risk for breast cancer were shown to benefit from intensive multimodal screening. However, increased sensitivity of combined imaging techniques might lead to an increased rate of core needle biopsies (CNB). The present study analyzed the association between radiological and patho-histological findings and their significance in patient management.

**Material and Methods:** 93 core needle biopsies from 65 high risk patients after multimodal imaging rounds were included in this retrospective study. Radiological changes were assessed according to the BI-RADS classification. CNB was performed ultrasound-, MRI-guided or stereotactically. Histological workup was in accordance with the current European Guidelines for Breast Cancer Screening and lesions were classified according to the B-classification. Subsequent breast surgery was performed in 38 (58.4%) patients. Histological diagnoses in CNB and surgical specimens (SR) were compared with respect to epithelial atypia and neoplastic lesions. Association between radiological and pathological findings was analyzed using chi-square test.

**Results:** Most frequent benign histological changes included fibroadenomatous hyperplasia (12.9%), UDH (11.8%), fibroadenomas (8.6%) and pseudoangiomatous stromal hyperplasia (6.5%). ADH was seen in 6.5% and DCIS in 8.6% of CNB specimens, respectively. Invasive carcinoma was diagnosed in 11.8% of cases. BI-RADS and B-classification of CNB were both significantly associated with reproducibility of histological diagnoses in subsequent SR specimens. Whereas reproducibility was excellent in B5 cases, no difference in reproducibility between B2 and B3 cases was noted. In these cases, the presence of atypical epithelial changes was discordant between CNB and SR in 33.3% for both B2 and B3 lesions, respectively. Particular histological changes showed a significant association with specific imaging modalities ($p = 0.029$). Of 65 patients, 7 (10.7%) were known to harbor BRCA 1/2 mutations. BRCA status was of marginal significance regarding the association with younger age ($p = 0.069$) and subsequent breast surgery ($p = 0.187$), independent of histological diagnosis of CNB. No significant correlation between BRCA mutation status and any of the specific histological changes listed above was found.

**Conclusions:** In a high-risk screening cohort, we identified specific histological changes frequently associated with particular imaging findings. An improved radiological and pathological characterization of these lesions might spare patients from unnecessary CNB. The validation of our results in a larger cohort is warranted.

**No conflicts of interest**

**319** Poster

**Breast-specific gamma imaging versus magnetic resonance imaging in ductal carcinoma in situ: A prospective head-to-head trial**

B.S. Ko[1], H.J. Kim[1], J.W. Lee[1], J.K. Kim[1], S.B. Lee[1], I.Y. Chung[1], B.H. Son[1], S.H. Ahn[1]. [1]*Asan Medical Center, Surgery, Seoul, South Korea*

**Background:** Ductal carcinoma in situ (DCIS) is very early cancer that is highly treatable, but accurate determination of the size or extent of the lesion is difficult. Breast magnetic resonance imaging (MRI) may provide an accurate assessment of tumor size. But there are limited data on the utility of breast-specific gamma imaging (BSGI) in DCIS. The aim of the study was to prospectively compare the accuracy of BSGI to MRI for the assessment of the size of DCIS.

**Material and Methods:** This single-center prospective study conducted from Jun 2013 to December 2014 at the Asan Medical Cancer included 135 patients with a histologically proven DCIS or DCIS with microinvasion (DCISM) by needle biopsy, who all underwent BSGI and MRI. Each longest diameter (LD) measurements were compared to histopathological LD. The measurements were validated using Bland and Altman analysis and Pearson's correlation. Bland and Altman agreement plot methodology resulting in dimensionless mean difference and 95% limits of agreement (LOA).

**Results:** Pathologic tumor size of the DCIS ranged from 0.2 to 12.0 cm (median 2.2 cm). Of 142 cases of biopsy-proven DCIS or DCISM in 135 women, 76.3% were detected with BSGI, and 95.0% were detected with MRI. Bland–Altman agreement plot analysis for the whole cohort revealed mean difference between MRI and histopathology (0.2901), 95% LOA (−2.6447 to 3.2249) compared with BSGI and histopathology (mean difference −0.2863, 95% LOA −2.9585 to 2.3860). Overall, Pearson's correlation of the size between BSGI and histopathology was 0.801 versus 0.777 between MRI and histopathology.

**Conclusions:** Although MRI is thought to be more sensitive than BSGI for detecting DCIS, BSGI comparable to MRI in the assessment of tumor size.

**No conflicts of interest**

**320** Poster

**Efficacy of positron emission mammography using fluorine-18-fluorodeoxyglucose in detection of residual lesion after neoadjuvant chemotherapy for operable breast cancer**

Y. Kojima[1], K. Tsugawa[1]. [1]*St. Marianna University School of Medicine, Surgery- division of breast and endocrine surgery, Kawasaki, Japan*

**Background:** Positron emission mammography (PEM) using (18)F-FDG has more sensitivity for detecting suspicious lesion in the breast compare to positron emission tomography (PET). There are several reports describing the efficacy of PET or PET/CT in evaluating remnant lesions after neoadjuvant chemotherapy, but few reports exist which describe the efficacy of PEM for this purpose. Recently, in cases with HER2 positive or triple negative (estrogen, progesterone and HER2 negative) breast cancer, high pathological complete response (CR) rate could be expected. Although, even in some cases with radiological findings indicating CR, remnant cancer cells were found. Previously, sensitivity and specificity of positron emission mammography (PEM) in assessment of neoadjuvant chemotherapy has reported as favorable as MRI. Our aim is to evaluate clinical accuracy of adding PEM to usual preoperative assessment of neoadjuvant chemotherapy effect in operable breast cancer.

**Methods:** Women who diagnosed as breast cancer between September 2013 and January 2014 were enrolled and underwent PEM with PET/CT after completion of neoadjuvant chemotherapy. Clinical and pathological

factors and MRI findings were compared with PET/CT and PEM. Images were analyzed visually and quantitatively by a radiologist.

**Results:** Seventeen patients were involved and, all cases were diagnosed as invasive ductal carcinoma. Among five patients who achieved pCR, although only one patient was diagnosed as CR by MRI, all five cases had no uptake on PEM. PEM findings consist of metabolic assessment using (18)F-FDG and could measure activity of tumor directly and identify pCR. On the other hand, among three patients with no FDG uptake on PEM, residual tumor cells were seen pathologically. Radiologic assessment of chemotherapy effect is based on blood flow loss or disappearance. Patients without PEM uptake having residual tumor, which may indicating the limit of resolution or decreased tumor activity. Actually, most of the cases that PEM could not detect residual lesion, had really small sized or predominantly in-situ lesion and which was thought to be the limit of resolution and also with the decreased activity.

**Conclusion:** This is a preliminary report to assess the usefulness of PEM in post-chemotherapy residual lesion diagnosis in breast cancer. PEM showed higher sensitivity than MRI. Further evaluation would be needed, and we are planning to run a prospective study to evaluate utility of PEM combined with MRI.

**No conflicts of interest**

## Thursday, 10 March 2016

**POSTER SESSION**

# Systemic Treatment

**321** Poster

### Long term effects of taxanes based neoadjuvant chemotherapy in advanced non-metastatic breast cancer

T. Mehmood[1], N. Siddiqui[1], A. Hameed[1]. [1]*Shaukat Khanum Memorial Cancer Hospital and Research Centre, Medical Oncology, Lahore, Pakistan*

**Background:** Pakistan has the highest rate of breast cancer for any South Asian population. We report on long term response and survival of primary non-metastatic breast cancer patients treated with neoadjuvant Adriamycin/Taxanes (AT) based regimens.

**Methods:** Between 1995 to 2009, we identified 517 women with pathologically confirmed breast cancer. All patients received neoadjuvant chemotherapy with AT based regimen followed by surgery. Median age was 43 years (range 17−71 years). AJCC stage; stage II 54%, stage III 46%. Axillary nodes were palpable in 72% of the patients at presentation. Histological sub-types were infiltrating ductal carcinoma 95%, infiltrating lobular carcinoma 3% and others 2% respectively. Pathological grade was I/II in 44% and grade III 56% of the patients. ER, PR, and Her2-neu receptors were positive in 44%, 40% and 24% respectively. 21% of the patients had triple negative breast cancer. Post operative radiotherapy was delivered to 94% of the patients. Patients with positive ER/PR receptors also received hormonal manipulation. Median follow-up duration was 7.6 years (range 3.5−8.2 years).

**Results:** Following neoadjuvant chemotherapy, pathological response was; complete response 13.5%, partial response 21%, stable disease 52% and progressive disease in 13% of the patients respectively. Breast conservation was possible in 36% of the patients. The 7 year overall survival (OS) and disease free survival (DFS) in patients with CR was 60% and 56% respectively. The 7 year OS and DFS in patients without CR was 33% and 29% respectively. On multivariate analysis T stage ($p = 0.001$) and response to neo-adjuvant chemotherapy ($p = 0.001$) were found to be independent predictors for OS and DFS.

**Conclusions:** Long term results shows that pathological response to neoadjuvant chemotherapy is a predictor of long term survival. Chemotherapy regimens with high response rates merit evaluation in randomized trials to improve outcome in locally advanced breast cancer.

**No conflicts of interest**

**323** Poster

### Safety and efficacy of bi-weekly eribulin therapy in elderly patients with metastatic breast cancer: Exploratory analysis of a Japanese multicenter phase 2 study (JUST-STUDY)

F. Hara[1], T. Nakayama[2], N. Masuda[3], T. Yoshinami[4], K. Watanabe[5], H. Kawaguchi[6], Y. Sagara[7], M. Sato[5], K. Aogi[1], K. Higaki[8], N. Matsunami[9], Y. Hasegawa[10], M. Takahashi[5], M. Mizutani[3], M. Itoh[8], K. Kimura[11], A. Matsukata[7], S. Morita[12], S. Ohtani[8]. [1]*NHO Shikoku Cancer Center, Breast Oncology, Matsuyama, Japan;* [2]*Osaka Medical Center for Cancer and Cardiovascular Diseases, Breast and Endocrine Surgery, Osaka, Japan;* [3]*NHO Osaka National Hospital, Breast Surgery, Osaka, Japan;* [4]*Osaka Medical Center for Cancer and Cardiovascular Diseases, Medical Oncology, Osaka, Japan;* [5]*NHO Hokkaido Cancer Center, Breast Surgery, Sapporo, Japan;* [6]*Matsuyama Red Cross Hospital, Breast Surgery, Matsuyama, Japan;* [7]*Hakuaikai Medical Corp. Sagara Hospital, Breast Surgery, Kagoshima, Japan;* [8]*Hiroshima City Hiroshima Citizens Hospital, Breast Surgery, Hiroshima, Japan;* [9]*Osaka Rosai Hospital, Breast Surgery, Sakai, Japan;* [10]*Hirosaki Municipal Hospital, Breast Surgery, Hirosaki, Japan;* [1]*Osaka Medical college Hospital, Breast Surgery, Takatsuki, Japan;* [12]*Kyoto University Graduate School of Medicine, Biomedical Statistics and Bioinformatics, Kyoto, Japan*

**Background:** Eribulin demonstrated a significant improvement in overall survival (OS) of patients with metastatic breast cancer (MBC) in a pooled analysis of two large randomized open-label Phase III clinical studies. However, eribulin at the standard dose and schedule (1.4 mg/m$^2$ on days 1 and 8 in every 3 weeks) frequently leads to adverse events, especially in elderly patients with comorbidities and increased susceptibility to toxicities. We have shown previously that bi-weekly eribulin therapy is effective and safe for patients unable to continue on the standard schedule of eribulin in a Japanese multicenter phase 2 study (JUST-STUDY) (Yoshinami T, et al. ASCO 2015 Abst. #1026). The aim of this exploratory analysis was to determine whether similar safety and efficacy were observed in elderly patients.

**Methods:** JUST-STUDY (UMIN 00000849) included patients treated with both anthracycline and taxane, and up to three prior chemotherapy regimens for MBC. Eribulin was initially administered at the standard dose and schedule, but the schedule was altered to bi-weekly without dose reduction, if any of administration criteria were not satisfied by day 8 of the 1st cycle or day 1 of the 2nd cycle, or remained unaltered if all administration criteria were met at both time points. The primary endpoints of this exploratory analysis were clinical benefit rate (CBR) of bi-weekly therapy based on RECIST v. 1.1 in the elderly cohort ($\geqslant$65 years) and safety. Secondary endpoints included time to treatment failure (TTF), and OS.

**Results:** Between July 2012 and April 2014, 86 patients were enrolled, and 42 patients were in bi-weekly schedule and 40 were in standard schedule. For this current exploratory analysis, there were 26 patients (31.7%) $\geqslant$65 years of age (12 in the bi-weekly group, 14 in the standard group). Reason of transition to bi-weekly therapy was mainly neutropenia (75.0%). Both cohorts of patients aged <65 years and $\geqslant$65 years had similar characteristics. In the elderly bi-weekly, the CBR was 33.3%, which were comparable to that of <65 years bi-weekly cohort (30.0%) and that in a domestic phase 2 study of eribulin (27.5%). The median TTF in the cohorts of $\geqslant$65 years bi-weekly, <65 years bi-weekly and overall study population were 75.0, 78.0 and 76.0 days, respectively. After transition to bi-weekly treatment, the incidence of Grade 3/4 leukopenia and neutropenia decreased. No severe adverse event was reported in both groups.

**Conclusions:** Bi-weekly eribulin therapy is effective and safe option for patients unable to continue on the standard schedule of eribulin in elderly patients who may be more susceptible to myelosuppression. Further investigation in pharmacogenetics should be warranted to examine the reason why efficacy results were almost similar in both groups, although relative dose intensity was lower in bi-weekly group compared to standard group.

**Conflict of interest:** Advisory Board: Satoshi Morita, Eisai. Corporate-sponsored Research: Fumikata Hara (Eisai, Chugai); Norikazu Masuda (Novartis, Astrazeneca, Pfizer, Lilly, Taiho, GSK). Other Substantive Relationships: Norikazu Masuda, Honoraria (Lilly, Chugai, Eisai, Astrazeneca, Sanofi, Kyowa-Hakko Kirin); Kenjiro Aogi, Honoraria (Astrazeneca, Eisai, ono, Ohtsuka, Sanofi, Daiichi Sankyo, Taiho, Chugai, Nihon Medi-physics, Becton Dickinson and company); Satoshi Morita, Honoraria (Eisai).

**324** Poster

**A patients' preference study on the treatment goals of neoadjuvant therapy of early breast cancer**

M. Thill[1], G. Isbary[2], G. Pisa[3]. [1]*AGAPLESION Markus-Krankenhaus Frankfurt, Klinik für Gynäkologie und Geburtshilfe, Frankfurt, Germany;* [2]*Roche Pharma AG, Roche Pharma AG, Grenzach-Wyhlen, Germany;* [3]*Kantar Health GmbH, Kantar Health GmbH, Munich, Germany*

**Background:** Physicians and authorities regard pathologic complete remission (pCR) as a distinct and relevant endpoint to assess the clinical benefit of a neoadjuvant therapy. We examined which treatment goals of a neoadjuvant therapy patients value as relevant.

**Material and Methods:** Preferences of patients regarding treatment goals of neoadjuvant treatment were assessed quantitatively by means of the Analytical Hierarchy Process (AHP) method. All study participants had been diagnosed with early breast cancer and had completed neoadjuvant treatment with chemotherapy and, in case of a positive HER2-status, with a monoclonal antibody targeted against HER2 6 to 36 months before they were interviewed. The criteria of the hierarchy model had been identified in a prior qualitative survey.

**Results:** Forty-one patients of whom 15 (36.6%) had HER2-positive disease, participated in the quantitative survey. Median age was 50 years (range 29−76). Patients ranked achieving a pCR as the most relevant treatment goal followed by disease-free survival, overall survival and the option of breast-conserving surgery. Avoiding treatment side effects was attributed the lowest significance.

| Treatment goals | Group weight | | | Consistence ratio |
|---|---|---|---|---|
| | Hierarchy level 0 | Hierarchy level 1 | Hierarchy level 2 | |
| **Efficacy** | **0.912** | | | **0.007** |
| Elimination of tumor cells | | 0.316 | | |
| Minimising the risk of tumor recurrence | | 0.256 | | |
| No shortening of lifetime by the disease | | 0.241 | | |
| Option of breast-conserving surgery | | 0.099 | | |
| **Avoiding side effects** | **0.088** | | | **0.005** |
| Side effects resulting in physical stress | | 0.050 | | |
| Fever | | | 0.011 | |
| Diarrhea | | | 0.008 | |
| Nausea | | | 0.015 | |
| Fatigue | | | 0.016 | |
| Side effects resulting in physical change | | 0.038 | | |
| Alopecia | | | 0.022 | |
| Weight gain | | | 0.016 | |

**Conclusion:** Patients regard achieving pCR as a distinct and relevant goal of neoadjuvant therapy and attribute this goal the highest priority.

**No conflicts of interest**

**325** Poster

**Treatment experience of triple-negative breast cancer in Saint-Petersburg City Clinical Oncology Dispensary**

A. Manikhas[1], R. Babeshkin[1], I. Grinev[1], L. Lee[1], A. Shemerovsky[2], G. Manikhas[1], A. Oganesyan[2], V. Skvortsov[2]. [1]*First Pavlov State Medical University of St. Petersburg, Saint-Petersburg City Clinical Oncology Dispensary. Department of mammology, St. Petersburg, Russian Federation;* [2]*Saint-Petersburg City Clinical Oncology Dispensary, oncomammology, Saint-Petersburg, Russian Federation*

**Objective:** development and implementation into City Clinical Oncology Dispensary's clinical practice the common approach to the treatment for triple-negative breast cancer patients.

**Materials and Methods:** 1018 patients are selected for the investigation (age 21 to 88, the average age is 52 years) with histologically verified invasive breast cancer I−IIIA stage triple-negative phenotype (TNBC). This TNBC patients were divided into 3 groups: Group A have been given neoadjuvant systematic therapy − 201 patients (in 19.7% cases). Group B have been given adjuvant treatment − 729 (in 71.6% cases). Group C have not been given any treatment except surgery due to some reasons (health or patient's refusal) − 88 (in 8.6% cases).

All the patients had been treated in City Clinical Oncology Dispensary since 2005 until 2011. They had different types of chemotherapy: CMF, FAC/FEC, taxane-comprising variations (T, TC, AT, TAC), as a surgical treatment either radical mastectomy (Madden) or the radical sectoral breast resection has been applied.

For all chosen groups disease-free survival is evaluated (DFS) with the investigation of minimum of 36 months. The analysis is performed using the international statistic program SPSS 20.0. Discrepancy was taken in account if $p < 0.05$.

**Results:** Recurrence rate (local, regional, farther) of the disease is definitely higher in group C in comparison to group A (35.8% vs 11.9%, $p < 0.05$); coincident data is obtained by analyzing the mortality rate from all causes (27.2% vs 8.5%, $p < 0.05$) and mortality rate from cancer (24.9% vs 6.8%, $p < 0.05$). For group A the DFS rates is significantly higher than for the patients not having taken the neoadjuvant therapy (90.8% vs 74.9%, $p < 0.05$).

**Conclusion:** Complex triple-negative breast cancer medicine therapy has to be started with neoadjuvant chemotherapy followed by the surgical and adjuvant treatment. This scheme has an incredibly important prognostic meaning dealing with TNBC and provides much better indexes in survival overall as well as in the disease-free survival.

**No conflicts of interest**

**326** Poster

**SafeHer Phase III study primary analysis: Safety of subcutaneous trastuzumab plus chemotherapy for early breast cancer**

J. Gligorov[1], B. Ataseven[2], M. Verrill[3], M. De Laurentiis[4], K.H. Jung[5], H.A. Azim[6], N. Al-Sakaff[7], S. Lauer[8], M. Shing[9], X. Pivot[10]. [1]*APHP-Tenon, IUC-UPMC- Sorbonne University, Paris, France;* [2]*Kliniken Essen-Mitte, Department of Obstetrics and Gynaecology, Essen, Germany;* [3]*Northern Centre for Cancer Care, Medical Oncology Department, Newcastle, United Kingdom;* [4]*National Cancer Institute "Fondazione Pascale", Breast Oncology Department, Naples, Italy;* [5]*Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea;* [6]*Cairo University, Clinical Oncology Department, Cairo, Egypt;* [7]*F. Hoffmann-La Roche Ltd, Global Pharma Development, Basel, Switzerland;* [8]*F. Hoffmann-La Roche Ltd, Biostatistics, Basel, Switzerland;* [9]*Genentech Inc., Global Pharma Development, South San Francisco, USA;* [10]*CHU Jean Minjoz, Chemotherapy − Oncology, Besançon, France*

**Background:** SafeHer (NCT01566721) is a Phase III, prospective, two-cohort, non-randomised, multi-centre, multi-national, open-label study, and the largest study (>2500 treated patients [pts]) to investigate 600 mg fixed-dose subcutaneous trastuzumab (Herceptin® SC [H SC]) to date. In SafeHer, 600 mg H SC was administered every 3 weeks (q3w) for 18 cycles as adjuvant therapy via hand-held syringe (Cohort A) or single-use injection device (Cohort B) +/− chemotherapy (CT) for HER2-positive early breast cancer (EBC). We report the primary safety analysis, which was planned to take place when all pts had received 18 H SC cycles and had completed safety follow-up (28 days after the last H SC cycle + 5-day window).

**Materials and Methods:** Key eligibility criteria were HER2-positive, stage I−IIIC EBC, baseline left ventricular ejection fraction $\geqslant$55% and no prior anti-HER2 therapy. The choice of concurrent or sequential CT partner for H SC was at the investigators' discretion, and some pts (limited to $\leqslant$10%) received H SC without any CT (to be reported later). Hormonal therapy/radiotherapy could be administered per local guidelines. Adverse events (AEs) and serious AEs (SAEs) were recorded/graded according to NCI-CTCAE 4.0; congestive heart failure (CHF), according to NCI-CTCAE 4.0/New York Heart Association functional classification. Laboratory parameters, vital signs and electrocardiogram data were also collected. Results are descriptive.

**Results:** N = 2577 pts were enrolled; the safety population is 2573 pts (four received no treatment), 2322 (90%) of whom completed treatment and 251 (10%) discontinued treatment. Overall, 1537 pts (60%) were treated with H SC + concurrent CT and 804 (31%) with H SC + sequential CT. The safety overview for the treatment period by cohort is shown in the table. As expected, AE rates varied according to the timing of CT.

**Conclusions:** SafeHer is the largest H SC study to date, with >2570 pts treated with H SC for HER2-positive EBC. This analysis identified no new safety signals and the H SC adjuvant profile is consistent with the known H adjuvant profile. SafeHer confirms the safety and tolerability of H SC 600 mg fixed dose q3w as adjuvant therapy with concurrent/sequential CT for HER2-positive EBC.

**Conflict of interest:** Ownership: NA-S, Roche shares. Advisory Board: JG, Roche; BA, Roche; MV: Fees from Roche; MDL, Novartis, Roche, Celgene, AstraZeneca, Genomic Health; HAA, Roche; XP, Roche, Novartis, Lilly, Pierre Fabre, Amgen, TEVA, Eisai. Corporate-sponsored Research: JG, Roche; BA, Roche; MV, Institutional funding from Roche; KHJ, Eisai Korea; HAA, Roche. Other Substantive Relationships: MV, Fees from speaking for Roche; NA-S, Roche employee; SL, Roche contractor; MS, Genentech employee.

Table (abstract 326): Safety overview for H SC + CT treatment period: first dose until 28 days after the last H SC dose (+ 5-day window)

| Adverse event(s) | Number of patients (%) | | | |
|---|---|---|---|---|
| | Cohort A | | Cohort B | |
| | Concurrent CT (n = 1084) | Sequential CT (n = 604) | Concurrent CT (n = 453) | Sequential CT (n = 200) |
| Any grade AE | 1015 (94) | 477 (79) | 424 (94) | 157 (79) |
| SAE | 179 (17) | 42 (7) | 73 (16) | 10 (5) |
| NCI-CTCAE ⩾grade 3 | 348 (32) | 66 (11) | 122 (27) | 22 (11) |
| NCI-CTCAE ⩾grade 3 of interest | | | | |
| Blood/lymphatic | 137 (13) | 7 (1) | 39 (9) | 2 (1) |
| Gastrointestinal | 51 (5) | 5 (1) | 16 (4) | 2 (1) |
| Infections | 44 (4) | 7 (1) | 14 (3) | 4 (2) |
| General disorders and administration site conditions | 31 (3) | 3 (<1) | 18 (4) | 2 (1) |
| Vascular | 30 (3) | 9 (1) | 15 (3) | 5 (3) |
| Respiratory | 12 (1) | 3 (<1) | 7 (2) | 2 (1) |
| Cardiac | 9 (1) | 10 (2) | 3 (1) | 0 |
| CHF | 1 (<1) | 6 (1) | 1 (<1) | 0 |

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**Longitudinal changes in the impact of the gene-expression profiles on the administration of adjuvant chemotherapy in early breast cancer patients − a nationwide study**

A. Kuijer[1], C. Drukker[2], S.G. Elias[3], C.H. Smorenburg[4], E.J.T. Rutgers[5], S. Siesling[6], T. Van Dalen[1]. *[1]Diakonessenhuis, Department of Surgery, Utrecht, Netherlands; [2]Albert Schweitzer Hospital, Department of Surgery, Dordrecht, Netherlands; [3]University Medical Center Utrecht, Department of Epidemiology- Julius Center For Health Sciences and Primary Care, Utrecht, Netherlands; [4]Antoni Van Leeuwenhoek Hospital − Netherlands Cancer Institute, Department of Medical Oncology, Amsterdam, Netherlands; [5]Antoni Van Leeuwenhoek Hospital − Netherlands Cancer Institute, Department of Surgery, Amsterdam, Netherlands; [6]Netherlands Comprehensive Cancer Organization Iknl, Department of Research, Utrecht, Netherlands*

**Purpose:** Ten years ago gene-expression profiles (GEP) were introduced to aid decision-making regarding administration of adjuvant chemotherapy (CT) in breast cancer patients. During this period national guideline adjustments led to a gradual expansion of the indication area for adjuvant CT. The aim of the present nation-wide study is to document the evolution of the proportion of patients receiving adjuvant CT in relation to the use of GEPs in patients in whom national guidelines formulated a new indication for CT over time.

**Methods:** Data patient-, tumor-, treatment and genomic profiling characteristics of all primary, unilateral, early breast cancer patients diagnosed between 2004–2006 (cohort I) and 2012–2014 (cohort II) were obtained from the Netherlands Cancer Registry (NCR). In accordance with the Dutch guideline a subgroup was identified with a newly formulated indication for CT over time. The administration of CT in relation to GEP use was assessed for both time periods.

Table 1. 70-gene signature (70-GS) and 21-recurrence score (21-RS) test results and the administration of adjuvant chemotherapy stratified for the two time periods

| | Cohort I: 2004–2006 | | Cohort II: 2012–2014 | |
|---|---|---|---|---|
| | n | CT (%) | n | CT (%) |
| **70-gene signature** | | | | |
| All [a] | 103 | 21.00% | 669 | 28.00% |
| Low risk | 69 | 1.00% | 466 | 6.00% |
| High risk | 34 | 62.00% | 184 | 83.00% |
| Unknown | – | – | 19 | 42.00% |
| Adherence to test result (CT) | | 85.60% | | 90.80% |
| **21-recurrence score** | | | | |
| All [a] | | n.a. | 11 | 18% |
| Low risk | | | 6 | 0% |
| Intermediate | | | 2 | 0% |
| High risk | | | 3 | 67% |
| Adherence to test result (CT) | | | | 88.80% |

[a] Patients with a new indication for adjuvant CT or ET according to the national guideline of 2012 who were eligible for receiving a GEP in both time periods (T1−4cN0M0 disease, <61 years of age) and received the 70-GS or 21-RS. Adherence to test result = proportion of patients with a low risk result and omission of CT or a high risk result and administration of CT.

**Results:** 56 669 patients were identified of whom 7208 (14%) were in the group in whom CT was not advised in the first period but indicated in the second. Overall, 6% of these patients in cohort I received CT compared to 34% in cohort II ($p < 0.001$). In patients <61 years with ER+ disease, 8% of patients in cohort I and 52% in cohort II received adjuvant CT without using a GEP (p 0.000) compared to 21% of patients in cohort I and 28% in cohort II who did receive a GEP (p 0.177). In the latter group the majority of patients was assigned to a low genomic risk profile (67% in cohort I and 69% in cohort II) and high adherence rates to the GEP test result were observed (85% vs. 91% for the respective periods, Table 1).

**Conclusion:** In patients with a guideline directed newly formulated CT indication approximately half of the patients received CT when the guideline was in effect. Use of GEPs was associated with a consistent proportion of patients receiving CT over time.

**No conflicts of interest**

**328** Poster

**Impact of the 70-gene signature on adjuvant systemic therapy decisions in Dutch early breast cancer patients: Preliminary results of a prospective multicentre observational study**

A. Kuijer[1], M. Straver[1], S.G. Elias[2], C. Smorenburg[3], A.C.M. Van Bommel[4], S. Linn[3], J. Wesseling[5], S. Siesling[6], E.J.T. Rutgers[7], T. Van Dalen[1]. *[1]Diakonessenhuis, Department of Surgery, Utrecht, Netherlands; [2]University Medical Center Utrecht, Department of Epidemiology- Julius Center For Health Sciences and Primary Care, Utrecht, Netherlands; [3]Netherlands Cancer Institute, Department of Medical Oncology, Amsterdam, Netherlands; [4]Leiden University Medical Center, Department of Surgery, Leiden, Netherlands; [5]Netherlands Cancer Institute, Department of Pathology, Amsterdam, Netherlands; [6]Netherlands Comprehensive Cancer Organisation Iknl, Department of Research, Utrecht, Netherlands; [7]Netherlands Cancer Institute, Department of Surgery, Amsterdam, Netherlands*

**Background:** gene-expression profiles, such as the 70-gene signature (70-GS), were developed for optimizing outcome prediction in early breast cancer patients and are increasingly used as an adjunct to conventional clinic-pathological prognostic factors to guide adjuvant chemotherapy (CT) decisions. The Dutch national guideline suggest the use of a validated gene-expression profiles in early stage breast cancer patients suffering from an oestrogen receptor (ER)+ invasive ductal carcinoma in whom controversy exists, based on conventional prognostic factors, regarding the benefit of adjuvant CT.

**Patients and Methods:** In this prospective observational multicentre study the impact of the 70-GS on adjuvant CT decisions in Dutch early stage breast cancer ER+ patients is assessed. Patients within the guideline-intended indication area who received the 70-GS were included. Adjuvant CT advice was stated by the treating physician before and after obtaining the 70-GS result.

**Results:** Until date 450 patients, treated in 31 hospitals, were enrolled. The 70-GS influenced the treatment decision in 307 (68%) of the patients. In 92 patients adjuvant CT would initially be omitted, in 31 (34%) of these patients adjuvant CT was nevertheless advised after obtaining the 70-GS result. In 185 patients adjuvant CT would have been administered without knowledge of the 70-GS, in 112 (61%) of these patients adjuvant CT could be withheld after obtaining the 70-GS result. In 172 patients the treating physician stated to be unsure about the CT decision. In all

three categories the 70-GS assigned the majority of patients to the low-risk category (Table 1). In 95% of patients the treating physician adhered to the 70-GS result and in 106 (62%) adjuvant CT was omitted.

| CT advice | 70-GS result | | Final CT advice after 70-GS | |
|---|---|---|---|---|
| prior to 70-GS | High-risk | Low-risk | CT | no CT |
| No CT | 37 (45%) | 55 (55%) | 31 (38%) | 61 (62%) |
| CT | 79 (43%) | 106 (57%) | 73 (39%) | 112 (61%) |
| Unsure/depends on the 70-GS | 67 (39%) | 106 (61%) | 66 (38%) | 106 (62%) |

**Conclusion:** use of the 70-GS in Dutch ER+ early breast cancer patients influenced CT treatment decision in 68% of the patients in whom based on conventional prognostic factors controversy exists regarding the benefit of adjuvant CT. 70-GS use was associated with high adherence rates to the test result and led to a decreased administration of adjuvant CT.

**No conflicts of interest**

**329** Poster

**Dexrazoxane added to adjuvant doxorubicin-based chemotherapy in breast cancer: A retrospective cohort study with comparative analysis of toxicity and survival**

E. Tahover[1], A. Segal[1], R. Isacson[1], O. Rosengarten[1], T. Grenader[1], M. Gips[1], N. Cherny[1], N. Heching[1], T. Tichler[1], L. Mesika[1], R. Catane[1], A. Gabizon[1]. *[1]Shaare Zedek Medical Center, Oncology, Jerusalem, Israel*

**Background:** Dexrazoxane is a cardioprotective agent for patients receiving doxorubicin who are at risk for cardiotoxicity. Concerns have been raised regarding the use of dexrazoxane, particularly in adjuvant therapy, because of the risk of interference with the antitumor effect of doxorubicin. We analyzed retrospectively a cohort of our institute database to assess the effect of dexrazoxane on myelosuppression in breast cancer patients receiving doxorubicin-based adjuvant therapy. Secondary objectives were febrile neutropenia, dose-schedule modifications, cardiac events, and overall survival.

**Patients and Methods:** 822 female patients receiving adjuvant doxorubicin and cyclophosphamide for breast cancer were included. 104 of them also received dexrazoxane. Blood counts were analyzed up to 30 days after last doxorubicin dose. Cardiac events (cardiac-related hospitalization, abnormal ECHO or MUGA scan) were collected from first doxorubicin dose to data cut-off date. Survival was defined as the time from first course of adjuvant chemotherapy to date of death from any cause.

**Results:** Median follow-up was 5.3 years for patients with dexrazoxane and 6.2 years for patients without dexrazoxane. Patients who received dexrazoxane were older (median, 59 vs 52 years), and more likely to receive dose-dense therapy (73% vs 59%) and adjuvant trastuzumab (29% vs 15%).

Dexrazoxane caused a significantly higher rate of hematological side effects: more patients developed neutropenia (45% vs. 31%, $p = 0.003$), anemia (86% vs. 73%, $p = 0.005$) and thrombocytopenia (37% vs. 22%, $p = 0.001$). Dexrazoxane also caused more febrile neutropenia hospitalizations (20% vs. 10% $p = 0.001$) and dose reductions (22% vs. 8% $p < 0.001$), but the frequency of dose delays was not different. The rates of neutropenia were significantly higher in the dose-dense therapy subgroup of patients treated with dexrazoxane (30% vs 16%, $p < 0.001$, for grades 3–4), but not in patients receiving treatment every 21 days.

The incidence of cardiac events was the same with and without dexrazoxane, and with or without trastuzumab.

There was a non-significant difference in survival in favor of the dexrazoxane group (6.5% vs 11.8%) and an older median age of death in the dexrazoxane group (65 vs 60 years). Most of the deaths (84%) occurred in patients who developed metastatic disease.

**Conclusion:** Adding dexrazoxane to doxorubicin causes higher rates of bone marrow suppression, with more febrile neutropenia and more dose reductions. There was no difference in the incidence of cardiac events, yet a cardioprotective effect cannot be ruled out given the design and limited power of our study. Dexrazoxane had no detrimental effect on survival, despite higher hematological toxicity, older median age, and a higher fraction of HER2-positive disease in the dexrazoxane group.

**No conflicts of interest**

**330** Poster

**Outcome of letrozole therapy after discontinuation of anastrozole due to intolerance in patients with breast cancer**

S. Dubey[1], Z. Win[2], K. Das[3]. *[1]Derriford Hospital, Oncology Department, Plymouth, United Kingdom; [2]Newcastle Freeman Hospital, Clinical Oncology, Newcastle, United Kingdom; [3]University Hospitals of Leicester, Department of Oncology, Leicester, United Kingdom*

**Background:** Non-steroidal aromatase inhibitors(AI) are standard of care in the treatment of postmenopausal women with hormone receptor positive breast cancer. However significant side-effects occur in almost 20–35% patients and leading to discontinuation of therapy in almost 11% patients. In clinical practice either switching to another AI or tamoxifen is usually considered in such situation. This study evaluated if patients who were intolerant of anastrozole would be able to continue AI therapy after switch to letrozole.

**Methods:** This was retrospective study looking at tolerance and outcome of letrozole use in patients of breast cancer who discontinued anastrozole due to side-effects. We reviewed hospital notes of patients of breast cancer who attended oncology follow up clinic at Derriford Hospital, Plymouth in the year 2013 and have had switch of AIs in the past due to side-effects. The cut off date for follow up analysis of data was August 2015.

**Results:** This study looked at the outcome of AI switch from anastrozole to letrozole in 32 patients. Of these, 31 patients were on adjuvant and 1 patient was on metastatic breast cancer treatment with anastrozole. The median duration of follow up of patients was 48.5 months (range 26–60 months).

The main side-effects leading to anastrozole discontinuation were musculoskeletal (63%), vasomotor (13%), gastrointestinal (10.5%) and neurological (10.5%).

Median duration of anastrozole in all patients before discontinuation was 7 months (range 2–25 months). Out of 32 patients who switched to letrozole after early discontinuation of anastrozole, 17 patients (53.1%) continued with letrozole therapy successfully with improvement in symptoms whereas 15 patients (46.9%) had to stop it due to intolerance and had further treatment with either exemestane or tamoxifen.

Among all patients, the median duration of letrozole after the switch was 24 months (range 2–54 months). The median duration of letrozole in 17 patients who successfully continued with letrozole was 36 months (range 23–54 months) as compared to 7 months (range 2–20 months) for 15 patients who had to discontinue letrozole subsequently due to intolerance. There was no significant difference between the prior anastrozole therapy duration among patients who tolerated letrozole as compared to those who did not with a median time of 8 months and 7 months, respectively.

**Conclusion:** This study suggests that more than half the patients who are intolerant of and have discontinued anastrozole due to side-effects are likely to continue with AI therapy when switched to letrozole.

**No conflicts of interest**

**331** Poster

**Prognostic value of VEGF-A in advanced breast cancer patients receiving bevacizumab and paclitaxel**

Y. Nishiyama[1], R. Nishimura[1], T. Osako[1], M. Fujisue[1], N. Arima[1], Y. Okumura[2]. *[1]Kumamoto Shinto General Hospital, Department of Breast Oncology, Kumamoto, Japan; [2]Kumamoto City Hospital, Department of Breast and Endocrine Surgery, Kumamoto, Japan*

**Background:** Vascular endothelial growth factor (VEGF), especially VEGF-A, is an important therapeutic target of breast cancer treatment using bevacizumab in randomized clinical trials. The addition of bevacizumab to chemotherapy improves progression-free survival (PFS) in metastatic breast cancer. However, the extent to which individual patients benefit from bevacizumab is still unclear. In this study, we investigated the efficacy of bevacizumab by assessing the plasma level of VEGF-A before and during treatment.

**Material and Methods:** We analysed 29 patients with a median age of 54 years (range, 36–81 years), who received bevacizumab in combination with paclitaxel. Out of these patients, there were 7 stage IV cases, 24 recurrent cases, and 2 locally advanced cases. In addition, there were cases with the following subtypes; luminal A (2 cases), luminal B (18 cases), HER2 enriched (1 case), and triple negative (8 cases). Patients received 0–5 regimens of chemotherapy prior to bevacizumab treatment. For the survival analyses, overall survival (OS) and PFS was evaluated in all the cases.

**Results:** The median PFS and OS after administration of bevacizumab were 12.3 months and 27.9 months, respectively. Moreover, the objective response rate was 44.8% (13/29 cases) and the clinical benefit rate was 55.2% (13/29 cases).

The VEGF-A plasma level was measured before administration of bevacizumab and paclitaxel and after the completion of two cycles of treatment. We dichotomized the plasma levels using the median pre-treatment VEGF-A level of 110 pg/ml. There was no significant difference in the response rate between the higher level group and the lower level group ($p = 0.198$). There was no difference in OS between the 2 groups. On the other hand, the changes in plasma level after treatment significantly correlated with the objective response rates; a significant decrease was seen in the PR cases ($p = 0.040$).

**Conclusion:** Bevacizumab targets VEGF-A rather than the tumor itself. The objective response rate showed that half of the patients responded to this treatment. Therefore, the sequential measurement of VEGF-A plasma level may be an important predictive factor in the treatment of breast cancer.

**No conflicts of interest**

**332** Poster

**Prospective observational cohort study of bevacizumab combined with paclitaxel as the first- or second-line chemotherapy for locally advanced or metastatic breast cancer (Study JBCRG-C05: B-SHARE)**

N. Kondo[1], Y. Yamamoto[2], H. Yamashiro[3], M. Kashiwaba[4], R. Nakamura[5], M. Takahashi[6], U. Toh[7], K. Tsugawa[8], K. Narui[9], K. Tamaki[10], T. Yoshinami[11], S. Ohtani[12], Y. Kai[13], T. Takano[14], Y. Yanagita[15], S. Morita[16], M. Toi[17], S. Ohno[18]. *[1]Nagoya City University Hospital, Department of Breast Surgery, Nagoya, Japan; [2]Graduate School of Medical Sciences- Kumamoto University, Department of Breast and Endocrine Surgery, Kumamoto, Japan; [3]Tenri Hospital, Department of Breast Surgery, Nara, Japan; [4]Iwate Medical University, Department of Surgery, Iwate, Japan; [5]Chiba Cancer Center, Department of Breast Surgery, Chiba, Japan; [6]NHO Hokkaido Cancer Center, Department of Breast Surgery, Sapporo, Japan; [7]Kurume University Hospital, Department of Surgery, Kurume- Fukuoka, Japan; [8]St. Marianna University School of Medicine Hospital, Division of Breast and Endocrine Surgery Department of Surgery, Kawasaki, Japan; [9]Yokohama City University Medical Center, Department of Breast and Thyroid Surgery, Yokohama, Japan; [10]Nahanishi Clinic Okinawa, Department of Breast Surgery, Naha, Japan; [1]Osaka Medical Center for Cancer and Cardiovascular Diseases, Department of Clinical Oncology, Osaka, Japan; [12]Hiroshima City Hiroshima Citizens Hospital, Department of Breast Surgery, Hiroshima, Japan; [13]Ueo Breast Cancer Hospital, Department of Surgery, Oita, Japan; [14]Toranomon Hospital, Department of Medical Oncology, Tokyo, Japan; [15]Gunma Prefectural Cancer Center, Department of Breast Oncology, Ota, Japan; [16]Kyoto University Graduate School of Medicine, Department of Biomedical Statistics and Bioinformatics, Kyoto, Japan; [17]Kyoto University Graduate School of Medicine, Breast Surgery, Kyoto, Japan; [18]The Cancer Institute Hospital of JFCR, Center of Breast Oncology, Tokyo, Japan*

**Background:** Metaanalyes of phase III trials of metastatic breast cancer showed that bevacizumab (Bmab) in combination with chemotherapy improves progression-free survival and overall response rate, but not overall survival compared with chemotherapy alone. Combining Bmab with paclitaxel (PTX) is one of the optional treatments for locally advanced or metastatic breast cancer in Japan. The Japan Breast Cancer Research Group (JBCRG) conducted a prospective observational multi-institutional cohort study, B-SHARE, to assess the efficacy and safety of first- and second line-Bmab combined with PTX for HER2-negative locally advanced or metastatic breast cancer in real-world routine practice.

**Patients and Methods:** The B-SHARE study enrolled 767 patients with HER2-negative locally advanced or metastatic breast cancer receiving Bmab in combination with PTX as the first- or second-line chemotherapy at 155 institutes in Japan from November 2012 to October 2014. Patients were treated with 28 day cycles of 10 mg/kg Bmab on days 1 and 15, and 90 mg/m$^2$ PTX on days 1, 8 and 15, followed by 1 week of rest until progression or unacceptable toxicity. We conducted the interim safety analysis of 537 patients (70%) who had terminated the Bmab combination therapy by the end of September 2015.

**Results:** Among the 537 patients in this interim analysis, 373 patients (69.5%) and 164 patients (30.5%) had Hormone receptor (HR)-positive and HR-negative (triple-negative) subtype, respectively. The median follow-up of the 537 patients was 6 months. The median age was 57.0 years and 91.5% of the patients had ECOG PS of 0 or 1. The median duration of Bmab + PTX therapy was 4.6 months. The median relative dose intensity of Bmab and PTX were 100% and 88.9%, respectively. The reasons for discontinuation of Bmab and PTX were disease progression (48.6% and 49.3%, respectively) and adverse events (AEs) (27.9% and 29.8%, respectively). Severe AEs were reported in 47 (8.8%) cases, and included 6 (1.1%) treatment-related deaths [3 liver dysfunction, 1 gastrointestinal (GI) perforation, 1 GI bleeding, 1 acute gastroenteritis]. Reported grade >3 AEs related to Bmab + PTX were hypertension (28.1%), neutropenia (25.9%), peripheral sensory neuropathy (6.5%), proteinuria (3.2%), congestive heart failure (CHF) (0.6%), GI perforation (0.6%) and bleeding (0.2%). None of the patients suffered thromboembolism and wound-healing complication of Grade >3.

**Conclusions:** Exposure to Bmab and PTX combination as the first- and second-line chemotherapy in clinical practice seems to be short compared with the results of randomized trials. The incidence of Bmab-related AEs of Grade >3 was consistent with the results of randomized trials, excluding thromboembolism and wound-healing complication. This combination therapy is a feasible option.

**No conflicts of interest**

**333** Poster

**The efficacy and safety of 4 cycles of tri-weekly nanoparticle albumin-bound paclitaxel (nab-PTX) followed by 4 cycles of FEC (5-fluorouracil, epirubicin, cyclophosphamide) as neoadjuvant chemotherapy for patients with HER2-negative primary breast cancer − A multicenter phase II study (KBCSG−TR1213)**

K. Tanaka[1], N. Masuda[1], N. Matsunami[2], T. Takashima[3], T. Morimoto[4], M. Mizutani[1], K. Yoshidome[5], H. Yasojima[1], H. Morishima[2], K. Hata[6], E. Shiba[7], S. Tominaga[8], T. Nishi[9], S. Kamigaki[10], T. Yoshinami[11], S. Munakata[12], M. Takeda[13], M. Tsujimoto[14], T. Nakayama[15]. *[1]National Hospital Organization- Osaka Natioal Hospital, Surgery- Breat Oncology, Osaka, Japan; [2]Osaka Rosai Hospital, Breast Surgery, Sakai, Japan; [3]Osaka City University Graduate School of Medicine, Surgical Oncology, Osaka, Japan; [4]Yao Municipal Hospital, Breast Surgery, Yao, Japan; [5]Osaka Police Hospital, Breast Surgery, Osaka, Japan; [6]Kishiwada City Hospital, Surgery- Breast Oncology, Kishiwada, Japan; [7]Osaka Breast Clinic, Breast Surgery, Osaka, Japan; [8]Higashiosaka City General Hospital, Breast Surgery, Higashiosaka, Japan; [9]Kaizuka City Hospital, Breast surgery, Breast surgery, Japan; [10]Sakai City Medical Center, Surgery, Sakai, Japan; [1]Osaka Medical Center for Cancer and Cardiovascular Diseases, Clinical Oncology, Osaka, Japan; [12]Sakai City Medical Center, Pathology, Sakai, Japan; [13]Yao Municipal Hospital, Surgical pathology, Yao, Japan; [14]Osaka Police Hospital, Diagnostic pathology, Osaka, Japan; [15]Osaka Medical Center for Cancer and Cardiovascular Diseases, Breast and Endocrine Surgery, Osaka, Japan*

**Background:** The standard adjuvant systemic chemotherapy to improve the survival of HER2-negative breast cancer (BC) patients (pts) is an anthracycline and taxane sequential combination regimen. Nanoparticle albumin-bound paclitaxel (nab-PTX) has been developed under the concept of improved drug delivery. There are some reports that the efficacy of nab-PTX is equals or more excellent compared with the other taxane among the patients with metastatic lesions. We have conducted a multicenter phase II study to evaluate the efficacy and safety of nab-PTX by setting neoadjuvant chemotherapy (NAC) instead of docetaxel or weekly paclitaxel (UMIN000008085).

**Material and Methods:** Women under 65 years of age with primary HER2-negative BC (cT1c−3cN0−1M0) were enrolled. Before surgery, pts received four cycles of nab-PTX (260 mg/m$^2$ q3w) followed by four cycles of FEC (5-fluorouracil; 500 mg/m$^2$, epirubicin 100 mg/m$^2$ and cyclophosphamide 500 mg/m$^2$ q3w). The primary endpoint was pathological complete response (CpCR; ypT0-is) rate, assessed by a central review committee. Secondary endpoints included clinical response, CpCRypN0, quasi-pathological complete response (QpCR) rates and safety. The study was designed to detect the expected pCR rate of 30%, with a threshold of >13.3% in at least 60 pts.

**Results:** From June 2012 to May 2013, 64 patients were enrolled. They had a median age of 49 [32−66] years, an estrogen receptor (ER) positive rate of 62.5% (40/64), and 60.9% (39/64) were premenopausal. Four pts discontinued nab-PTX due to progressive disease, and in four pts the nab-PTX dose was reduced to 220 mg/m$^2$ due to adverse events (AE). Among the 64 pts assessable for pathologic response, 20.3% (95% confidence interval (CI), 10.2–29.8%) experienced CpCR and 12.5% (95% CI, 4.4–20.6%) had a near pathological complete response (few remaining cancer cells), resulting in a QpCR of 32.8% (95% CI, 23.4–42.2%). The rate of CpCRypN0 rate was 17.2%. The CpCR rate was 17.5% (95% CI, 5.7–29.3%) in pts with ER(+) and 25% (95% CI, 7.7–42.3%) in pts with ER(−), respectively. Clinical response rate following the initial nab-PTX regimen was 46.9%. The overall clinical response rate after completion of FEC was 73.4% (47/64); 82.5% (33/40) in pts with ER(+) and 58.3% (14/24) in pts with ER(−). Breast-conserving surgery was performed in 46.8% of pts. AE exceeding grade 3 were observed in 39 pts (60.9%); and the most common AE were neutropenia (43.8%), febrile neutropenia (14.1%), alanine amino transferase (ALT) elevation (9.4%), fatigue (7.8%), and nausea (6.3%).

**Conclusion:** In HER2-negative pts, NAC with nab-PTX followed by FEC was basically consistent with the results of other preceding regimens using taxane and anthracycline-based drugs. The AE were tolerable. Further studies of this regimen in larger numbers of pts are ongoing (KBCSG-TR1315).

**Conflict of interest:** Other Substantive Relationships: Chugai Pharmaceutical Co., Ltd., AstraZeneca plc, Eisai Co., Ltd., Kyowa Hakko Kirin Co., Ltd., Novartis Pharma.

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**The role of cyclin D1 in planning of endocrine therapy for women of postmenopausal age with breast cancer (5 years follow-up)**

A. Manikhas[1], V. Skvortsov[1], G. Manikhas[1], R. Babeshkin[2], I. Grinev[2], A. Shemerovsky[1]. [1]*City Clinical Oncology Dispensary, Department No.1, St. Petersburg, Russian Federation;* [2]*Pavlov First Saint Petersburg State Medical University, Department of Oncology, St. Petersburg, Russian Federation*

**Background:** Tamoxifen is the primary drug in breast cancer endocrine therapy. The research of biomarkers is one of the most actual problems in prognosis of tamoxifen adjuvant therapy. The most perspective biomarker is cyclin D1. It plays a central role in cell cycle regulation, modulates the estrogen receptors activity and influence on the effectiveness of treatment with antiestrogens and aromatase inhibitors. The objective of our work was to evaluate the effectiveness of tamoxifen in adjuvant therapy of hormone-receptor-positive breast cancer in women of postmenopausal age with cyclin D1 expression and to compare the effectiveness of tamoxifen and anastrozole in adjuvant therapy of women with cyclin D1 expression more than 30%.

**Material and Methods:** We have researched retrospective group of 140 patients with hormone-receptor-positive T1−2N0−1M0 breast cancer that have been on regular medical check-up for a period of 5 years or who had previously undergone treatment. On the basis of archive histological material we have revealed cyclin D1 in tumor cells. To compare the effectiveness of tamoxifen and anastrozole we have additionally researched another group of 50 patients with breast cancer and cyclin D1 expression more than 30% that had been on regular anastrozole treatment for 5 years.

**Results:** Patients (n = 62) with lack of cyclin D1 expression or with its low quantitative value (according to our data less than 30%) had neoplastic process progression in 3 (4.8%) cases throughout the 5 years of tamoxifen adjuvant therapy. On the contrary, women (n = 78) with moderate and high cyclin D1 expression (more than 30%) had a relapse of tumor in 63 (81%) cases. Thus, according to the 5 years follow-up period distant metastasis is prognosed to be observed in patients with moderate and high cyclin D1 expression ($p < 0.001$).

The average period of tumor relapse and progression in patients with cyclin D1-positive breast cancer was 20 months. In 5 years follow-up period patients (n = 50) who had cyclin expression more than 30% and had been receiving anastrozole in adjuvant regime, tumor relapse and progression was observed in 4 (8%) cases.

**Conclusion:** Women with hormone-receptor-positive cyclin D1-negative breast cancer on early stages have more prolonged non-relapse period during the tamoxifen adjuvant therapy. Patients with cyclin D1-positive breast cancer are less sensitive to tamoxifen and in adjuvant regime should receive therapy with other effective equivalent drugs (aromatase inhibitors). It is necessary to continue the research of cyclin D1 as biomarker that could influence on the choice of treatment between tamoxifen and aromatase inhibitors.

**No conflicts of interest**

**335** Poster

**Use of neoadjuvant chemotherapy in locally advanced breast cancer in the Netherlands**

P.E.R. Spronk[1], A.C.M. Van Bommel[1], S. Siesling[2,3], M.J.T. Baas-Vrancken Peeters[4], C.H. Smorenburg[5]. [1]*Leiden University Medical Centre, Surgery, Leiden, Netherlands;* [2]*Comprehensive Cancer Centre the Netherlands IKNL, Epidemiology, Utrecht, Netherlands;* [3]*University of Twente, MIRA Biomedical science and Technical Medicine, Twente, Netherlands;* [4]*Netherlands Cancer Institute/Antoni van Leeuwenhoek, Surgery, Amsterdam, Netherlands;* [5]*Netherlands Cancer Institute/Antoni van Leeuwenhoek, Medical Oncology, Amsterdam, Netherlands*

**Background:** Neoadjuvant chemotherapy (NAC) is the treatment of choice for patients with locally advanced breast cancer (LABC). The aim of this study is to examine the use of NAC for LABC in all Dutch hospitals participating in breast cancer care and to assess what patient, tumour and hospital characteristics influence its use.

**Material and Methods:** Data were derived from the national multidisciplinary NABON Breast Cancer Audit (NBCA), regarding all women aged >18 years and newly diagnosed with LABC from January 2011 to September 2013. Multivariable logistic regression was used to assess the association between the use of NAC and patient, tumour and hospital related factors.

**Results:** Of 1419 woman diagnosed with LABC, 70% were treated with NAC. This percentage varied from 12.5% to 90% between hospitals and did not increase over time. Factors associated with the use of NAC included young age, large tumour size, more advanced nodal disease and triple negative or hormone-receptor negative tumours. Also patients treated in hospitals with a multidisciplinary preoperative work-up and participation in neoadjuvant studies were more likely to receive NAC. However, considerable variation between hospitals remained after case-mix correction.

Table 1. Multivariable odds ratios (ORs) for receipt of NAC among 1419 stage III patients 2011 through 2013

| | OR | 95% CI | P-value |
|---|---|---|---|
| Age | | | 0.000 |
| <40 | 0.92 | 0.44−1.94 | |
| 40−49 | ref. | | |
| 50−59 | 0.67 | 0.41−1.09 | |
| 60−69 | 0.51 | 0.31−0.84 | |
| ⩾70 | 0.03 | 0.02−0.05 | |
| Histologic subtype | | | 0.145 |
| ductal | ref. | | |
| lobular | 0.58 | 0.34−0.98 | |
| both | 1.19 | 0.33−4.29 | |
| other | 0.55 | 0.20−1.53 | |
| Multifocal | | | 0.997 |
| yes | ref. | | |
| no | 1.00 | 0.67−1.50 | |
| Tumor size | | | 0.000 |
| ⩽5 cm | ref. | | |
| >5 cm | 5.68 | 2.34−13.79 | |
| Clinical nodal status | | | 0.000 |
| cNx/N0 | ref. | | |
| cN1 | 1.32 | 0.86−2.04 | |
| cN2 | 2.93 | 1.18−7.29 | |
| cN3 | 10.28 | 4.18−25.25 | |
| Receptor status | | | 0.000 |
| Triple negative | 2.35 | 1.40−3.93 | |
| HR−, Her2+ | 3.37 | 1.67−6.78 | |
| HR+, Her2+ | 0.91 | 0.51−1.60 | |
| HR+, Her2− | ref. | | |
| Type of surgery | | | 0.026 |
| Breast conservation therapy | 2.05 | 1.09−3.84 | |
| Mastectomy | ref. | | |
| Multidisciplinary team | | | 0.021 |
| Yes | 1.98 | 1.11−3.53 | |
| No | ref. | | |
| Type of hospital | | | 0.569 |
| General | 1.20 | 0.73−1.98 | |
| Top clinical | ref. | | |
| Academic | 1.50 | 0.64−3.47 | |
| Hospital surgical volume | | | 0.729 |
| <100 | 1.19 | 0.69−2.06 | |
| 100–200 | ref. | | |
| >200 | 1.27 | 0.70−2.31 | |
| Study participation | | | 0.005 |
| Yes | 1.80 | 1.20−2.70 | |
| No | ref. | | |

**Conclusions:** There is considerable variation in the use of NAC for LABC in the Netherlands. Although various patient, tumor and institutional factors are associated with the use of NAC in LABC, these can only explain part of the observed variation in treatment patterns between hospitals.

**No conflicts of interest**

**336** Poster

**Do elderly patients complete their planned adjuvant breast cancer chemotherapy? A comparison of patients aged 60−64, 65−69 years and over 70 years**

P.V. Joshi[1], F.E. Chamberlain[2], J.W. King[2]. [1]*Mount Vernon Cancer Centre, Breast Oncology Unit, London, United Kingdom;* [2]*Royal Free Hospital, Oncology, London, United Kingdom*

**Background:** Breast cancer prevalence increases with age, but most adjuvant trials exclude older patients. The benefit from adjuvant chemotherapy is mostly extrapolated for older populations, who are more likely to have co-morbidities/impaired performance status, and not represent the clinical trial population. We reviewed our local practice to see how much chemotherapy our older patients actually receive.

**Methods and Materials:** A retrospective, single-centre audit of patients over 60 years, treated with adjuvant chemotherapy for breast cancer from 2010–2015 at the Royal Free Hospital, London. Data was collected from clinical and pharmacy records. Primary outcomes were the type of intended chemotherapy, the percentage delivered and the frequency of dose reductions.

**Results:** 84 patients received adjuvant chemotherapy: 32 were aged 60−64 years, 33 were 65−69 years and 19 were over 70 years. The majority had T2 tumours (50%; 73%; 63%), were node positive (56%; 67%; 74%) and HER2 positive (69%; 73%; 53%), while hormone positivity declined with age (88%; 73%; 42%) (60−64 yrs; 65−69 yrs; >70 yrs, respectively).

Patients aged 60−64 yrs were most likely to receive FEC/FEC-T, and on average completed 95.8% of their planned chemotherapy, with 25.3% of cycles dose reduced and 9.1% stopping chemotherapy early. 26.3% of patients >70 yrs stopped chemotherapy early, with 35.1% of cycles delivered at a reduced dose (Table 1).

Table 1. Chemotherapy delivered

| Age group | Number of chemotherapy cycles (% of intended) | | | | Number of regimes discontinued early |
|---|---|---|---|---|---|
| | Intended | Actually delivered | With dose reduced | Delayed | |
| 60−64 yrs (n = 32) | 190 | 182 (95.8%) | 48 (25.3%) | 6 (3.2%) | 8 (25.0%) |
| 65−69 yrs (n = 33) | 182 | 175 (96.2%) | 88 (11.0%) | 20 (10.6%) | 3 (9.1%) |
| 70+ yrs (n = 19) | 94 | 78 (83.0%) | 33 (35.1%) | 6 (6.4%) | 5 (26.31%) |

**Conclusions:** There were differences in the baseline characteristics of patients over 65 yrs who were offered adjuvant chemotherapy compared to younger patients: patients over 65 yrs were more likely to be ER-ve and/or HER2+ve. Patients over 65 were more also likely to have multiple dose reductions, discontinue chemotherapy early and were least likely to receive third generation chemotherapy, even for node positive disease.

Patients who do not complete their adjuvant chemotherapy may not derive the benefit in 10 year survival proposed by the tool nhs.predict. This should be taken into consideration when counselling elderly patients for adjuvant chemotherapy.

**No conflicts of interest**

**337** Poster

**Prognostic factors in patients with operable breast cancer who received neoadjuvant chemotherapy**

J. Horiguchi[1], D. Takata[1], R. Nagaoka[1], T. Fujii[1], A. Sato[1], H. Tokiniwa[1], T. Higuchi[1], S. Uchida[1], M. Tsuboi[1], R. Yajima[1], M. Kikuchi[1], Y. Ino[2], T. Oyama[3]. *[1]Gunma University Hospital, Breast and Endocrine Surgery, Maebashi, Japan; [2]Kusunoki Hospital, Surgery, Fujioka, Japan; [3]Gunma University Hospital, Pathology, Maebashi, Japan*

**Background:** Neoadjuvant chemotherapy (NAC) is applied to patients who are candidates for adjuvant chemotherapy. Some of patients receiving NAC achieve a pathological complete response (pCR). The presence of circulating tumor cells (CTCs) is associated with survival time of advanced or metastatic breast cancer. However, the prognostic significance is not clear in operable breast cancer. The aim of this study is to evaluate clinical factors and CTC before NAC, and to study whether the factors have a prognostic impact on these patients.

**Patients and Methods:** A total of 121 women with stage II/III breast cancer received neoadjuvant chemotherapy (NAC) between April 2008 and July 2013 at Gunma University Hospital. NAC consisted of anthracycline and paclitaxel chemotherapy and additional trastuzumab treatment for patients with HER2-positive tumors. CTCs were evaluated before NAC. After NAC, 121 patients received breast-conserving surgery or mastectomy with lymph node dissection. Pathological complete response (pCR) was defined as no invasive cancer in the breast.

**Results:** The age of patients ranged from 28 to 78 (median 51). 67 patients had Stage II disease and 54 had Stage III disease. Subtypes of tumors were classified into 4 groups according to ER, PgR and HER2 status: 39 luminal type, 28 luminal-HER2 type, 19 HER2 type, and 35 triple negative type. CTC was detected in 20 (16.5%) of 121 patients. CTC-positive patients were seen more frequently in those with Stage III disease than those with Stage II disease. A pCR was achieved in 34 (28%) of 121 patients. Clinical stage (II vs III) and subtype (HER2 vs non-HER2) were associated with pCR. There was no association between CTC detection and pCR. Disease-free survival was better in patients with small tumor, early stage disease, and pCR. In non-pCR patients, CTC-negative patients showed a better DMFS than CTC-positive patients.

**Conclusion:** CTC before NAC in patients with operable breast cancer is a possible prognostic factor.

**No conflicts of interest**

**338** Poster

**Docetaxel-associated myalgia–arthralgia syndrome in patients with breast cancer**

I. Voutsadakis[1], C. Seguin[2]. *[1]Sault Area Hospital, Medical Oncology, Sault Ste Marie, Canada; [2]Sault Area Hospital, Clinical Trials, Sault Ste Marie, Canada*

**Background:** With the increasing use of taxanes in clinical oncology, the myalgia–arthralgia syndrome (M-AS), an adverse effect of these drugs is becoming a common clinical problem. Information on its predisposing factors and prevention or therapy is sparse. We describe our experience with the syndrome.

**Patients and Methods:** Women who had received docetaxel as part of the FEC-D(T) regimen for the treatment of an early breast cancer were identified from the records of our department and retrospectively reviewed. Demographic, disease, adverse effect and treatment data were extracted. The group of patients who developed M-AS after docetaxel treatment was compared with those who did not to identify risk factors for the syndrome. Effectiveness of various treatments used for M-AS was reviewed. Patients without complete follow-up data on adverse effects or receiving taxanes for another diagnosis or in the metastatic setting were excluded.

**Results:** Sixty-seven patients were included in the analysis. The M-AS occurred after the first docetaxel administration in 19 patients. From the 48 patients that did not develop the syndrome, three patients had been prescribed gabapentin or pregabalin prophylactically or had been taking these medications for other reasons. The remaining 45 patients were included in the control group for the current analysis. There was no difference between the two groups regarding age, menopause status, stage of the cancer or histology. Patients with the M-AS were more likely to have an increased BSA and to have their docetaxel treatment discontinued before completing the three intended cycles. Treatments used for the M-AS included acetaminophen, NSAIDs, the two atypical anti-epileptics, gabapentin and pregabalin, extended corticosteroids and opioids or combinations.

**Conclusion:** The docetaxel associated M-AS is a significant cause of not completing treatment with the drug. Possible risk factors and effectiveness of treatments for the syndrome are presented.

**No conflicts of interest**

**339** Poster

**Extending preoperative indication for systemic therapy to patients with early-stage breast cancer using multiparametric high-field breast MRI**

A.M.T. Schmitz[1], W.B. Veldhuis[1], M.B.E. Menke-Pluijmers[2], W.J.M. Van der Kemp[1], T.A. Van der Velden[1], M.A. Viergever[1], W.P.T.M. Mali[1], M.C.J.M. Kock[3], P.J. Westenend[4], D.W.J. Klomp[1], K.G.A. Gilhuijs[1]. *[1]University Medical Center Utrecht, Department of Radiology/Image Sciences Institute, Utrecht, Netherlands; [2]Albert Schweitzer hospital, Department of Surgery, Dordrecht, Netherlands; [3]Albert Schweitzer hospital, Department of Radiology, Dordrecht, Netherlands; [4]Albert Schweitzer hospital, Department of Pathology, Dordrecht, Netherlands*

**Background:** Preoperative systemic therapy is a clinically accepted approach for locally-advanced and lymph-node-positive breast cancer, enabling patient-tailored therapy. For early-stage breast cancer, however, preoperative indication for systemic therapy has fallen short owing to inaccurate preoperative tumor characterization. Multiparametric breast MRI may compensate for these inaccuracies. The objective of this study is to establish a preoperative decision model for early breast cancer.

**Material and Methods:** Patients eligible for breast-conserving therapy were consecutively included. Patients underwent conventional diagnostic workup and one preoperative multiparametric 7-tesla breast MRI. The postoperative (gold standard) indication for systemic therapy was established from resected tumor and lymph-node tissue, based on 10-year risk-estimates of breast cancer mortality and relapse using Adjuvant! Online. Preoperative indication was estimated using similar guidelines, but from conventional preoperative diagnostic workup. Agreement was established between preoperative and postoperative indication, and MRI-characteristics were used to improve agreement with resected tissue. MRI-characteristics included phospomonoester/phosphodiester (PME/PDE) ratio on 31-phosphorus spectroscopy ($^{31}$P-MRS), apparent diffusion coefficients on diffusion-weighted imaging, and tumor size on dynamic-contrast enhanced (DCE)-MRI. A decision model was built to estimate the postoperative indication from preoperatively available data.

**Results:** We included 46 women (age: 43−74 yrs) with 48 invasive carcinomas. Postoperatively, 26 patients (57%) had negative, and 20 patients (43%) had positive indication for systemic therapy. Using conventional workup, positive preoperative indication agreed excellently with positive postoperative indication (N = 8/8; 100%). Negative preoperative

indication was correct in only 26/38 (68%) patients. However, $^{31}$P-MRS score ($p = 0.030$) and tumor size ($p = 0.002$) were associated with the postoperative indication. The decision model shows that negative indication is correct in 21/22 (96%) patients when exempting tumors larger than 2.0 cm on DCE-MRI or with PME>PDE ratios at $^{31}$P-MRS.

**Conclusions:** Preoperatively, a positive indication for systemic therapy is highly accurate. A negative indication is highly accurate (96%) for tumors sized $\leqslant$2.0 cm on DCE-MRI and with PME$\leqslant$PDE ratios on $^{31}$P-MRS.

**No conflicts of interest**

**340** Poster

**Bone health and adherence to vitamin D and calcium use in early breast cancer patients on endocrine therapy with aromatase inhibitors**

E. Vrdoljak[1], Z. Soldic[2], L. Boskovic[1], M. Jazvic[2], N. Dabelic[2], B. Petric Mise[1], D. Gugic[3], L. Bozac Radolovic[4], J. Jovic Zlatovic[5], L. Vazdar[6], M. Gasparic[7], M. Petkovic[8]. *[1]University Hospital Center Split, Clinic for oncology and radiotherapy, Split, Croatia; [2]University Hospital Center Sestre Milosrdnice, Clinic for oncology and nuclear medicine, Zagreb, Croatia; [3]University Hospital Center Osijek, Department for radiotherapy and oncology, Osijek, Croatia; [4]General Hospital Pula, Department for oncology and hematology, Pula, Croatia; [5]General Hospital Sibenik − Knin County, Department for internal medicine, Sibenik, Croatia; [6]University Hospital Center Sestre Milosrdnice, Clinic for tumors, Zagreb, Croatia; [7]PLIVA Croatia Ltd., Medical Affairs, Zagreb, Croatia; [8]University Hospital Center Rijeka, Clinic for radiotherapy and oncology, Rijeka, Croatia*

**Background:** Randomized trials involving aromatase inhibitors (AIs) in the adjuvant treatment of breast cancer patients have reported increased osteoporosis and fracture risk. Bone loss can be reduced with vitamin D and calcium supplementation. The aim of this analysis was to investigate the adherence to vitamin D and calcium use in postmenopausal breast cancer patients receiving adjuvant endocrine therapy with non-steroidal AIs.

**Material and Methods:** In this prospective, multicenter, non-interventional study newly diagnosed patients and those already receiving non-steroidal AIs for up to 3.5 years were included. Standard clinical practice was analyzed which included utilization of densitometry before initation of AIs therapy and use of vitamin D, calcium and/or bisphosphonate therapy. Patients were asked whether they were instructed by their oncologist to take vitamin D and calcium, and if they replied positively, they were reporting the number of doses that were omitted on monthly basis.

**Results:** A total of 438 female patients were included in the study and were followed-up for an average 23.5$\pm$4.9 months. Median endocrine therapy duration before study recruitment was 10.5 months (interquartile 4.8–26.6). Patients' age ranged from 58 to 71 years (median 64). Densitometry was done in 142 patients (32.4%) before initiation of endocrine therapy, and in additional 38 (8.6%) patients at second visit. Vitamin D and calcium were prescribed to 71.7% of patients at least at some time point during the study. Patients who took more than 80% of the doses were considered adherent. Self-reported adherence was 88.4%. There was the tendency of more bone side effects (arthralgia, bone pain, joint swelling and musculoskeletal stiffness) in patients who took vitamin D and calcium, 24.76% vs. 16.26% ($p = 0.0568$). Osteoporosis was diagnosed in 26 patients (5.9%) of total study population. Bisphosphonates were prescribed to 54/438 (12.3%) patients, while only 19 (35.2%) of them had osteoporosis. Vitamin D and calcium were prescribed more often to the patients with T score lower than −2.5 or T score between −2.5 and −1 than to the patients with T score higher than −1 (>95% vs. 83.5%; $p = 0.0117$).

**Conclusion:** In this analysis, lack of oncologists' adherence to the guidelines on bone health in early breast cancer patients receiving AIs was observed. Additionally, significant proportion of patients do not adhere to the vitamin D and calcium use, making this even more hazardous for bone health in postmenopausal breast cancer patients receiving AIs.

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**No conflicts of interest**

**341** Poster

**Anthracylines and adjuvant chemotherapy: are we too concerned about long term cardiac issues?**

J. Fraser[1], P. McIlroy[1], S. Reid[2]. *[1]Beatson West of Scotland Cancer Centre, Breast Oncology Team, Glasgow, United Kingdom; [2]Glasgow Royal Infirmary, Department of Nuclear Cardiology, Glasgow, United Kingdom*

**Background:** Patients receiving anthracycline containing chemotherapy regimes may be at late risk of developing cardiomyopathy or congestive heart failure. Epirubicin containing regimens are now favoured over doxorubicin due to proven lower cardiotoxicity. We aimed to determine the rate of long term late onset cardiac associated conditions.

**Methods:** Multi gated acquisition (MUGA) scans have been routinely undertaken pre chemotherapy within our centre since 2002 to assess cardiac functional status and suitability for anthracycline containing treatment. Left ventricular ejection fraction (LVEF) is considered normal if >55%, with 51−55% low normal and <50% abnormal with a +/− 5% variation. A follow up review of a previous audit of 151 non-selected sequentially treated adjuvant breast patients treated between August 2002 and June 2003 and aged between 29−69 yrs (median 55 yrs) was performed. The previous audit examined utility, cost-effectiveness and predictive use of MUGA scans regarding underlying, undetected cardiac issues that might have resulted in changes to planned anthracycline chemotherapy (San Antonio 2004 poster #5070). All patients underwent a pre-treatment MUGA scan. No patient received Trastuzumab. Chemotherapy regimes included either doxorubicin 60 mg/m$^2$/cycle ($\times$4 cycles) or epirubicin 60–100 mg/m$^2$/cycle ($\times$4 cycles) in association with other chemotherapy agents and within TACT and TanGo adjuvant trials. Follow up information at 12−13 years has been obtained from hospital and general practitioner records including drug prescription resources regarding patient outcomes to June 2015.

**Results:** Of the original 151 patients, data will be presented regarding rates of cardiac events, cardiac conditions, cardiac related deaths and other causes of morbidity and mortality. There have been 8 patients lost to follow up. Of the remaining 143, 46 patients have died, 25 of metastatic breast cancer, 3 of second malignancies, 2 of non-malignant causes and 2 of cardiac events. Further information will be presented at conference in respect to 14 deaths whose cause is currently unknown (death registry being investigated). Ninety-seven patients remain alive, 57 are alive and well, 21 currently have medication controlled hypertension, 4 are currently being treated for metastatic breast cancer, 5 have other malignancies. Ten patients have current cardiac conditions.

**Conclusion:** Whilst some causes of deaths are still to be determined, there are a low number of cardiac deaths reported to date and only around 10% cardiac morbidity at 12−13 yrs follow up of which some may be unrelated to anthracycline exposure. Is it time to consider if we are *too* concerned about this late effect in the modern chemotherapy era?

**No conflicts of interest**

**342** Poster

**FDG PET/CT to predict pathologic complete response to neoadjuvant systemic treatment in breast and axilla in triple negative and in HER2-positive breast cancer**

M. Van Ramshorst[1], S. Teixeira[2], K. Pengel[3], K. Gilhuijs[4], R. Valdes Olmos[2], S. Rodenhuis[1], E. Rutgers[5], W. Vogel[2], G. Sonke[1], M.J. Vrancken Peeters[5]. *[1]Netherlands Cancer Institute, Medical Oncology, Amsterdam, Netherlands; [2]Netherlands Cancer Institute, Nuclear Medicine, Amsterdam, Netherlands; [3]Netherlands Cancer Institute, Radiology, Amsterdam, Netherlands; [4]University Medical Center Utrecht, Radiology/Image Sciences Institute, Utrecht, Netherlands; [5]Netherlands Cancer Institute, Surgical Oncology, Amsterdam, Netherlands*

**Background:** FDG PET/CT can visualize metabolic activity in primary breast cancers and involved lymph nodes and may be used to predict response to neoadjuvant systemic treatment. However, it is currently unclear if the metabolic response has similar significance and cut-off levels in primary tumors and in nodal disease, and whether these are consistent across tumor subtypes.

**Methods:** PET/CT following 18F-FDG administration was sequentially performed in stage II and III triple negative (TN) and HER2-positive (HER2+) breast cancer patients at baseline (PET1), after 2−3 weeks (PET2) and after 6−8 weeks (PET3) of neoadjuvant systemic therapy. Absolute $SUV_{max}$ and relative changes in $SUV_{max}$ were determined separately in FDG-avid breast tumors and lymph nodes. These PET response variables were categorized according to quartiles, and pathologic complete response (pCR, defined as no invasive tumor cells) rates were calculated within each category. Fisher's exact test was used to test for significance.

**Results:** 78 TN and 75 HER2+ tumors were available for analyses. The pCR rate was 44% in TN and 53% in HER2+ tumors. The metabolic responses of the primary tumor and the associated lymph nodes correlated poorly (Spearman's rho correlation coefficient = 0.10–0.52). Therefore, we assessed the association between metabolic response and pCR separately for breast and for lymph nodes. In TN tumors, the relative change in $SUV_{max}$ between PET1 and PET3 was the best predictor of pCR. If $SUV_{max}$ decreased >75%, the breast pCR rate was 94% (15/16; $p < 0.001$) and the lymph node pCR rate was 79% (15/19; $p = 0.003$). In HER2+ tumors, the absolute $SUV_{max}$ at PET2 was the best predictor of pCR. If $SUV_{max}$ was 2.4

or less, the breast pCR rate was 81% (13/16; p = 0.08) and if $SUV_{max}$ was 1.7 or less, the lymph node pCR rate was 93% (14/15; p < 0.01; Table 1).

Table 1. Quartile categories of change in $SUV_{max}$ (PET1 − PET3) and corresponding pCR rate in TN tumors and quartile categories of $SUV_{max}$ at PET2 and corresponding pCR rate in HER2+ tumors

| Breast | Total | pCR | | p | Axilla | total | pCR | | p |
|---|---|---|---|---|---|---|---|---|---|
| | | n | % | | | | n | % | |
| **TN** | | | | | | | | | |
| Δ (%) PET1 & PET3 | | | | <0.001 | Δ (%) PET1 & PET3 | | | | <0.001 |
| 0−25% decrease | 5 | 1 | 20% | | 0−25% decrease | 1 | 0 | 0% | |
| 25−50% decrease | 13 | 3 | 23% | | 25−50% decrease | 9 | 2 | 22% | |
| 50−75% decrease | 30 | 15 | 50% | | 50−75% decrease | 12 | 3 | 25% | |
| 75–100% decrease | 16 | 15 | 94% | | 75–100% decrease | 19 | 15 | 79% | |
| **HER2+** | | | | | | | | | |
| $SUV_{max}$ PET2 | | | | 0.08 | $SUV_{max}$ PET2 | | | | <0.01 |
| >3.7 | 13 | 5 | 38% | | >2.6 | 10 | 7 | 70% | |
| >2.9 & ⩽3.7 | 14 | 8 | 57% | | >2.1 & ⩽2.6 | 11 | 5 | 45% | |
| >2.4 & ⩽2.9 | 13 | 10 | 77% | | >1.7 & ⩽2.1 | 9 | 9 | 100% | |
| ⩽2.4 | 16 | 13 | 81% | | ⩽1.7 | 15 | 14 | 93% | |

**Conclusions:** To accurately predict pCR in the primary tumor and lymph nodes with FDG PET/CT during neoadjuvant treatment, the metabolic responses of both anatomical locations must be evaluated separately, and with cut-off values that are specific for the different tumor subtypes.

**No conflicts of interest**

**343** Poster

**Safety analyses of the first 110 patients treated with dual HER2-blockade in the TRAIN-2 study**

M. Van Ramshorst[1], E. Van Werkhoven[2], A. Honkoop[3], V. Dezentje[4], I. Oving[5], I. Mandjes[2], I. Kemper[1], J. Stouthard[1], S. Rodenhuis[1], S. Linn[1], G. Sonke[1]. *[1]Netherlands Cancer Institute, Medical Oncology, Amsterdam, Netherlands; [2]Netherlands Cancer Institute, Biometrics, Amsterdam, Netherlands; [3]Isala, Medical Oncology, Zwolle, Netherlands; [4]Reinier de Graaf Gasthuis, Medical Oncology, Delft, Netherlands; [5]Ziekenhuisgroep Twente, Medical Oncology, Almelo, Netherlands*

**Background:** The optimal neoadjuvant chemotherapy regimen in combination with dual HER2-blockade with trastuzumab and pertuzumab is unknown. Anthracycline-free schedules may be preferable to reduce toxicity. The TRAIN-2 study evaluates the relative efficacy and toxicity of weekly paclitaxel/carboplatin versus FEC (5-fluorouracil, epirubicin, cyclophosphamide), both in combination with trastuzumab and pertuzumab. Here, we report the toxicity data during neoadjuvant treatment of the first 110 patients.

**Methods:** The TRAIN-2 study is a multicenter trial in stage II and III HER2-positive breast cancer. Patients are randomly assigned to receive 3 cycles of paclitaxel (80 mg/m$^2$ day 1 and 8), trastuzumab (6 mg/kg, loading dose 8 mg/kg), carboplatin (AUC=6 mg/ml·min) [PTC] plus pertuzumab (420 mg, loading dose 840 mg) or 3 cycles of 5-fluoruoracil (500 mg/m$^2$), epirubicin (90 mg/m$^2$), cyclophosphamide (500 mg/m$^2$) and trastuzumab [FECT] plus pertuzumab, followed by 6 additional cycles of PTC plus pertuzumab in both arms (NCT01996267). Toxicities according to CTCAE 4.03 are described according to treatment arm.

Table 1. Most relevant grade 3−4 toxicity (%) per treatment arm according to CTC criteria v4.03

| | FECT-Ptz (n = 55) | | PTC-Ptz (n = 55) | |
|---|---|---|---|---|
| | Grade 3 | Grade 4 | Grade 3 | Grade 4 |
| Hematological toxicity | | | | |
| Anemia | 25 | 0 | 13 | 0 |
| Neutropenia | 36 | 18 | 47 | 4 |
| Trombocytopenia | 13 | 5 | 11 | 2 |
| Febrile neutropenia | 7 | 0 | 0 | 0 |
| Non-hematological toxicity | | | | |
| Fatigue | 4 | 0 | 7 | 0 |
| Diarrhea | 5 | 0 | 18 | 0 |
| ALAT elevated | 4 | 0 | 7 | 0 |
| Peripheral polyneuropathy | 4 | 0 | 5 | 0 |
| Electrolyte disturbances | 2 | 0 | 7 | 2 |
| Ejection fraction decrease | 2 | 0 | 0 | 0 |

**Results:** This analysis includes 55 patients in each arm (Table 1). Neutropenia was the most common hematological adverse event occurring at a similar rate in both arms. G-CSF support was initiated in 40% of patients in the FECT-arm and in 35% in the PTC-arm. Febrile neutropenia was rare and did not occur in the PTC-arm. The most common grade 3−4 non-hematological toxicity was diarrhea followed by ALAT increase, fatigue, and electrolyte disturbances. Asymptomatic ejection fraction decrease grade 2−3 was observed in 7% in the PTC-arm and in 5% in the FECT-arm. One patient, in the PTC-arm, experienced acute myocardial infarction followed by left ventricular dysfunction. Peripheral neuropathy grade 2 or 3 was seen in 31% and 5% in the PTC-arm and in 24% and 4% in the FECT-arm. Eighty percent of patients in the PTC-arm and 82% in the FECT-arm received all nine cycles. Dose reduction was needed in 60% in the PTC-arm and in 51% in the FECT-arm.

**Conclusions:** Neutropenia was common in both arms and can be managed with G-CSF support and dose reductions. Febrile neutropenia and cardiac toxicity were rare with both regimens. Diarrhea was seen according to the known toxicity profile of pertuzumab. Patient accrual is expected to be completed Q1 2016.

**Conflict of interest:** Advisory Board: SCL is an advisory board member for Cergentis, Novartis, Roche, and Sanofi. Other Substantive Relationships: The TRAIN-2 study is supported by a research grant from Roche; SCL has received institutional research support funding from Amgen, AstraZeneca, Genentech, Roche, and Sanofi.

**344** Poster

**Can early response after the first cycle of neoadjuvant chemotherapy for breast carcinoma on diffusion-weighted magnetic resonance imaging predict the pathological outcome?**

M. Keupers[1], G. Clinckemaillie[1], L. Cardoen[1], A. Poppe[2], P. Neven[3], H. Wildiers[4], A. Smeets[3], A. Laenen[5], F. De Keyzer[1], C. Van Ongeval[1]. *[1]University Hospitals Leuven, Radiology, Leuven, Belgium; [2]University Hospitals Leuven, Obstetrics and Gynaecology, Leuven, Belgium; [3]University Hospitals Leuven, Multidisciplinary Breast Center, Leuven, Belgium; [4]University Hospitals Leuven, Oncology, Leuven, Belgium; [5]Catholic University Leuven, Biostatistics and Statistical Bioinformatics Centre L-BioStat, Leuven, Belgium*

**Background:** Magnetic resonance imaging (MRI) has proven to be a very useful tool in monitoring neoadjuvant chemotherapy (NACT). In diffusion-weighted (DW-) MRI, the apparent diffusion coefficient (ADC) is a quantitative marker for the water diffusivity, which in tumours is inversely correlated with cellular density. The goal of this study is to evaluate initial ADC, as well as early changes in tumour volume and ADC after the first cycle of NACT, correlating these results with pathologic outcome after completion of NACT and surgery.

**Material and Methods:** In this prospective study, 27 patients aged 32−68 (median 50) years received NACT (written consent was acquired). Pathological response was recorded according to the Miller & Payne (MP) score, dividing patients into three response categories: complete response (pCR, MP=5), partial response (pPR, MP=2−4) and no response (pNR, MP=1). The administered chemotherapy regimen is 3xFEC (5fluoracil, epirubicin, cyclophosphamide) and 3xTaxotere. All patients underwent a DW-MRI (1.5T Siemens Aera, Germany) before the start of NACT and on the day of the second NACT session two weeks later. The tumour volume was delineated by two independent radiologists according to the b1000 hyperintensity. The Kruskal–Wallis test is used to test differences in volume decrease or ADC increase between the three response categories.

**Results:** Intraclass correlation coefficients were high for both volume (0.98 [0.96;0.99]) and ADC (0.82 [0.66;0.91]), indicating a very good inter-rater reliability. Averaged over both raters, the mean pre-NACT ADC (in $\times 10^{-5}$ mm$^2$/s) was 99.7 for pCR, which is slightly lower than the values found in pPR (106.3) and pNR (102.2), but without reaching significance. (Note: pNR was only found in 2 patients, of which one had a very good initial response on FEC but tumour growth during Taxotere therapy). An ADC increase was seen in 20 patients (74%) after one cycle of NACT, of which 10 had pCR, 8 pPR and 2 pNR. For both readers, there is a clear difference in median ADC increase for both pCR (15.4, IQR 4.3–26.7) and pPR (8.1, IQR 6.2–11.3) groups, again not reaching significance (p = 0.42). In the subgroup of patients with ADC increase of 15, pCR was found in 83% (5/6) of cases. All 27 patients had a volume decrease after one cycle of NACT, of which 12 (44%) had pCR, 13 (48%) pPR and 2 (7%) pNR. For both readers, there is a clear but non-significant (p = 0.41) difference in median volume decrease for pCR (2.84 ml, IQR 1.85–5.31), pPR (1.87 ml, IQR 0.98–4.03) and pNR (1.68, IQR 1.60–1.77).

**Conclusions:** According to literature, a low pre-NACT ADC value can predict response for NACT, although this could not be confirmed from our limited patient group. Also, no significant associations were found between early response and pCR, although an ADC increase of at least $15 \times 10^{-5}$ mm$^2$/s did predict pCR in 83% of patients.

**No conflicts of interest**

**345** Poster

**The prognosis of 123 super-elderly breast cancer patients**

R. Shimazaki[1], R. Nakamura[1], N. Shiina[1], T. Miyaki[1], N. Yamamoto[1], M. Miyazaki[2]. [1]*Chiba Cancer Center, Breast Surgery, Chiba, Japan;* [2]*Department of General Surgery, Chiba University Graduate School of Medicine, Chiba, Japan*

**Background:** Current study of evidence-based medicine for breast cancer does not include super-elderly patients aged 80 years or older and no standard treatment such as surgery, radiation and medical therapy has been established for such patients. In this study, we investigated whether the existing standard-of-care treatment for younger breast cancer patients also provides a good prognosis for super-elderly patients and assessed whether this treatment meets the standard of care for super-elderly patients.

**Material and Methods:** 1001 breast cancer patients aged 60 years or older underwent surgery at our hospital. The patients were divided into two age groups consisting of a super-elderly group (123 patients aged 80 years or older) and a younger age (control) group (878 patients aged between 60 and 79 years). Overall survival (OS) and disease-specific survival (DSS) were compared between the two groups.

**Results:** The rate of patients with a tumor size T2, T3 or T4 ($p < 0.0001$) or with PR-negative ($p = 0.042$) or HER2-negative ($p = 0.042$) tumors was significantly higher in the super-elderly group compared to the control group. OS and DSS were significantly shorter in the super-elderly group compared to the control group ($p < 0.0001$, $p = 0.015$). Among the patients with ER-negative tumors, DSS was significantly shorter in the super-elderly group compared to the control ($p = 0.013$), whereas among the patients with ER-positive tumors, no significant difference in DSS was observed between the two groups ($p = 0.855$). ER-negative ($p = 0.003$), PR-negative ($p = 0.003$) tumors and lymphovascular invasion ($p = 0.042$) were found to be adverse prognostic factors in the super-elderly group. We also found that 15.1% of patients with ER-negative tumor in the super-elderly group underwent standard-of-care chemotherapy.

**Conclusions:** Although a good prognosis for super-elderly patients with ER-positive breast cancer was observed, the current standard-of-care treatment was not sufficiently performed for those with ER-negative breast cancer and prognosis was poor. The establishment of the safety and effective adjuvant therapy for super-elderly patients with ER-negative breast cancer remains a challenge for the future.

**No conflicts of interest**

**346** Poster

**Male breast cancer − outcome with adjuvant treatment**

B. Yadav[1], S. Sharma[1], R. Singh[2], S. Ghoshal[1]. [1]*Postgraduate Institute of Medical Education & Research, Radiation Oncology, Chandigarh, India;* [2]*Postgraduate Institute of Medical Education & Research, General Surgery, Chandigarh, India*

**Background:** To analyze outcome in male breast cancer (MBC) patients with adjuvant treatment.

**Material and Methods:** From 1991 to 2013, 68 men with breast cancer were retrospectively analyzed for demographic, clinico-pathological and treatment outcomes. Disease-free survival (DFS) was defined as time duration from diagnosis to first recurrence. Overall survival (OS) was defined as time duration from pathologic diagnosis to death or last follow-up with any death defined as an event. DFS and OS were estimated using Kaplan–Meier method and compared between patients receiving and not receiving adjuvant treatment using log-rank test.

**Results:** Mean age was 55 years (range 30−76). Right, left and bilateral BC was seen in 37 (54%), 30 (44%) and 1 (1%) men respectively. Mean duration of symptoms was 25 months (range 1–240). Comorbidity and family history was present in 22 (36%) and 3 (4%) men respectively. Mean tumor size was $5 \times 5$ cm (range $1 \times 1$–$10 \times 10$ cm). Nipple was involved in 24 (35%) men. Early, locally advanced and metastatic disease was seen in 27 (39%), 29 (43%) and 13 (19%) patients respectively. Majority 51 (84%) had IDC histology. In radically treated 56 men, NACT with FAC regimen was given to 10 (18%) patients; with CR in 4 (40%) and PR in 6 (60%) patients. Mastectomy was done in 48 (86%) and WLE in 8 (14%) men. Margins and nodes were positive in 13 (23%) and 30 (54%) men respectively. ER, PR and Her2neu positive were 22 (39%), 12 (22%) and 2 (3.5%) patients respectively. Adjuvant radiotherapy, chemotherapy and tamoxifen was received by 45 (80%), 25 (45%) and 37 (66%) men respectively. Median follow up was 52 months (range 1–278). Local recurrence occurred in 8 (14.5%) and distant metastasis in 18 (33%) men respectively. DFS and OS at 10 years was 41% and 49% respectively. DFS and OS was significantly better in men with adjuvant radiation (53% vs 12%, $p = 0.002$ and 57% vs 22%, $p = 0.005$ respectively) and hormonal therapy (58% vs 14%, $p = 0.004$ and 58% vs 39%, $p = 0.036$). Chemotherapy had no impact on DFS and OS.

**Conclusion:** Adjuvant radiotherapy and hormonal therapy significantly improve DFS and OS in MBC patients. Chemotherapy had no impact on DFS and OS.

**No conflicts of interest**

Table 1. Patient characteristics for 56 patients

| Characteristic | | No. of patients (%) |
|---|---|---|
| Laterality | Right | 28 (50) |
| | Left | 27 (48) |
| | Bilateral | 1 (2) |
| Comorbidity | Yes | 22 (39) |
| | No | 34 (61) |
| Tumor | T1T2 | 27 (48) |
| | T3T4 | 29 (52) |
| Histology | IDC | 47 (87.5) |
| | Other | 9 (12.5) |
| Grade | I&II | 42 (75) |
| | III | 10 (18) |
| | Unknown | 4 (7) |
| Margins involved | Yes | 13 (23) |
| | No | 43 (77) |
| Nodes | Negative | 26 (46) |
| | Positive | 30 (54) |
| Oestrogen receptor | Positive | 22 (39) |
| | Negative | 12 (22) |
| | Unknown | 22 (39) |
| Progesterone receptor | Positive | 12 (22) |
| | Negative | 22 (39) |
| | Unknown | 22 (39) |
| Chemotherapy | Yes | 25 (45) |
| | No | 31 (55) |
| Radiotherapy | Yes | 45 (80) |
| | No | 11 (20) |
| Tamoxifen | Yes | 37 (66) |
| | No | 19 (44) |

**347** Poster

**Efficacy of a half-dose pegfilgrastim for dose-dense doxorubicin and cyclophosphamide in Japanese breast cancer patients**

Y. Mizuno[1], H. Fuchikami[1], N. Takeda[1], Y. Inoue[2], H. Seto[3], K. Sato[1]. [1]*Tokyo-West Tokushukai Hospital, Breast Oncology Center, Tokyo, Japan;* [2]*Inoue Ladies Clinic, Obstetrics and Gynecology, Tokyo, Japan;* [3]*Seto Hospital, Obstetrics and Gynecology, Saitama, Japan*

**Background:** In many countries, 6 mg pegfilgrastim was used to reduce the risk of febrile neutropenia (FN). However, based on the results from internal clinical trials, the Japanese Ministry of Health, Labour and Welfare approved the use of 3.6 mg pegfilgrastim for the prevention of FN in September 2014. In those trials, the docetaxel, doxorubicin, and cyclophosphamide (TAC) regimen has been used in a phase II dose-finding study, and the docetaxel and cyclophosphamide (TC) regimen has been used in a phase III randomized trial. However, clinical trials for the use of 3.6 mg pegfilgrastim with dose-dense chemotherapy have not yet been performed. Therefore, in this study, we aimed to evaluate the efficacy of 3.6 mg pegfilgrastim for dose-dense doxorubicin and cyclophosphamide (AC) in Japanese breast cancer patients.

**Material and Methods:** Since 6 mg pegfilgrastim has not been approved in Japan, we performed comparisons between dose-dense AC with 3.6 mg pegfilgrastim support and EC (epirubicin and cyclophosphamide) regimen. Therefore, a retrospective review was performed for patients who received 3.6 mg pegfilgrastim after each dose-dense AC (doxorubicin 60 and cyclophosphamide 600 mg/m$^2$, respectively; every 14 days for 4 cycles) and for those who received EC (epirubicin 90 and cyclophosphamide 600 mg/m$^2$, respectively, every 21 days for 4 cycles). We assessed the occurrence of FN in the first cycle of chemotherapy, dose delay, regimen change, and hospitalization because of neutropenia were evaluated. According to the policies of our institutional ethics committee, general consent was obtained from all patients receiving medical care.

**Results:** In total, 75 patients with stage I−III invasive breast cancer were enrolled between November 2013 and October 2015, including 18 patients in the dose-dense AC with 3.6 mg pegfilgrastim support group (dose-dense AC group) and 57 patients in the EC group). There was no occurrence of FN in the first cycle of chemotherapy in the dose-dense AC group; FN was observed in 7 of the 57 patients (12.3%) in the EC group ($p = 0.34$). The rate of patients who received their planned dose on time was similar in

both groups (16 of 18 patients in the dose-dense AC group and 54 of 57 patients in the EC group). There were no patients who had regimen change or hospitalization because of neutropenia in the dose-dense AC group. In the EC group, regimen change and hospitalization because of FN were observed in one patient each, respectively.

**Conclusion:** This is the first study to evaluate the efficacy of 3.6 mg pegfilgrastim for dose-dense chemotherapy. Although this study was based on a retrospective chart review of a small number of patients, we demonstrated that 3.6 mg pegfilgrastim was effective for the primary prevention of FN treated with dose-dense AC in Japanese breast cancer patients.

**No conflicts of interest**

**348** Poster

**Weight change in breast cancer patients during chemotherapy: A meta-analysis**

M. Van den Berg[1], R. Winkels[1], E. Kampman[1]. [1]*Wageningen University, Human Nutrition, Wageningen, Netherlands*

**Background:** Weight gain during chemotherapy for women with breast cancer is commonly reported. However, there are important differences between studies that examined weight gain during chemotherapy; e.g. the amount and type of chemotherapy, sample size, menopausal status and study design. The purpose of this meta-analysis is to quantify changes in body weight during chemotherapy for women with breast cancer, taking into account the differences mentioned.

**Materials and Methods:** We identified relevant studies using PubMed, Scopus and Embase databases. The search was limited to human studies published in English until 2014. Studies of early stage breast cancer patients treated with chemotherapy were included if they reported at least body weight before and after chemotherapy. In addition, also type of chemotherapy must be reported. Both observational and intervention studies were included. Intervention studies were only included if they included a control group receiving usual care. Data were pooled with a random effects meta-analysis and weight changes (95% confidence intervals) were reported.

**Results:** 26 studies were included in this meta-analysis. Preliminary overall results of this meta-analysis showed an increase in weight during chemotherapy for breast cancer patients of 2.28 kg (95% CI: 1.63–2.92), with a high degree of heterogeneity ($I^2$= 91.1%). Stratified analysis will be presented that explore possible sources of heterogeneity.

**Conclusion:** Despite the high heterogeneity, this meta-analysis suggest significant weight gain during chemotherapy for women with breast cancer.

**No conflicts of interest**

**349** Poster

**Results of a phase II trial of abiraterone acetate plus prednisone in patients with a molecular apocrine HER2-negative locally advanced or metastatic breast cancer (UCBG 2012-1)**

T. Grellety[1], H. Bonnefoi[1], O. Tredan[2], M. Saghatchian[3], F. Dalenc[4], A. Mailliez[5], T. L'Haridon[6], P. Cottu[7], S. Abadie-Lacourtoisie[8], B. You[9], M. Mousseau[10], J. Dauba[11], F. Del Piano[12], I. Desmoulins[13], F. Coussy[14], J. Grenier[15], G. MacGrogan[16], C. Orsini[17], M. Pulido[18], A. Gonçalves[19]. [1]*Institut Bergonié, Department of Medical Oncology, Bordeaux, France;* [2]*Centre Léon Bérard, Department of Medical Oncology, Lyon, France;* [3]*Gustave Roussy, Department of Medical Oncology- Breast Cancer Unit, Villejuif, France;* [4]*Institut Claudius Regaud- IUCT-Oncopole, Medical Oncology Department, Toulouse, France;* [5]*Centre Oscar Lambret, Breast Cancer Department, Lille, France;* [6]*Centre Hospitalier Départemental Vendée, Medical Oncology Department, La Roche sur Yon, France;* [7]*Institut Curie, Department of Medical Oncology, Paris, France;* [8]*Centre Paul Papin, Medical Oncology Department, Angers, France;* [9]*Teaching Hospital-Lyon-Sud University, Medical Oncology Department, Lyon, France;* [10]*CHU Grenoble, Department of Medical Oncology, Grenoble, France;* [1]*Centre Hospitalier Layné, Department of Medical Oncology, Mont-de-Marsan, France;* [12]*Hôpital du Leman, Department of Gynecologic Surgery, Thonon-Les-Bains, France;* [13]*Centre GF Leclerc, Department of Medical Oncology, Dijon, France;* [14]*Institut Curie, Department of Medical Oncology, St Cloud, France;* [15]*Institut Sainte-Catherine, Department of Medical Oncology, Avignon, France;* [16]*Institut Bergonié, Department of Pathology, Bordeaux, France;* [17]*UNICANCER, R&D, Paris, France;* [18]*Institut Bergonié, Clinical and Epidemiological Research Unit, Bordeaux, France;* [19]*Institut Paoli-Calmettes, Department of Medical Oncology, Marseille, France*

**Background:** Several expression array studies identified molecular apocrine as a subtype of breast cancer (BC) that expresses androgen receptors (AR) but not oestrogen receptors (represents up to 20% of triple negative BCs). We performed a multicenter single arm phase II trial in women with AR-positive triple-negative metastatic or inoperable locally advanced BC to assess the efficacy and safety of abiraterone acetate (AA) plus prednisone.

**Material and Methods:** Patients presenting with a metastatic or locally advanced centrally reviewed triple negative (ER, PR, HER2) and AR positive ($\geqslant$10% by immunohistochemistry) BC were eligible. Any number of previous lines of chemotherapy was allowed. AA 1000 mg was administered once a day with prednisone 5 mg twice a day until disease progression or unacceptable toxicity. Primary endpoint was clinical benefit rate (CBR) defined as the proportion of patients presenting a complete response (CR), partial response (PR), or stable disease (SD) $\geqslant$6 months. Secondary endpoints were objective response rate (ORR), progression-free survival (PFS), safety and tolerability (NCI-CTCAE v4.0). The treatment was deemed interesting for further research if a clinical benefit at 6 months was observed in at least 8/28 eligible and evaluable patients (>25%).

**Results:** One hundred and forty-six patients from 27 centres consented for IHC central review. Of patients with sufficient tissue, 37.7% (52/138) were AR-positive and triple negative. Thirty-four patients were included from July 2013 to December 2014. Thirty patients were eligible and evaluable for the primary end-point (3 progressed before the end of cycle one, one not eligible). Median age was 62.5 years (range 39−86). Majority of the patients had visceral metastasis and received a median of 2.5 (0−9) prior lines of chemotherapy for advanced disease. CBR at 6 months was 20.0% (6/30; 95% CI: 7.7–38.6) including 1 CR and 5 SD $\geqslant$6 months. One patient in SD became a PR at 12 months; the ORR was 6.7% (95% CI: 0.8–22.1). Median PFS was 2.8 months (95% CI: 1.7−5.4). Five patients were still under treatment (1 patient in CR on treatment for 23.4 months; 1 patient in PR for 17.6 months; 3 patients in SD for 6.4, 9.2 and 14.5 months). Fatigue (17.6%), hypertension (11.8%), and hypokalaemia (8.8%) were the most common drug-related adverse events with the majority being grade 1 or 2. Two patients presented with treatment-related serious adverse events: one hypokalaemia and one adrenal insufficiency grade 3.

**Conclusions:** While from a statistical point of view our data does not allow a rejection of the null hypothesis, from a clinical perspective our results are important. At the time of this analysis, 5 patients remain on treatment with prolonged clinical benefits. A translational research program is currently ongoing to identify predictive factors of response to anti-androgen therapy.

**No conflicts of interest**

**350** Poster

**Randomized, open-label, phase II study comparing the efficacy and the safety of cabazitaxel versus weekly paclitaxel given as neoadjuvant treatment in patients with operable triple negative or luminal B/HER2 normal breast cancer (GENEVIEVE)**

S. Paepke[1], J. Huober[2], K. Sherko[3], H. Eidtmann[4], M. Untch[5], S. Dan Costa[6], J.U. Blohmer[7], W. Eiermann[8], B. Gerber[9], C. Hanusch[10], J. Hilfrich[11], C. Jackisch[12], A. Schneeweiss[13], C. Denkert[14], K. Engels[15], P. Klare[16], P. Fasching[17], N. Burchardi[18], S. Loibl[19], G. Von Minckwitz[18]. [1]*TU München, Frauenklinik und Poliklinik der TU München, München, Germany;* [2]*Universitätsklinikum Ulm, Frauenklinik, Ulm, Germany;* [3]*Klinikum Essen Mitte, Frauenklinik, Essen, Germany;* [4]*Universitätsklinikum Schleswig-Holstein Kiel, Frauenklinik, Kiel, Germany;* [5]*HELIOS Klinikum Berlin-Buch- Berlin, Frauenklinik, Berlin, Germany;* [6]*Klinikum der Otto-v.-Guericke-Universität Magdeburg, Frauenklinik, Magdeburg, Germany;* [7]*Charite − Universitätsmedizin Berlin, Frauenklinik, Berlin, Germany;* [8]*Isarklinikum- IOZ München, Onkologisches Zentrum, München, Germany;* [9]*Klinikum Südstadt Rostock, Frauenklinik, Rostock, Germany;* [10]*Rotkreuzklinikum München, Frauenklinik, München, Germany;* [1]*Eilenriede Klinik Hannover, Frauenklinik, Hannover, Germany;* [12]*Klinikum Offenbach, Frauenklinik, Offenbach, Germany;* [13]*Universitätsklinikum Heidelberg, Frauenklinik, Heidelberg, Germany;* [14]*Charite − Universitätsmedizin Berlin, Pathologie, Berlin, Germany;* [15]*Zentrum für Pathologie- Zytologie und Molekularpathologie Neuss, Pathologie, Neuss, Germany;* [16]*Praxisklinik Berlin, Senologie, Berlin, Germany;* [17]*Universitätsklinikum Erlangen, Frauenklinik, Erlangen, Germany;* [18]*German Breast Group, Medicine and Research, Neu-Isenburg, Germany;* [19]*German Breast Group, Medicine and researchg, Neu-Isenburg, Germany*

**Background:** Cabazitaxel is a new taxoid promoting the tubulin assembly in vitro and stabilizing microtubules against cold-induced depolymerization as efficiently as docetaxel. It has shown superior survival against mitoxantrone plus prednisone in docetaxel pre-treated hormone refractory metastatic prostate cancer patients leading to its registration. A favorable toxicity profile with a low rate of alopecia was shown.

The GENEVIEVE study compares cabazitaxel to weekly paclitaxel, which is currently most widely used in breast cancer patients.

**Methods:** GENEVIEVE (NCT01779479) is a prospective multicenter, randomized, open label phase II study investigating efficacy and safety of cabazitaxel.

Patients with uni- or bilateral primary breast cancer (stage cT3/T2/T1c and cN+/T1c and pNSLN+), tumor lesion $\geqslant$2 cm (palpation) or $\geqslant$1 cm (sonography) and centrally confirmed triple-negative (TNBC) or luminal B/HER2− disease were randomized to four cycles cabazitaxel (25 mg/m$^2$ i.v.) q3w vs. 12 cycles paclitaxel (80 mg/m$^2$ i.v.) q1w. Randomization was stratified by nodal status and subtype.

Primary objective is pathologic complete response (pCR, ypT0/is ypN0/+). Secondary objectives are pCR in stratified subgroups and by other definitions, objective response rate, pCR and local recurrence free survival in patients with clinical complete response and negative core biopsy before surgery, breast conservation rate, toxicity, compliance, survival rates and biomarkers predicting response.

Assuming a pCR rate of 15% in controls and targeting a smallest clinical improvement of 10% (25% pCR in experimental arm), a total of 326 patients (163/arm) are required for the one-sided Fisher's exact test ($\alpha$=0.1) to show superiority of cabazitaxel with 80% power.

**Results:** 333 patients were recruited (4/2013–6/2015) in 44 German centers, 166 in the cabazitaxel, 167 in the paclitaxel arm. Baseline characteristics were well balanced; median age was 51 (23−78) years in the cabazitaxel and 53 (25−77) years in the paclitaxel arm. 39/40% of the patients presented with TNBC, 41/43% with cN+, 98/96% with cT1/2, 85/86% with ductal invasive, 66/62% with G3 tumors, respectively.

The pCR rate was 1.8% (3/166; 95% CI: 0.37, 5.19) with cabazitaxel compared with 10.8% (18/167; 95% CI: 6.51, 16.50) with paclitaxel (p = 1.000 for planned one-sided test; p = 0.001 for exploratory two-sided test). The difference in pCR rates was 9.0% (95% CI: 4.67, 13.27).

**Conclusion:** The GENEVIEVE study showed no short-term effect of cabazitaxel in TNBC or luminal B/HER2− primary breast cancer. Final efficacy and safety data will be presented at the meeting.

**No conflicts of interest**

**351** Poster

**Clinical outcomes of neoadjuvant chemotherapy (NC) with or without anthracyclines in different invasive breast cancer (IBC) subtypes in a mono-institutional series**

A. Ferro[1], R. Triolo[1], O. Caffo[1], A. Caldara[1], B. Mattia[2], M. Bonzanini[2], E. Leonardi[2], M. Pellegrini[3], D. Bernardi[3], M. Valentini[3], D. Mangiola[1], E. Galligioni[1]. [1]*Santa Chiara Hospital, Medical Oncology, Trento, Italy;* [2]*Santa Chiara Hospital, Surgical and Molecular Pathology, Trento, Italy;* [3]*Santa Chiara Hospital, Mammography, Trento, Italy*

**Background:** The clinical outcomes of IBC pts who received NC could be different by Subtypes.

**Methods:** We retrospectively reviewed the clinical records of 252 pts treated with NC for stage II−III IBC from 2000 to 2015.

For each pt we recorded baseline tumor size, type of NC, type of surgery (S), pathological response (pCR defined as the absence of invasive cells in the breast and the lymph nodes regardless of DCIS).

IHC subtypes were defined according to ER and PgR expression, Ki-67 level, and HER2 status:

Luminal A (LA): ER and PR+, HER2−ve and Ki67 <20% (4.3%)
Luminal B (LB): ER and/or PR+, HER2−ve and Ki67 $\geqslant$20% (34.7%)
Luminal HER2 (LHER2): ER and/or PR+, HER2+ and any Ki67 (23.6%)
HER2 positive (HER2+): neg ER and PR, HER2+ and any Ki67 (12.6%)
TN: ER−ve and PR−ve, HER2−ve and any Ki67 (19.4%)
Unknown in 33 cases (5.6%)

pCR and OS outcomes also on the basis of both pre- and post-NC Ki67 levels were assessed.

**Results:** Median age was 50 yrs (range 25−75). The NC consisted of an anthracyclines (A) followed by taxanes (T) in all HER2− (153 pts), associated with weekly carboplatin (C) in 21 of TN (10 pts ongoing) and of T + trastuzumab (H) +/− A (32) or C (46 pts) in HER2+ disease. Only 22 pts did not receive surgery: 5 for distant progression disease (PD) and 17 because still on NC. Quadrantectomy was performed in 134 pts (58.3%).

pCR was achieved in 59 pts (25.6%) with further 5 pts showing a RT $\leqslant$1 mm. Fast clinical (after only one course of chemotherapy) response was more frequently associated to pCRs.

All but 21 HER2+ pts (98) received H obtaining pCR in 38.4% of cases regardless chemotherapy type (A-based 37.5% vs C- 39.1%). Eight of 11 pts (72.7%) who received C addition underwent surgery with pCR (BRCA-1 positive in 2 of these pts); an additional 10 patients are currently in treatment. The median Fup was 52 mo (range 1–182 mo). The 5y-RFS and OS were higher in whom achieved pCR than those did not (RFS 93.8% vs 67.8%; p = 0.001 and OS 95.8% vs 76.0%; p = 0.007).

Median Ki67 in pretreated core biopsy was 40 compared to 30% in post-NC RT. Pts with high (>30%) post-NC PI showed significantly higher risk for relapse (5y-RFS 49.3%; p = 0.001) and death (5yOS 56.4%; p = 0.007) compared with pts with <15% (RFS 93.6% and OS 89.6%) or >15−30 Ki67 levels (RFS 73.0% and OS 82.6%).

Table: Relationship between pCR and Sub, ki67 and PD

| | LA (%) | LB (%) | LHER2 (%) | HER2+ | TN (%) | Median Ki67 | PD (%) |
|---|---|---|---|---|---|---|---|
| pCR | 0 | 8.2 | 31.0 | 52.0 | 36.4 | 47.4 | 5.8 |
| No pCR | 100 | 91.8 | 69.0 | 48.0 | 63.6 | 38.1 | 34.3 |
| p value | <0.0001 | | | | | <0.0001 | <0.0001 |

**Conclusions:** The pCR rate was significantly higher in aggressive subtypes HER2+ and TN than luminals. Pts achieving pCR showed better RFS and OS compared to no pCR pts. Interestingly high pre-NC PI seems to predict the possibility obtaining pCR, while post-NC PI seem to be of prognostic value in pts who do not receive pCR.

**No conflicts of interest**

**352** Poster

**An audit of survival of secondary triple negative breast cancer patients and their response to systemic chemotherapy within the metastatic setting**

H. Passant[1]. [1]*Velindre Cancer Centre, Clinical Oncology, Cardiff, United Kingdom*

**Background:** Triple negative breast cancer (TNBC) is a subtype that carries a poor prognosis, exacerbated by lack of effective therapies. An audit was undertaken to determine the post-recurrence survival of triple negative patients within a single centre in South Wales and their response to systemic therapy. The proportion of patients presenting with visceral metastases, brain metastases and bone only metastases was calculated and the effect of site of metastatic disease on survival determined. The proportion of patients receiving 1$^{st}$ line, 2$^{nd}$ line and subsequent chemotherapy and the response rate to chemotherapy was investigated.

**Methods:** Using the Velindre Cancer Centre Secondary Breast Cancer database 91 women presenting with metastatic triple negative breast cancer between March 2010 to June 2014 were identified. The impact of site of metastases, performance status, age, stage and grade of tumour on survival in this group was examined. In addition we evaluated their response to each line of chemotherapy received.

**Results:** Of the Cohort of 91 patients, 87 had distant metastatic disease and 4 had inoperable loco regional recurrence. Mean follow up was 35.3 months. Median duration from presentation with primary breast cancer to presentation with secondary breast cancer was 26 months. Median survival time from presentation with secondary breast cancer for the cohort of patients was 9.3 months. 57/87 (65%) presented with visceral metastases. The median survival for this group was 9.26 months. For the patients presenting with brain metastases; 23/87 (26.4%) the median survival was 4.4 months. Of the 91 patients, 54 received chemotherapy (59.3%) and 37 did not receive chemotherapy. The survival of patients receiving chemotherapy was 12.2$\pm$1.7 months, compared to those who did not receive chemotherapy, 3.9$\pm$0.6 (P < 0.001).

32% of the 54 patients receiving chemotherapy showed a response to 1st Line therapy. A further 21% of patients showed an initial response to chemotherapy on an interval staging scan but progressed on treatment. A further 9% had stable disease. 30% had documented progression throughout treatment.

27 patients received second line chemotherapy. 15% showed a response to therapy with a further 7% an initial response and later progression. 11% had stable disease.

14 patients received third line chemotherapy. 8% showed response, 17% had stable disease.

None of the 3 patients receiving fourth line chemotherapy showed a response to treatment.

**Conclusion:** Secondary TNBC carries a poor prognosis in line with previous published series. Response to systemic chemotherapy in this group is poor following first line treatment and the risk benefit to the patient should be carefully considered prior to 3$^{rd}$ and 4$^{th}$ line chemotherapy.

**No conflicts of interest**

**353** Poster

**A single centre experience of neoadjuvant chemotherapy for invasive breast cancer**

H. Passant[1], J. Watts[2]. [1]*Velindre Cancer Centre, Clinical Oncology, Cardiff, United Kingdom;* [2]*Cardiff University, Medical School, Cardiff, United Kingdom*

**Background:** Neoadjuvant chemotherapy (NACT) for breast cancer is a therapeutic alternative for certain high-risk breast cancers according to tumour biology, inoperable disease and tumours of ⩾cT2/cN2. NACT offers several clinical advantages; it can downsize inoperable tumours, allow the option of breast-conserving surgery instead of mastectomy and enables the monitoring of response. In patients with estrogen receptor-negative tumours, a survival advantage has been seen in those achieving a pathological complete response (pCR) compared to those with residual disease following NACT.

An overview of NACT at a single cancer centre in Cardiff was performed, focusing on response and its determining factors. Given prognostic implications of dose delays (DDs) and dose reductions (DRs) following neutropenic events (NEs), the use of primary (PP) and secondary (SP) prophylaxis was also reviewed.

**Materials and Methods:** Retrospective data was collected from 08/05/10−08/05/15 using an electronic database. 197 patients were included. 5 bilateral cancers and 2 patients with axillary primaries gave 204 separate tumours. Response was determined by comparing the sum of the largest dimension of tumour foci between baseline and surgery using RECIST guidelines.

PP was assessed by: 1. Comparing cycle 1 NE rate in those given cycle 1 PP versus those without; 2. Comparing cycle 4 NE rate in those given PP from cycle 4 (before docetaxel switch) versus those at the same stage without.

**Results:** 186 cancers (91%) had a measurable pathological response. Overall pCR was 22% (n = 41) with the highest rate in the triple-negative group (n = 19; 37%). 52% (n = 97) of cancers had a pathological partial response (pPR), within which there was a 69% change range in aggregate measure. 65 patients had HER2+ cancers, 61 received neoadjuvant trastuzumab. 161 patients received GCSF at some point; 133 PP (118 from cycle 1; 15 from cycle 4), 43 SP. 58 patients had ⩾1 NE (total NEs=72). 21 occurred with FEC75T, 19 without prophylaxis. 16 occurred with FEC100T, all despite PP. The most common cycle after which NE occurred was cycle 4 (24 NEs). Overall cycle 1 NE rate was 9% (11/118) in those given PP and 13% (10/79) in those without PP. All FEC100T patients received PP with a NE rate of 11% (6/53). For FEC75T patients, cycle 1 NE rate in those given PP was 0% (0/9) and 18% (6/33) in those without PP. Overall cycle 4 NE rate was 27% (4/15) in patients given delayed PP and 30% (8/27) in those without. NEs caused 22/67 DRs and 14/45 DDs.

**Conclusion:** Overall pCR was better than expected whilst subtype-specific pCR matched published standards. Partial responders require greater subcategorisation. Review of criteria for PP from cycle 1 of FEC75T is needed. Delayed PP at docetaxel switch could be considered in regimen-based subpopulations.

**No conflicts of interest**

**354** Poster/Poster Spotlight

**Doxorubicin/cyclophosphamide with concurrent versus sequential docetaxel as neoadjuvant treatment in patients with breast cancer − 5-year disease-free and overall survival data**

B. Vriens[1], M. Aarts[1], S. Van Gastel[2], F. Van den Berkmortel[3], T. Smilde[4], L. Van Warmerdam[5], M. De Boer[1], D.J. Van Spronsen[6], P. Peer[7], V. Tjan-Heijnen[1]. [1]*Maastricht University Medical Center, Medical Oncology, Maastricht, Netherlands;* [2]*Comprehensive Cancer Center the Netherlands, Cancer Registry, Nijmegen, Netherlands;* [3]*Zuyderland Hospital, Medical Oncology, Heerlen, Netherlands;* [4]*Jeroen Bosch Hospital, Medical Oncology, 's Hertogenbosch, Netherlands;* [5]*Catharina Hospital, Medical Oncology, Eindhoven, Netherlands;* [6]*Canisius-Wilhelmina Hospital, Medical Oncology, Nijmegen, Netherlands;* [7]*Radboud Institute for Health Sciences, Biostatistics, Nijmegen, Netherlands*

**Background:** Taxanes have an established role as (neo)adjuvant treatment of breast cancer. Previously, we reported the results from a Dutch phase III neoadjuvant chemotherapy study, showing a pCR in the breast in 21% of patients treated with a sequential taxane-containing chemotherapy schedule and in 16% of patients treated with a concurrent schedule (odds ratio 1.44; 95% confidence interval (CI) 0.67–3.10) (Vriens B. et al., Eur J Cancer 2013; 49: 3102−10). Now we report on the follow-up analyses.

**Material and Methods:** Women with newly diagnosed breast cancer were randomly assigned to neoadjuvant chemotherapy of four cycles of doxorubicin and cyclophosphamide followed by four cycles of docetaxel (AC 60/600 − T 100 mg/m$^2$) or six cycles of TAC (75/50/500 mg/m$^2$) every 3 weeks. Primary endpoints of the current analysis concern the 5-year disease-free (DFS) and overall survival (OS).

**Results:** In total, 201 patients were included. Baseline characteristics were well balanced. After a median follow-up of six years, 5-year DFS was 81% for patients in the AC-T group and 71% for patients who received TAC (log-rank P = 0.015; HR = 0.53; 95% CI 0.32 to 0.89). Five-year OS was also superior for the AC-T arm: 84% versus 76%, respectively (log-rank P = 0.041; HR = 0.54; 95% CI 0.30 to 0.98). A more detailed analysis will be presented at the meeting.

**Conclusions:** AC-T in sequence with a lower cumulative dose per agent outperformed concurrent TAC with improved 5-year DFS and OS.

Support: Unrestricted grants from sanofi-aventis NL BV and Amgen BV INTENS study GOV No. NCT00314977.

**Conflict of interest:** Other Substantive Relationships: Unrestricted grants from sanofi-aventis NL BV and Amgen BV.

**355** Poster

**A randomized, double-blind, placebo-controlled window of opportunity trial evaluating clinical effects of high dose vitamin D in patients with breast cancer**

A. Arnaout[1], S. Robertson[2], C. Addison[3], N. Chang[2], M. Clemons[4]. [1]*Ottawa Hospital Regional Cancer Centre, Surgery, Ottawa- Ontario, Canada;* [2]*Ottawa Hospital, Pathology, Ottawa, Canada;* [3]*Ottawa Hospital Research Institute, Cancer Therapeutics, Ottawa, Canada;* [4]*Ottawa Hospital Regional Cancer Centre, Oncology, Ottawa- Ontario, Canada*

**Background:** Considerable epidemiologic and preclinical laboratory data suggest that there is a role for vitamin D in breast cancer therapy through its tumor suppressive effects. The objective of this study was to assess the biologic effects of short term high dose vitamin D intake on breast tumor biology as demonstrated by changes in biomarkers of proliferation and apoptosis through a "window of opportunity" trial.

**Materials and Methods:** This is a prospective, randomized, double blind, placebo-controlled phase 2 trial assessing the effect of high dose (40,000 IU) of oral vitamin D3 on breast cancer biology in patients awaiting surgical management of their primary breast cancer. Eligible patients took the study drug for at least 2 weeks leading up to the day of surgery. Pre- and post-25-OH vitamin D blood levels were obtained. In addition, tumor biomarkers including the Ki67 index (marker of proliferation) and caspase 3 (marker of apoptosis) analyzed on the original diagnostic core biopsy sample and then compared to a repeated analysis on the tissue obtained at the time of the definitive surgical procedure.

**Results:** 80 patients completed the study; 38 in the control group and 42 in the vitamin D group. The mean duration on the study was 19 days. Within the study cohort, 16/80 (64%) were ER positive, 55/80 (55%) were PR positive, 65/80 (61%) were Her2 negative. Mean overall baseline blood 25-OH Vitamin D levels in the study cohort was 76.4 nmol/L, which increased to 241.9 nmol/L in the vitamin D treated group (p = 0.0001). Mean Ki67 level at baseline was 35.4% overall and there was no statistically significant difference in the ki67 obtained from the surgical specimen between the treatment group (mean = 39.3%) and the control group (41.0%). Baseline caspase 3 level was 31.2% overall and there was no statistically significant difference in the caspase 3 obtained from the surgical specimen between the treatment group (mean = 13.1%) and the control group (15.6%). However, the overall caspase 3 level (14%) obtained from the surgical specimen from both study groups was significantly lower than that at obtained from the core biopsy at baseline (31.2%) (p = 0.04).

**Conclusion:** This is the first prospective randomized trial evaluating the effect of short term, high dose vitamin D on the in vivo markers of proliferation and apoptosis. No significant difference was seen in these markers as a result of vitamin D intake, despite significantly higher circulating levels of 25-OH vitamin D in the blood. A significant reduction in caspase 3 was noted in both study arms when comparing the biopsy sample to the surgical specimen, which could be due to a reduction in apoptosis activity or technical factors affecting the measurement of caspase 3.

**No conflicts of interest**

**356** Poster

**Cardiac events and cardiac monitoring in adjuvant trastuzumab patients at The Christie: A retrospective audit**

A. Conway[1], H. Mitchell[1], D. Morrisey[1], A. Armstrong[1], A. Wardley[1], S. Howell[1]. [1]*Christie Hospital NHS Foundation Trust, Medical Oncology, Manchester, United Kingdom*

**Background:** Adjuvant trastuzumab (Herceptin ®) reduces breast cancer mortality in Her2-positive early breast cancer patients. The HERA trial

and NICE (2006) guidance stipulated LVEF >55% prior to trastuzumab treatment, exclusion of patients with certain cardiac comorbidities and 3-monthly LVEF monitoring on therapy (with trastuzumab suspension if LVEF declined). In 2009 National Cancer Research Institute (NCRI) published modified guidance recommending a more proactive approach to monitoring, including an echocardiogram prior to chemotherapy so that anthracycline could be avoided if there was concern about cardiac function, and management of cardiac dysfunction to maximise the number of patients benefitting from adjuvant trastuzumab. We present The Christie NHS Foundation Trust data before and after introduction of the NCRI guidance.

**Methods:** A complete audit cycle compared the frequency of LVEF monitoring and interventions of patients commenced on adjuvant trastuzumab for HER2-positive breast cancer from January to December 2010 and June to November 2014.

**Results:** In 2010, of 172 patients initiated on trastuzumab, 99% had pre-trastuzumab LVEF measurement but only 74% had a pre-chemotherapy LVEF performed. Seven patients (4%) did not complete trastuzumab; 5 due to symptomatic/persistent decline in LVEF. LVEF declined in 10 (5%) of patients. ACE-inhibitor initiation and cardiology referral were undertaken in 3 (60%) and 5 (71%) of cases respectively. In those with LVEF decline, 60% (n = 6) completed trastuzumab.

Following recommendations that NCRI guidance be standard of care, in a re-audit over 6 months in 2014, of 104 patients commenced on trastuzumab 98% had pre-chemotherapy LVEF performed. Of 5 patients (5%) who did not complete trastuzumab only 1 was due to a decline in LVEF. LVEF declined in 10 patients (10%); but 9 (90%) completed planned trastuzumab with commencement of ACE-inhibitor (+/− β-blocker) +/− cardiology referral.

In both cohorts, no patients treated with anthracycline chemotherapy (n = 217) who had both pre- and post-chemotherapy scans (n = 158) demonstrated an asymptomatic decline in LVEF.

**Conclusion:** Adherence to the 2009 NCRI guidelines improved the ability to complete adjuvant trastuzumab which is essential to optimal treatment of patients with HER-2 positive early breast cancer. The utility of echocardiography after anthracycline before trastuzumab needs reviewing.

**References**

Jones AL, et al, Br J Cancer. 2009 Mar 10; 100(5): 684−92.

**No conflicts of interest**

**357** Poster

**Toxicity of (neo)adjuvant chemotherapy in BRCA1- and BRCA2-associated versus sporadic breast cancer patients**

J. Drooger[1], B. Heemskerk-Gerritsen[1], N. Smalllenbroek[1], C. Epskamp[2], C. Seynaeve[1], A. Jager[1]. *[1]Erasmus MC Cancer Institute, Medical Oncology, Rotterdam, Netherlands; [2]Sint Franciscus Gasthuis, Medical Oncology, Rotterdam, Netherlands*

**Background:** Treatment with (neo)adjuvant chemotherapy for breast cancer, as currently given, causes cell damage by induction of double-strand DNA breaks. Because BRCA1 and BRCA2 proteins play a role in repair of DNA damage, the efficacy of (neo)adjuvant chemotherapy in BRCA1/2-associated breast cancer patients (having an impaired DNA repair mechanism) may be increased, but as a downside be associated with more chemotherapy-related toxicity. We performed a single center retrospective cohort study to examine potential differences in (neo)adjuvant chemotherapy-related toxicity between BRCA1/2-associated and sporadic breast cancer patients.

**Patients and Methods:** We selected all female patients who were treated at the Erasmus MC Cancer Institute, Rotterdam, the Netherlands, with (neo)adjuvant chemotherapy for primary or loco-regional recurrence of breast cancer (PBC/LR) between 1−1–2004 and 31−12–2014. The primary outcome was the relative total dose intensity (RTDI), which accounts for reductions, delays and premature discontinuations of a treatment. The RTDI was calculated for anthracyclines and taxanes separately. Secondary outcomes were the occurrence of febrile neutropenia, delay in chemotherapy administration, and altered chemotherapy regimen due to toxicity.

**Results:** In total, 701 patients treated for PBC/LR were eligible for data-analysis. There were 86 PBC/LRs in patients with a BRCA1/2 mutation (n = 68 BRCA1 and n = 18 BRCA2). The mean RTDI for anthracyclines was not significantly different between both groups (98.7% in the BRCA1/2, and 96.6% in the sporadic group, p = 0.27). Also the mean RTDI for taxanes was not significantly different between the groups (93.6% in the BRCA1/2-associated, and 90.0% in the sporadic group, p = 0.12). Linear regression analysis revealed no significant effect of BRCA1/2 mutation carriership on the RTDIs. No significant differences were found in the percentages of patients presenting with febrile neutropenia (21% in the BRCA1/2-associated, and 17% in the sporadic group, p = 0.42), with a delay in chemotherapy administration (anthracyclines: 15% in both groups, p = 0.97; taxanes: 4% in the BRCA1/2-associated, and 10% in the sporadic group, p = 0.13) or with an altered chemotherapy regimen (9% in the BRCA1/2-associated, and 11% in the sporadic group, p = 0.73). Additionally, the odds ratios showed no significant effect of BRCA1/2 mutation carriership on the secondary outcome variables.

**Conclusion:** The lack of differences in (neo)adjuvant chemotherapy-related toxicity between BRCA1/2-associated and sporadic breast cancer patients suggests that the DNA damage repair mechanism of non-cancer cells with only one normal copy of either the BRCA1 or BRCA2 gene is sufficiently functional to handle acute chemotherapy-associated toxicity.

**No conflicts of interest**

**358** Poster

**Cobimetinib (COBI) + Paclitaxel (PTX) as first-line treatment in patients (pts) with advanced triple-negative breast cancer (TNBC): Interim safety review of the ongoing phase 2 COLET study**

S.B. Kim[1], D. Miles[2], T. Velu[3], J. Garcia-Saenz[4], E. Tan-Chiu[5], J.H. Sohn[6], L. Dirix[7], M. Borms[8], J.I.D. Mingorance[9], M.C. Liu[10], M. Moezi[11], M. Kozloff[12], J. Sparano[13], J. Hsu[14], S. Brian[15], V. McNally[16], A. Brufsky[17]. *[1]Asan Medical Center, Dept of Medicine, Seoul, Korea; [2]Mount Vernon Cancer Centre, Medical Oncology, London, United Kingdom; [3]Chirec Cancer Institute, Medical Oncology, Brussels, Belgium; [4]Hospital Clinico San Carlos, Medical Oncology, Madrid, Spain; [5]Florida Cancer Research Institute, Medical Oncology, Plantation, USA; [6]Severance Hospital- Yonsei University Health System, Medical Oncology, Seoul, Korea; [7]Sint-Augustinuskliniek, Medical Oncology, Wilrijk, Belgium; [8]AZ Groeninge, Medical Oncology, Kortrijk, Belgium; [9]Hospital Infanta Cristina, Medical Oncology, Badajoz, Spain; [10]Koo Foundation Sun Yat-Sen Cancer Center, Medical Oncology, Taipei, Taiwan; [11]Cancer Specialists of North Florida, Medical Oncology, Jacksonville, USA; [12]Ingalls Memorial Hospital, Oncology/Hematology, Harvey, USA; [13]Montefiore Einstein Cancer Center, Oncology, Bronx, USA; [14]Genentech Inc., Biostatistics, South San Francisco, USA; [15]Genentech Inc., Product Development Oncology, South San Francisco, USA; [16]Roche Products Ltd., Clinical Development, Welwyn Garden City, United Kingdom; [17]Magee Women's Hospital, Hematology-Oncology, Pittsburgh, USA*

**Background:** COBI is a potent, highly selective MEK inhibitor that has shown improved clinical outcomes when combined with vemurafenib, compared with vemurafenib alone, in $BRAF^{V600}$-mutated metastatic melanoma. Preclinical models imply that up-regulation of the MAPK pathway confers resistance to taxane therapy. Since most TNBC pts develop resistance to taxanes and many TNBC tumors harbor genetic alterations in the MAPK pathway, the combination of a taxane and a MEK inhibitor may be beneficial.

**Methods:** COLET (EudraCT number, 2014–002230−32) is a multistage study to evaluate safety and efficacy of COBI + PTX in pts with metastatic or locally advanced TNBC and no prior systemic therapy for metastatic disease. The study has 2 stages: a safety run-in stage of approximately 12 pts, followed by a randomized stage in which approximately 100 pts will be randomized (1:1) to receive COBI + PTX or placebo + PTX. Pts will receive PTX 80 mg/m$^2$ on Days 1, 8, and 15 and COBI/placebo 60 mg/day on Days 3−23 of each 28-day cycle until disease progression or unacceptable toxicity. An interim safety review of the run-in stage was planned after 12 pts completed at least 1 cycle of treatment. Initiation of the randomized stage was conditional on this review, results of which are presented here.

**Results:** Between Mar 12, 2015, and Jun 8, 2015, 16 pts were enrolled in the safety run-in stage. All were female, and the median age was 55 years. At data cutoff (Jun 25, 2015), 12 pts had completed at least 1 cycle; all 16 pts received at least 1 dose of study treatment and were included in the safety review. Median time on treatment was 47 days (range, 1−85). Most pts tolerated COBI + PTX; only 1 pt discontinued treatment because of an AE (PTX-related infusion reaction at the start of Cycle 2). 94% of pts had ⩾1 adverse event (AE). The most common (⩾20%) AEs of any grade were diarrhea (63%), rash (44%), nausea (38%), and alopecia, pyrexia, stomatitis, vomiting, and abdominal pain (all 25%). 7 pts (44%) had grade 3 AEs; there were no grade 4−5 AEs. Ocular toxicity has been reported with MEK inhibitors; in this study, 1 pt had a grade 1 AE of increased macular drusens (yellow deposits under the retina). Preliminary efficacy results (data cutoff Aug 3, 2015) of 16 pts were unconfirmed partial response (n = 7), stable disease (n = 4), and progressive disease (n = 2); 3 pts had not completed a tumor assessment.

**Conclusions:** The safety profile of COBI + PTX was consistent with known safety profiles of each drug, with no exacerbation of anticipated COBI or PTX toxicities and no new safety signals. This is the first study evaluating COBI + PTX in TNBC. Results support further evaluation, and enrollment to the randomized stage was opened (primary efficacy outcome

of progression-free survival). Pts in the safety run-in stage continue to be followed up for long-term safety and disease progression.

**Conflict of interest:** Ownership: Sparano, stock options (Metastat); Hsu, Employee, salary, stock (Genentech); Simmons, Employee, salary, stock (Genentech); McNally, Employee, salary, stock (Roche). Advisory Board: Miles, Roche, GNE, Amgen, Celgene; Kozloff, Genentech Roche; Sparano, T-DM1 Ad board, MM-121 Advisory board, Fulvestrant ad board, Abraxane ad board, Maraviroc observations study), Genentech/Roche, Merrimack, AstraZeneca, Celgene, Pfizer; Brufsky, Genentech; Corporate-sponsored Research: Kim, Novartis, GSK, Sanofi; Tan-Chiu, Florida Cancer Research Institute (PI); Sparano, Genentech/Roche, Novartis, Merrimack, Medimmune. Other Substantive Relationships: Miles, Speaker (Roche); Tan-Chiu: Investigator (Florida Cancer Research Institute); Borms, Consultant (Roche; grant); Kozloff, Consultant (Genentech Roche), Investigator (Genentech Roche), Speaker (Genentech Roche); Sparano, Consultant (Metastate, Prescient Therapeutics), Research Funding (Takeda), Honoraria (Genentech/Roche, Celldex), Other (patent, royalties; Genomic Health); Brufsky, Consultant (Genentech).

**359** Poster

**Low relapse rate with a non-anthracycline (nonA)-containing taxane (Tax)-based chemotherapy (CTx) for HER2-normal early stage breast cancer (ESBC): Mature results of a single institution experience**

G. Gullo[1], D. Tryfonopoulos[2], J. Ballot[3], J. Gannon[4], C. Lowry[3], A.M. Defrein[5], M. Donohoe[6], T. Lyons[5], J. Crown[4]. [1]*St Vincents University Hospital, Medical Oncology Department, Dublin, Ireland;* [2]*Agios Savvas Cancer Center, Medical Oncology, Athens, Greece;* [3]*St Vincents University Hospital, Medical Oncology Clinical Research Unit, Dublin, Ireland;* [4]*St Vincents University Hospital, Pharmacy Department, Dublin, Ireland;* [5]*St Vincents Private Hospital, Medical Oncology Unit, Dublin, Ireland*

**Background:** Anthracycline-containing regimens (AReg) became an established standard (neo)adj CTx for ESBC following fairly consistent demonstration of a modest superiority over older anti-metabolite/alkylating Regs. Intriguingly, substantial translational data suggest that this superiority was limited to pts with HER2-altered BrCa, although HER2 is not a target for A. Data from Press et al (JCO 2012) support the hypothesis that this phenomenon is due to co-amplification of topoisomerase 2 in 1/3 of HER2 amplified. A are cardiotoxic (including late onset of cardiomyopathic congestive heart failure) and potentially leukaemogenic. The non-A Reg TC (docetaxel/cyclophosphamide) produced superior outcomes compared to AC in a USONC trial. In late 2006 we established a routine, uniform policy of non-AReg CTx for ESBC, using TC for all pts receiving (neo)adj CTx for HER2-normal ESBC. We report this large single department unselected experience.

**Materials and Methods:** We performed a retrospective analysis of pts treated at our Department with at least 1 cycle of (neo)adj TC (docetaxel 75 mg/m$^2$ and cyclophosphamide 600 mg/m$^2$ IV every 3 weeks) for ESBC before the end of 2010. Pts were identified by systematic analysis of the dataset of the Pharmacy Departments. Information on tumour characteristics [e.g. axillary lymph nodes (N) metastases, hormonal receptors (HR) and HER2 status] were retrieved. Pts with node-positive (N+) ESBC received TC $\times$6 cycles, and pts with high-risk node-negative (N−) [e.g. primary tumour (T) >2 cm, or HRneg, or T >3 cm] ESBC received TC $\times$4 cycles. Pts received adjuvant hormone therapy and radiotherapy as per standard of care. From 2008 on many better risk HR+/N− patients were not given CTx due to Oncotype availability.

**Results:** A total of 450 female pts treated between September 2006 and December 2010 were identified and included in this analysis. Pts characteristics are: median age 57 yrs (range 31−76), N− 237 (53%), N+ 213 (47%), hormone receptors positive (HR+) 379 (84%), triple-negative (TN) 72 (16%). The database was locked as of 31/10/2015. Median follow up from first cycle of CTx is 6.7 yrs (range 4.8−9). 55 BrCa-specific relapse events have been observed accounting for an overall Relapse-Free Survival (RFS) rate of 88%. The Overall Survival (OS) rate in the whole cohort is 90%. The RFS and OS rates for the different pts subgroups are reported in the table.

| | DFS rate | OS rate |
|---|---|---|
| All pts (N = 450) | 88% | 90% |
| HR+/N− (N = 191) | 95% | 95% |
| HR+/N+ (N = 187) | 84% | 88% |
| TN/N− (N = 47) | 91% | 91% |
| TN/N+ (N = 25) | 56% | 60% |

**Conclusions:** These mature data suggest that the prognosis for 5-yrs OS for pts with HER2neg HR+ ESBC (regardless of nodal status) and for TN N− ESBrCa treated with nonAReg is excellent. To date no random assignment trial has shown superior survival for any A over non-A regimen in Her2neg ESBC. N+TN ESBrCa remains a significant clinical challenge.

**No conflicts of interest**

**360** Poster

**Adherence to oral adjuvant hormonal therapy in women with breast cancer: intentional and unintentional influencing factors**

B. Cotter[1], M. Corrigan[1]. [1]*Cork University Hospital, Academic Surgery, Cork, Ireland*

The role of anti-oestrogen therapies such as tamoxifen and aromastase inhibitors is well established in the management paradigm of hormone sensitive breast cancer. The aim of this study was to assess adherence levels to oral adjuvant hormonal therapy in women with breast cancer, primarily focusing on the intentional and unintentional influencing factors.

**Methods:** A patient focused, medication specific questionnaire, focusing on intentional and unintentional adherence influencing factors was designed, psychometrically tested and distributed to a cohort study of 212 patients with ER/PR positive breast cancer, currently prescribed an anti-oestrogen therapy. The questionnaire was completed anonymously by consecutive patients attending follow-up breast clinics over a 6 month period. Psychometric analysis including factor analysis, reliability and validity testing was conducted. Levels of medication adherence, intentional factors (i.e. health & medication beliefs) and unintentional factors (i.e. medication planning strategies) were evaluated.

**Results:** The mean age of women involved in the study was 59.2 years. 77.7% of women took between 1−3 tablets per day. 83.4% of women underwent lumpectomy/Wide local excision whilst 28.9% underwent mastectomy prior to oral medication. 72.2% of women believed that having cancer in the past would affect their future health. The majority of women involved in the study shared similar medication beliefs. 42.5% agreed and 25.9% strongly agreed that oral medications allowed them to have a better quality of life. In relation to medication adherence the majority of patients had a specific planning strategy (92%) relating to their oral medications.

**Conclusion:** Adherence to oral hormonal therapy in women with breast cancer is key to optimal therapeutic outcomes. Assessing both intentional and unintentional factors is essential for clinicians to understand individual barriers to adherence.

**No conflicts of interest**

**361** Poster

**Adjuvant chemotherapy with 3-weekly cyclophosphamide and dose dense paclitaxel in early breast cancer patients older than 65 years, a retrospective study**

C. Fontaine[1], S. Joris[1], L. Decoster[1], L. Vanacker[1], D. Schallier[1], M. Vanhoeij[2], G. Verfaillie[2], J. Lamote[2], J. De Grève[1]. [1]*UZ Brussels, Medical Oncology, Jette, Belgium;* [2]*UZ Brussels, Surgical Oncology, Jette, Belgium*

**Introduction:** Adjuvant treatment decisions in older breast cancer (BC) patients (pts) have to be weighed against life expectancy, comorbidities, and functional status. Based on the superiority of four cycles of adjuvant docetaxel/cyclophophamide to standard doxorubicin and cyclophosphamide in older BC pts we previously implemented this regimen in our institution. Due to the high rate of G3/4 non-hematologic toxicities (43%) and hospitalizations (27%) with this regimen, we adopted an alternative combination therapy consisting of weekly paclitaxel and 3-weekly cyclophosphamide in early BC pts above 65 years.

**Purpose:** The objectives of this study were to analyze the relative dose density, the hematologic and non-hematologic toxicities of this regimen as well as disease-free and overall survival in the older BC group.

**Methods:** A single center retrospective analysis was performed in all pts aged $\geqslant$65 years with early breast cancer (EBC) treated with (neo)adjuvant chemotherapy consisting of 4 cycles of cyclophosphamide at 600 mg/m$^2$ every three weeks and 12 cycles of weekly paclitaxel at 80 mg/m$^2$ followed by irradiation and endocrine therapy in case of hormone sensitivity.

**Results:** A total of 27 pts were included in the study with a mean age at diagnosis of 70 years (65−83 yrs). Most of the tumors were small (T1 28%; T2 53%) and invasive ductal carcinomas (71%), but were relatively high grade (G2 50%; G3 40%). Only ten percent were triple negative and 17 percent were Her2 amplified. Lymph node involvement was present in eighteen pts (N1: 7; N2: 5; N3: 6). Only seven out of 27 pts (26%) could complete the four cycles of adjuvant chemotherapy without dose reduction. Seven pts (26%) prematurely interrupted chemotherapy due to non-hematologic toxicities [allergic reaction G2: 1; heart failure G4: 1; anorexia G3: 1; skin rash G2: 2; polyneuropathy (PNP) G2: 2]. Most non-hematologic toxicities were G1/2: asthenia G1/2 (70%), PNP G1/2 (52%)

and alopecia G1/2 (33%). Despite the use of G-CSF, four pts (14%) developed a grade 4 neutropenia. Hospitalization was necessary in 4 pts due to pneumonitis G4 (lethal 1), heart failure G4 (1), seroma infection G2 (1) and diarrhea G3 (1). After a median follow-up of 18 months the progression free and overall survival were both 96.3%.

**Conclusion:** This is the first retrospective study of the adjuvant combination of cyclophosphamide and paclitaxel in the older BC pts above 65 yrs old. This regimen appears less toxic than the docetaxel/cyclophosphamide regimen. Selection and close monitoring of this elderly patient population remains a challenge for medical oncologists.

**No conflicts of interest**

## Friday, 11 March 2016

**POSTER SESSION**

# Advanced Disease

**362** Poster

### Patient's clinical, pathologic and therapy features related to bone metastases and survival in breast cancer

B. Merck[1], J.M. Redín[2], C. Barrios[3], A. Barrasa[4]. [1]*Universidad Cardenal Herrera CEU, Surgery, Valencia, Spain;* [2]*Universidad Cardenal Herrera CEU, Physiotherapy, Valencia, Spain;* [3]*Universidad Católica de Valencia, Surgery, Valencia, Spain;* [4]*Universidad Cardenal Herrera CEU, Biomedical Science, Valencia, Spain*

**Background:** Bone metastasis is a frequent event in breast cancer patients. Actual treatment enhances overall survival; however there are differences in patient's outcome. Relevant factors related to bone lesions have been analyzed and survival repercussion evaluated.

**Patients and Method:** A retrospective analysis of our prospectively collected database yielded 114 women treated with zoledronic acid for bone metastases between July 2009 and June 2010. Analyzed factors were: synchronous versus metachronous presentation; unique bone lesion against multiple metastases; hormonal status; and presence or not of extraosseous disease.

**Results:** Fifteen patients were excluded from analysis. Age ranged between 26 and 79 years, 48.5% were premenopausal. Staging at the time of breast cancer diagnosis was: cM0:78;cM1:21. Surgery was the first treatment for 68 patients, while 30 cases had systemic approach. Time between primary cancer and bone metastases diagnosis ranged between 0 (Stage IV) and 311 months. 27 patients presented isolatedbone lesions located on sacrum, ribs, sternum, vertebral body, acetabulum, humerus, pelvis and scapula. Pain(39.4%), asymptomatic (29.3%) and impaired biochemical blood analysis (27.3%) were the principal clinical presentations of the bone lesion. Extraosseous failure happened in 64.6% of patients during follow up. Bone metastases treatment included surgery (8 patients), radiation therapy (43.3%), chemotherapy (60%), hormonal therapy (68%) and 22 patients were additionally castrated.

A significant relationship ($p < 0.001$) was found for hormonal status and unique bone metastases, metastases biopsy and castration; M0/M1 at breast cancer diagnosis and primary treatment, axillary lymphadenectomy and adjuvantchemotherapy; Unique bone lesions were more often biopsied, surgically managed and less frequent in postmenopausal women. Additional visceral and/or central nervous system metastases were related to reduced survival.

**Conclusions:** Two patterns of bone dissemination have been found. Younger premenopausal women with unique bone and high rate of visceral and or CNS disease presented a low overall survival. A second group included older women, postmenopausal, presenting multiple bone metastases, usually on hormonal treatment and with a favorable prognosis.

**No conflicts of interest**

**363** Poster

### Breast cancer in eldery patients: A single center experience

A. Fachinetti[1], C. Chiappa[1], G. Dionigi[1], F. Rovera[1]. [1]*University of Insubria Varese, Department of Surgical and Morphological Sciences, Varese, Italy*

**Background:** Elderly population is increasing and consequently the number of elderly breast cancer patients. According to data of the Italian Cancer Registry, 15% of all breast cancer patients is diagnosed in women older than 65 years.

Unfortunately, there is no consensus or sure guidelines on how to treat this group of patients. It is generally assumed that breast cancer characteristics and behaviour are more favourable among older patients than younger patients. Despite this favourable disease pattern, some recent studies suggest that elderly patients are often undertreated compared to younger patients.

**Material and Methods:** The primary aim of this study was to analyse the surgical management and the post operative outcome in elderly patients in a Breast Unit. The second aim was also to evaluate the biological characteristics of the primary tumor, the patients' comorbidities and the time of hospitalization.

This study enrolled 98 patients, aged 80 years or older, who underwent surgery for breast cancer in the period January 2012 to May 2015.

Co-morbidity was classified according to the Adult Co-morbidity Evaluation-27 index (ACE-27), wich divided co-morbidity into different organ systems: cardiovascular, respiratory, gastrointestinal, renal, endocrine, neurological, psychiatric, rheumatologic, immunological and malignancy.

**Results:** Ninty-eight patients were included (median age 83 years). We recorded data regarding type of tumor, stage at the diagnosis, surgical procedure, co-morbidities and surgical outcome.

Forty-eight percent had mastectomy and 52% underwent to breast conservative surgery. Seventy-two percents had sentinel lymph node biopsy. The majority of the tumors were Luminal A with a moderate grade of differentiation, only 20% were G3. Seventy percent of patient underwent to complete adjuvant radiotherapy after breast conservative surgery. Almost all patients received adjuvant hormonal treatment, only 13% received also adjuvant chemotherapy.

No adverse event were recorded during the hospitalization.

The median follow up period was 36 months and we observe seven death due to disease progression.

**Conclusion:** Advanced age should not be considered a limitation to surgical treatment by itself, although there are no standard guidelines for elderly breast cancer patients. Breast cancer surgical treatment in elderly patients, in our experience, is feasible and safe with a low risk of complications and with a short hospitalization.

Additional evidence to support clinical practice is still needed to improve and individualize oncogeriatric care.

**No conflicts of interest**

**364** Poster

### Thyroid diseases in patients with breast cancer

C. Chiappa[1], A. Fachinetti[1], G. Dionigi[1], F. Rovera[1]. [1]*University of Insubria Varese, Department of Surgical and Morphological Sciences, Varese, Italy*

**Background:** The possible existence of a correlation between thyroid diseases and breast cancer has been evaluated during last decades, but the relationship between these two pathological conditions remains controversial. The dependence of breast cancer by hormonal substances and controversial data shown in literature on the relationship between thyroid function of patients and the neoplastic disease suggested that the expression of thyroid hormone receptors could be an important marker in the characterization of breast cancer.

**Materials and Methods:** During the period January 2009 − December 2013, 867 patients were treated for breast cancer at the Breast Unit (5 male, average age 61 years). We analyzed the incidence and the characteristic of thyroid disease in these patients.

**Results:** In 725 cases a ductal carcinoma was detected, in 71 lobular carcinoma, the remaining 71 were distributed among less frequent histological types. Among these 867 patients, 141 (16%) were affected by benign or malignant thyroid disease, while the remaining 725 had no history of thyroid disease. The analysis of 141 patients with thyroid disease established that 138 cases were benign disease, whereas the remaining 3 were malignant. Fifty-three patients had autoimmune thyroid disease, while the remaining 88 had a non-autoimmune thyroid disease. We found statistically significant association between breast cancer and chronic autoimmune thyroiditis ($p < 0.03$), post-menopausal age ($p < 0.003$) and the correlation between estrogen receptor positivity in breast cancer and chronic autoimmune thyroiditis ($p < 0.03$). There were no statistically significant differences regarding the characteristics of breast cancer such as family history, tumor size, lymph node metastases, distant metastases, clinical stage and histo-pathology, grading, estrogen and progesterone receptor profile and the expression of Ki67, p53 and HER2.

**Conclusions:** The relationship between breast cancer and thyroid disease remains controversial also related to the contradictory results reported in the literature. It appears to be an association between autoimmune thyroid disease, specifically chronic autoimmune thyroiditis and the occurrence of breast cancer at young age. However, it remains to be investigated the pathophysiological mechanism linking the two entities. Multicentric studies are needed to confirm the correlation between these two diseases, in order to accurately identify a subpopulation of high risk patients for developing breast cancer.

**No conflicts of interest**

**365** Poster

**Surgical treatment of hereditary breast cancer**

C. Chiappa[1], A. Fachinetti[1], G. Dionigi[1], F. Rovera[1]. [1]*University of Insubria Varese, Department of Surgical and Morphological Sciences, Varese, Italy*

**Background:** The vast majority of breast cancers are sporadic; about 5−7% appears as hereditary breast cancers, defined as an aggregation of breast and/or ovarian cancers with two or more first-degree relatives affected with demostration of genetic mutation. Presentation is an early age; often it appears bilateral and multifocal/multicentric. The well-known genes mainly involved are BRCA1 and BRCA2, respectively located on chromosomes 17 and 13. The risk of developing a contralateral breast cancer is higher than 30%. Risk reduction options include three different categories: surveillance diagnostics, drug-prevention and prophylactic surgery. The risk reduction surgical procedures are represented by prophylactic bilateral mastectomy, reducing the risk of about 90% and bilateral salpingo-oophorectomy, which reduces the risk of ovarian cancer of about 98% and the risk of breast cancer of 50%.

**Materials and Methods:** Since 2008 to July 2014 56 patients with hereditary breast cancer were treated in our Breast Unit. Thirty had BRCA1 mutation and 26 BRCA2. Fifty-three patients (95%) were female and 3 (5%) male; the average age was 46.2 years (range 23−77 years).

**Results:** Globally 80 surgical procedures were performed, 20 patients underwent more than one operation, for relapse, second cancer or contralateral breast cancer. Eight developed a local relapse, with an average time of 105 months (range 42–192 months), while 9 developed a contralateral tumor. Regarding contralateral breast cancers, 4 were synchronous while 5 metachronous. The 80 procedures were divided in: 23 mastectomies, 44 lumpectomy and 5 local excisions. The last 8 procedures were performed prophylactically. Seven prophylactic contralateral skin nipple-sparing mastectomy and 1 skin-sparing mastectomy were performed. In one case, there was necrosis of the latissimus dorsi flap used for reconstruction. Twenty-two patients underwent axillary lymph node dissection d'emblèe. Thirty-eight patients underwent sentinel lymph node biopsy. In 14 cases the intraoperative frozen examination demonstrated metastases in the sentinel lymph node, and we proceeded to complete axillary lymph node dissection immediately. Of the 72 breast cancers 53 (74%) were invasive ductal carcinoma; 14 cases (19%) ductal carcinoma in situ; 2 cases (3%) were lobular carcinoma in situ; in the other 2 cases (3%) invasive lobular carcinoma and in 1 (2%) case neuroendocrine carcinoma of the breast were detected. Sixty-four carcinomas (89%) were unifocal, 6 (8%) bifocal and only 2 multifocal (3%). The grading was: in 3 cases (4%) grading 1, 38 (53%) grading 2 and 31 (43%) grading 3.

**Conclusions:** The management of high risk women is complex and should be performed in a Breast Unit were a multidisciplinary team could take charge the patient in order to offer woman a path that can reconcile her willingness to oncological security.

**No conflicts of interest**

**366** Poster

**Management of advanced breast cancer patients with eribulin − the experience of three UK teaching hospitals**

M. Jafri[1,2], R. Kussaibati[3], H. Ghoz[2], C. Draycott[1], N. Kazi[3], I. Fernando[1,3], M. Tsalic[3], D. Rea[1,2]. [1]*University Hospital Birmingham, Oncology, Birmingham, United Kingdom;* [2]*City Hospital, Oncology, Birmingham, United Kingdom;* [3]*Heart of England Foundation Trust, Oncology, Birmingham, United Kingdom*

**Background:** The EMBRACE study showed eribulin treatment c.f. physician's choice was associated with a significant improvement in overall survival (OS) of 13.2 c.f. 10.5 months after prior treatment with anthracyclines and taxanes in women with advanced breast cancer. We describe the clinical outcomes of individuals treated with eribulin in routine clinical practice.

**Materials and Methods:** All patients treated with eribulin between January 2011 and January 2015 treated at three Birmingham teaching hospitals by eight oncologists were identified using pharmacy records. Data was collated on: histological data, previous treatments, response to treatment, dose intensity and overall survival.

**Results:** 55 patients were identified with a median age of 56 years. 41 (75.5%) were ER positive and 14 (24.5%) ER negative. 45 (82%) were Her2 negative and 10 (18%) Her2 positive. 80% had ductal, 12.7% had lobular, 3.7% medullary and 3.7% had a mixed carcinoma. Patients received a median of 3 prior treatments, 2 endocrine treatments and 3 prior chemotherapy treatments. Patients received a median of 4 cycles (1−11). 70% of patients received 100% of the dose, 22% of patients received at least one dose delay. Treatment with eribulin was associated with an OS of 13 (6−9-19) months. OS was significantly longer in patients who received eribulin as a third line treatment c.f. fourth or more (18 months (95% CI 10.5–25.4) c.f. 9(95% 5.97–12.03) $p \leqslant 0.05$). OS of patients achieving partial response or stable disease was significantly longer than those who had progressive disease (15 c.f. 6 months ($p \leqslant 0.005$). No difference in OS was demonstrated dependent on ER or Her2 status. Presence of visceral metastases was a poor prognostic sign associated with a 9 month median survival.

**Conclusion:** Eribulin treatment is associated with similar OS to that demonstrated in clinical trials and other UK series. Survival appeared longer in those patients who were less heavily pre-treated i.e. received eribulin no more than third line. OS was equivalent regardless of whether patients had a partial response or stable disease. In routine practice, eribulin is an effective anti-cancer agent.

**No conflicts of interest**

**367** Poster

**STEPAUT: Efficacy and safety of everolimus plus exemestane in patients with HR+, HER2− advanced breast cancer progressing on/after prior endocrine therapy, in routine clinical practice**

G. Steger[1], M. Hubalek[2], G. Pfeiler[3], R. Greil[4], L. Ohler[5], R. Helfgott[6], E. Petru[7], B. Mraz[8], M. Hennebelle[8], I. Winiger[8,9], M. Gnant[10]. [1]*Medical University of Vienna, Department of Oncology and Comprehensive Cancer Center, Vienna, Austria;* [2]*Medical University of Innsbruck, Department of Obstetrics and Gynecology, Innsbruck, Austria;* [3]*Medical University of Vienna, Department of Gynecology and Gynecological Oncology-Comprehensive Cancer Center, Vienna, Austria;* [4]*Medical University of Salzburg, Department of Oncology, Salzburg, Austria;* [5]*Saint Joseph's Hospital of Vienna, Department of Oncology, Vienna, Austria;* [6]*Hospital Sisters of Charity, Department of Surgery, Linz, Austria;* [7]*Medical University of Graz, Department of Obstetrics and Gynecology, Graz, Austria;* [8]*Novartis Pharma GmbH, Oncology, Vienna, Austria;* [9]*Novartis Pharma AG, Basel, Switzerland;* [10]*Medical University of Vienna, Department of Surgery and Comprehensive Cancer Center, Vienna, Austria*

**Background:** In the pivotal BOLERO-2 trial, everolimus (EVE) + exemestane (EXE) more than doubled median progression-free survival (PFS) in hormone receptor-positive (HR+), human epidermal growth factor-receptor 2 (HER2)-negative advanced breast cancer (ABC) recurring/progressing on/after prior non-steroidal aromatase inhibitors (NSAIs). STEPAUT, an Austrian non-interventional study, evaluated the efficacy and safety of EVE+EXE in routine clinical practice in a similar pt population (N = 300). Results from the first interim analysis are reported here.

**Materials and Methods:** The study included 150 postmenopausal pts aged ⩾18 yrs, with HR+, HER2− ABC without symptomatic visceral metastasis, who received EVE+EXE in routine clinical practice, after disease recurrence/progression on/after NSAIs. The primary endpoint was PFS; secondary endpoints included response per RECIST v1.1 and safety.

**Results:** At data cut-off date (19 May 2015), median duration of follow-up was 6.05 mo. Overall, 134 pts (median age, 65 yr) were evaluable for safety and efficacy. Median time from initial diagnosis to study enrolment was 7.19 yr. NSAIs (83.3%) and chemotherapy (47.3%) were the most common prior therapies. The majority of pts received 10 mg EVE (n = 89, 60.1%) and 59 pts (39.9%) received 5 mg EVE. Of these, 54 pts (40.3%) and 37 pts (27.6%) continued on 10 mg and 5 mg EVE, respectively. Median PFS with 10 mg EVE was 9.83 mo (95% CI, 6.43–10.30) and was longer than with 5 mg EVE (4.97 mo, 95% CI, 3.13–10.03). Median PFS of pts who switched from 5 mg to 10 mg EVE was 6.83 mo, (95% CI, 2.57–15.40). Best overall response rate was 14.49% (CR, 0.72%, PR, 13.77%, SD, 13.64%). Overall, 27.6% of pts required therapy interruption and 58.7% of pts discontinued treatment, mainly due to disease progression (52.2%) or adverse events (AEs, 34.8%). Mean time periods from therapy initiation to interruption were 1.4 mo (10 mg) and 0.9 mo (5 mg). Interruptions due to AEs were higher with 5 mg (83.3%) vs 10 mg (66.7%). Median time to first AE was 0.63 mo. Most frequent AEs (all grades) were stomatitis (46%), exanthema (27.3%) and dyspnoea (23.3%). Grade 3 or 4 AEs reported were stomatitis (3.3%), weight loss (3.3%), and inappetence (2.7%). The frequency of AEs with 10 mg was comparable to 5 mg EVE. Serious AEs were reported for 29.3% of pts. Post-study regimens included endocrine therapy (35.3%), chemotherapy (30.9%), and others (33.8%).

**Conclusions:** Real world data from STEPAUT are consistent with BOLERO-2 data, and support EVE+EXE regimen as a suitable treatment option in HR+, HER2− ABC recurring or progressing on/after prior NSAIs. EVE 10 mg may be the preferred starting dose in routine clinical practice, owing to better efficacy and tolerability. Treatment interruption, instead of dose reduction, may be more effective in managing AEs.

**Conflict of interest:** Advisory Board: Prof Guenther Steger, Amgen, Roche, Novartis, Pfizer; Prof Richard Greil, Various advisory boards; Prof Gnant, Amgen, Asta Zeneca, GlaxoSmithKline, Roche, Novartis, Nanostring Technologies. Corporate-sponsored Research: Prof Gnant,

Sanofi Aventis, Novartis, Roche, Glaxo Smithkline, Pfizer; Prof Richard Greil, Research funding. Other Substantive Relationships: Prof Edgar Petru, Honoraries for lectures; Bernhard Mraz and Mathias Hennebelle, employees of Novartis Pharma GmbH in Austria.

**368** Poster

**Estimation of efficacy and safety of Genexol-PM, a Cremophor-free, polymeric micelle formulation of paclitaxel, in recurrent or metastatic breast cancer patients**

S.S. Kang[1], H. Lee[1], M. Hur[1], S. Ko[1], C. Yoon[1], S. Kang[1], J. Roh[2]. *[1]Dankook University- Cheil General Hospital, Surgery, Seoul, South Korea; [2]Dankook University- Cheil General Hospital, Medical Oncology, Seoul, South Korea*

**Background:** Genexol®-PM is a Cremorphor EL (CrEL)-free polymeric micelle formulation of paclitaxel that allows higher-dose administration with less hypersensitivity. This study was conducted to evaluate the response and safety of Genexol®-PM monotherapy in patients with recurrent or metastatic breast cancer (MBC).

**Material and Methods:** A total of forty-eight patients with recurrent or MBC, ECOG performance status $\leqslant$2 received Genexol®-PM by intravenous infusion at 300 mg/m$^2$ over 3 h every 3 weeks in the inpatient setting with premedication until disease progression or intolerability. Response to therapy was assessed after every 3 cycles using the Response Evaluation Criteria in Solid tumors (RECIST) guideline (version 1.1) and adverse events were evaluated according to the NCI Common Terminology Criteria for Adverse events, Version 3.0.

**Results:** A total of 290 chemotherapy cycles were administered, with a median of 6 cycles per patient (range, 1−16). The overall response rate was 52.1% with 1 complete response (CR) and 24 partial responses (PR). Of 11 patients who received Genexol®-PM as a first-line therapy, there were 5 responses (45.5%). Disease control rate (CR + PR + stable disease) was 64.6% (first-line: 72.7%, second-line: 53.8%, respectively). The median time to progression (TTP) was 6.0 months (range, 2.0−36 months). The common grade 3/4 non-hematologic toxicities were peripheral neuropathy (n = 22, 45.8%) and myalgia (n = 5, 10.4%). Hematologic toxicities were grade 3 and 4 neutropenia (n = 15, 31.3% and n = 6, 12.5%, respectively), and grade 1 and 2 thrombocytopenia (n = 7, 14.6%). No febrile neutropenia was observed.

**Conclusions:** Genexol®-PM, a CrEL-free, polymeric micelle formulation of paclitaxel chemotherapy showed significant antitumor activity with relatively low incidence and severity of toxicity in spite of a high paclitaxel dose in patients with MBC. Although further studies with larger sample size and different dosing schedules are warranted, this study suggests that Genexol®-PM monotherapy may be a candidate as a reasonable treatment for MBC patients.

**No conflicts of interest**

**369** Poster

**Preoperative breast MRI for the assessment of the size of ductal carcinoma in situ**

M. Rayzah[1], S. Nam[1]. *[1]Samsung Medical Center, General Surgery Breast Division, Seoul, South Korea*

**Objective:** To determine whether magnetic resonance imaging (MRI) can assess the size of ductal carcinoma in situ (DCIS) more accurately than mammography and ultrasonography using the histopathological dimension of the surgical specimen as the reference measurement.

**Materials and Methods:** This is a retrospective review study from a Samsung Medical Center (SMC) database of breast cancer. Preoperative contrast-enhanced MRI, mammography and ultrasonography were performed to detect and assess the size of DCIS in 131 patients. The greatest dimensions of DCIS determined by the imaging modalities were compared with the histopathological dimensions of the surgical specimen. Intra-class coefficients were calculated to check the agreement among the MRI, mammography and ultrasonography measurements. The Wilcoxon signed-rank test was used to evaluate the statistical significance of the differences in size between MRI, mammography or ultrasonography and histopathology.

**Results:** Of the 131 patients, 126 (96.18%) underwent MRI, 103 (78.63%) underwent mammography, and 121 (92.37%) underwent ultrasonography. The mean lesion size was 3.882 cm on histopathology, 3.595 cm on MRI, 2.879 cm on mammography and 2.327 cm on ultrasonography, and the difference among modalities was statistically significant. The correlation coefficient between histopathological measurement and MRI was 0.837, versus 0.461 between histopathology and mammography and 0.284 between histopathology and ultrasonography. The lesion size was correctly estimated ($\pm$5 mm), under-estimated (<5 mm), or over-estimated (>5 mm), respectively, by MRI in 60%, 19% and 21% of cases, by mammography in 38%, 31% and 31% of cases and by ultrasonography in 24.43%, 62.6% and 12.98% of cases, respectively.

**Conclusion:** MRI was more accurate for the detection and assessment of the size of DCIS than mammography and ultrasonography.

**No conflicts of interest**

**370** Poster

**Screening and management of cardiovascular risk in Belgian women $\geqslant$65 years with metastatic breast cancer treated with anthracyclines: An interim analysis of the MYCARD study**

I. Deleu[1], T. Velu[2], R. D'Hondt[3], I. Marinovic[4], C. Fontaine[5]. *[1]AZ Nikolaas, Medical Oncology, Sint-Niklaas, Belgium; [2]Chirec Cancer Institute, Oncology, Brussels, Belgium; [3]AZ Damiaan, Internal Medicine-Medical Oncology, Oostende, Belgium; [4]Teva Pharma Belgium, Medical Affairs, Wilrijk, Belgium; [5]Free University Brussels, Medical Oncology, Brussels, Belgium*

**Background:** Belgium has the highest incidence of breast cancer (BC) among the most affected countries in the world. Given the negative effect of anthracyclines (ANCs) and menopause on the cardiovascular (CV) system, cardiac parameters should be considered when therapy is planned for patients with metastatic BC (mBC) aged $\geqslant$65 years.

**Materials and Methods:** Open-label, multicenter, prospective, observational study at 20 specialized BC treatment centers in Belgium (NCT01555944). An equal number of consecutive patients aged $\geqslant$65 years with 1st or 2nd-line mBC will be treated with liposomal or nonliposomal ANCs; maximum of 160 patients per arm at national level. Routinely performed CV parameters will be recorded before, during, and after ANC treatment. Descriptive statistics and SAS v9.1.3 will be employed. Primary objectives are to evaluate the prevalence of CV risk factors and cardiac function before ANC treatment, observe the management of CV risk during and after ANC treatment, and compare liposomal with nonliposomal ANC therapy on cardiac function, outcomes, and quality of life. Secondary objectives include evaluations of preliminary efficacy and CV events.

**Results:** As of 17 August 2015, 56 patients (median age 74 years) were enrolled in either the liposomal ANC arm (n = 42 [75%]; nonpegylated [n = 38] or pegylated [n = 4] liposomal doxorubicin) or the nonliposomal ANC arm (n = 14; epirubicin [n = 9] or doxorubicin [n = 5]). Median BMI for patients was 27 kg/m$^2$. Menopause was reported in 59% of patients (data missing: 41%). Median age at primary BC and mBC diagnosis was 63 and 73 years, respectively. Of the 19 (34%) patients who had previously received ANC therapy at a mean cumulative dose of 261 mg/m$^2$, 16 were enrolled in the liposomal arm. Radiotherapy was received by 59% of patients. Baseline CV variables were not always routinely measured: BP was missing in 14%, ejection fraction (EF) in 20% and glucose in 37.5% of patients. Thus, descriptive analysis was performed for CV variables alone. Median systolic/diastolic BP and left ventricular EF were 134/80 mmHg and 65%, respectively. Median total cholesterol, LDL, HDL, and triglycerides were 204, 115, 59, and 125 mg/dL, respectively; 41% of patients received hypolipidemic drugs. Median HbA1c was 36 mmol/mol. At least 1 CV risk factor (eg myocardial infarction, arrhythmia, heart failure, familial heart disease, diabetes type 1 or 2) was reported in 52 (93%) patients. Overall, no statistically significant differences were observed in demographic variables and medical history between both treatment groups.

**Conclusions:** In clinical practice, CV risk factors are not routinely measured in this preselected, elderly population. Optimal detection and management of CV risk factors, before embarking on ANC therapy is essential to prevent CHF, even in the metastatic setting. Follow-up data will be presented at the meeting.

**Conflict of interest:** Corporate-sponsored Research: Grant (TEVA), Employee of Teva Pharma Belgium.

**371** Poster

**Use of bone-targeted agents (BTAs) to prevent skeletal-related events (SREs) in patients with advanced breast cancer and bone metastases (BMs) in a real-world setting**

R. Von Moos[1], D. Henry[2], J.J. Body[3], A. Rider[4], J. De Courcy[4], Y. Qian[5], D. Bhowmik[5], G. Hechmati[6], F. Gatta[6]. *[1]Kantonsspital Graubünden, Department of Onkologie/Hämatologie, Chur, Switzerland; [2]Joan Karnell Cancer Center- Pennsylvania Hospital, Department of Medicine, Philadelphia, USA; [3]CHU Brugmann- ULB, Department of Medicine, Brussels, Belgium; [4]Adelphi Real World, Bollington, United Kingdom; [5]Amgen Inc., Global Health Economics, Thousand Oaks, USA; [6]Amgen Europe GmbH, Global Health Economics, Zug, USA*

**Background:** Bone is the most common site of distant metastasis in patients with advanced breast cancer. Current bone health guidelines (ASCO, NCCN, ESMO) recommend patients should be prescribed a BTA

in combination with standard systemic therapies if BMs are present. BTAs are approved to prevent SREs that often cause debilitating bone pain and negatively impact on a patient's quality of life. The Adelphi Breast Cancer Disease-Specific Programme was used to understand real-world BTA treatment patterns.

**Material and Methods:** A multi-country cross-sectional survey of 290 oncologists conducted between February-April 2015 in 6 countries (Belgium, France, Germany, Italy, Spain and the United Kingdom). Physicians completed comprehensive record forms capturing information about the next 8 consecutive patients being treated for advanced breast cancer and a further two patients with the additional criterion of presence of BMs. Data collected included pain state (diagnosis and current), analgesic use, use of a BTA, reasons behind BTA treatment decisions, patient-reported outcomes and anti-cancer treatments.

**Results:** Data were captured for a total of 1408 patients with breast cancer with BMs; 77% of patients were hormone receptor positive; 21% were hormone receptor negative; for 2% data were unknown. The most common anti-cancer treatments patients were receiving were letrozole (20%) and paclitaxel/bevacizumab (7%). Patients were, on average, 11 months post BMs diagnosis with half (47%; n = 665) having experienced mild pain and 20% (n = 293) moderate/severe pain. A total of 16% (n = 219) of patients had experienced $\geqslant$1 SRE at time of BMs diagnosis. Of the 958 patients experiencing pain at the time of the survey, almost all (97%; n = 927) were taking analgesics, including 28% (n = 266) receiving strong opioids. Among the 1408 patients with BMs, 88% (n = 1238) were treated with a BTA (initiated within 3 months of BMs diagnosis in 81%; n = 1003). Main reasons for initiating BTA treatment were to manage bone pain (33%; n = 336) and perceived high risk of bone complications (31%; n = 313). A total of 170 patients with BMs were not receiving a BTA, the main reasons for not prescribing a BTA were: very recent diagnosis (41%; n = 70); perceived low risk of bone complications (18%; n = 30); and short life expectancy (10%; n = 17).

**Conclusions:** Patient management in the real-world setting appears to reflect current guidelines with the majority of patients receiving a BTA within 3 months of initial diagnosis. Where there is delay or no intention to initiate a BTA, a perceived low risk of SREs and short life expectancy were the most commonly reported reasons.

**Conflict of interest:** Ownership: Y Qian, G Hechmati − Amgen stock. Advisory Board: R von Moos − Amgen, Novartis, Roche, BMS, GSK; D Henry − Amgen. Corporate-sponsored Research: D Henry − Amgen. Other Substantive Relationships: Y Qian, D Bhowmik, G Hechmati, F Gatta − employees of Amgen; R von Moos − Speaker honoraria Amgen, Novartis, GSK; A Rider, J De Courcy − Employees of Adelphi Real World, paid consultants of Amgen.

**373** Poster

**TNM classification: Is there need for revision of pN3a breast cancer?**

T. Van Nijnatten[1], M. Moossdorff[2], L. De Munck[3], M. Vane[1], B. Goorts[1], K. Keymeulen[2], M. De Boer[4], L. Boersma[5], B. De Vries[6], R. Beets-Tan[7], M. Lobbes[8], M. Smidt[2]. *[1]Maastricht University Medical Center +, Radiology and Nuclear Medicine/Surgery, Maastricht, Netherlands; [2]Maastricht University Medical Center +, Surgery, Maastricht, Netherlands; [3]Netherlands Comprehensive Cancer Organisation, Research, Utrecht, Netherlands; [4]Maastricht University Medical Center +, Internal Medicine, Maastricht, Netherlands; [5]Maastricht University Medical Center + Maastro Clinic, Radiation Oncology, Maastricht, Netherlands; [6]Maastricht University Medical Center +, Pathology, Maastricht, Netherlands; [7]The Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital, Radiology, Amsterdam, Netherlands; [8]Maastricht University Medical Center +, Radiology and Nuclear Medicine, Maastricht, Netherlands*

**Background:** According to the current 7th edition of the TNM classification, pN3a stage in breast cancer patients consists either of presence of an infraclavicular lymph node metastasis (with a maximum of 9 lymph node metastases (LNM) in total) or presence of >10 axillary LNM. Both subgroups are considered as similar pathologic nodal stage. The aim of this study is to determine whether the prognosis of pN3a stage based on an infraclavicular LNM is different compared to >10 axillary LNM in breast cancer patients.

**Material and Methods:** Data were obtained from the National Cancer Registry. All patients were diagnosed between 2005 and 2008 with primary invasive epithelial breast cancer. Patients were subdivided in pN3a stage based on an infraclavicular LNM (with a maximum of 9 LNM in total) versus >10 axillary LNM. Exclusion criterion was distant metastases at time of diagnosis. Disease-free survival (DFS) included any local, regional, or contralateral recurrence or distant metastasis within 5 years. Kaplan–Meier curves provided information on DFS after 5 years and overall survival (OS) after 8 years. In addition, an univariable cox proportional hazards model was used to measure the effect between both subgroups for DFS and OS, respectively.

**Results:** A total of 1,788 patients with a pN3a stage were included. In 83 patients pN3a stage was based on the presence of an infraclavicular LNM (4.6%) and in 1705 patients because of >10 axillary LNM (95.4%). Five year follow-up was available for 1,293 patients (72.3%). DFS and OS were significantly superior in patients with pN3a stage based on an infraclavicular LNM compared to >10 axillary LNM (70.7% versus 55.7%, HR = 0.56, p = 0.016 and 63.9% versus 55.7%, HR = 0.62, p = 0.010) (Table 1).

Table 1. Results of Cox proportional hazards model for DFS and OS in pN3a stage breast cancer

| | Hazard Ratio (95% CI) | P-value |
|---|---|---|
| DFS | | 0.018 |
| >10 axillary LNM (n = 1235) | Reference | |
| Infraclavicular LNM [a] (n = 58) | 0.56 (0.35–0.91) | |
| OS | | 0.010 |
| >10 axillary LNM (n = 1705) | Reference | |
| Infraclavicular LNM [a] (n = 83) | 0.62 (0.43–0.89) | |

CI, confidence interval.
[a] Infraclavicular LNM with a maximum of 9 LNM in total.

**Conclusion:** Although pN3a stage based on an infraclavicular LNM is rare, its prognosis is better than pN3a stage defined as >10 axillary LNM, suggesting that the pN3a stage consists of a heterogeneous population with different survival outcomes. Therefore, we recommend a re-evaluation of pN3a stage.

**No conflicts of interest**

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**Primary tumor maxSUV by $^{18}$F-FDG PET/CT after neoadjuvant chemotherapy as predictive value for the pathologic response in locally advanced breast cancer**

S.H. Kang[1], S. Kwon[2]. *[1]Keimyung University Hospital, General Surgery, Daegu, South Korea; [2]Keimyung University Hospital, Pathology, Daegu, South Korea*

**Background:** The aim of this study is to evaluate the correlation of metabolic response by using maxSUV of F-18 fluorodeoxyglucose positron emission tomography/computed tomography (FDG-PET/CT) in tumor after neoadjuvant chemotherapy (NAC) with pathologic response in locally advanced breast cancer.

**Material and Methods:** This study included 26 patients with locally advanced breast cancer who had NAC and radical surgery from September 2007 to January 2015 in our institute. We retrospectively reviewed clinico-pathologic factors as age, pre-NAC clinical stage, chemotherapy regimen, clinical, metabolic and pathologic response to NAC, operation. We used the RECIST guideline to confirm the clinical response. For the pathologic response, the complete response (CR) was defined as no invasive focus in operation specimen and the partial response (PR) was defined as any invasive focus present. We divided total patients to pathologic CR (pCR), pathologic PR (pPR) and non responder (pNR). Also, by max SUV in $^{18}$FDG-PET/CT, metabolic response was described as metabolic complete response (mCR) and metabolic partial response (mPR); mCR was defined as complete resolution of hot uptake of primary tumor and mPR was defined as reduced uptake but not suitable for mCR. We compared clinical and metabolic response with pathologic response. To assess the predictive value of maxSUV for response of chemotherapy, we calculated reduction rate (RR) of maxSUV, it means a ratio of maxSUV after NAC to maxSUV before NAC. Receiver operating characteristic (ROC) anlaysis was conducted to determine the abilities of RR of maxSUV and maxSUV after NAC to predict NAC response.

**Results:** Before NAC, clinical state of total patients showed stage 2 was 12 (46.2%), stage 3 was 14 (53.8%) cases. Adriamycin based regimen was used in 10 patients (38.5%), and adriamycin plus taxane regimen was used in 16 patients (61.5%). All patients showed reduced maxSUV after NAC. Six patients (23.1%) showed mCR. Mean value of maxSUV before and after NAC was 12.5 (2.6–26.5) and 5.2 (1.0–16.4). Mean RR of maxSUV was 60.4%. After operation, pCR was achieved in 4 patients (15.4%), pPR in 14 patients (53.8%), pNR in 8 patients (30.7%). And among 6 mCR patients, 4 patients showed pCR and 2 patients showed pPR. The pCR group showed that mean value of post-NAC maxSUV is lower (p = 0.009) and higher RR of maxSUV (82.1%, p = 0.004) than pPR and pNR group. We found the optimal cutoff value of post-NAC maxSUV and RR predicting pCR and pPR, which were 5.4 and 56%. In analysis for correlation with pathologic response, both cut off values were statistically significant in univariate analysis, however, post-NAC maxSUV 5.4 or less was the only

independent significant factor in multivariate analysis (odds ratio 21.4, p = 0.018).

**Conclusions:** The maxSUV on tumor after NAC can predict the chemoresponse in locally advanced cancer.

**No conflicts of interest**

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**Metronomic combination of vinorelbine (VNR) and capecitabine (CAPE) in HER2-negative advanced breast cancer (ABC) patients (pts): Preliminary results of efficacy and safety of the VICTOR-2 study**

M.E. Cazzaniga[1], L. Porcu[2], L. Cortesi[3], A. Ferzi[4], F. Giovanardi[5], M. Ciccarese[6], P. Pugliese[7], S. Della Torre[8], M. Nicolini[9], C. Verusio[10], E. Piazza[11], L. Zanlorenzi[12], M. Comandè[13], L. Clivio[2], V. Torri[2]. *[1]AO San Gerardo, Medical Oncology, Monza, Italy; [2]Istituto Mario Negri, Oncology Unit, Milano, Italy; [3]University of Modena and Reggio Emilia, Hematology and Respiratory Diseases, Modena, Italy; [4]AO Legnano, Medical Oncology, Legnano, Italy; [5]Ospedale di Guastalla, Medical Oncology, Guastalla, Italy; [6]AO Vito Fazio, Medical Oncology, Lecce, Italy; [7]AO Sant'Anna, Medical Oncology, Como, Italy; [8]AO Garbagnate, Medical Oncology, Garbagnate, Italy; [9]AUSL Romagna, Medical Oncology, Rimini, Italy; [10]AO Busto Arsizio, Medical Oncology, Saronno, Italy; [1]AO Sacco, Medical Oncology, Milano, Italy; [12]AO Busto Arsizio, Medical Oncology, Busto Arsizio, Italy; [13]AO Serbelloni, Medical Oncology, Gorgonzola, Italy*

**Background:** One of the main objectives in the treatment of ABC pts is the preservation of QoL, also by limiting chemotherapy (CHT)-related toxicities. Metronomic CHT (mCHT) is a novel way of administering cancer drugs at doses higher than the MTD with lower side effects. Grade 3−4 neutropenia, neuropathy and gastro-intestinal toxicity are frequently observed when VNR and CAPE are used at standard doses. We recently published the results of the VICTOR-1 study, demonstrating that the mVRL-CAPE leads to a very low incidence of Grade 3−4 toxicities. The VICTOR-2 study was designed aiming to confirm the efficacy and safety data of the previous trial. Here we present for the first time data of efficacy and safety.

**Materials and Methods:** The treatment consisted of VNR 40 mg thrice a week + CAPE 500 mg thrice-a-day, continuously, as 1st or further lines of treatment. One cycle was conventionally defined as 3 weeks of treatment. Main inclusion criteria were: measurable or evaluable HER2-negative disease, HR known status. mCHT-related toxicity was collected by using NCI-CTCAE Version 4.02 Criteria.

**Results:** From September 2011 to May 2015, 85 pts entered the study, of whom 74 (87.1%) are evaluable for toxicity at the time of the present analysis. Median age was 66 years (38−86). A total of 669 cycles were administered; median number of cycles per patient was 6.5 (1−55). Thirty-eight (79.2%) out of 84 patients have discontinued the treatment mainly for progressive disease (76.3%). Only 3 pts (7.9%) have discontinued due to CHT toxicity. Table 1 summarizes the toxicity observed.

Table 1. Toxicity observed in N = 669 cycles of chemotherapy

| Toxicity | Grade 3 | Grade 4 | Any grade |
|---|---|---|---|
| Leucopenia | 3 | 2 | 14 |
| Febrile neutropenia | 0 | 3 | 5 |
| Non-febrile neutropenia | 6 | 2 | 11 |
| Thrombocytopenia | 2 | 0 | 8 |
| Anaemia | 1 | 0 | 15 |
| Diarrhoea | 4 | 0 | 49 |
| Nausea | 4 | 0 | 61 |
| Vomiting | 3 | 0 | 19 |
| Mucositis | 1 | 1 | 7 |
| Fever | 0 | 0 | 5 |
| Asthenia | 2 | 0 | 52 |
| Alopecia | 0 | 0 | 2 |
| Allergy | 3 | 0 | 4 |

Grade 3−4 toxicity was observed in 4.3% and 1.2% of the cycles, respectively. Interestingly, the highest incidence of Grade 3−4 toxicity was observed during the first 3 cycles (8.5% and 3.5%), whereas it seems that there is no dose-cumulative effect (any Grade 3−4 toxicity: cycles 4−6: 4.2%; cycles 7−9: 2%; cycles >9: 1.4%).

Twenty-eight (37.8%) pts had VNR dose reduction, mainly due to G2 neutropenia (4/28, 14.3%), whereas 21 pts (28.4%) had CAPE reduction, mainly for cutaneous toxicity (5/21, 23.8%). Clinical Benefit Rate, evaluated in 75% of the enrolled pts, was 80% (70−88%), with no differences according to the line of treatment: 81% (54−96%) for 1st-line vs 73% (58−85%) for ⩾2nd-line.

**Conclusion:** These preliminary results of a large Phase II study confirm that the metronomic combination of VNR and CAPE in ABC pts is active and well tolerated, with a very low incidence of side effects, thus being a valid option of treatment both as 1st or further lines of treatment for HER2-negative BC patients.

**No conflicts of interest**

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**N-1 study with S-1 + low dose docetaxel for advanced breast cancer patients**

A. Tangoku[1]. *[1]Tokushima University Graduate School, Department of Thoracic- Endocrine Surgery and Oncology, Tokushima, Japan*

**Background:** We have reported the efficacy of S-1 combined with low dose docetaxel (S-1+DOC). It showed good response rate (ORR) and complete response (CR) could be realized within three months (4 cycles). But this therapy was difficult to keep compliance, because S-1 is oral medicine. To improve pathological CR (pCR) rate, we planned new protocol of primary chemotherapy.

**Methods:** Patients with operable breast cancer (stage II-III) were treated with i.v. docetaxel (40 mg/m$^2$) on day 1 and oral S-1 (80 mg as FT/m$^2$/day) on days 1 to 14 every 3 weeks for 4 cycles. According to the RECIST criteria, patients with CR underwent operation, partial response were continued more 4 cycles of S-1+DOC. Stable disease or progressive disease cases were added EC or trastuzumab and paclitaxel (HT) according to their HER2 status. Supportive therapy was provided for typical adverse events. Primary endpoint is pCR rate. Secondary endpoints are ORR, breast conservation rate and safety.

**Results:** Between May 2009 and October 2013, 70 patients entered the study. After 4 cycles of S-1+DOC, CR was noted in 4 cases, PR in 49 cases, SD in 14 cases, and PD in 3 cases. 9 cases of SD and 2 cases of PD underwent EC, 5 cases of SD and 1 case of PD underwent HT. Among 70 assessable patients, 32.9% achieved pCR. ORR was 80.0%. According to subtype, pCR rate is 20.0% in Luminal A type, 40.0% in Luminal HER2 type, 54.5% in HER2 type, 42.8% in Basal type. Breast conservation rate was 82.9%, although the patients who could continue S-1 more than 80% was 72.9%. Adverse events over grade 3 were leucopenia, neutropenia, anemia, peripheral sensory neuropathy, muscle pain, nausea, vomiting, diarrhea, anorexia, constipation, and nail change. Grade 3, 4 of neutropenia was noted in 50.0%. Overall survival showed superior in CR case even in the case of Luminal type A.

**Conclusion:** S-1 with low dose DOC therapy showed prior response to previous protocol with EC followed by taxane. Compliance of S-1 intake by supportive care is a key to establish the best response. The results suggested S-1 combined with low dose docetaxel could become an effective chemotherapy for Luminal type patients.

**No conflicts of interest**

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**A real-world evidence study of patients with hormone receptor-positive locally advanced or metastatic breast cancer at primary diagnosis**

E. Bastiaannet[1], J. Charman[2], T. Børge Johannesen[3], S. Schrodi[4], S. Siesling[5], L. Van Eycken[6], P.M. Walsh[7], R.A. Audisio[8], P.G. Boelens[1], C.J.H. Van de Velde[1]. *[1]LUMC, Surgery, Leiden, Netherlands; [2]National Cancer Intelligence Network, Public Health England, Birmingham, United Kingdom; [3]Cancer Registry of Norway, Kreftregisteret, Oslo, Norway; [4]Munich Cancer Registry, Depatment of Medical Informatics- Biometry and Epidemiology- Ludwig-Maximilians-University, Munich, Germany; [5]Netherlands Cancer Registry, Comprehensive Cancer Organization of The Netherlands, Utrecht, Netherlands; [6]Belgian Cancer Registry, Stichting Kankerregister-Fondation Reistre du Cancer, Brussels, Belgium; [7]National Cancer Registry, Cork, Ireland; [8]University of Liverpool, St Helens Teaching Hospital, St Helens, United Kingdom*

**Background:** The ongoing Phase III FALCON study (NCT01602380) will assess the efficacy of fulvestrant 500 mg versus anastrozole in patients with hormone receptor (HR)-positive locally advanced/metastatic breast cancer (LA/MBC) who have received no prior endocrine therapy (ET), including patients diagnosed with LA/MBC at the time of their primary diagnosis. However, epidemiological data for such patients are lacking. We analyzed data from European cancer registries to assess the proportion of postmenopausal women with HR-positive LA/MBC who have advanced disease at primary diagnosis.

**Materials and Methods:** This is an international, observational, retrospective study conducted by the European Registry of Cancer Care (EURECCA). Data for this analysis were collected from national/regional

Table (abstract 377): Breast cancer patient groups

| Group | England [a] | Norway | Ireland | Germany [b] | Belgium [c] | The Netherlands | Total |
|---|---|---|---|---|---|---|---|
| All postmenopausal breast cancer cases 2000–2014 | 125,408 | 27,159 | 19,179 | 40,181 | 6658 | 98,095 | 316,680 |
| Known HR-status and cancer stage (% [d]) | 61,428 (49.0) | 12,962 (47.7) | 15,393 (80.3) | 32,218 (80.2) | 4848 (72.8) | 95,782 (97.6) | 222,631 (70.3) |
| HR-positive disease and known cancer stage (% [e]) | 53,197 (86.6) | 11,012 (85.0) | 12,693 (82.5) | 28,264 (87.7) | 4197 (86.6) | 81,591 (83.2) | 190,954 (85.8) |
| HR-positive LA/MBC at primary diagnosis (% [f]) | 4484 (8.4) | 802 (7.3) | 1257 (9.9) | 4085 (14.5) | 503 (12.0) | 7871 (9.6) | 19,002 (10.0) |
| HR-positive LA/MBC at primary diagnosis and subsequent ET [g] | 2796 (62.4) | 445 [g] (74.4 [h]) | 1019 (81.1) | 2526 (61.8) | 443 (88.1) | 6928 (88.0) | 14,157 (74.5) |

ET, endocrine therapy; HR, hormone receptor; LA/MBC, locally advanced/metastatic breast cancer.
[a] 2010–2014 data only.
[b] Regional dataset (Munich).
[c] 2008 data only.
[d] % of all breast cancer.
[e] % of confirmed HR-status/cancer stage.
[f] % of HR-positive.
[g] % of HR-positive LA/MBC at primary diagnosis.
[h] Of 603 patients with recorded follow-up.

cancer registries representing Belgium, England, Germany, Ireland, Norway and The Netherlands. Postmenopausal patients with HR-positive breast cancer diagnosed from January 2000 to December 2014 were included. Data were analyzed for the proportion of patients with HR-positive breast cancer with recorded cancer stage who had LA/MBC at the time of their primary diagnosis. Results are presented descriptively.

**Results:** Overall, 316,680 postmenopausal women with breast cancer were included; HR status and cancer stage were confirmed for 222,631 (70.3%). Of these patients, 85.8% (190,954/222,631) had confirmed HR-positive breast cancer. In total, 10.0% (19,002/190,954) of patients with HR-positive disease had LA/MBC at primary diagnosis; subsequent ET was documented for 74.5% (14,157/19,002) of these patients. Data for individual countries are included in the Table.

**Conclusions:** These real-world data describe a substantial proportion of patients with HR-positive breast cancer who had LA/MBC at primary diagnosis and who had no record of ET; the size of this proportion varies across European countries.

**Conflict of interest:** Advisory Board: Riccardo Audisio has served as a scientific advisor to Nutricia.

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**Incidence of previously diagnosed other primary multiple malignancies in breast cancer patients; a retrospective statistical evaluation in 2007−2014**

A. Kovács[1], T. Parris[2], K. Helou[2]. [1]*Sahlgrenska University Hospital, Dept. of Clinical Pathology and Genetics, Gothenburg, Sweden;* [2]*Institute of Clinical Sciences- Sahlgrenska Cancer Center- Sahlgrenska Academy at the University of Gothenburg, Dept. of Oncology, Gothenburg, Sweden*

**Background:** The incidence of other primary malignant tumors, occurring before the breast carcinoma was detected, increased from 3% to 7% during 2007–2014. We especially analyzed those breast cancer patients, who had more than one previous primary malignancy.

**Material and Methods:** Using clinical records from the Dept. of Clinical Pathology and Genetics, we performed a retrospective search for other types of previously diagnosed primary malignancies in **4,850 patients** registered with newly diagnosed primary invasive and/or in situ breast carcinomas during an **8-year period (2007−2014)**.

**Results:** 454 primary malignant tumors were diagnosed in 221 patients, including two male patients, during this eight year period. We found 10 breast cancer patients with several (2−4) previous primary malignancies.

The most striking increase in incidence was found among the gynecological tumors (endometrium and ovarian adenocarcinomas) and malignant melanoma. The number of gastrointestinal malignancies showed an irregular, but relatively high incidence during this time per

**Conclusions:** Identifying the type of different coexisting primary malignancies may awake a special clinical vigilance for oncologists, warranting new screening programs for cancer patients to detect certain second or third, etc. primary malignancies at an early stage. The overall survival rates for cancer patients have improved tremendously during the past 40 years, in part because of individually tailored therapies. As cancer patients live longer, they have elevated risk to develop later primary malignancies in other organs. Patients with several primary malignancies need special treatment strategies, regarding the previously administered radio-and/or chemotherapy to avoid excessive cytotoxic harm due to cumulative effect of all applied therapies.

**No conflicts of interest**

Table (abstract 378): Primary malignant tumor preceding newly diagnosed primary invasive and/or in situ breast carcinomas

| Patient no. | → | → | → | → | |
|---|---|---|---|---|---|
| 1 | Ovarian carcinoma | Endometrium carcinoma | | | Breast cancer |
| 2 | Urinary bladder carcinoma | Rectum adenocarcinoma | | | Breast cancer |
| 3 | Lymphoma | Endometrium adenocarcinoma | | | Breast cancer |
| 4 | Malignant melanoma, invasive type | Thyroid gland carcinoma | | | Breast cancer |
| 5 | Urinary bladder carcinoma | Endometrium adenocarcinoma | | | Breast cancer |
| 6 | Colon adenocarcinoma | GIST in small intestine | | | Breast cancer |
| 7 | Mucoepidermoid cancer in the gum | Rectum adenocarcinoma | | | Breast cancer |
| 8 | Endometrium adenocarcinoma | Colon adenocarcinoma | Malignant melanoma, invasive type on the leg | Spindle cell sarcoma of the upper arm | Breast cancer |
| 9 | Ovarian carcinoma | Colon adenocarcinoma | | | Breast cancer |
| 10 | Endometrium adenocarcinoma | Rectum adenocarcinoma | Rectum adenocarcinoma | | Breast cancer |

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**Search for appropriate treatment strategy using fulvestrant for postmenopausal ER-positive advanced or recurrent breast cancer patients in Japan (JBCRG-C06; Safari)**

H. Kawaguchi[1], N. Masuda[2], T. Nakayama[3], K. Aogi[4], K. Anan[5], Y. Ito[6], S. Ohtani[7], N. Sato[8], S. Saji[9], E. Tokunaga[10], S. Nakamura[11], Y. Hasegawa[12], M. Hattori[13], T. Fujisawa[14], S. Morita[15], M. Yamaguchi[16], T. Yamashita[17], Y. Yamamoto[18], S. Ohno[19], M. Toi[20]. *[1]Matsuyama Red Cross Hospital, Breast Surgery, Matsuyama, Japan; [2]NHO Osaka National Hospital, Department of Surgery- Breast Oncology, Osaka, Japan; [3]Osaka Medical Center for Cancer and Cardiovascular Diseases, Department of breast and endocrine surgery, Osaka, Japan; [4]Shikoku Cancer Center, Department of Breast Oncology, Matsuyama, Japan; [5]Kitakyushu Municipal Medical Center, Department of Surgery, Kitakyushu, Japan; [6]The Cancer Institute Hospital of JFCR, Breast Medical Oncology Department, Tokyo, Japan; [7]Hiroshima City Hiroshima Citizens Hospital, Department of Breast Surgery, Hiroshima, Japan; [8]Niigata Cancer Center Hospital, Department of Breast Oncology, Niigata, Japan; [9]Fukushima Medical University, Department of Medical Oncology, Fukushima, Japan; [10]Kyushu Cancer Center, Department of Breast Oncology, Fukuoka, Japan; [1]Showa University Hospital, Showa University School of Medicine- Department of Surgery- Division of Breast Surgical Oncology, Tokyo, Japan; [12]Hirosaki Municipal Hospital, Department of Breast Surgery, Hirosaki, Japan; [13]Aichi Cancer Center Hospital, Department of Breast Oncology, Nagoya, Japan; [14]Gunma Prefectural Cancer Center, Department of Breast Oncology, Ohta, Japan; [15]Kyoto University Graduate School of Medical, Department of Biomedical Statistics and Bioinformatics, Kyoto, Japan; [16]JCHO Kurume General Hospital, Department of Breast Surgery, Kurume, Japan; [17]Tokyo Metropolitan Cancer and Infectious Diseases Center Komagome Hospital, Department of Breast Surgery, Tokyo, Japan; [18]Kumamoto University-Graduate School of Medical Sciencies, Department of Breast and Endocrine Surgery, Kumamoto, Japan; [19]The Cancer Institute Hospital of JFCR, Breast Oncology Center, Tokyo, Japan; [20]Kyoto University Graduate School of Medicine, Department of Breast Surgery, Kyoto, Japan*

**Background:** After the CONFIRM trial, fulvestrant 500 mg (F500) became a standard treatment for patients with estrogen receptor positive (ER+) advanced/metastatic breast cancer (AMBC) and progression on hormonal treatment. This retrospective study evaluated the effect of clinical background and treatment line on time to treatment failure (TTF) in patients with AMBC receiving F500 in Japan (UMIN 000015168).

**Material and Methods:** Patients starting treatment with F500 between Nov 2011 (F500 approval in Japan) and Dec 2014 were registered. The relationship between baseline clinical/pathological factors, treatment line, and TTF (time from start to cessation of F500 treatment for any reason, including toxicity and death) were analyzed (Kaplan–Meier methods). Univariate analysis of TTF data was performed by Cox hazards model using: age, histological type, histological/nuclear grade, visceral-metastases, stage, PgR, HER2, period from AMBC diagnosis to F500 use, treatment line of F500, prior chemotherapy. Hazard ratios (HR), 95% confidence intervals (CI) and p values are reported. All tests were two-sided.

**Results:** Data for 1072 patients at 16 sites were available; 1031 patients (96.2%) were evaluable for efficacy. Median age was 64 yrs; 21.5% had advanced disease; 78.5% recurrent disease; 32.4% visceral metastases. Histology: 82.3% ductal; 4.7% lobular; 13.1% other. Hormonal receptor status: ER+/PgR+ 69.5%; ER+/PgR− 25.4%; ER+/PgR unknown 5.0%. HER2 status was documented in 909 patients; 21.5% were HER2+. F500 was administered as 1st-line treatment in 2.0%, 2nd-line in 22.6%, 3rd-line in 26.8%, and ⩾4th-line in 48.6%. Median follow up was 18.0 months (mo) from F500 treatment (0.1–44.9), median TTF was 5.4 mo (4.7−5.7). In the univariate analysis, younger patients (<65 yrs vs. ⩾65 yrs; HR=0.84, 95% CI=0.73–0.96; p = 0.009), longer period from AMBC diagnosis to F500 use (<3 yrs vs. ⩾3 yrs; HR=0.87, 95% CI=0.76–1.00; p = 0.047), earlier F500 use (⩾4th vs. 3rd vs. 2nd vs. 1st line; HR=0.83, 95% CI=0.77–0.90; p < 0.001) and no prior chemotherapy (yes vs. no; HR=0.74, 95% CI=0.65–0.84; p < 0.001) were associated with longer TTF. Histological type, histological/nuclear grade, visceral metastases, stage, PgR, HER2 did not influence TTF. In the multivariate analysis, longer period from AMBC diagnosis to F500 use (<3 yrs vs. ⩾3 yrs; HR=0.60, 95% CI=0.51–0.70; p < 0.001), earlier F500 use (⩾4th vs. 3rd vs. 2nd vs. 1st line; HR=0.83, 95% CI=0.70–0.84; p < 0.001) and no prior chemotherapy (yes vs. no; HR=0.69, 95% CI=0.60–0.80; p < 0.001) were associated with longer TTF. Three patients (0.8%) had severe adverse events.

**Conclusions:** Our findings suggest that F500 is more effective when used as an earlier treatment line for AMBC. F500 efficacy is affected by longer period from AMBC diagnosis to F500 use and no prior chemotherapy, and not affected by HER2 status or presence of visceral metastases.

**Conflict of interest:** Other Substantive Relationships: N. Masuda, Chugai, Astrazeneca, Eisai, Kyowa Kirin; T. Nakayama, Chugai, AstraZeneca, Novartis; S. Saji, lecture fee from AstraZeneca; S. Morita, AstraZeneca (honorarium).

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**Hormonal receptors, Her2/neu status and Ki-67 index as prognostic markers of survival in breast cancer patients with central nervous system metastases**

F. Porras-Reyes[1], I. Sollozo-Dupont[1], N. Castañeda-Soto[2], E. Bargalló-Rocha[3], Y. Villaseñor-Navarro[4], H.A. Maldonado-Martínez[1], G. Alamilla-García[2], V.M. Pérez-Sánchez[1]. *[1]Instituto Nacional de Cancerología, Surgical Pathology, México, Mexico; [2]Instituto Nacional de Cancerología, Medical Oncology, México, Mexico; [3]Instituto Nacional de Cancerología, Surgical Oncology Breast Cancer, México, Mexico; [4]Instituto Nacional de Cancerología, Department of Radiology and Imaging, México, Mexico*

**Background:** Treatment responsiveness in breast cancer (BC) is usually determined by the presence of estrogen receptors (ER), progesterone receptors (PR) and human epidermal growth-factor (Her2/neu) status. Although pathologists have demonstrated the importance of proliferation markers (e.g. Ki-67) in the prognosis of BC, little is known about its predictive value on survival in patients with central nervous system (CNS) metastases. The purpose of this study was to verify the impact of hormone receptors and Her2/neu on survival in BC women with CNS metastases, and to evaluate Ki-67 as a useful marker to predict the clinical prognosis of these patients.

**Material and Methods:** Primary tumors from 100 metastatic BC were retrospectively examined and classified into six groups according to its immunohistochemical (IHC) profile. The criteria used for their classification is resumed in table 1. To evaluate the prognostic value of biomarkers on survival, the primary tumors were classified according to the hormone receptor status and Her2/neu expression. Furthermore, the survival of each group was also evaluated adding the marker of proliferation Ki-67. For statistical analysis, a Fisher's exact test and Kaplan–Meier methods were used.

Table 1. Criteria used for tumor classification

| Category | Criteria used in this study |
|---|---|
| Luminal A (LUMA) | ER score >200, HER2−, Ki67 <15% |
| Luminal B (LUMB) | ER score 11–199 or PR score >10, HER2−, and Ki67 >15% |
| Triple Negative (TPN) | ER−, PR−, HER2− |
| HER-2 | ER−, PR− and HER2 3+ |
| Luminal A–HER2 Hybrid (LAHH) | ER score >200, HER2 3+ and Ki67 <15% |
| Luminal B– HER2 Hybrid (LBHH) | ER score 11–199 or PR score >10, HER2 3+ and Ki67 >15% |

**Results:** Our results show that TPN had a significant high frequency (35%, p < 0.05), followed by Her2/neu group (21%) and LUMB (21%). The remaining 23% it was distributed as follow; 5% for LAHH, 7% for LUMA and 8% for LBHH. According to our analysis, there were no statistical significant differences between groups when the survival was calculated considering only hormone receptors and Her2/neu (p < 0.4). Nevertheless, the enhanced Ki-67 expression (>15%) in TPN, significantly reduces survival (31 months, p = 0.002), in comparison with TPN with low expression of Ki-67 (<15%) (115 months). Likewise, Ki-67 overexpression diminishes median survival for patients with primary Her2/neu+, including both hybrids (120 months vs 42 months), as well as, the survival LUMB (111 months for LUMA vs 38 months for LUMB).

**Conclusion:** In this study CNS metastases were more common associated with TPN primary tumors. Additionally, our results suggest that in BC patients with CNS metastases, the prognostic of the treatment is not determined solely on primary ER, PR and Her2 analysis. IHC evaluation of Ki67 appears to be a better survival biomarker.

**No conflicts of interest**

**381** Poster

**Expression of stem and epithelial mesenchymal transition markers during metastatic progression of breast cancer**

L. Viberg[1]. *[1]Karolinska Institutet, Oncology Pathology, Stockholm, Sweden*

Many biological process such as enhanced growth factor signaling, inhibition of apoptosis and acquired drug resistance are key components for breast cancer metastasis. However, accumulating data indicates that cancer stem cell (CSC) with tumor initiating capacity and epithelial mesenchymal transition (EMT) are highly involved in the metastatic

progression of breast cancer. Breast cancer characteristics with respect to the predictive biomarkers ER, PR, HER2 and Ki-67 have been shown to occasionally switch throughout tumor progression. It is currently not known whether stem and EMT markers in metastatic tumors differ from corresponding primary tumors. To address this, we have performed immunohistochemical assessments and global geneexpression analysis of primary tumors and corresponding metastases from 20 patients. All patients were diagnosed with breast cancer during the years 1992 to 2009 in Stockholm, Sweden. Metastatic lesions were micro dissected from the following organs brain (n = 6), axillary lymph nodes (n = 10), colon (n = 2), skin (n = 5), lung (n = 1), uterus (n = 1), bone (n = 6) and liver (n = 2). A tissue microarray was made with cores from tumors and metastases. Immunohistochemistry for the stemness markers (ALDH1, CD44, OCT3/4 and Nanog) and epithelial mesenchymal transition (EMT) markers (N-cadherin, E-cadherin and VIM3B4). Stainings were scored by two independent researchers and the consensus values were considered as the final value. Among the stemness markers evaluated, none of the proteins were significantly differentially expressed in metastases compared to its respective primary tumor. However out of three EMT markers analyzed, N-cadherin was found to be upregulated in metastases significantly ($p = 0.0435$, Wilcoxon matched-pairs signed rank test) compared to the respective primary tumors. Apart from the protein expression, we have acquired the whole transcriptomic profiling by retrieving RNA from formalin-fixed archive material by Sensation plus kit (Affymetrix). Gene level normalization was done using Expression console (Affymetrix) with RMA algorithm. EMT gene ontology (GO) term (GO:0001837) genes and stem cell population maintenance (GO:0019827) genes will be analyzed on primary versus matched metastasis gene expression values. This will identify significantly differentially expressed genes involved in these two process in metastases compared to the corresponding primary tumors. Using this data, we will understand the significance of stem cell and EMT process involvement in breast cancer tumor progression.

**No conflicts of interest**

**382** Poster

**Outcomes of incidental breast nodules, overview of imaging and histopathology**

S.Y. Ham[1], B. Ko[2], S. Shin[3]. *[1]Korea Univ. Anam Hospital, Radiology, Seoul, Korea; [2]Ulsan University Hostpital, Surgery, Ulsan, South Korea; [3]Korea University Hospital, Oncology, Seoul, South Korea*

**Purpose:** An increasing number of breast lesions are noted in chest CT scan, for the purpose of screening or follow evaluation for malignancy evaluation detected. The aim of this study was to review the rate of referrals to the breast section for assessment of lesions identified on CT and to evaluate the imaging findings and histopathology in case of biopsy, excision.

**Materials and Methods:** A retrospective review was undertaken of CT examinations conducted over a period of 7 years. All patients (with no previous history of breast cancer) whose report contained the keyword “recommand breast U or mammography”and who were referred to a specialist breast center for assessment were reviewed. CT lesion morphology and enhancement pattern were identified and compared with the final diagnostic outcome. The imaging findings were classified into to three groups, mass, asymmetry, calcifications. The site, location and extent or mass size were recorded.

**Results:** 61 patients were identified by retrospective analysis, incidental breast lesions, of which 11 (18%) were malignant. This gave a positive predictive value (PPV) for malignancy of 14.7%. The histopathology types were invasive ductal carcinoma (7), ductal carcinoma in situ (1), phyllodes tumor (1), medullary carcinoma (1), lymphoma (1). The best morphological predictor of malignancy was spiculation (PPV, 68%) and enhancement (PPV, 48%), whereas calcification patterns (PPV, 27%). Malignant lesions were likely to be larger (mean, 21.5 mm) than benign lesions (mean, 17.2 mm). As an associated findings, axillary nodes enlargement and regional parenchymal retraction are more common in malignancy. Combined malignancy were colon cancer (5), hepatocellular ca (2), lymphoma (1), thyroid ca (2), lung cancer (3), Two of them were triple cancer, lung, thyroid, breast and breast, lung and colon cancers.

**Conclusions:** In conclusion, 18% of incidental breast lesions in this large series of patients proved to be as breast cancers, particularly irregular spiculated masses with enhancement. Careful evaluation for incidentally detected breast lesions are should be followed, especially in cancer follow up patients.

**No conflicts of interest**

**384** Poster

**Metronomic chemotherapy is well tolerated, less toxic and as effective as standard chemotherapy. Results from the XeNa trial; a randomized phase 2 trial combining vinorelbine and capecitabine in the treatment of advanced HER2 negative breast cancer**

A.S. Brems-Eskildsen[1], S. Linnet[2], A. Luczak[3], H. Nielsen[4], P. Vestlev[5], E.H. Jacobsen[6], J. Neimann[1], C.B. Jensen[1], T. Dongsgaard[2], S.T. Langkjer[1]. *[1]University Hospital of Aarhus, Department of Oncology, Aarhus, Denmark; [2]Hospital of Herning, Department of Oncology, Herning, Denmark; [3]University hospital of Aalborg, Department of Oncology, Aalborg, Denmark; [4]Hospital of Hillerød, Department of Oncology, Hillerød, Denmark; [5]Hospital of Roskilde, Department of Oncology, Roskilde, Denmark; [6]Hospital of Esbjerg, Department of Oncology, Esbjerg, Denmark*

**Background:** Metronomic treatment is hypothesized to be less toxic and more effective compared to standard treatment. The continuously low dose administered theoretically affects the angiogenesis in tumors. Vinorelbine is effective especially in the combination with other treatments and the toxicity profile of capecitabine and vinorelbine is not overlapping. Long term disease control is beneficial to the patients with disseminated breast cancer.

**Material and Methods:** We have tested the metronomic treatment principle in a randomized phase 2 setting combined with standard Xeloda treatment in the XeNa trial with Clinical Trials.gov identifier number: NCT0141771. 120 patients with disseminated or locally advanced HER2 negative breast cancer are included by June 2015. Randomization are between Arm A: “vinorelbine (Navelbine Oral®)” 60 mg/m$^2$ day 1 + day 8 in the first cycle followed by 80 mg/m$^2$ day 1 + day 8 in the following cycles or Arm B: continually “vinorelbine (Navelbine Oral®)” 50 mg three times a week. “Capecitabine (Xeloda®)” 1000 mg/m$^2$ twice a day for day 1−14 is administered in both arms. Dose reduction is allowed if toxicity is unacceptable.

**Results:** The study population is well balanced in the two study arms. The number of patients presenting with visceral metastasis was 80% and the number of patients with ”no visceral” metastasis was 16%. The reported adverse events in the standard versus metronomic arm are presented in Table 1. The grade 3 and 4 toxicity profile of the metronomic arm seems beneficial as the number of febrile neutropenia (3 versus 2), alopecia (6 versus 0) and thromboembolic events (6 versus 2) were lower in arm B.

The response rate is 21.4% (arm A) versus 20.8% (arm B). The clinical benefit rate is 61.9% (arm A) versus 60.4% (arm B).

Table 1.

| Adverse event | Number of events | | | |
|---|---|---|---|---|
| | Standard arm | Metronomic arm | Difference | Total |
| Grade 1 | 405 | 307 | 98 | 714 |
| Grade 2 | 192 | 166 | 26 | 358 |
| Grade 3 | 68 | 69 | 1 | 137 |
| Grade 4 | 13 | 4 (+1 grad 5) | 8 | 18 |
| Total | 778 | 548 | 240 | 1227 |

Preliminary calculation of progression free survival and overall survival shows equal effect as mean time to progression is 228 days (confidence interval 175–281) in arm A and 199 days (confidence interval 147–250) in arm B, and overall survival is 285 days (confidence interval 229–341) in arm A and 247 days (confidence interval 193–301) in arm B.

**Conclusion:** The study meets its primary endpoint by determining an equal overall response rate of 21% in both treatment arms. The secondary endpoints determining the toxicity and safety of the treatment reveal a lower frequency of adverse events in the metronomic treatment arm and the combined treatment is considered safe. Preliminary efficacy data shows equal time to progression and overall survival. Survival data will be updated upon time for the congress.

Acknowledgement: The clinical study is supported by Pierre Fabre.

**No conflicts of interest**

**385** Poster

**Tissue microRNAs predicting the pattern of breast cancer metastases**

S.P. Gampenrieder[1], H. Hackl[2], G. Rinnerthaler[1], M. Steiner[1], C. Hufnagl[1], C. Hauser-Kronberger[3], B. Mlineritsch[1], R. Greil[1]. *[1]Paracelsus Medical University Salzburg, IIIrd Medical Department-Salzburg Cancer Research Institute with Laboratory of Immunological and Molecular Cancer Research and Center for Clinical Cancer and Immunology Trials, Salzburg, Austria; [2]Innsbruck Medical University, Division of Bioinformatics- Biocenter, Innsbruck, Austria; [3]Paracelsus Medical University Salzburg, Department of Pathology, Salzburg, Austria*

**Background:** The location of metastases is one of the principal prognostic factors for patients with metastatic breast cancer (MBC), whereat visceral disease (VD) generally predicts poor survival. The exact mechanisms influencing the propensity of breast cancer cells to infiltrate certain tissue types are not known yet. Here we investigate the role of miRNAs in this context.

**Patients and Methods:** A genome-wide miRNA profiling using high-throughput TaqMan® Array Human MicroRNA Cards enabling quantification of 754 unique human miRNAs was performed. Formalin-fixed paraffin-embedded specimens from the primary tumor of 42 patients with MBC were analyzed. VD was defined as metastases in liver, lungs, adrenal glands, peritoneum or pleura, brain and dura. Overall survival (OS) was defined as time between diagnosis of MBC and death from any cause. Differential miRNA expressions between VD and non-VD (NVD) were selected by moderated t-test (limma) and spearman rank correlation. Association of miRNA expression with OS were analyzed using Kaplan–Meier survival curves and Cox proportional hazard model applied to patients with high vs low miRNA expression (median dichotomization).

**Results:** In our cohort 26 patients (52%) and 16 (38%) had VD and NVD, respectively. VD strongly correlated with poor overall survival (median OS 20.7 months vs. 58.2 months; HR 2.88, 95% CI 1.27 to 6.50; P = 0.011). The expression levels of 32 miRNAs were significantly associated with VD: miR-106b-5p, -532-5p, -20a-5p, -425-5p, -224-5p, -30a-5p, -155-5p, -106a-5p, -660-5p, -30d-5p, -203a, -30d-5p, -17-5p, -19b-3p, -708-5p, -211-5p, -151a-3p, -518f-3p, -185-5p, -93-5p, -519d-3p, -550a-5p, -130b-3p, -34a-5p, -19a-3p, -296-5p, -9-5p, -143-5p, -30d-3p, -9-3p, -571, -210-3p (all except miR-143-5p with higher expression levels in VD). Twelve of these miRNAs were also significantly correlated with prognosis of metastatic disease (Table).

| | VD vs. NVD log2FC (−ΔΔCT) | P | OS HR (95% CI) | P |
|---|---|---|---|---|
| miR-20a-5p | 1.91 | 0.0027 | 2.80 (1.24–6.31) | 0.0128 |
| miR-532-5p | 1.90 | 0.0018 | 2.98 (1.29–6.92) | 0.0109 |
| miR-30a-5p | 1.88 | 0.0063 | 2.53 (1.17–5.45) | 0.0177 |
| miR-224-5p | 1.84 | 0.0045 | 3.56 (1.46–8.69) | 0.0052 |
| miR-708-5p | 1.58 | 0.0125 | 2.61 (1.17–5.81) | 0.0187 |
| miR-106a-5p | 1.51 | 0.0084 | 3.35 (1.51–7.42) | 0.0029 |
| miR-660-5p | 1.47 | 0.0097 | 7.02 (2.65–18.61) | 0.0001 |
| miR-17-5p | 1.45 | 0.0118 | 3.36 (1.52–7.43) | 0.0028 |
| miR-425-5p | 1.43 | 0.0032 | 2.97 (1.32–6.70) | 0.0087 |
| miR-30d-5p | 1.42 | 0.0115 | 3.26 (1.43–7.39) | 0.0048 |
| miR-34a-5p | 1.10 | 0.0264 | 3.20 (1.39–7.35) | 0.0061 |
| miR-143-5p | −1.93 | 0.0389 | 0.33 (0.11–0.93) | 0.0369 |

Currently these data are validated in a further patient cohort. The validated results will be presented at the meeting.

**Conclusion:** Determination of tissue microRNAs in the primary tumor could help to predict both prognosis and the pattern of breast cancer metastases. Here 32 candidate miRNAs were identified probably involved in tissue specific metastatic spread.

**No conflicts of interest**

**386** Poster

**Metastatic pattern of infiltrating lobular carcinoma of the breast − emphasis on gastric metastases**

A. El-Hage[1], C. Ruel[2], W. Afif[3], H. Wissanji[2], J.C. Hogue[4], C. Desbiens[5], G. Leblanc[3], E. Poirier[5]. *[1]CHU de Québec − Université Laval, Surgery, Québec City, Canada; [2]Laval University, Surgery, Québec City, Canada; [3]Montreal University, Surgery, Montréal, Canada; [4]CHU de Québec, Center for Breast Diseases, Québec, Canada; [5]CHU de Québec − Université Laval, Center for Breast Diseases, Québec City, Canada*

**Background:** Breast invasive ductal carcinoma (IDC) and invasive lobular carcinoma (ILC) have different patterns of metastases, but the exact pattern of metastases from ILC is poorly known because of the lower frequency of ILC compared to IDC. This study aimed to determine the frequency of ILC metastases in atypical locations, with an emphasis on gastric metastases.

**Materials and Methods:** Patients with ILC treated at the Saint-Sacrement Hospital (Quebec City, Canada) and the Maisonneuve-Rosemont Hospital (Montreal, Canada) between January 2003 and December 2009 were retrospectively reviewed. Demographic, clinical, and follow-up data were retrieved from the medical charts. Metastases that were diagnosed during follow-up were recorded.

**Results:** Among the 481 patients with ILC, 74 (15.4%) were diagnosed with metastases after a median follow-up of 46 months (1 to 74 months). Among these 74 patients, 41.9% had metastases in atypical sites. Five patients were diagnosed with gastric metastases of ILC.

**Conclusion:** Metastases of breast ILC to atypical sites might be more frequent than previously reported. Clinicians should keep a high level of suspicion when a patient with a history of ILC develops digestive symptoms. It is also important to differentiate metastases from a primary GI tumor by using immunohistochemical markers and comparing biopsies with the breast primary carcinoma. Systemic treatment with hormonal therapy or chemotherapy might be a good option. Surgery should be used only for emergencies or palliation or in much selected cases of solitary GI metastases.

**No conflicts of interest**

**387** Poster

**Etirinotecan pegol (EP) significantly improves overall survival in patients with advanced breast cancer (aBC) and a history of brain metastases (BM)**

J. O'Shaughnessy[1], H. Rugo[2], A. Awada[3], C. Twelves[4], E. Perez[5], S.A. Im[6], P. Gómez-Pardo[7], L. Schwartzberg[8], V. Diéras[9], D. Yardley[10], D. Potter[11], A. Mailliez[12], A. Moreno-Aspitia[5], J.S. Ahn[13], C. Zhao[14], U. Hoch[14], M. Tagliaferri[14], A. Hannah[15], J. Cortés[16]. *[1]Baylor Sammons Cancer Center- Texas Oncology- US Oncology Research, Medical Oncology, Texas, USA; [2]University of California, School of Medicine, San Francisco- CA, USA; [3]Jules Bordet Institute, Medical Oncology Clinic, Brussels, Belgium; [4]University of Leeds and St. James's University Hospital, Medical Oncology, Leeds, United Kingdom; [5]Mayo Clinic, Medical Oncology, Jacksonville- FL, USA; [6]Seoul National University Hospital- Cancer Research Institute- Seoul National University College of Medicine, Medical Oncology, Seoul, Korea; [7]Vall d'Hebron Institute of Oncology, Medical Oncology, Barcelona, Spain; [8]The West Clinic, Medical Oncology, Nashville- TN, USA; [9]Institut Curie, Medical Oncology, Paris, France; [10]Sarah Cannon Research Institute, Medical Oncology, Nashville-TN, USA; [1]University of Minnesota, Department of Medicine and Masonic Cancer Center, Minneapolis- MN, USA; [12]Centre Oscar Lambret, Medical Oncology, Lille, France; [13]Samsung Medical Center- Sungkyunkwan University School of Medicine, Department of Medicine, Seoul, Korea; [14]Nektar Therapeutics, Medical Oncology, San Francisco- CA, USA; [15]Consultant, Medical Oncology, Sebastopol- CA, USA; [16]Ramon y Cajal University Hospital, Medical Oncology, Madrid, Spain*

**Background:** The long-acting topoisomerase 1 inhibitor EP preferentially accumulates in tumor tissue in preclinical animal models, including the brain, providing sustained SN38 levels (Hoch et al AACR 2014). The phase 3 BEACON trial included patients with a history of BM as detailed below. Findings from the preplanned subgroup analysis are reported herein.

**Materials and Methods:** BEACON compared EP (145 mg/m$^2$ q21d) with treatment of physician's choice (TPC) in patients with aBC previously treated with an anthracycline, taxane, and capecitabine. Patients with a history of BM that had been previously subjected to prior definitive therapy were eligible provided local therapy was completed (surgery, whole brain or stereotactic radiation) and corticosteroids discontinued ⩾3 weeks prior to randomization.

**Results:** Of the 852 patients randomized, 67 had a history of BM (EP, n = 36; TPC, n = 31); 37 (EP, n = 19; TPC, n = 18) had stable brain lesions on radiographic imaging at baseline; subgroups were balanced for baseline characteristics and Graded Prognostic Assessment (GPA) indices. Survival analyses revealed a significant reduction in the risk of death with EP relative to TPC (HR 0·51; 95% CI 0.30–0.86; P < 0.01), and a doubling of median OS (10.0 months vs 4.8 months); 12-month survival rates were 44.4% and 19.4%, respectively. Use of EP led to improved OS within GPA subgroups (0−2.0 and 2.5−4.0, HR=0.27 and 0.54, respectively). Treatment was well tolerated as previously reported. Fewer patients randomized to EP experienced grade ⩾3 toxicity (50% versus 70%), with neutropenia occurring in 33% on TPC (vs 15% on EP); grade 3 diarrhea occurred infrequently (6% vs 4% on EP and TPC, respectively) and no grade 4 diarrhea was reported.

**Conclusions:** The significant benefit observed in patients with a history of BM in BEACON is supported by preclinical data and suggests that EP is a promising investigational therapy for aBC. Further studies are warranted.

**No conflicts of interest**

**388** Poster

**Nanosize is not enough: Response according to sites of disease in a population of advanced breast cancer (ABC) patients treated with nab-paclitaxel**

M. Ciccarese[1], L. Petrucelli[1], L.I. Lupo[1], V. Saracino[1], A. Gambino[1], G. Cairo[1], V.E. Chiuri[1], E. De Matteis[1], R. Forcignanò[1], G. Surico[1].
[1]*Vito Fazzi Hospital, Oncology Department, Lecce, Italy*

**Background:** Nab-paclitaxel is a colloidal suspension of paclitaxel and serum albumin that can be administered in ABC from a second-line treatment and beyond, with a schedule of 260 mg/m$^2$ every three weeks. This analysis includes ABC patients (pts) treated in a single institution with nab-paclitaxel according to regular schedule. We assessed the response to nab-paclitaxel according to site of disease (liver vs other) and the relationship between dose intensity and efficacy of the drug.

**Material and Methods:** We retrospectively evaluated 30 pts with Her-2 negative ABC treated with nab-paclitaxel from December 2012 up today, in a single site. Median age was 69 years (44−84), median time from primary diagnosis was 47 mths (0–329), median sites of disease was 2 (1−7), visceral 63% (liver 52%, other visceral sites 48%), bone only disease 0%, luminal A pts n = 4 (13.3%), luminal B pts n = 17 (56.7%), triple negative pts n = 4 (13.3%), not evaluable pts n = 5 (16.7%). Median number of treatment for ABC was 4 (1−6), median number of lines before nab-paclitaxel was 2 (0−6).

We assessed the relation between dose intensity of nab-paclitaxel (Hryniuk method) and response. Moreover, we evaluated the relation between the efficacy of the drug and response of specific sites of disease (liver vs other).

**Results:** Twenty-seven pts were evaluable for response, with ORR (CR+PR) 56% (n = 15) and CB (CR+PR+SD) 59% (n = 16). Percentage of PD according to sites is more evident in pts with liver metastasis versus not liver (Table 1).

Table 1.

| Site | Progression | |
|---|---|---|
| | % | n |
| Liver | 70 | 7/10 |
| Lung | 8 | 1/12 |
| Bone | 15 | 2/13 |
| Soft tissue | 20 | 2/10 |
| LN | 8 | 1/13 |
| Brain | 100 | 3/3 |
| Skin | 0 | 0/4 |
| Other | 40 | 2/5 |

Eight out of 27 pts showed a discordant response for sites: 5 pts liver PD/SD on the other sites; 3 pts lung response greater than other sites (PR vs SD, SD vs PD). Median percentage of projected DI was 76.9% (55.1–100.0). No relationship was seen neither between DI and RR, nor between line of nab-paclitaxel (3rd vs 4th, i.e.) and DI.

**Conclusions:** The dose intensity did not affect RR, neither for triple negative or endocrine responsive subtypes. A discordant degree of benefit was seen for sites of disease (lung, soft tissue, LN vs liver).

A possible reason could be the heterogeneity of biologic barriers, such as microvessel density, that limits the delivery of the drug in specific sites. This finding was biased by a limited sample, but could be a generating hypothesis for a larger observational study.

**No conflicts of interest**

**389** Poster

**Phase 1b/2 trial of BI 836845, an insulin-like growth factor (IGF) ligand-neutralising antibody, in combination with exemestane and everolimus in postmenopausal women with hormone receptor-positive, locally advanced or metastatic breast cancer: Preliminary results of the Phase 1b part**

J. Cortés[1,2], N. Martinez Jáñez[3], M.P. Sablin[4], J.A. Pérez-Fidalgo[5], P. Neven[6], E. Hedayati[7], A. Ballester[8], M.P. Ehrhart[9], D. Chin-Lun Huang[10], T. Bogenrieder[11], P. Schmid[12]. [1]*Ramon y Cajal University Hospital, Department of Medical Oncology, Madrid, Spain;* [2]*Vall d'Hebron Institute of Oncology VHIO, Department of Oncology, Barcelona, Spain;* [3]*Hospital Universitario Ramón y Cajal, Department of Medical Oncology, Madrid, Spain;* [4]*Institut Curie, Department of Medical Oncology, Paris, France;* [5]*Hospital Clínico Universitario Valencia, Department of Haematology and Medical Oncology, Valencia, Spain;* [6]*UZ Leuven, Multidisciplinary Breast Center, Leuven, Belgium;* [7]*Karolinska Institutet and University Hospital, Department of Oncology-Pathology, Stockholm, Sweden;* [8]*Boehringer Ingelheim España S.A., Department of Medical Oncology, Barcelona, Spain;* [9]*Staburo GmbH, Munich, Germany on behalf of Boehringer Ingelheim Pharma GmbH & Co. KG;* [10]*Boehringer Ingelheim Taiwan Limited, Medical, Taipei, Taiwan;* [1]*Boehringer Ingelheim RCV, Medical, Vienna, Austria;* [12]*Barts Cancer Institute, Queen Mary University of London, Centre for Experimental Cancer Medicine*

**Background:** Dysregulation of insulin-like growth factor (IGF) signalling is associated with acquired resistance to hormone therapy in breast cancer (BC). BI 836845, an IGF ligand-neutralising antibody, binds to IGF-1 and IGF-2, inhibits growth-promoting signalling and mitigates AKT activation induced by everolimus (Ev). This ongoing Phase 1b/2 trial evaluates BI 836845 combined with exemestane (Ex) and Ev in hormone receptor-positive (HR+)/HER2-negative (HER2−) locally advanced or metastatic BC (Study 1280.4; NCT02123823). Preliminary results of the Phase 1b part are presented.

**Materials and Methods:** The "3+3 design" dose-escalation part of the study enrolled postmenopausal women with HR+ (oestrogen and/or progesterone)/HER2− locally advanced or metastatic BC not amenable to curative therapy, which recurred or progressed and was refractory to non-steroidal aromatase inhibitors. Patients (pts) were administered escalating doses of BI 836845 (750 or 1000 mg/week, 1-hour intravenous infusion) in combination with standard doses of oral Ex (25 mg/day) and Ev (10 mg/day) in 28-day cycles until disease progression, intolerable adverse events (AEs) or other reasons for withdrawal. Primary endpoints were occurrence of dose limiting toxicity (DLT) and determination of the maximum tolerated dose (MTD) based on the number of pts with DLT during the first cycle.

**Results:** As of the data cut-off date, 18 pts were treated (750 mg, n = 3; 1000 mg, n = 15). Median age (range) was 65 (49−76) years. Five (27.8%) pts discontinued due to progressive disease (750 mg, n = 3; 1000 mg, n = 2); 13 pts are still on treatment. During the first cycle, 0/3 pts and 1/6 evaluable pts (grade 3 stomatitis) had a DLT in the 750 mg and 1000 mg groups, respectively. Therefore, the MTD was determined to be 1000 mg BI 836845 in combination with 25 mg Ex and 10 mg Ev. The most common drug-related AEs were hyperglycaemia and mucosal inflammation (each n = 12; 66.7%), which were manageable and mostly grade 1/2 (one grade 3 hyperglycaemia in the 1000 mg group). Of the pts with hyperglycaemia, three had diabetes mellitus and one hyperglycaemia as baseline conditions. No drug-related AEs led to discontinuation. No dose reductions/interruptions due to AEs (all causality) were required for BI 836845 or Ex; 11 pts (all in the 1000 mg group) required dose reduction of Ev due to AEs. No dose-related differences in laboratory assessments were observed.

**Conclusions:** The MTD of BI 836845 was 1000 mg/week in combination with Ex 25 mg/day and Ev 10 mg/day, which was also determined as the recommended Phase 2 dose. This triple combination demonstrated a clinically manageable safety profile, consisting of AEs commonly listed for Ex+Ev alone without the need to reduce the Ev approved dose. The Phase 2 part of the study is currently ongoing.

**Conflict of interest:** JC, Advisory board (Roche, Celgene), Speaker honoraria (Roche, Celgene, Novartis, Eisai); M-PS, Steering committee member (Boehringer Ingelheim); AB, DC-LH, TB, Employment (Boehringer Ingelheim); M-PE: Employment (Staburo GmbH, Munich, Germany on behalf of Boehringer Ingelheim). Nothing to declare: NMJ, JAP-F, PN, EH, PS.

**390** Poster

**Prognostic factors affecting ipsilateral tumor recurrence and distant metastasis after breast-conserving surgery**

A. Aktas[1], L. Yeniay[1], M. Kapkac[1], R. Yilmaz[1]. [1]*Ege University Hospital, General Surgery, İzmir, Turkey*

**Background:** The purpose of the study is to evaluate treatment results after breast-conserving surgery and determine the effects of risk factors and prognostic factors on recurrence, metastasis, general and illness-free survival and mortality.

**Material and Methods:** 1388 women were included in our study that have been discussed previously in our Ege University breast diseases council, undergone breast-conserving surgery with no preoperative metastasis, personal data of whom have been accessed completely. Data was reviewed retrospectively.

**Results:** Patients varied from ages 24 to 85 with average age being 51.3±11.0. General survival changed between 12 and 282 months while average survival rate was 68.2±35.2 months. Illness-free period varied between 3 and 246 months with an average survival of 64.0±33.1 months. During the follow-up, 93 patients out of our 1388 were found to have recurrences (6.7%). 67 out of 93 patients had local, 15 had regional and 11 had locoregional recurrence. 112 patients out of 1388 had distant metastasis during the follow-up (8.1%) while 52 (3.7%) had exitus due to breast cancer. It was proved that many parameters such as surgical margin, existence of microcalcification in mammography, TNM staging, ER, PR, p53, c-erB-2, HER2/neu, ki67, subgroups, HG (histological grade), NG (nuclear grade), MBRG (Nottingham-modified Bloom–Richardson grading system), lymphovascular invasion, ESTS (Environment soft tissue spread); direct-lymphatic-vascular spread had effect on recurrence and/or metastasis. High HG, NG and MBRG levels, hormone receptor negativity, presence of lymphovascular invasion and surgical margins are found to be the major influential factors for recurrence based on our multivariate analysis. Besides many other factors, the TNM stage and the high number of metastatic lymph nodes are found as risk factors of distant metastasis.

**Conclusion:** The results of our study showed the importance of early diagnosis in breast cancer once more.

**No conflicts of interest**

**391** Poster

**Phase II study of single agent oral vinorelbine as a first line treatment for postmenopausal patients with locally recurrent or metastatic breast cancer previously treated with anthracycline or taxanes**

M. Elebrashi[1]. [1]*Mansoura University, Clinical Oncology, Dakahlia, Egypt*

**Background:** Breast cancer arises in about 48% of patients older than 65 years and more than 30% occurs in those over 70 years. Elderly patients tolerate chemotherapy poorly compared to their younger counterpart. Chemotherapy is indicated in elderly patients with advanced breast cancer resistant to hormonal treatment or with visceral disease. Oral chemotherapy may offer the specific advantage of fewer and shorter hospital visits, delayed use of central venous access and maintained social activities. Oral vinorelbine has demonstrated similar activity as IV formulation with better patient convenience in metastatic breast cancer.

This study examined the efficacy and safety of oral vinorelbine as 1st line treatment in elderly metastatic breast cancer patients.

**Patients and Methods:** 50 postmenopausal patients with histologically proven metastatic breast cancer were enrolled in the study between June 2012 and June 2015. All patients presented with anthracyclines +/− taxanes WHOP <2, with adequate bone marrow, renal and liver functions, all patients had measurable disease and were treated with oral vinorelbine 60 mg/m$^2$/week until disease progression, death or unacceptable toxicity. Oral serotonin antagonist was given 30−60 minutes prior to each administration of oral vinorelbine. The use of prophylactic or curative GCSF is allowed. The primary end points was toxicity, the secondary end points were PR, PFS & OS. Assessment of response was done every 8 weeks.

**Results:** All patients were evaluated for response, toxicity & survival. The median age was 75 years (range 68−80 years), median number of weekly oral vinorelbine was 32 (range 20−88). The overall response rate was 48% (CR 14%, PR 34%), stable disease was observed in 20 patients (40%) and 6 patients (12%) experienced disease progression. Response rate observed by disease site, sites were found in 30% of patients with liver metastases, 40% of patients with lung metastases, 60% of patients with skin metastases, 60% of patients with lymph node metastases. No WHO grade 4 toxicities were noted, 2 patients (4%) had G3 anemia and 4 patients (8%) G2 neutropenia. The most frequent adverse events were G2 nausea & vomiting (4%), fatigue (4%), alopecia (4%) and neuropathy (2%). The median DFS and survival were 14 and 20 months respectively.

**Conclusion:** Oral vinorelbine is an active, safe, feasible and effective chemotherapy in recurrent or metastatic breast cancer elderly patients resistant to hormonal therapy or with visceral metastases.

**No conflicts of interest**

**392** Poster

**Changes in hormone receptors and Her2 status in the metastases of 21 autopsies in patients with primary breast cancer: A probabilistic approach**

F. Porras-Reyes[1], I. Sollozo-Dupont[1], E. Bargalló-Rocha[2], Y. Villaseñor-Navarro[3], M. López-Estrada[1], M.D.L. Suárez-Roa[1], F. Vaca-Paniagua[1], J. Mejía-Gómez[4], C. Rojas-Cervantes[1], H.A. Maldonado-Martínez[1], V.M. Pérez-Sánchez[1]. [1]*Instituto Nacional de Cancerología, Surgical Pathology, México, Mexico;* [2]*Instituto Nacional de Cancerología, Surgical Oncology Breast Cancer, México, Mexico;* [3]*Instituto Nacional de Cancerología, Department of Radiology and imagin, México, Mexico;* [4]*Instituto Nacional de Cancerología, Surgical Oncology, México, Mexico*

**Background:** Dissemination and growth of cells in metastatic sites are responsible for most breast cancer deaths. Nevertheless, our knowledge of how cancer cell populations change during metastatic progression is limited. Difficulties are mainly associated to the acquisition of tissue, especially repeated sampling of multiple lesions. Considering this fact, tumor specimens obtained at autopsy might be particularly valuable for the study of biological process involved in the tumor metastatic progression, including molecular mechanisms.

In the current study we will provide a probabilistic approach associated to the loss of expression of estrogen and progesterone receptors (ER and PR), as well as HER2 expression, in the metastases from primary breast cancer patients.

**Material and Methods:** The immunohistochemical findings correspond to the analysis of 150 metastases from 21 patients and the probability associated to biomarkers lost was calculated following a mathematical model based in the total probability theorem.

**Results:** Despite all of the patients had multiple tumors, the most common sites were lungs (18 out of 21 patients), liver (14 out of 21), lymph chains (13 out of 21), adrenals (9 out of 21) and central nervous system (9 out of 21). The median for the number of metastases was 7 (maximun 14, minimun 3). Concerning to the histologic types, it was identified ductal carcinoma 62%, mixed 19% (ductal and lobullar carcinoma), lobular carcinoma 14% and metaplastic carcinoma 5%.

The independent probability of bidirectional changes (+ to −, or − to +) of each biomarker indicated that the highest changes corresponded to PR and ER, reaching a rate of 20% to 70% for the different metastases including diaphragm, lung, lymph node chains, esophagus, bone marrow, ovary, liver, kidney, adrenals, thyroid and contralateral breast. Meanwhile, smallest changes were those registered for HER2 (0% to 20%). Next, we calculated in an independent manner, the total probability associated to biomarkers lost. By mean of this, it was determined that in ~92% of the metastatic sites, the PRs were lost; while the associated loss of ER was ~70%. Interestingly, our analysis revealed a reduction in loss of Her2 expression (~15%). For all the cases, a receptor-negative primary tumor was accompanied by receptor-negative recurrence.

**Conclusion:** Our results suggest that in recurrent breast cancer, the prognostic of the treatment could be strongly determined, not only by the loss of ER, but also by the loss of PRs. Nevertheless, future studies are required in order to establish a better correlation between several biomarkers at different recurrent tumor samples.

**No conflicts of interest**

**393** Poster

**Whole body diffusion-weighted MRI in metastatic breast cancer patients: The Luton & Dunstable experience**

P.V. Joshi[1], A.R. Padhani[1], M. Kosmin[1], E. Chapman[2], C.J. Jayasekera[2], M.L. Ah-See[1]. [1]*Mount Vernon Cancer Centre, Breast Oncology, London, United Kingdom;* [2]*Luton and Dunstable Hospital, Oncology, Luton, United Kingdom*

**Aim:** Whole-body MRI with diffusion sequences (WB-DW-MRI) is a relatively new imaging modality in the assessment of disease extent and treatment response for patients with metastatic breast cancer (MBC). Our aim was to audit the use of WB-DW-MRI in MBC in a single breast unit and evaluate the impact on treatment strategy.

**Materials and Methods:** A retrospective audit was performed of WB-DW-MRI use in MBC patients treated at Luton and Dunstable hospital, UK over an 18 month period (22/2/2011 to 13/09/2012). Patient notes were used to assess the impact of WB-DW-MRI on treatment received.

**Results:** 19 patients were identified. 3 patients were excluded due to missing notes. 16 patient were assessed in total.

The median patient age was 46 years (range 41−65). 70 WB-DW-MRI scans were performed, with a median number of 4.5 scans per patient (range 1−10). 14/16 (87.5%) had bone-predominant MBC. 42 WB-DW-MRI were performed with a concurrent chest, abdominal and pelvic CT (CT-CAP). In 24 cases (57.1%), WB-DW-MRI and CT-CAP demonstrated comparable disease. In 16 cases (38.1%), WB-DW-MRI showed progressive disease (11/16 bone, 4/16 liver and 2/16 brain) not seen on CT. For 9 patients, WB-MRI resulted in a treatment change due to disease progression not detected by CT (21.4%).

**Conclusions:** WB-DW-MRI is being utilised in a small cohort of MBC patients with bone-predominant MBC to assess treatment response. Our audit has shown that in 38.1% of cases where both a WB DW-MRI and CT-CAP were performed, the WB-DW-MRI was superior in detecting disease progression and in 21.4% of cases resulted in a therapy change that would not have occurred if CT-CAP had been the sole imaging modality.

Further research is required to compare WB-DW-MRI with current imaging modalities (radionuclide bone scan and CT scans), to assess whether earlier detection of disease progression with WB-DW-MRI alters outcome, namely overall survival and quality of life.

**No conflicts of interest**

## Friday, 11 March 2016

**POSTER SESSION**

# Basic Science and Translational Research

**394** Poster

### Sperm-associated antigen 9 (SPAG9), a putative target for early detection and targeted therapy of breast cancer

N. Gupta[1], N. Jagadish[1], S. Agarwal[1], D. Parashar[1], A. Suri[1]. [1]*National Institute of Immunology, Cancer Microarray- Genes and Protein Laboratory, Delhi, India*

**Background:** Breast cancer is the most common cause of cancer related mortality in women. Around 15% breast cancers are designated as triple-negative for which treatment modalities are limited. Till date, there have been no tumor biomarkers validated and incorporated into oncologic practice for the early diagnosis of breast cancer. In the present study, we investigated SPAG9 expression, humoral immune response and its association with disease progression in breast cancer.

**Material and Methods:** SPAG9 gene and protein expression was examined in breast cancer patients specimens by reverse-transcription (RT)-Polymerase chain reaction (PCR) and immunohistochemical (IHC) analysis. Immunoreactivity score (IRS) was determined to study the association of SPAG9 with various histotypes and grades of breast cancer. Also, circulating auto-antibodies against SPAG9 were investigated in patient's sera by ELISA. SPAG9 mRNA and protein expression was also investigated in breast cancer cells of different hormone receptor status and different subtypes by employing RT-PCR, real time PCR, Western blotting, indirect immunofluorescence (IIF) and fluorescence activated cell sorting (FACS). Gene silencing approach was employed in triple-negative breast cancer cells, MDA-MB-231, to assess its role on various malignant properties *in vitro* and *in vivo*.

**Results:** Our RT-PCR and IHC analyses revealed SPAG9 expression in 88% breast cancer specimens independent of tumor stages and grades. Further, the humoral immune response against SPAG9 was detected in 80% breast cancer patients with SPAG9-expressing tumors. Also, our data indicated significant association of SPAG9 with the predicted high risk of breast cancer recurrence. SPAG9 mRNA and protein expression was detected in all breast cancer cells. IIF results showed that SPAG9 was predominantly localized in the cytoplasm of breast cancer cells. FACS analysis revealed distinct SPAG9 surface localization in breast cancer cells. Moreover, gene silencing of SPAG9 resulted in significant reduction in cellular proliferation, colony forming ability, migration, invasion and cellular motility of MDA-MB-231 cells. Further, ablation of SPAG9 expression resulted in reduction in the tumor growth of human breast cancer xenograft in nude mice in vivo.

**Conclusions:** Collectively, our data indicated that SPAG9 is expressed in breast cancer patients and has the ability to generate humoral response. In addition, SPAG9 downregulation in triple negative breast cancer cells alter the various malignant properties of breast cancer. Our data suggest that SPAG9 may be used in early detection and diagnosis of breast cancer and may be a potential target for therapeutic use.

**No conflicts of interest**

**395** Poster

### How to reduce Ki 67 variability jointly evaluating histological grade

M. Izquierdo[1], I. Rodriguez[1], F. Tresserra[2], M. Mallafre[1], R. Fabregas[1]. [1]*University Hospital Quiron Dexeus, Gynaecology, Barcelona, Spain;* [2]*University Hospital Quiron Dexeus, Histology, Barcelona, Spain*

**Background:** Proliferative tumor activity measured immunohistochemically by Ki 67 has high variability. Clinical use can be improved if it is considered together with the histological grade.

**Material and Methods:** Ki 67 value had been studied in 566 breast cancers since 2007 to 2013 at our institution using MIBI monoclonal antibody. The histological grade and hormonal receptor status were also evaluated.

**Results:** Histological grade was I in 293 (51.7%) tumours, grade II in 219 (38.7%) and III in 54 (16.8%) tumours. Estrogen receptor was positive in 166 (29.5%) tumours and progesterone receptor was positive in 95 (16.8%) tumours.

None of the tumours with Ki 67 value lower than 10% had histological grade III. Only 7% of tumours with histological grade I had a Ki 67 higher than 25%.

**Conclusions:** It has to be considered to repeat and confirm the values of Ki 67 higher than 25% with histological grade I, and Ki 67 values lower than 10% in tumours with histological grade III.

**No conflicts of interest**

**396** Poster

### High expression of Herceptin biosimilar in stir bioreactor

S. Teimourian[1]. [1]*Iran University of Medical Sciences, Medical Genetics, Tehran, Iran*

**Background:** Herceptin is a humanized monoclonal antibody (mAb) which is used for specific management of metastatic breast cancer in patients with overexpression of HER2 receptor. In this study, we have attempted to develop a biosimilar version of Herceptin mAb.

**Methods:** According to in silico studies, the heavy and light chains of Herceptin mAb were designed and constructed. The recombinant constructs were cloned in PVITRO2-neo plasmid and then transfected in CHO-K1 cell line. Stable transformants were selected on G418 containing medium. Cell were then adapted to serum free medium suspension culture in final concentration of 0.5mM L-glutamine. Biological activity of produced antibody in comparison with Herceptin was tested by killing activity in SK-BR3 human breast cancer cell lines.

**Results:** Our results indicated the equal expression level of heavy and light chains. The yield of purified mAb was between 230 to 280 μg/ml/day using stir tank bioreactor. According to the results, the produced mAb had similar affinity to $HER2^+$ tumor cells to that of Herceptin.

**Conclusion:** High-level recombinant protein expression can be achieved by amplification of the recombinant gene with a selectable marker, such as G418). Keeping concentration of glutamine at 0.5 mM, which related to ammonia will extend cultures from 1 week to 2 weeks with a 1.9-fold increase in MAb titers.

**No conflicts of interest**

**397** Poster

### Low ATM protein expression in malignant tumor as well as cancer associated stroma is an independent prognostic factor in a retrospective study of early stage hormone negative breast cancer

X. Feng[1]. [1]*British Columbia Cancer Agency- Vancouver Island Center, Medical Oncology, Victoria, Canada*

**Introduction:** The serine/threonine protein kinase ataxia telangiectasia mutated (ATM) is critical in maintaining genomic integrity. Upon DNA double-strand breaks, ATM phosphorylates key downstream proteins including p53 and BRCA1/2, most common sporadic and inheritable mutated genes in breast cancer, thereby orchestrating complex signaling pathways involved in cell cycle arrest, DNA repair, senescence and apoptosis. Although sporadic mutation of ATM occurs rarely in breast cancer, the status of its protein expression and its clinical significance in breast cancer remains not well established. Our study is sought out to investigate the influence of ATM protein in both tumor and cancer associated stromal on clinical outcome in hormone positive (HPBC) and hormone negative (HNBC) early stage breast cancer (EBC).

**Methods:** Tissue microarrays (TMA), containing formalin-fixed, paraffin embedded resected tumors from two cohorts of patients (HPBC cohort: n = 130; HNBC cohort: n = 168) diagnosed at the Tom Baker Cancer Centre, Calgary, Canada, were analyzed for ATM protein expression using fluorescence immunohistochemistry (IHC) and automated quantitative analysis (AQUA). ATM expression level were measured within the tumor as

a whole (tATM) as indicated by pan-cytokeratin expression, tumor nuclear compartment (nATM) as indicated by both DAPI and pan-cytokeratin positive, and cancer associated stromal (csATM) as indicated by vimentin-positive and pan-cytokeratin-negative. ATM expression levels within these compartments were correlated with clinical outcome.

**Results:** While tATM and nATM were significantly lower in tumors compared to normal breast epithelial tissues, csATM was significantly higher than the corresponding normal tissue compartment. In addition, the median expression level of both tATM and nATM were two to three-fold lower ($p < 0.001$) in HNBC than in HPBC. In both HNBC and HPBC cohorts, patients with low tATM, nATM and csATM tumors had significantly poorer survival outcomes than those with a high tATM, nATM and csATM, but this effect was more pronounced in HNBC. A multivariate analysis demonstrates these biomarkers predict survival independent of tumor size and lymph nodes status, only in HNBC cohort ($p < 0.001$).

**Conclusions:** Low ATM protein expression in both malignant tumor and stromal compartments likely contributes to the aggressive nature of breast cancer and is an independent prognostic factor associated with worse survival in HNBC patients.

**No conflicts of interest**

**398** Poster

**Interleukin-8 in progression of ER-positive and ER-negative breast cancer patients**

N. Todorovic-Rakovic[1], J. Milovanovic[1], Z. Abu Rabi[1]. [1]*Institute for Oncology and Radiology of Serbia, Department of Experimental Oncology, Belgrade, Serbia*

**Background:** Interleukin-8 (IL-8) is a multifunctional cytokine, linked to cancer progression. Biological functions of IL-8 are associated with aggressive potential of estrogen receptor (ER)− breast cancer which is characterized with increased expression of IL-8. In contrast to that, less is known about the role and significance of IL-8 in ER+ breast cancer and about the influence of its expression on clinical course of disease in ER+ breast cancer patients.

**Material and Methods:** The study included 91 postmenopausal primary breast cancer patients (clinical stage I/II) with favorable clinicopathological parameters, mostly with negative lymph node status. These patients didn't receive any kind of adjuvant therapy according to valid protocol at that time. IL-8 levels were determined in primary tumor tissue homogenates by ELISA according to manufacturer's instructions (RayBio Human IL8 ELISA kit). The same primary tumor tissue homogenates were used for ER determination by classical biochemical method. ER levels $\geqslant$10 fmol/mg were considered as positive.

**Results:** There was no statistically significant correlation ($p = 0.2$, Spearman rank order) between ER and IL-8 expression and no statistically significant difference between quantitative IL-8 levels in ER− and ER+ subgroups ($p = 0.06$ Mann Whitney test), although median values of IL-8 in ER-negative subgroup was 387 pg/mg versus 76 pg/mg in ER-positive subgroup. This implies that breast cancer patients with higher levels of IL-8 have lower level of ER. When patients were stratified according to their ER status and using the median IL-8 level for the whole group of breast cancer patients (88.82 pg/mg), it was obvious that IL-8 expression had no influence on survival of ER− breast cancer patients, but had significant influence on survival of ER+ breast cancer patients ($p = 0.04$, Log rank). Patients with ER+IL-8− phenotype had almost twice longer median relapse free survival time (150 months) than patients with ER+IL-8+ phenotype (85 months). Also, the number of relapses in ER+IL-8− subgroup was 18 versus 38 in ER+IL-8+ subgroup.

**Conclusion:** Our findings indicate the more complex association between ER and IL-8 in breast cancer and significant role of IL-8 in progression of ER+ tumors, in contrast to the previously accepted hypothesis that IL-8 expression is important feature which exclusively influence the course of disease in ER− breast cancer patients.

**No conflicts of interest**

**399** Poster

**The effect of VEGF peptide vaccine on inhibition of metastasis in mice breast cancer model**

B. Fazeli Delshad[1,2], F. Soltanpour Gharibdousti[1,2], R. Falak[3], M. Ganjalikhani-Hakemi[1], G.A. Kardar[2]. [1]*Isfahan University of Medical Sciences, Department of Immunology- School of Medicine, Isfahan, Iran;* [2]*Tehran University of Medical Sciences, Immunology Asthma & Allergy Research Institute, Tehran, Iran;* [3]*Iran University of Medical Sciences, Department of Immunology- School of Medicine, Tehran, Iran*

**Introduction:** Breast cancer is the most prevalent cancer in the women that cancer cells metastasis to different tissues and impair the function of them. Cancer cells for growth and development secret some metastatic factors that one of them is vascular endothelial growth factor (VEGF). Already peptide based vaccines are one of the immunotherapy approaches. In this study a peptide based vaccine designed and used for induction of immune system against of VEGF molecule.

**Material and Methods:** By bioinformatics, a part of the VEGF molecule was selected as a peptide based vaccine and conjugated with the KLH carrier. BALB/c mice divided into three groups that one group received peptide vaccine and then 4T1 breast cancer model was created, the second group were only 4T1 breast cancer model and third group were negative control. The mice serums were taken at intervals and the titration of serum IgG against VEGF was measured using ELISA. The weights of the mice in all of the groups as well as the primary tumor volume in vaccinated and tumoral group were measured respectively.

**Results:** The titer of anti-VEGF IgG had significantly increased in vaccinated group compared to tumoral group. Tumor growth in the vaccinated group compared to tumoral group showed the dramatic decrease. As well as the survival rate in the vaccinated group was more than the tumoral group and less than the negative control group.

**Conclusion:** The results of this research show that the designed peptide based vaccine to be able to inhibit the growth and spread of tumoral cells in murine model.

**No conflicts of interest**

**400** Poster

**Immunohistochemical expression of carbonic anhydrase IX, cellular tumor antigen p53, and apoptosis regulator Bcl-2 in triple-negative breast cancer**

I. Alvir[1], P. Ozretić[2], B. Sarčević[3], A. Roguljić[4], L. Beketić-Orešković[5]. [1]*Clinical Hospital Center "Sestre milosrdnice"- University Hospital for Tumors, Department of Gynecologic Oncology, Zagreb, Croatia;* [2]*Ruder Bošković Institute, Division of Molecular Medicine, Zagreb, Croatia;* [3]*Clinical Hospital Center "Sestre milosrdnice"- University Hospital for Tumors, Department of Pathology, Zagreb, Croatia;* [4]*Clinical Hospital Center "Sestre milosrdnice"- University Hospital for Tumors, Department of Radiotherapy and Internal Oncology, Zagreb, Croatia;* [5]*University of Zagreb School of Medicine and Clinical Hospital Center "Sestre milosrdnice"- University Hospital for Tumors, Department of Radiotherapy and Internal Oncology, Zagreb, Croatia*

**Background:** Tumor hypoxia is an important indicator of malignant disease prognosis, associated with aggressive tumor growth, early metastasis and poor response to the treatment. In hypoxic conditions an increased expression of p53 can occur, along with induction of apoptosis via Bcl-2. Our previous study showed that the high expression of a hypoxic marker carbonic anhydrase IX (CA-IX) was a strong independent prognostic indicator for shorter overall (OS) and recurrence-free survival (RFS) in patients with invasive ductal breast carcinoma (Beketic-Oreskovic et al. Pathol Oncol Res, 2011; 17: 593−603).

**Aim:** The aim of this study was to examine the expression of a hypoxic marker carbonic anhydrase IX (CAIX), Bcl-2 as a marker of apoptosis, and tumor suppressor protein p53, as prognostic parameters in patients with triple negative breast cancer.

**Material and Methods:** Immunohistochemical expressions of CAIX, Bcl-2 and p53 were analyzed on paraffin-embedded tumor tissues from 64 female TNBC patients, and correlate with standard clinico-pathological parameters and patients' overall survival.

**Results:** Expression of Bcl-2 was in negative correlation with histological tumor grade ($p = 0.036$), while p53 expression was in positive correlation with both tumor grade and tumor size ($p = 0.033$ and $p = 0.010$, respectively). There was no significant correlation among the expressions of any examined markers. Patients with "high" tumor Bcl-2 expression (above cut-off values) have shorter OS (HR 4.31, 95% CI 0.50–37.44, $p = 0.020$), while there was no correlation between expression of CAIX, p53, Ki-67 and patients' survival. In multivariate analysis Bcl-2 was shown to be an independent prognostic indicator for OS in TNBC patients (HR 10.45, 95% CI 2.23–49.02, $p = 0.003$).

**Conclusions:** High proportion of TNBC samples showed high expression of hypoxic marker CAIX, as well as tumor suppressor protein p53 and proliferation index KI-67. Increased expressions of CAIX, p53, and KI-67 were not connected with decreased patients' survival. However, patients with "high" tumor Bcl-2 expression have shorter overall survival, and expression of anti-apoptotic protein Bcl-2 was an independent prognostic indicator for decreased overall survival for patients with TNBC. With the "cut-off" values of Bcl-2 expression we were able to distinguish TNBC patients with better or worse prognosis.

**No conflicts of interest**

**402** Poster

**Shifts in miRNA expression pattern can lead to the loss of contact inhibition in breast cancer cells**

V. Halytskiy[1]. [1]*Palladin Institute of Biochemistry of the National Academy of Sciences of Ukraine, Molecular Immunology Department, Kiev, Ukraine*

**Background:** Loss of contact inhibition is one of the most prominent features of transformed cells, resulting in uncontrolled cell proliferation and movement. This research aims to identify in what way the shifts in expression of non-coding RNAs, especially miRNAs, can affect the signal pathways responsible for contact inhibition.

**Material and Methods:** MiRNA targets within gene transcripts were predicted in silico using TargetScan software.

**Results:** MiRNAs, hyperexpression of which is essential for abnormal proliferation and surviving of breast cancer cells, can affect the Hippo pathway. MiRNAs miR-27 and miR-155 can silence transcripts of WWC1 (KIBRA) and LATS2 genes. Transcripts of STK4 (MST1) and STK3 (MST2) genes carry targets of miR-18 and, respectively, miR-19, miR-21 and miR-375. MiRNAs miR-21 and miR-27 can silence LATS1 and SAV1 genes, respectively. At the same time, down-regulation of miR-15/16 and miR-205 allows hyperexpression of YAP1 and, respectively, WWTR1 (TAZ) genes which transcripts carry targets of these miRNAs. Hippo pathway failure allows YAP1/TAZ entry into the nucleus.

Overexpressed miRNAs can silence genes encoding the FAK/Src kinase pathway. Transcripts of PTK2 (FAK) and SPRY2 genes contain targets of miR-221/222 and, respectively, miR-21 and miR-27. MiRNAs miR-23a/b, miR-181, miR-221/222 can suppress ARHGEF7 gene encoding PIXB. Target for miR-221/222 is revealed also in PAK1 gene.

In addition, overexpressed miRNAs (miR-18, miR-19, miR-21, miR-23, miR-27, miR-29, miR-155, miR-181, miR-206, miR-221/222, miR-375) silence some other genes that encode key molecules responsible for cell-cell adhesion − E-cadherin, nectins 1, 3, nectin-like molecules 1, 2, 4, occludin, vinculin and connexin 43. MiRNAs miR-19 and miR-23 suppress ACTN1 and ACTN2 genes encoding $\alpha$-actinins. As a result, formation of intercellular contacts and cytoskeleton ultrastructure, responsible for contact inhibition, is affected. At the same time, down-regulation of other miRNAs (miR-128, miR-31, miR-143, miR-145, miR-15/16, miR-204, miR-125, miR-185) allows overexpression of PVR gene which transcript contains many targets for these miRNAs. PVR gene encodes nectin-like molecule 5 that is important for metastasis of cancer cells.

**Conclusions:** Shifts in miRNA expression profile can affect the Hippo cascade as well as FAK/Src pathway and disrupt cell-cell adhesion. This alteration leads to attenuation and nullification of the contact inhibition signals as well as reduces or prevents their generation. Furthermore, many genes responsible for the contact inhibition are involved also in establishment of the cell adhesion and polarity. Silencing of these genes not only leads to the loss of contact inhibition but also impairs cell polarity and randomizes mitotic spindle orientation. As a result, transformed cells form irregular multi-layer conglomerates.

**No conflicts of interest**

**403** Poster

**Induction of Hsp70 in human breast cancer cells treated with Hsp90 inhibitors: a predictive marker and promising target for the tumor radiosensitization**

V. Kudryavtsev[1], A. Khokhlova[1], V. Mosina[1], Y. Makarova[1], A. Kabakov[1]. [1]*A.F. Tsyb Medical Radiological Research Center, Department of Biochemistry, Obninsk, Russian Federation*

**Background:** Several inhibitors of the 90 kDa heat shock protein (Hsp90) activity were characterized as potential radiosensitizers for malignancies; however, the radiosensitivity of some tumors is not enhanced by such inhibitors. Therefore, biomarkers are needed to predict the tumor radiation response in the context of Hsp90-inhibiting treatments. Implication of the inducible 70 kDa heat shock protein (Hsp70) in the breast cancer cell response to co-treatments with the Hsp90 inhibitors and radiation was analyzed in the present study.

**Material and Methods:** Cells cultured from different human breast carcinomas were treated with Hsp-inhibiting drugs or/and gamma-photon radiation. In the comparative experiments, cell cultures of the human normal (non-cancerous) epithelium were subjected to the same treatments. The post-treatment cell death/survival was evaluated in clonogenic assays and MTT-test. The levels of Hsp70 induction were determined on a microscope by measuring the fluorescence intensity per cell in the cell preparations stained with an antibody specific to inducible Hsp70.

**Results:** It was found that clinically achievable (nanomolar) concentrations of 17AAG and NVP-AUY922 (inhibitors of the Hsp90 chaperone activity) exerted radiosensitizing effects only if the early pronounced Hsp70 induction was observed in target cells following the drug treatments. When the drug-induced radiosensitization did take place, its degree positively correlated with the level of Hsp70 induction in the drug-treated cells. According to the data obtained, quantitative determination of inducible Hsp70 in the drug-treated normal and cancer cells enables to predict (i) which breast tumors will be susceptible to such radiosensitizers and (ii) which concentrations of 17AAG or NVP-AUY922 can ensure the preferential cytotoxicity within the target tumor and minimal damage to normal adjacent tissues. Therefore, quantified expression of inducible Hsp70 can define a potential of either Hsp90 inhibitor as a selective radiosensitizer for human breast tumors. Importantly, the Hsp70 induction in the drug-treated breast cancer cells appears to be a cytoprotective response that may impair the antitumor effects of Hsp90 inhibition. It was here demonstrated that combination of the Hsp70-inducing Hsp90 inhibitor (17AAG or NVP-AUY922) with one of known inhibitors of the Hsp induction (quercetin, triptolide, KNK437, NZ28) prevented up-regulation of Hsp70 in the co-treated cancer cells and significantly enhanced the radiosensitization of them.

**Conclusions:** The easily detectable Hsp70 induction can be a useful marker predicting the breast tumor response to Hsp90-inhibiting radiosensitizers. Besides, targeting the treatment-responsive Hsp70 induction in breast cancer cells may improve the outcome of radiotherapy.

**No conflicts of interest**

**404** Poster

**Collection of breast venous blood during sentinel node biopsy**

G. Mitchell[1], L. Webber[1], F. Collier[2]. [1]*University Hospital Geelong, Surgery, Geelong, Australia;* [2]*University Hospital Geelong, Medical Research, Geelong, Australia*

**Background:** Circulating tumour cells and tumour markers are generally measured in the peripheral circulation; however a source closer to the breast tissue could be more informative. Although the veins from the breast drain in multiple directions, the lateral thoracic vein (LTV) is often exposed during sentinel node biopsy (SNB) procedure. We propose that, (i) during SNB the LTV can be cannulated for collection of blood, and (ii) LTV blood contains higher concentrations of breast factors than blood collected in a peripheral site. The aim of the study is to assess the feasibility and validity of collecting breast venous blood from breast cancer patients at the time of their surgery.

**Methods:** Patients (n = 28 women) undergoing SNB were identified and consent obtained. A radioactive tracer and blue dye were injected prior to surgery. During SNB, blood was collected simultaneously from the LTV and a peripheral site (leg or lower arm). Levels of radioactivity (counts/sec) and the intensity of the blue dye (at 540 nm) were measured in the two samples. Levels of 17$\beta$-oestradiol were also measured by immunoassay (detectable limit 70 pmol/L).

**Results:** LTV Blood was successfully collected in 25/28 patients. Both concentration of the blue dye and levels of radioactivity were higher in the plasma samples from the LTV compared to the peripheral site ($p < 0.0001$ and $p = 0.002$ respectively, Wilcoxon matched-pairs signed rank test of relative data). Oestradiol was elevated by 20% in LTV blood when detectable (12 patients, $p = 0.001$).

**Conclusion:** Collection of breast venous blood during SNB is feasible in most cases. It can be validated as breast venous blood by measuring its radioactivity, blueness and/or 17$\beta$-oestradiol content compared to peripheral blood.

**No conflicts of interest**

**405** Poster

**Flutamide effects on cell proliferation and steroid hormone secretion in human and canine inflammatory breast cancer cell lines**

S. Caceres[1], L. Peña[2], M. Illera[1], B. Monsalve[1], W. Woodward[3], J. Reuben[4], J. Illera[1]. [1]*Universidad Complutense De Madrid, Fisiologia Animal, Madrid, Spain;* [2]*Universidad Complutense De Madrid, Medicina Y Cirugia Animal, Madrid, Spain;* [3]*The University of Texas Md Anderson Cancer Center, Radiation Oncology, Houston, Usa;* [4]*The University of Texas Md Anderson Cancer Center, Hematopathology, Houston, Usa*

**Background:** Inflammatory breast carcinoma (IBC) is a special type of breast cancer with a poor survival rate and accounts for 6% of diagnosed breast cancers. Estrogens are the main hormones implicated in tumor progression. The role of androgens on breast cancer is on rise in research, trying to propose anti-androgen therapeutic strategies. The aim of this study was to know the effects of flutamide (anti-androgen drug) on cell proliferation and steroid production (based on steroidogenic enzymes and hormones) in two cancer IBC triple negative cell lines (SUM-149 and IPC-366, human and canine, respectively).

**Material and Methods:** IPC-366 was cultured in Dulbecco's modified Eagle medium nutrient mixture F-12 Ham (DMEM/F12) and SUM149

was maintained in Ham's F-12 media. Flutamide concentrations added to the culture media were: 5 μM, 10 μM, and 15 μM for 72 hours. Steroid hormones determination in culture media (pregnenolone (P5), progesterone (P4), dihydroepiandrostenedione (DHEA), androstenedione (A4), testosterone (T), dihydritestosterone (DHT), 17β-estradiol (E2) and estrone sulphate (SO4E1)) were assayed by EIA previously validated. Immunohistochemistry (IHC) analysis of the steroidogenic enzymes CYP11A1, 3β-HSD, CYP19A1, 17β-HSD and 5α-reductase were assayed in pellets from treated and control groups in both cell lines.

**Results:** Percentage of cell proliferation showed a decrease in all treatments in IPC-366 and SUM149. Regarding hormonal secretion, in treated groups changes in hormone concentrations were dose dependent. In treated groups there was an increased in steroid secretion as showed the high levels found in P5, P4 and A4. T and DHT concentrations were higher in treated groups, in contrast to E2 levels that decreased in the treated groups. 17β-HSD and 5α-reductase by IHC showed a high expression in treated groups. As DHEA levels showed a decreased it is assumable that androgen synthesis is mediated by P4 pathway.

**Conclusion:** We can conclude that IPC-366 and SUM149 treated with flutamide reduced the proliferation of neoplastic cells and cause significant changes in steroid hormone secretion by increasing T production leading to a decrease in E2 levels. Further studies should clarify the effectiveness and mechanism of action of anti-androgens drugs opening a future approach for IBC and triple negative breast cancer.

**No conflicts of interest**

**406** Poster

**High nuclear expression of RBM3 is associated with an improved prognosis of clinical outcome in breast cancer**

S.Y. Kwon[1], S.H. Kang[2], Y.N. Kang[1], M. Choe[1], I. Hwang[1], J.H. Cho[2]. *[1]Keimyung University School of Medicine, Pathology, Daegu, South Korea; [2]Keimyung University School of Medicine, Surgery, Daegu, South Korea*

**Background:** The RNA-binding motif protein 3 (RBM3) is produced by hypoxia and low temperature and has been known as a proto-oncogene. Recently, high nuclear expression of RBM3 has been reported to be associated with good prognosis in colon cancer, prostate cancer, ovarian cancer, and malignant melanoma. Also very limited studies of RBM3 in breast cancers are reported.

**Material and Methods:** The nuclear RBM3 expression was examined using a tissue microarray from 361 patients for invasive mammary carcinomas. Other immunohistochemical staining for ER, PR, and Her2 was performed to compare the expression with that of RBM3. For scoring of RBM3 expression, a combined nuclear score of NF (nuclear staining fraction) × NI (nuclear staining intensity) was used. Also additional study for western blotting for breast cancer cell lines was performed.

**Results:** The combined nuclear score of RBM3 expression was divided into 2 groups (low expression, ⩽4, and high expression, >5). Total 248 (68.7%) of 361 was high nuclear RBM3 expression. High nuclear RBM3 expression was significantly associated with a prolonged disease free survival, the overall survival, expression of ER and PR, T1 and 2 stage, and high histologic grade. The result of western blotting study for several breast cancer cell lines revealed increased RBM3 expression in normal breast cell lines (MCF10A and 184B5) and luminal types (MCF7, T47D, and ZR75−1) and triple negative types (MDA-MB-231 and BT-20). However, in case of HER2 rich type, such as HCC1954 showed decreased RBM3 expression.

**Conclusions:** Our results showed that high nuclear RBM3 expression in breast cancers are strongly associated with a prolonged disease free time and overall survival. Also it is very close relationship with good prognostic markers of hormonal receptors such as ER and PR in breast cancer. Therefore, high nuclear RBM3 expression can be a critical biomarker of favorable clinical outcomes in breast cancer.

**No conflicts of interest**

**407** Poster

**Triple-negative breast cancer: New therapeutic options via signalling transduction cascades**

U. Andergassen[1], A. Koelbl[1], U. Jeschke[1]. *[1]University of Munich, Klinik Und Poliklinik Fur Frauenheilkunde Und Geburtshilfe, Munchen, Germany*

**Background:** Triple negative breast cancer is a highly aggressive type of mammacarcinoma. It is defined by a rather weak expression of Estrogen-, Progesterone- and Her2-Receptor, and is therefore difficult to treat, resulting low disease-free and overall survival rates of the affected patients. Hence it is important to find new therapeutic options.

**Methods:** We analysed the incidence of some molecules from different signal transduction cascades, which are known to correlate with triple negative breast cancer, by immunohistochemistry, and correlated the expression of these molecules to different tumour traits, like size, grading, menopausal stage, histology, lymph node affection and remote metastasis formation, furthermore to the incidence of local and lymph node recurrence and metastasis by statistical analysis.

**Results:** Some statistically significant correlations were found for a number of tumour characteristics and signalling molecules. HIF1α is correlated to tumour grading, β-catenin to the menopausal state of the patient, and Notch1 bears a relation to lymph node affection. In terms of different recurrences, a correlation of β-catenin to metastasis formation and lymph node recurrence could be shown, as well as coherences between XBP1 and lymph node recurrence, Notch1 and metastasis formation and FOXP3 and the occurrence of local recurrence.

**Conclusion:** The presented results are in accordance with formerly published studies and therefore might comprise chances to develop new therapeutical strategies, which could help to treat this aggressive form of breast cancer in a manner, by which side effects would be reduced and therapeutical efficiency is increased.

**No conflicts of interest**

**408** Poster

**Hormone sensitivity in breast cancer cells under hypoxia: The role of estrogen receptor and Snai1 signaling pathways**

A. Scherbakov[1], L. Stefanova[2], M. Krasil'nikov[2]. *[1]N.N. Blokhin Russian Cancer Research Center, Laboratory of Molecular Endocrinology and Laboratory of Clinical Biochemistry, Moscow, Russian Federation; [2]N.N. Blokhin Russian Cancer Research Center, Laboratory of Molecular Endocrinology, Moscow, Russian Federation*

**Background:** The transcription factors Snai1 and Snai2/Slug are key players in the loss of cell adhesion and the epithelial-to-mesenchymal transition (EMT), one of the important steps in breast cancer progression. Snai1 mediates the loss of E-cadherin-associated cell-cell contacts, the increase in the expression of mesenchymal markers, and the progression to fibroblast-like phenotype of breast cancer cells. Hormonal signaling plays the significant role in breast cancer development and treatment, but relationship between Snai1 and estrogen receptor (ERα) pathways remain unclear, especially under stress conditions such as hypoxia.

The main **Purpose** of the project was to study a relationship between Snai1 signaling pathway, the hormonal response and the tolerance of breast cancer cells to hypoxia.

**Material and Methods:** MCF-7 and MCF-7/HER2 (ERα+, hormone responsive) and MDA-MB-231, HBL-100, SKBR3 (ERα−, hormone resistant) breast cancer cells were cultured in standard DMEM medium supplemented with 7% fetal calf serum. Estrogen receptors and Snai1 expression were assessed by immunoblotting; α-tubulin antibody was used as loading control. The transcriptional activity of Snai1 was determined by reporter luciferase assay.

**Results:** We have established a direct relation between one of epithelial-mesenchymal proteins, Snai1, and the tolerance of breast cancer cells to hypoxia. The Snai1 involvement in the regulation of cell survival under hypoxia has been demonstrated. Snai1 protected breast cancer cells from hypoxic stress when ERα was down-regulated in ERα-positive cells under hypoxia. At the same time the experiments with MCF-7/HER2 and SKBR3 cells showed that HER2/ERBB2 was not involved in the response of breast cancer cells to hypoxia. Moreover the ERα-dependent suppression of Snai1 as well as Snai1 activation in the hormone resistant breast cancer cells has been observed. Snai1 involvement in doxorubicin resistance has been revealed.

**Conclusions:** The results demonstrate the protective role of Snai1 in breast cancer in hypoxic conditions, and show that Snai1 pathway may serve as perspective target in the treatment of hormone resistant breast cancer. Snai1 inhibition can help to sensitize breast cancer to doxorubicin.

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**No conflicts of interest**

**409** Poster

**Can we get accurate biomarker (ER, PR, Her2 and Ki67) information from core needle biopsy specimens in invasive breast cancer?**

H. Nagaoka[1], T. Takahashi[1], K. Endo[1], Y. Ohta[2]. *[1]Ogawa Redcross Hospital, Department of Breast and Endocrine Surgery, Hiki- Saitama, Japan; [2]Ogawa Redcross Hospital, Department of Central Laboratory, Hiki- Saitama, Japan*

**Background:** Accurate evaluation of biomarker [estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor type 2 (Her2) and Ki67] status is important for primary breast cancer patients to

determinate their course of therapy. We usually obtained these information from core needle biopsy specimens (CNBs) preoperatively, but diagnostic differences between CNB and surgically resected specimens (SRs) was not available. We investigate the correlation of ER, PR, HER-2 and Ki67 status in the CNBs with those observed in SRs.

**Material and Methods:** A total of 144 patients with invasive ductal carcinoma without preoperative therapy were included in this retrospective study. CNB was underwent with 16Gauge needle under ultrasound-guide and 3−5 specimens were taken. ER, PR, Her2 and Ki67 status were determined by immunohistochemistry in invasive margin of tumor. ER and PR (>3: Allred score), Her2 (score 3: ASCO/CAP), Ki67 (>14%: Ki67 labeling index) were evaluated as positive case. We made a comparison between the results of CNBs and SRs.

**Results:** The sensitivity, specificity, accuracy were well enough in ER (70.8%, 94.4%, 87.2%), PR (74.2%, 95.8%, 87.8%), Her2 (97.2%, 83.3%, 96.2%) status, while but it seems to be worse in Ki67 (70.2%, 85.7%, 74.2%). We sought the factors which drive down the diagnostic rate, clinicopathological characteristics(age, tumor size, lymphnode status, histological grade) and the number of CNBs were not concerned their accuracy.

**Conclusions:** CNB can be useful for ER, PR and HER2 status determination, while its usefulness for Ki67 status is limited. We should use caution to evaluate tumor proliferation with CNBs.

**No conflicts of interest**

**410** Poster

**Macrophage content by CD163 expression is strongly related to vascular invasion and interval breast cancer**

T.A. Klingen[1], Y. Chen[2], H. Aas[3], E. Wik[4], L.A. Akslen[4]. *[1]Vestfold Hospital Trust, Centre for Cancer Biomarkers CCBIO- Department of Clinical Medicine- Section for Pathology- University of Bergen- Department of Pathology- Vestfold Hospital Trust, Tønsberg, Norway; [2]Vestfold Hospital Trust, Centre for Cancer Biomarkers CCBIO- Department of Clinical Medicine- Section for Pathology- University of Bergen − Department of Pathology- Akershus University Hospital, Lørenskog, Norway; [3]Vestfold Hospital Trust, Departement of Surgery, Tønsberg, Norway; [4]University of Bergen, Centre for Cancer Biomarkers CCBIO- Departement of Clinical Medicine- Section for Pathology- University of Bergen − Department of Pathology- Haukeland University Hospital, Bergen, Norway*

**Background:** Tumor associated macrophages resembles M2 macrophages, promotes tumor invasion and show strong expression of CD163 in breast cancer. We here investigated the association between CD163 positive macrophages and vascular invasion, molecular subgroups (St Gallen consensus 2013), mode of detection, and outcome.

**Materials and Methods:** We performed a population based retrospective study of invasive breast cancers from the Norwegian Breast Cancer Screening Programme in Vestfold County (2004–2009) including 199 screen-detected and 83 interval cancers. Immunohistochemical staining for CD163 positive macrophages were quantified and dichotomized as high (upper quartile) and low expression. Lymphatic vessel involvement (LVI) and blood vessel invasion (BVI) were recorded separately based on immunohistochemical staining (D2−40 and CD31 antibodies).

**Results:** High CD163 was associated with BVI (OR=4.1; $p < 0.001$), LVI (OR=3.1; $p < 0.001$) and with interval cancers compared to screening tumors (OR=4.4; $p < 0.001$). Median CD163 counts were 42% in Luminal A, 42% in Luminal B (Her2 neg), 50% in Luminal B (Her2 pos), 59% in Her2 type and 62% in Triple negative tumors (Kruskal–Wallis test, $p < 0.001$). In univariate survival analyses, cases with high level of CD163 positive cells (upper quartile) were significantly associated with poorer disease specific survival compared to cases with low CD163 ($p = 0.005$).

Table: Association between CD 163 expression in hot spot counts, categories of vessel invasion and detection method

| Variable | | Cases | CD163 | | | |
|---|---|---|---|---|---|---|
| | | | Low[a] | High[a] | Odds ratio | p-value[b] |
| BVI | Negative | 239 | 194 (81) | 45 (19) | 1 | <0.001 |
| | Positive | 43 | 22 (51) | 21 (49) | 4.1 (2.1−8.1) | |
| LVI | Negative | 212 | 174 (82) | 38 (18) | 1 | <0.001 |
| | Positive | 70 | 42 (60) | 28 (40) | 3.1 (1.7−5.5) | |
| Detection | Screening | 200 | 170 (85) | 30 (15) | 1 | <0.001 |
| | Interval | 82 | 46 (56) | 36 (44) | 4.4 (2.5−8.0) | |

[a] Number of cases (%) for high [upper quartile] and low CD163 expression.
[b] Pearson's chi square test.

**Conclusions:** High CD163 expression in breast cancer is strongly related to blood and lymph vessel invasion as well as detection between screening intervals. Furthermore, the presence of high CD163 is associated with non-luminal molecular subgroups and poor prognosis.

**No conflicts of interest**

**411** Poster

**Contribution of estrone-sulfate to cell proliferation in aromatase-inhibitor resistant breast cancer**

T. Higuchi[1], M. Endo[2], T. Hanamura[3], T. Gohno[2], T. Niwa[2], Y. Yamaguchi[4], J. Horiguchi[1], T. Oyama[5], I. Takeyoshi[6], S.I. Hayashi[2]. *[1]Gunma University Hospital, Breast and Endocrine Surgery, Maebashi, Japan; [2]Graduate School of Medicine- Tohoku University, Molecular and Functional Dynamics, Sendai, Japan; [3]Shinshu University School of Medicine, Surgery, Matsumoto, Japan; [4]Saitama Cancer Center, Research Institute for Clinical Oncology, Saitama, Japan; [5]Graduate School of Medicine- Gunma University, Diagnostic Pathology, Maebashi, Japan; [6]Graduate School of Medicine- Gunma University, Visceral and Thoracic Organ Surgery, Maebashi, Japan*

**Background:** Aromatase Inhibitors (AIs) are first-choice drugs for estrogen-receptor (ER) positive postmenopausal breast cancer patients, and their efficacies are validated by some big trials, but some patients do not respond to AIs and experience recurrence. Several AI-resistant mechanisms were has been reported by our laboratory and other researchers, but the whole mechanism remains to be solved. In this study, we now present the possibility of another dual-blockade treatment for steroid metabolism.

**Material and Method:** We introduced plasmids carrying aromatase gene to MCF-7 cells whose ER activity could be visually monitored by expression of green fluorescent protein (GFP). These candidate-cell lines were cultured in estrogen-depleted medium including testosterone and letrozole for three months, visually monitoring GFP as ER activity. We finally established ER-positive Letrozole-Resistant cell lines (LR cell lines), and analyzed the AI-resistant mechanism of LR cell lines.

**Results:** In LR cell lines, mRNA expression of steroid sulfatase (STS) and four organic anion transporter peptides (OATPs) involved in metabolism of estrone sulfate (E1S) were induced, but there was no change in mRNA expressions of efflux drug transporters, aromatase-catabolic enzyme, enzymes related with production for estrogenic androgen, androgen receptor and its target genes. It was suggested that E1S-STS pathway probably was involved in AI-resistance of LR cell lines rather than AR activity, estrogenic-androgen, efflux transporter and catabolic enzyme related with AI. Furthermore, LR cell lines proliferated by E1S in dose-dependent manner more than their parental cells, but there was no difference of proliferation when estrone and estradiol treated. STS inhibitor administered with letrozole was inhibitory to proliferation of LR cells. LR cells were also inhibited by SERM and SERD. In mRNA analysis of clinical primary tissues of postmenopausal patients, expression of STS mRNA significantly correlated with those of three OATPs which were induced in LR cell lines. Additionally, mRNA expression of STS also strongly correlated with that of OATP different from those induced in LR cells, suggesting that mRNA expression of OATPs in primary tissue is different from AI-resistant one.

**Conclusion:** In this study, we first demonstrated that the contribution of E1S to ER-positive breast cancer in the context of AI resistance. This model could present the possibility of dual-blockade treatments to AI-resistant breast cancer in combination with AI.

**No conflicts of interest**

**412** Poster

**Selective FGFR inhibitor, AZD4547, modulates bone microenvironment by suppressing RNAKL/M-CSF/Osteocalcine induced osteoclastogenesis in FGFR-amplified breast cancer**

Y.J. Choi[1], J. Kang[1], H.J. Lee[1], U. Jo[1], S.I. Park[2], J.W. Bae[1], K.H. Park[1]. *[1]Korea University Anam Hospital, Internal Medicine, Seoul, Korea; [2]Korea University College of Medicine, Biochemistry, Seoul, Korea*

**Background:** Fibroblast growth factor receptor (FGFR) are important molecules that control bone formation and bone metastases. Luminal-B type breast cancers are more proliferative, more likely to metastasize to bone than luminal-A type tumors and associated with FGFR amplification. In this study, interaction between FGFR-amplified breast cancer cell and bone microenvironment was investigated with selective FGFR-tyrosine kinases inhibitor (FGFR-TKI), AZD4547.

**Materials and Methods:** FGFR1-amplified breast cancer cell line (MDA-MB-134-IV) and FGFR2-overexpressed MCF-7 cells were used. Pre-osteoblast cells (MC3T3-E1) and human osteosarcoma cells (MG-63) were used as cells in bone microenvironment. Western blot analysis and ELISA were used to evaluate protein expression in cells and supernatants of cells, respectively. Quantitative RT-PCR was used to assess gene expression in MC3T3-E1 and MG-63 cells. Effect of AZD4547 were used to assess gene or protein expression in cells and osteoclastogenesis assay. Micro-CT and histopathology was used for evaluation of tumor growth in vivo.

**Results:** AZD4547 significantly inhibits growth of FGFR-amplified breast cancer cell line in MTT assay. Supernatants of MDA-MB-134-IV cells significantly activated FGFR1 on osteoblast and induced RNAKL/M-CSF/Osteocalcin expression in MC3T3-E1 and MG-63 cells. A selective inhibition of FGFR by AZD4547 significantly decreased expression of RNAKL/M-CSF/Osteocalcin, which were induced by supernatants of MDA-MB-134-IV cells. Additionally, ligand or MDA-MB-134IV supernatant-induced osteoclastogenesis were significantly inhibited by AZD4547 in bone marrow monocytes. Also, AZD4547 significantly inhibited tumor growth of MDA-MB-134 xenografts and modulated bone microenvironment.

**Conclusions:** Taken together, our results suggest that selective inhibition of FGFR might have therapeutic effect by modulating bone microenvironment as well as cytotoxicity in FGFR-amplified breast cancer with bone metastasis.

**No conflicts of interest**

**413** Poster

**Evaluation of the relationship among Topoisomerase II alpha expression, chemotherapeutic sensitivity, and prognostic factors in breast cancer**

H. Tokiniwa[1], J. Horiguchi[1], D. Takata[1], R. Nagaoka[1], N. Rokutanda[1], A. Sato[1], T. Higuchi[1], S. Obayashi-Uchida[1], M. Tsuboi[1], I. Takeyoshi[1], T. Oyama[2], Y. Iino[3]. *[1]Gunma University Graduate School of Medicine, Thoracic and Visceral Organ Surgery, Maebashi- Gunma, Japan; [2]Gunma University Graduate School of Medicine, Diagnostic Pathology, Maebashi-Gunma, Japan; [3]Kusunoki Hospital, Breast Center, Fujioka- Gunma, Japan*

**Background:** It is important to search for prognostic factors that are useful in estimating an individual patient's risk or to predict response to a specific therapy. Topoisomerase II alpha (Topo IIa) is involved in DNA replication and is a molecular target for anthracycline-based chemotherapy. The collagen gel droplet-embedded culture-drug sensitivity test (CD-DST) is an in vitro chemosensitivity test that has several advantages over conventional tests. The objective of this study was to evaluate of the relationship among Topo IIa expression, chemotherapeutic sensitivity, and prognostic factors in breast cancer.

**Materials and Methods:** CD-DST was performed in 125 patients with breast cancer between July 2001 and December 2006. The specimens obtained during surgery were used for the CD-DST and immunohistological examination of Topo IIa expression. Chemotherapeutic sensitivity to the anticancer drugs epirubicin (EPI), Adriamycin (ADM), Paclitaxel (PAC), Docetaxel (DOC) and 5-FU was estimated using CD-DST. We investigated the correlation of levels of Topo IIa expression within tumor cells were compared with clinicopathological factors and chemotherapeutic sensitivity.

**Results:** Statistically significant differences were observed between Topo IIa overexpression, nuclear grade ($p < 0.001$), ER expression ($p = 0.028$) and Ki-67 LI ($p < 0.001$). Results obtained from the CD-DST showed the chemosensitivity to each anticancer drug to be EPI, 76%; ADM, 26%; PAC, 43%; DOC, 71% and 5-FU, 21%. There was no statistically significance between clinicopathological factors, Topo IIa overexpression and chemosensitivity for EPI, ADM, 5-FU. Chemosensitivity for DOC was significantly correlated with HER2 status and cell proliferation.

**Conclusions:** Topo IIa overexpression was associated with poor prognostic factors such as histological grading, cell proliferation. In this study, there was no significance between Topo IIa overexpression and chemosensitivity. And we could not show the role of Topo IIa as a chemosensitivity marker.

**No conflicts of interest**

**414** Poster

**Biomarkers to distinguish hazardous from harmless ductal carcinoma in situ (DCIS) of the breast**

L. Visser[1], L. Elshof[1], K. Van de Vijver[2], E. Groen[2], F. Nieboer[1], M. Maaker[1], M. Schaapverld[3], E. Rutgers[4], E. Lips[1], J. Wesseling[1]. *[1]Dutch Cancer Institute − Antoni van Leeuwenhoek Hospital, Molecular Pathology, Amsterdam, Netherlands; [2]Dutch Cancer Institute − Antoni van Leeuwenhoek Hospital, Pathology, Amsterdam, Netherlands; [3]Dutch Cancer Institute − Antoni van Leeuwenhoek Hospital, Psychosocial research and Epidemiology, Amsterdam, Netherlands; [4]Dutch Cancer Institute − Antoni van Leeuwenhoek Hospital, Surgery, Amsterdam, Netherlands*

**Background:** The incidence of DCIS has increased since the introduction of population-based screening. This has not resulted in a decrease in invasive breast cancer incidence, implying overdiagnosis exists. All women with DCIS are still intensively treated, by surgery, radiotherapy, and/or hormonal treatment, although only a minority will develop a subsequent invasive breast cancer. As we cannot discriminate such hazardous from harmless DCIS lesions, accurate prognostic biomarkers are urgently needed. In the current study we aim to identify molecular markers for DCIS aggressiveness, using a large population-based cohort.

**Patients and Methods:** We used a population-based, nation-wide cohort consisting of 10,090 women treated for primary DCIS between 1989 and 2004 with a median follow-up time of 10.7 years. Within this cohort, a case–control study was set up to analyse which markers are associated with progression to invasive breast cancer. Patients with a subsequent ipsilateral invasive breast cancer were defined as "cases", patients without a subsequent invasive cancer in the same follow up period were defined as "controls". We have collected FFPE tissue blocks of 287 "cases" (matched DCIS and iiBC specimen) and 1149 "controls". A first study using this population-based cohort will involve immunohistochemistry (IHC) on 200 "cases" and 500 "controls" for an 8-marker IHC panel (ER, PR, HER2, Ki67, p16, p53, COX-2, and Annexin A1). Molecular subtypes of the DCIS and invasive breast cancer lesions will be determined and intra-individual heterogeneity will be assessed. IHC marker expression will be both compared between "cases" and " controls" as well as between DCIS lesions and its subsequent invasive breast cancer. In a second study, DNA and RNA will be isolated from these specimens, using laser microdissection, and extensive molecular profiling will be performed.

**Results:** We have collected FFPE tissue blocks of 287 "cases" and 1149 "controls" (86% of requested material) from 56 participating hospitals. At present all the specimens of the "cases" and "controls" have been centrally reviewed for extensive morphological characteristics by a panel of breast pathologists. Only a small part (14%) of the specimens had to be excluded from the study population. IHC staining of the tissue specimens, using the 8-marker IHC panel is ongoing.

**Conclusion:** Within a nation-wide cohort of 10,090 patients diagnosed with primary DCIS, we were able to collect tissue material of a representative case–control series of 200 "cases" with subsequent invasive breast cancer and 500 invasive breast cancer-free "controls". This is the first time such a large unique, unbiased DCIS series, with long-term follow-up is analysed integrating clinical, histological, and immunohistochemical data.

**No conflicts of interest**

**415** Poster

**Troglitazone inhibits NF-κB and AP-1-mediated MMP-9 expression and invasion of breast cancer cell**

K. Seon Kwang[1], K. Sang Yull[1], J. Sung Hoo[1], Y. Hyun Jo[1], L. Seung Joo[1]. *[1]Chonbuk National University Hospital, Surgery, Jeon-ju, Korea*

**Purpose:** Peroxisome proliferator-activated receptor gamma (PPARg) inhibits proliferation and invasion of cancer cells and might be a potential therapeutic target of breast cancer. Matrix metalloproteinases (MMPs) are key enzymes for invasion and metastasis. Among them, MMP-9 expression is associated with breast cancer invasion. 12-O-tetradecanoyl phorbol-13-acetate (TPA) treatment induces MMP expression by activating transcription factors such as NF-κB and activator protein-1 (AP-1). In this study, we investigated the effect of PPARg ligands on TPA-induced MMP-9 expression and cell invasion using breast cancer cells.

**Methods:** To investigate the effect of troglitazone on TPA-induced MMP-9 expression, we performed zymography, western blots, real-time PCR, and luciferase assays on MCF-7 cells. In vitro Matrigel invasion assays were also used to investigate the inhibition by troglitazone of invasion on MCF-7 cells.

**Results:** We treated the MCF-7 cells with the synthetic PPARγ ligand troglitazone at concentrations with no obvious cytotoxicity. TPA treatment increased MMP-9 expression and cell invasion and these effects were decreased by troglitazone. TPA substantially increased DNA binding by NF-κB and AP-1. Pretreatment with troglitazone inhibited TPA-stimulated NF-κB and AP-1 DNA binding. The selective PPARγ antagonist GW9662 did not block troglitazone-mediated inhibition of MMP-9 expression in TPA-treated MCF-7 cells.

**Conclusion:** These results suggested that troglitazone inhibited TPA-induced MMP-9 expression and cell invasion on MCF-7 cells through a PPARγ-independent mechanism.

**No conflicts of interest**

**416** Poster

**The genomic profile of BRCA1-associated estrogen-receptor (ER) positive breast cancer does not resemble BRCA1-associated ER negative cancers, but is more similar to BRCA2-associated breast cancer**

E.H. Lips[1], R. Debipersad[1], E. Scheerman[1], L. Mulder[2], L.E. Van der Kolk[3], J. Wesseling[1], F.B.L. Hogervorst[1], P.M. Nederlof[1]. *[1]Netherlands Cancer Institute Antoni van Leeuwenhoek hospital, Pathology, Amsterdam, Netherlands; [2]Netherlands Cancer Institute Antoni van Leeuwenhoek hospital, Molecular Pathology, Amsterdam, Netherlands; [3]Netherlands Cancer Institute Antoni van Leeuwenhoek hospital, Clinical Genetics, Amsterdam, Netherlands*

**Background:** Most breast cancers arising in BRCA1-mutation carriers are estrogen receptor negative (ER−). However, 10 to 20% of BRCA1-associated breast cancers are estrogen receptor positive (ER+). As these tumors arise more often in older patients, and have less aggressive tumor characteristics, it has been suggested that these tumors are 'sporadic' and not BRCA1-driven. With the introduction of targeted treatments specific for tumors with a non-functioning BRCA1 or BRCA2 gene, the question whether the BRCA genes are impaired in the tumor, is highly relevant. Therefore, we typed BRCA1 mutated ER+ tumors on the genomic level.

**Material and Methods:** Genomic profiling of 16 ER+ BRCA1 mutated tumors was performed as well as BRCA1 promoter methylation and LOH analysis. Results were compared to 57 ER− BRCA1 associated tumors, 36 ER+ BRCA2 associated tumors, and 182 ER+ sporadic tumors. Clinico-pathological variables were compared between subgroups.

**Results:** Only 2 out of 16 (12.5%) ER+ BRCA1 associated tumors showed a BRCA1-like genomic profile, while 86% of all ER− BRCA1-associated tumors show this genomic profile. Interestingly, 10 out of 16 (62.5%) ER+ BRCA1-associated tumors showed a BRCA2-like genomic profile. BRCA1 promoter methylation was absent in ER+ BRCA1-associated tumors, similar to ER− BRCA1-associated tumors. In 10 out of 12 ER+ BRCA1 mutated tumors loss of the wild-type BRCA1 allele was observed, fitting a tumor suppressor gene scenario. Histopathological variables in ER+ BRCA1 mutated tumors were more similar to ER+ BRCA2 mutated tumors and to sporadic ER+ tumors than to ER− BRCA1 mutated tumors.

**Conclusions:** The genomic profile of BRCA1-associated ER+ tumors was highly similar to BRCA2 mutated ER+ tumors, and not to BRCA1-associated ER− tumors or sporadic ER+ tumors. This suggests that the genomic profile is driven by both hormonal status and the loss of a BRCA gene. LOH analysis indicated that also in ER-BRCA1-mutated tumors complete loss of the BRCA1 gene plays a crucial role in tumorigenesis. A clinical consequence would be that ER+ BRCA1-associated breast tumors are probably highly sensitive to PARP inhibitors, similar to ER− BRCA1-associated breast cancers. However, as ER+ BRCA1-mutated tumors clearly have different tumor characteristics compared to ER− BRCA1-mutated tumors, they should be considered as a special group, and response to therapies exploiting the BRCA1 gene defect should be specifically monitored in this subgroup.

**No conflicts of interest**

**417** Poster

**Identification of breast cancer-specific signatures in saliva metabolites using capillary electrophoresis mass spectrometry**

H. Jinno[1], T. Murata[2], S. Makoto[3], S. Masahiro[4]. *[1]Teikyo University School of Medicine, Surgery, Tokyo, Japan; [2]Saitama Municipal Hospital, Surgery, Saitama, Japan; [3]Tokyo Medical University, Surgery, Tokyo, Japan; [4]Keio University, Institute for Advanced Biosciences, Tokyo, Japan*

**Background:** Saliva is an easily accessible and informative biological fluid which has high potential for the early diagnosis of diseases. Saliva-based diagnostics, particularly those based on metabolomics technology, offer a promising clinical strategy by characterizing the association between salivary analytes and a particular disease. The aim of this study is to investigate potential biomarkers in human saliva to facilitate the early diagnosis of breast cancer.

**Methods:** We conducted a comprehensive metabolite analysis of saliva samples obtained from breast cancer patients (n = 90) and healthy controls (n = 20), using capillary electrophoresis time-of-flight-mass spectrometry (CE-TOF-MS). Statistical analyses were performed by using a nonparametric Mann–Whitney U-test, multiple logistic regression and the receiver operating characteristics (ROC) to evaluate the predictive power of biomarkers.

**Results:** The median age was 61 years (range, 26−81 years) for breast cancer patients and 29 years (range, 22−50 years) for healthy controls. Of all breast cancer patients, 74 patients had invasive ductal carcinoma, 14 had ductal carcinoma in situ and 3 had invasive lobular carcinoma. Fourteen patients were clinical stage 0, 43 were stage I, 28 were stage II, 4 were stage III, and one patient was stage IV. Before collecting salivary sample, 21 patients received chemotherapy, 30 received endocrine therapy, and 3 received excisional biopsy.

After removing the concomitantly observed peaks and noise peaks, totally 205 peaks derived from the metabolites were observed. Among these peaks, some potential salivary biomarkers demonstrated significantly higher concentrations in breast cancer patients comparing with healthy individuals ($p < 0.05$). Especially, salivary biomarkers obtained from patients with IDC before neoadjuvant treatments tended to be higher concentrations than those obtained after treatment. Of these, five metabolites (Choline, Isethionate, Cadavarine, N1-Acetylspermidine, and Spermine) showed high the area under the ROC curves (AUCs) values; 0.850, 0.819, 0.809, 0.765, and 0.716, respectively.

**Conclusions:** Salivary metabolites are promising biomarkers for the early diagnosis of breast cancer.

**No conflicts of interest**

**418** Poster

**Characterization of cancer-associated adipocytes and evaluation of its role in breast cancer**

H. Fujimoto[1,2], K. Fujisaki[2], T. Sangai[2], T. Nagashima[2], M. Sakakibara[2], M. Miyazaki[2]. *[1]Saitama Medical Center- Saitama Medical University, Department of Breast Surgery, Kawagoe City- Saitama, Japan; [2]Chiba University Graduate School of Medicine, Department of General Surgery, Chiba city, Japan*

**Background:** There is growing evidence that interactions between cancer cells and stromal tissue contribute to the progression of cancer. However little attention was focused on the interaction between adipocytes and cancer cells. One of the reasons is the difficulty in culturing mature adipocytes. To solve this problem, we isolated and embedded primary adipocytes from human breast cancer tissue into a three-dimensional collagen gel. Then, we compared the phenotype of normal breast adipocytes (NBAs) and cancer-associated adipocytes (CAAs).

**Material and Methods:** In 27 breast cancer patients undergoing mastectomy, mammary adipose tissue was obtained from the breast quadrant bearing the tumor and corresponding non-tumoral quadrant. Adipose tissue was digested with a collagenase and isolated NBAs and CAAs were cultured in collagen gels to mimic the in vivo environment. To examine the phenotype of CAAs, immunohistochemistry, qRT-PCR, and cell proliferation assays were performed. Migration of MCF7 and MDA-MB-231 cells was assessed in NBA- and CAA-conditioned media. Cytokine levels in conditioned media were measured by cytokine array. Migration assays were repeated using conditioned media containing neutralizing antibodies.

**Results:** In collagen gel culture, NBAs and CAAs lost their lipid content and grew with a spindle-like shape. The cell number of CAAs increased significantly than that of NBAs. qRT-PCR analysis of isolated adipocytes showed that CEBP/a expression levels in CAAs were lower than those in NBAs. In co-cultures with MCF7 or MDA-MB-231 cells, NBAs exhibited increased cell proliferation. These observations suggested that CAAs had a more immature phenotype than NBAs. Furthermore, we examined the effect of media conditioned by NBAs and CAAs on cell proliferation and migration of MCF7 or MDA-MB-231 cells. Although there was no significant difference on the proliferation, MCF7 and MDA-MB-231 showed significantly higher migration in a CAA-conditioned medium than in an NBA-conditioned medium (1.8-fold, $p = 0.011$ and 1.8-fold $p = 0.013$, respectively). To identify factors responsible for activation of breast cancer cell migration, we analyzed the conditioned media using a cytokine array. It revealed higher levels of interleukin-6 (IL-6) and monocyte chemoattractant protein-1 (MCP-1) in the CAA-conditioned medium. Increases in IL-6 and MCP-1 mRNA expression were also observed in CAAs compared with that in NBAs. To confirm the effects of IL-6 and MCP-1 produced by CAAs on cell migration, we neutralized the conditioned media using antibodies against IL-6 and MCP-1. Inhibition of IL-6 or MCP-1 significantly reduced the migration of MCF7 and MDA-MB-231 cells (from25% to 40% reduction).

**Conclusions:** Adipocytes revert to an immature and proliferative phenotype in the presence of cancer cells, and promote cancer cell migration via adipokines including IL-6 and MCP-1.

**No conflicts of interest**

**419** Poster

**Clinicopathological pattern and immunohistochemical expression of tumor associated macrophages (TAMs) in triple negative breast cancer patients in Pakistan**

M. Rehman[1], S. Afzal[1], N.R. Hamdani[1]. *[1]Armed forces institute of pathology, Histopathology, Rawalpindi, Pakistan*

**Background:** Triple negative breast cancers (TNBC) are the most aggressive breast cancer subtypes characterized by lack of expression of

estrogen(ER), progesterone (PR) and Her-2-neu receptors. These tumors lack both definitive prognostic factors and selected targeted therapies. Presence of tumor associated macrophages (TAMs) in breast cancer stroma is associated with dismal prognosis and increase metastatic potential. Targeting Tumor associated macrophages can be used as specific therapy in triple negative breast cancers. This study investigated the immunohistochemical expression and prognostic value of tumor associated macrophages and their relationship in triple negative Pakistani breast cancer patients.

**Material and Methods:** TAMs expression was analysed immunohistochemically by using CD 68 antibodies, in a prospective series in 150 cases in breast cancer patients diagnosed and treated between 2013 to 2015 at CMH Rawalpindi, Pakistan with simultaneous application of ER, PR and Her-2-neu receptor antibodies. CD 68 positive TAMs were calculated in three tumor stroma areas and categorized into low and high groups using 26 CD68+ TAMs/tumor stroma was used as cut off value.

**Results:** See the tables. Out of 150 patients 59 were classified as TAMs high infiltrative group whereas 91 were classified as TAMs low infiltrative group. The median number of CD 68+ cells was 22±14 cells/high power field and the range was 5−40/high power field. Presence of High infiltrative TAMs group was associated with mostly grade II and grade III tumors of breast cancer.

Table 1. Clinical characteristics

| Characteristic | Number of cases (n) | Percentage (%) |
|---|---|---|
| Age (years) | | |
| Mean±SD | 50.94±11.77 | |
| Range | 32−79 | |
| Age specific group | | |
| Premenopausal | 85 | 56.66 |
| Postmenopausal | 65 | 43.33 |
| Tumour laterality | | |
| Right | 82 | 54.8 |
| Left | 68 | 45.2 |
| Tumour size (cm) | | |
| Mean±SD | 5.24±2.23 | |
| Range | 1.8–10.5 | |
| T stage | | |
| p T1 | 16 | 10.6 |
| p T2 | 77 | 51.33 |
| p T3 | 46 | 30.6 |
| p T4 | 11 | 7.3 |

Table 2. Pathological characteristics

| Characteristic | Number of cases | Percentage |
|---|---|---|
| Histological tumour type | | |
| Invasive ductal carcinoma | 137 | 91.3 |
| Medullary carcinoma | 2 | 1.3 |
| Metaplastic carcinoma | 4 | 2.6 |
| Invasive lobular carcinoma | 7 | 4.6 |
| Histological grade | | |
| Grade I | 16 | 10.6 |
| Grade II | 123 | 82 |
| Grade III | 11 | 7.3 |
| Lymphovascular invasion | | |
| Present | 79 | 52.66 |
| Absent | 71 | 47.33 |
| Axillary lymph nodes | | |
| Positive | 105 | 70 |
| Negative | 42 | 28 |
| None identified | 3 | 2 |

**Conclusion:** Expression of CD 68+ TAMs is related to high grade, high stage and predicts poor survival. Targeted therapies against TAMs can be beneficial to patients who have triple negative breast cancer.

**No conflicts of interest**

**420** Poster

**Does the pre-treatment neutrophil/lymphocyte ratio and platelet/lymphocyte ratio correlate with clinicopathological characteristics in primary breast cancer patients?**

V. Kalles[1], G. Boutsikos[1], I. Tsouknidas[1], I. Papapanagiotou[1], M. Konstantinou[1], A. Tselos[1], G. Georgiou[2], E. Kalogera[2], G. Xanthopoulou[1], N. Ivros[1], G. Pechlivanides[1]. *[1]Naval and Veterans Hospital of Athens, 2nd Department of Surgery, Athens, Greece; [2]Hellenic Anticancer Institute, Research Center, Athens, Greece*

**Background:** The inflammation mechanism is an established key factor of tumor progression in most human cancers. Peripheral blood-derived inflammation-based scores such as the neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) have recently been proposed as prognostic markers in solid tumours. The aim of the present study is to assess the correlation between NLR and PLR and the pathologic characteristics of the tumor.

**Material and Methods:** In the present cohort study, preoperative complete blood counts, as well as pathology results of 67 patients (mean age 60.9 years) that underwent surgery for primary breast cancer were retrospectively reviewed. Patients with hematologic disease, ongoing infection, recent steroid therapy, or diseases that result in elevated inflammatory markers were excluded from the study. Patients who received neoadjuvant therapy prior to surgery were also excluded.

**Results:** Mean preoperative values of NLR and PLR were 2.25 and 133.5, respectively. Patients with node-positive disease had significantly elevated NLR compared to those with node-negative disease ($p < 0.05$). Furthermore, the NLR was observed to increase in a stepwise manner according to tumor size (T1 vs T2 vs T3) ($p < 0.05$). Additionally, increased NLR was associated with advanced disease stage (Stage I < Stage II < Stage III) ($p < 0.01$). A marginally insignificant association between preoperative NLR and higher tumor grade was also observed ($p = 0.0536$). On the other hand, the NLR was not observed to correlate with the presence of lymphovascular invasion (LVI). Meanwhile, the PLR correlated significantly with advanced disease stage ($p < 0.01$), but there was no evidence of significant correlation between PLR and tumor size, nodal status, tumor grade and LVI. Regarding axillary nodal involvement, ROC curve analysis showed that for a cutoff point of NLR = 1.90 the sensitivity and specificity were 73% and 61%, respectively (AUC: 0.6614, $p < 0.05$).

**Conclusions:** Our results indicate that preoperative NLR is significantly associated with the two of the most important prognostic factors for breast cancer, tumor size and axillary lymph node involvement. In contrast, increased preoperative PLR was associated only with advanced disease stage. The reliability of both NLR and PLR as an inexpensive prognostic indicator for breast cancer patients needs to be further evaluated.

**No conflicts of interest**

**421** Poster

**In vitro and in vivo effects of fulvestrant combined with trastuzumab in breast cancer with estrogen receptor-positive and HER-2/neu-overexpressing**

Q. Chen[1], K. Wu[1], Y. Lu[1], L. Ding[1]. *[1]Xin Hua Hospital Affiliated to Shanghai Jiao Tong University School of Medicine, General Surgery, Shanghai, China*

**Background:** Both estrogen receptor (ER) and HER-2/neu are critical therapeutic targets in breast cancer. A large amount of literature has demonstrated extensive interactions between the signaling pathways of the two receptors. This suggests a dramatic therapeutic effect may appear in the ER-positive and HER-2/neu-overexpressing breast cancer patients if the two receptors are targeted simultaneously. This hypothesis was tested both in vitro and in vivo.

**Methods:** ER(+), HER-2/neu-overexpressing human breast cancer cells ZR-75−1 and BT-474 were cultured in the presence of the selective estrogen receptor downregulator fulvestrant or the anti-HER-2/neu therapeutic antibody trastuzumab, or both. The effects on cell growth, cell apoptosis and cell cycle distribution were examined. Moreover, effects of fulvestrant and/or trastuzumab on the tumor growth in vivo xenograft models were also observed.

**Results:** The cell proliferation was increasingly inhibited by fulvestrant, trastuzumab or both when the drug concentration added, with a $CI_{ED50}$ of 0.629 in the cell ZR-75−1 and a $CI_{ED50}$ of 0.513 in the cell BT-474. The BT-474 cell apoptosis rates distinctly increased when fulvestrant was added alone or with trastuzumab ($P < 0.05$), but not distinctly varied in the presence of trastuzumab alone ($P > 0.05$). Moreover, it is not distinctly varied on the ZR-75−1 cell apoptosis rates neither in the presence of fulvestrant and trastuzumab alone or both($P > 0.05$). The cell accumulation in the G1 phase of the cell cycle was enhanced in both the two cell lines, with a decrease in S phase ($P < 0.05$). Using a BALB/c athymic ZR-75−1

or BT-474 in vivo xenograft models, the drug combination (Fulvestrant 4.0 mg/body s.c. weekly, trastuzumab 2.5 mg/kg i.p. twice weekly in ZR-75−1 xenograft model and fulvestrant 2.5 mg/body s.c. weekly, trastuzumab 2.0 mg/kg i.p. twice weekly in BT-474 xenograft model) showed a stronger inhibition of tumor growth compared to either single agent, and no significant variation of weight was observed in all the groups.

**Conclusions:** The combination of fulvestrant and trastuzumab is demonstrated to generate synergistic growth inhibition and enhancement of $G_1$ cell cycle accumulation both in the human breast cancer cell lines ZR-75−1 and BT-474, but no significant variation in cell apoptosis. In vivo, drugs combined produce a greater cytostatic effect. These results suggest that targeting ER and HER-2/neu simultaneously may represent a powerful approach to the treatment of breast cancer expressing ER and overexpressing HER-2/neu.

**No conflicts of interest**

**422** Poster

**Development and efficacy evaluation of smart nanocarriers for targeting breast cancers**

S. Talluri[1], S. Pindiprolu[2], R. Janarthanam[1], G. Kuppusamy[1]. *[1]JSS College of Pharmacy, Pharmaceutics, Ootacamund, India; [2]JSS College of Pharmacy, Pharmacology, Ootacamund, India*

**Background:** Among 7.6 million cancer related deaths reported in 2008 globally, 458,000 deaths are due to breast cancers. In addition, the incidence of breast cancer is also very high both in developed and developing countries. Several nanocarrier-based drugs have been approved for treating cancers as they offer several advantages − protection of drug from degradation in serum; prevention of interactions with various other biological constituents. Nano-carrier based albumin bound paclitaxel nanoparticles (Abraxane ®), liposomal doxorubicin (Myocet ®) and pegylated liposomal doxorubicin (Doxil ®) have been approved for treating metastatic and recurrent breast cancers. However, several side effects have been reported. Therefore, a novel smart-drug approach is needed to specifically target breast carcinoma cells, using simultaneous delivery of chemotherapeutic agents and chemosensitizer. Quercetin has distinguishing feature to suppress the transcription factor linked to chemoresistance and drug transporters which is now being co-administered with another chemotherapeutic drug Doxorubicin. And application of pH-sensitive lipids to formulate pH sensitive liposomes for tumor specific drug delivery. The objective of this study is to develop pH-sensitive liposomes encapsulating Quercetin (chemosensitizer) and Doxorubicin to overcome multidrug resistance (MDR) in breast cancer cells.

**Materials and Methods:**

1. Preparation of PEGylated pH-Sensitive Liposomes
2. Determination of Entrapment Efficiency (EE) and Drug Loading (DL)
3. Particle Size, Zeta Potential and Morphology
4. Drug release
5. Cytotoxicity study
6. Cell uptake study

**Results:** The pH sensitive liposomes have a mean diameter of 142 nm and a low polydispersity index 0.20 with a high drug-loading efficiency ranging from 78.2% to 91.6%. The in vitro drug release profiles show that the pH sensitive liposomes exhibit a controlled drug release behavior with the maximum and minimum unloading percentages of 62.7% at pH 4.7 and 21.6% at pH 7.4, respectively. The pH sensitive liposomes displayed a superior ability in inhibiting the proliferation of MCF-7/MDR cells. This hypothesis is justified by the confocal images exhibiting the accumulation of doxorubicin in the nuclei of cancer cells.

**Conclusion:** By this study, pH-responsive liposomes were developed have exhibited improved efficacy against MDR breast cancer cells. The results make us to believe that by encapsulating chemotherapeutic agents and chemosensitizers in nanoparticles have enhanced efficacy and minimized side effects. MDR cancer chemotherapy can be developed based on the platform presented in this study.

**No conflicts of interest**

**423** Poster

**Utilisation of reverse phase protein array analysis to identify signalling pathways activated in lobular breast cancer**

K. Teo[1], M. Tenhagen[2], A. Byron[1], P. Derksen[2], V. Brunton[1]. *[1]Institute of Genetics and Molecular Medicine- University of Edinburgh, Edinburgh Cancer Research Centre, Edinburgh, United Kingdom; [2]University Medical Center Utrecht, Department of Pathology, Utrecht, Netherlands*

**Background:** Invasive lobular carcinoma (ILC) is the second commonest histological subtype of breast cancer after invasive ductal carcinoma (IDC), with these entities accounting for approximately 12% and 80% of cases respectively. ILC is associated with a number of distinct clinico-pathologic features and is understudied as a breast cancer subtype. In comparison with IDC, ILC has an increased propensity for multi-focal and bilateral spread, and is also associated with an unusual pattern of metastatic dissemination, to sites such as the gastro-intestinal tract, peritoneum and ovary. Histologically, ILC appears as small, round cells that infiltrate in single files, with a tendency to surround normal structures in a targetoid manner, and these features are attributed to the early loss of membranous E-cadherin expression − a hallmark of the lobular phenotype. The biological mechanisms underpinning the differences between ILC and IDC are not fully understood, and elucidation of these is necessary in order to highlight novel therapeutic strategies for this patient group.

**Materials and Methods:** Cell lines derived from a mouse model of ILC (mILC), based on mammary-specific inactivation of p53 and E-cadherin, were compared with those derived from controls based on p53 inactivation only. For pathway analysis profiling, three biological replicates of each cell line were submitted for reverse phase protein array (RPPA) analysis using a panel of 120 antibodies. Changes were validated by Western blotting analysis, which included human ILC and IDC cell lines. In addition, immunohistochemistry was performed upon human tissue micro-arrays (TMAs) developed by each centre, and comprising a total of 171 lobular breast cancer patient samples.

**Results:** RPPA revealed an increase in Akt-mediated signalling in the E-cadherin negative mILC cells, with increased expression of pIGF-1R, pAkt, pMTOR and pGSK-3β, and decreased expression of the downstream pro-apoptotic protein pBAD. A statistically significant difference in activated Akt status was also found when human ILC and IDC lines were compared, with increased expression of pAkt in the human ILC line IPH926 compared to MCF7 cells ($p < 0.01$). Staining of the TMAs for pAkt revealed expression of activated Akt in the majority of ILC tumours (65%). Interestingly low/absent expression of the tumour suppressor and negative regulator of Akt, PTEN was also observed in the majority of ILC cases (76%).

**Conclusions:** These findings suggest that patients with ILC may benefit from therapies targeting the PI3K/Akt pathway, such as small molecular Akt inhibitors. We are in the process of assessing the role of downstream pathway members, and plan to determine the response of primary patient-derived ILC cells to Akt inhibitors in vitro.

**No conflicts of interest**

**424** Poster

**Androgen receptor expression in breast cancer and its correlation with clinico-pathological parameters**

S.K. Gupta[1], A. Gupta[1], M. Kumar[2]. *[1]Institute of Medical Sciences, Department of General Surgery, Varanasi, India; [2]Institute of Medical Sciences, Department of Pathology, Varanasi, India*

**Background:** Breast cancer is the commonest cancer amongst women. It is a heterogeneous disease with varying molecular and clinical characteristics. Hormones play an important role in breast carcinogenesis and the prognostic and predictive role of estrogen (ER) and progesterone receptor (PR) is well established. The role of androgen receptors (AR) is still unclear. The aim of this study was to evaluate androgen receptor expression in breast cancer and correlate it with ER, PR, HER2-neu status and clinico-pathological parameters.

**Material and Methods:** 80 cases of histologically proven breast cancer were included after clearance from the Institute Ethics Committee and informed consent. The following clinical and pathologic parameters were assessed; age, menopausal status, parity, family history, tumour size, lymph node status, histological type and grade of the tumour. Immunohistochemical evaluation was done for ER, PR, AR and HER2-neu status and cases were labeled as positive if >10% tumour cells showed nuclear staining.

**Results:** Clinical attributes of the study population showed that 50% of the patients were >45 years of age and postmenopausal. Majority of the cases had tumors >5 cm (70%) and lymph node involvement (65%). 72 cases (90%) were infiltrating ductal cancer. 60% had Grade 3 tumors and the remaining had Grade 2 tumors. Expression of the steroid receptors ER, PR and AR was observed in 32 (40%), 34 (42.5%) and 36 (45%) cases respectively. HER2-neu positivity (3+) was seen in 28 cases (35%). 22 cases (27.5%) were triple negative of which 10 cases (45.4%) were AR positive. There was no significant correlation between age, parity, family history, tumor size and lymph node involvement with AR expression. AR expression was significantly higher in postmenopausal women ($P < 0.01$). While the AR expression was higher in Grade 2 tumors as compared to Grade 3 tumors, the difference was not significant.

**Conclusions:** The fact that AR was the most frequently expressed marker, indicates that it has some role in breast carcinogenesis. Larger data sets will help in better defining the interplay between the various receptors and the potential role of AR as a target of endocrine therapy.

**No conflicts of interest**

**425** Poster

**Clinical and histological characteristics of triple-negative breast cancer in Chinese patients**

W. Wang[1], H. Xing[1], L. Tang[1]. [1]*China-Japan Union Hospital of Jilin University, Department of Breast Surgery, Changchun, China*

**Background:** Triple negative breast cancer (TNBC) is a heterogeneous subtype of breast cancer that is defined by lacking the expression of estrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor-2 (HER-2). It is characterized by high malignancy, high recurrence rate and poor prognosis. TNBC is not responsive to conventional hormonal and targeted therapies due to the absence of receptors. TNBC exhibits a significant racial disparity in incidence and outcomes, however, few reports have focused on the TNBC incidence and histological characteristics in Chinese TNBC patients. In this study, we sought to evaluate the differences in clinical and histological features of patients with TNBC.

**Material and Methods:** The clinical records of breast cancer patients who were diagnosed as well as treated at the Department of Breast Surgery, China-Japan Union Hospital between July 1, 2011 and June 30, 2015 were retrospectively reviewed. 114 consecutive female patients diagnosed with TNBC confirmed by surgery and pathological examinations were involved in the study. Age of onset and tumor characteristics (tumor size, lymph node metastasis, distant metastasis, tumor grade, pathological stage, histological type, and the expression of main distinguishing markers) were chosen as baseline data to assess. The clinical and pathological information of breast cancer registry database was reviewed and approved by the Ethics Committee of Jilin University. The statistical analysis was implemented by SPSS 20.0.

**Results:** During the last 4 years, TNBC accounted for 10.41% (114/1095) of all breast cancers in our hospital. The onset age widely ranged from 28 to 87 years old, yet TNBC occurred mainly in younger age groups (35−55 years), with a median age of 43. TNBC displayed a high histological grade and high incidence of lymph node metastasis. The histological types of TNBC were 52.63% IDC (60/114), 27.19% AMC (31/114), and 20.18% other types (23/114). 84 (73.68%) of the 114 TNBC patients were without the expression of the basal markers EGFR, while CK5/6 were detected in 73 (60.04%) patients. A high positive rate (85.96%) of E-cadherin staining was noted. Overall, Ki67 was positive (>30%+) in 73 (60.04%) cases, and no distinguishing difference between moderately positive (30−60%+) and highly positive (>60%+) was observed, with percentage of 30.70% and 33.33% respectively. Positive (>50%+) P53 only took up 39.47% of the 114 cases. The study demonstrated a statistically significant link between the basal marker expression and the clinical and pathological prognostic parameters.

**Conclusions:** The clinical and pathological characteristics of TNBC cases may elucidate the implications of the underlying distinction between TNBC and other breast cancer subgroups in terms of tumor biology.

**No conflicts of interest**

**426** Poster

**Estrogen receptor β governs proliferation of breast cancer stem cells and can be targeted by endocrine therapy**

M. Ran[1]. [1]*Karolinska Institutet, Oncology Pathology, Stockholm, Sweden*

**Background:** Breast cancer cells with stem cell characteristics (CSCs) are a phenotypic distinct cell population with tumor-initiating capability and able to differentiate into the heterogeneous tumor mass. CSCs depict the features of mammary stem cells (MSCs) by expressing the embryonic stem cell genes SOX2, Nanog and OCT4, and can be identified by their unique cell-surface antigenic profile CD24−/CD44+ and ALDH1$^{high}$. In vitro, CSCs can be cultured as mammospheres. Previous studies have indicated that CSCs are important for tumor relapse, metastasis and therapeutic resistance. Two estrogen receptors (ER) exist; ERα and ERβ. Although ERα expression can be identified within around 75% of primary breast tumors, CSCs are ERα negative and considered estrogen non-responsive. Instead, estrogens are thought to stimulate CSCs through paracrine regulation.

**Methods:** Characterization of patient derived CSCs and breast cancer cell lines were determined by immunostaining and RT-PCR for their ERβ expression and stem cell markers. Knockdown experiments were performed to investigate the role of ERβ in CSCs phenotype maintenance. Mammosphere formation assays were performed by using ERβ specific ligands. Human transcriptome array 2.0 was performed to identify the gene sets and signaling pathways after ERβ stimulation in mammospheres. This specific ERβ stimulated gene signature was further assessed for the clinical relevance using three breast cancer microarray datasets with comprehensive clinical-pathological and survival data. Xenografts models have been used to study the ERβ role in tumor initiation and progression.

**Results:** We here identify expression of the ERβ in CSCs as well as in MSCs correlating with phenotypic stem cell markers. We show that ERβ is responsible for the proliferative role of estrogens in CSCs and thereby essential for tumor growth. Knock-down of ERβ causes a reduction of mammosphere formation in both MCF7 and MDA-MB231 cell-lines (41% and 27% respectively), as well as in patient-derived cancer cells (44% reduction). In addition, activation of ERβ in mammospheres by a selective agonist shows induction of HIF1-signaling by global gene expression analysis. We also observe an induction of glucose metabolism associated signaling pathways and show that stimulating ERβ in CSCs can impair the activity of mitochondria and therefore increase glucose uptake through glycolysis. Furthermore, the ERβ activated gene signature in mammospheres correlates to poor outcome in three independent breast cancer cohorts. While the ER-antagonist tamoxifen and the ERα-blocker fulvestrant are alone insufficient to block CSCs proliferation, whereas an inhibitor of ERβ can reduce tumor initiation and reinforce tamoxifen-mediated inhibition of tumor growth.

**Conclusion:** We suggest that ERβ is a mediator of estrogen action and a novel target for endocrine therapy in CSCs.

**No conflicts of interest**

**427** Poster

**Cancer stem cell (CSC) and epithelial mesenchymal transition (EMT) in triple negative breast cancer**

Y. Ishikawa[1], T. Oyama[2], A. Katayama[2], T. Handa[2], H. Tokiniwa[3], J. Horiguchi[3], Y. Iino[4]. [1]*Tokyo Medical University Hachioji Medical Center, Breast Oncology, Tokyo, Japan;* [2]*Gunma University Graduate School of Medicine, Diagnostic Pathology, Gunma, Japan;* [3]*Gunma University Graduate School of Medicine, Thoracic and Visceral Organ Surgery, Gunma, Japan;* [4]*Kusunoki Hospital, Surgery, Gunma, Japan*

**Background:** Cancer stem cell (CSC), which has ability of pluripotency and self-replication and resistance to chemotherapy, is an origin of various differentiated cancer cells. CSCs are very important in the cancer progression, invasion and metastasis and they are considered to be formed by Epithelial Mesenchymal Transition (EMT) of tumor cells. In breast cancer, recently CD44−CD24+ with ALDH+ was reported to be a potent marker of stem cells. Triple negative breast cancer (TNBC), ER(−) PR(−) HER2(−), is usually poor prognosis subtype and against of the therapy compered to non-TN subtype. On the other hand, TNBC has some groups of better prognosis, for example apocrine carcinoma and adenoid cystic carcinoma.

In this study, we analyzed the expression of EMT-related factors (TWIST, Claudin-4, E-cadherin) and CSC markers (ALDH1, CD44, and CD24) in TNBC and non TNBC.

**Materials and Methods:** Tumor tissues, which were operated at Gunma University in 1999–2002 and 2008–2010, were obtained from 250 patients of primary breast cancer. DCIS were excluded in this study. We made Tissue Microarray (TMA) and analyzed immunohistochemical (ER, PgR, HER2, EGFR, CK5/6, stem cell markers, and EMT rerated-factors) and clinicopathological features to classify the tumors into intrinsic subtypes and histological classification, examine the expression of CSC and EMT markers and prognosis.

**Results:** Out of 250 cases, 82 cases (32.8%) were TNBC. 24 cases of TNBC (29.3%) were basal-like subtype. Cell with CD44+CD24−ALDH1+ was significantly higher in TNBC than in non-TNBC ($p = 0.01$) and CD44+CD24− was higher in non-basal like subtype of TNBC ($p = 0.02$). In the TNBC, TWIST expression ($p = 0.01$) were higher than in non TNBC. No relation was found between CSCs and EMT expression and prognosis.

**Conclusion:** These results suggested that combination of several markers of CSCs and EMT will reveal a special group of TNBC. Furthermore, cases are needed in this study, we will report with additional studies.

**No conflicts of interest**

**428** Poster

**Suppression of MUC1 alters tumorigenicity and metastatic ability in human breast cancer cells**

W. Wang[1], Y. Guo[2], H. Xing[1], L. Tang[1]. [1]*China-Japan Union Hospital of Jilin University, Department of Breast Surgery, Changchun, China;* [2]*China-Japan Union Hospital of Jilin University, Department of Neurosurgery, Changchun, China*

**Background:** MUC1 is a transmembrane glycoprotein aberrantly expressed in breast cancers. Overexpression and hypoglycosylation of MUC1 in cancer cells compared with normal epithelial cells are likely to alter its function and affect the behavior of breast cancer cells; moreover, MUC1 is involved in diverse signaling pathways that have been linked to tumorigenesis, functioning either in promoting cell proliferation and invasion or regulating cell transcription. Previous studies have showed that MUC1

plays an important role in tumorigenesis and progression of breast cancer; however, the mechanism remains unclear.

**Material and Methods:** To investigate MUC1 function in breast cancer cells with high endogenous expression, that is, cells likely to have evolved with active MUC1 signaling; we used small interfering RNA (siRNA) to knockdown MUC1 in human breast cancer MCF-7 cells. We then analyzed several genes on proliferation or apoptosis signaling pathway, including Wnt/β-catenin, MAPK, NF-κB, TGF-β, growth factor receptor signaling pathways by cDNA microarray analysis to identify alterations regulated by MUC1. Proliferation, migration and invasion, aggregation and apoptosis changes in MUC1 silencing cells were analyzed compared with MCF-7 wild type. In vivo assays were performed in nude mice, in order to study the tumorigenicity of MCF-7 cells with or without MUC1 silencing.

**Results:** MCF-7 cells were chosen for high expression of MUC1, after siRNA transfection, consistent MUC1 silencing had been found, and transcription of several genes was altered, including c-myc, cyclin-D1, NF-κB, VEGF, MAPK, TGF-β signal molecular genes. MCF-7 cells behaved as expected for loss of an oncogene: MUC1 siRNA correlates with increased apoptosis, decreased proliferation and reduced invasion. We further investigated the possible mechanisms by Western blotting and immunoprecipitation, Wnt/β-catenin and apoptotic pathways were analyzed. We found that MUC1 silencing inhibited cell proliferation by blocking the nuclear translocation of β-catenin and decreasing the expression of Cyclin D1 and c-Myc, moreover, induced apoptosis by the activation of caspase-3 and its substrate PARP, upregulation of p53, Bax and mitochondrial cytochrome C, activation of caspase-8 and caspase-9. Consistent with this finding, we observed that suppression of MUC1 was associated with β-catenin nuclear localization in tumor tissues and decreased expression of Cyclin D1 and c-Myc in breast carcinoma specimens.

**Conclusions:** These results indicate a critical role for MUC1 in the development of tumorigenesis and development, suggesting MUC1 as a potential target for the diagnosis and chemoprevention of human breast cancer.

**No conflicts of interest**

**429** Poster

**Prognostic relevance of PIK3CA mutations in breast cancer patients treated with primary dose-dense epirubicin/cyclophosphamide → dose-dense docetaxel**

V. Cocciolone[1], A. Tessitore[1], E. Ricevuto[1], V. Mastroiaco[1], L. Rinaldi[2], S. Paradisi[2], A. Irelli[2], T. Sidoni[2], A. Dal Mas[3], G. Coletti[3], A. Ciccozzi[4], V. Resta[5], A. Bafile[5], E. Alesse[1], C. Ficorella[1], K. Cannita[2]. *[1]University of L'Aquila, Department of Clinical Applied Sciences and Biotechnologies, L'Aquila, Italy; [2]San Salvatore Hospital, Medical Oncology, L'Aquila, Italy; [3]San Salvatore Hospital, Pathology, L'Aquila, Italy; [4]San Salvatore Hospital, Breast Diagnostics, L'Aquila, Italy; [5]San Salvatore Hospital, Breast Unit, L'Aquila, Italy*

**Background:** PIK3CA activating mutations are reported in about 25% of breast cancers (BC), with proved predictive and prognostic role after neoadjuvant chemotherapy (CT). A phase I/II study of dose-dense (dd) anthracyclinetaxane CT was planned to define recommended dose (RD) of dd Docetaxel (D) following dd Epirubicin/Cyclophosphamide (EC) and to evaluate safety and activity and correlation with PIK3CA mutations.

**Material and Methods:** 41 operable(18)/locally-advanced(22)/inflammatory(1) BC patients (pts) enrolled. Tumor features (2 pts with bilateral BC): ER and/or PR+/HER2−, 4; HER2+, 23; triple negative (TNBC), 6. Schedule: E(90 mg/m$^2$)–C(600 mg/m$^2$) q14. To evaluate D RD, a dose de-escalation from 65 mg/m$^2$ to 60, 55 and 50 mg/m$^2$ if a limiting toxicity occurred was planned. Trastuzumab (T) (4 mg/kg) was added in HER2+ pts. Pegylated G-CSF scheduled d2. Dose-limiting toxicities (DLTs): G4 haematological; G3 non-haematological; any toxicity resulting in >2 weeks delay; limiting left ventricular ejection fraction reduction, arrhythmia, symptomatic heart failure. pCR was defined as absence of invasive tumor on breast and nodes. Pre-treatment DNA was extracted from fresh (8) and FFPE (23) tissue samples; direct sequencing of exons (ex) 9 and 20 of PIK3CA is ongoing to evaluate the impact on response and survival.

**Results:** 60 mg/m$^2$ was D RD in combination with T in HER2+ pts (DLTs: G3 asthenia, 2 pts; G2 asthenia >2 weeks, 1 patient); 65 mg/m$^2$ was D RD in HER2− pts (DLTs: G3 hand-foot syndrome, 1 patient; G2 anemia >2 weeks, 1 patient). Cumulative G3−4 adverse events: neutropenia 27%, vomiting 2%, transaminases increase 2%, asthenia 17%, myalgia 5%. No severe cardiac toxicity occurred. pCR rate: 15.7% (6/38 evaluable pts) in the ITT analysis, 16.7% (6/36) in the as-treated analysis (HER2+, 20%; triple negative, 33%; ER+/HER2−, 8%), 18.4% (7/38) in the whole population treated with sequential EC and taxanes, as 1 of 2 pts with allergic reaction to D who continued with nab-paclitaxel had a pCR (HER2+, 23.8%; TNBC, 33%; ER+/HER2−, 7.7%). Median follow-up: 25 months; median Disease-Free Survival: overall, 52 mo, HER2+, nr, TNBC, 7.5 mo, HR+/HER2−, 52 mo; median Overall Survival: overall, nr, HER2+, nr; TNBC, 33 mo; HR+/HER2−, nr. So far, 9 tumor samples were analyzed for both exons 9 and 20 of PIK3CA. For ex 9, all samples analyzed were wild-type; for ex 20, the same mutation G>A (M1043I), not yet described, was detected in 2 samples from HER2+ BC (ER−/PgR−, 1; ER+/PgR+, 1), from pts who did not had pCR and are currently disease-free.

**Conclusions:** dd E (90 mg/m$^2$)–C (600 mg/m$^2$)→D (60 mg/m$^2$) and (65 mg/m$^2$) with or without T, respectively, can be recommended as a safe and active neoadjuvant regimen in BC. Mutation analysis on PIK3CA is currently under evaluation and in progress.

**No conflicts of interest**

**430** Poster

**The role and correlation of histopathological parameters in grading of phyllodes tumors of the breast: An institutional experience in India**

S. Sharma[1], M. Valiathan[1]. *[1]Kasturba Medical College- Manipal University- Manipal, Pathology, Udupi, India*

**Background:** Phyllodes tumors of the breast are fibroepithelial neoplasms that have the potential for recurrence. Grading into benign, borderline and malignant categories is based on a constellation of histologic characteristics. Although these features have been useful to some extent in predicting biologic behavior, specific parameters that can define the likelihood for recurrence are not universally accepted.

**Materials and Methods:** The aim of the study is to examine and assess the role of pathologic parameters in defining malignancy and hence in determining the biologic behaviour of Phyllodes tumor of the breast. All cases diagnosed between January 1997 to December 2014 in Department of Pathology, Kasturba Medical College, Manipal, India were evaluated for the study. Patient details along with macroscopic findings and histologic featuress were reviewed. Classification into benign, borderline and malignant categories was done according to Moffat CJC et al in their clinico-pathological review of Phyllodes tumors of breast in 1995.

**Results:** Total 112 cases of Phyllodes tumor of breast were identified. Overall incidence of breast carcinoma was found to be 1.5% while that of Phyllodes was 3.1% among breast malignancies. In 3 cases gross details were unavailable, hence were excluded. 109 cases studied, the age ranged from 17 years to 72 years (Mean age 39.9 years). 48.5% cases showed involvement of right sided breast. 4 cases had bilateral tumor. 74 cases were benign; 24 were borderline and 11 were found to be malignant. In <25 years age group out of total 14 cases, 10 were benign while 4 were borderline. In 26−39 year age group, out of total 30 cases, 23, 4 and 3 cases were benign, borderline and malignant respectively. 65 tumors occurred in patients more than or equal to 40 years of age, 41 were benign while 16 and 8 were borderline and malignant respectively. Tumor size ranged from 1.5 to 16 cms. Grossly 91 cases were well circumscribed. Presence of macroscopic cystic degeneration, necrosis, hemorrhage and ulceration of overlying skin along with microscopic margins, extent of stromal overgrowth, hypercellularity and atypia, mitotic count, presence of myxoid degeneration, hemorrhage, necrosis, multinucleated giant cells and pseudoangiomatous stromal hyperplasia were studied. Extent of epithelial hypercellularity, any epithelial metaplasia and adjoining breast changes were documented.

**Conclusions:** This study reveals that careful and thorough appraisal of light microscopic morphologic findings remains the mainstay in the evaluation and grading of Phyllodes tumor of the breast. Histological grade was found to correlate positively with increasing age of the patient, tumor size and microscopically with increase in mitotic count, necrosis, stromal cellularity and atypia. An inverse correlation with epithelial hyperplasia was noted.

**No conflicts of interest**

**431** Poster

**SPARC mRNA expression in phyllodes tumors of the breast using RNAscope in situ hybridization assay: Its clinical implication and comparison with immunohistochemistry**

J.S. Lee[1], G.E. Kim[1], M.H. Park[2], J.H. Yoon[2]. *[1]Chonnam National University Hwasun Hospital, Pathology, Jeollanam-do, Korea; [2]Chonnam National University Hwasun Hospital, Surgery, Jeollanam-do, Korea*

**Background:** Phyllodes tumors (PTs) of the breast are rare biphasic tumors with the potential for invasion and metastasis. Secreted protein acidic and rich in cysteine (SPARC) plays a crucial role in the process of tumor invasion and metastasis in some tumors. Matrix metalloproteinases (MMPs) degrade all components of the extracellular matrix and facilitate

tumor invasion and metastasis. Our aim was to assess the expression of SPARC mRNA in PTs and to determine its association with SPARC protein expression and the grade and clinical behavior of PTs. Another objective was to assess the association of SPARC with MMP-2 and MMP-9 expression in PTs.

**Material and Methods:** SPARC mRNA expression was determined by RNAscope in situ hybridization (ISH) in eighty-two PTs (50 benign, 22 borderline, and 10 malignant) using tissue microarray. Additionally, expression of SPARC, MMP-2 and MMP-9 was examined by immunohistochemistry (IHC).

**Results:** Although some SPARC mRNA was detected in epithelial component, it appeared concentrated mainly in the stromal compartment of PTs. SPARC protein IHC showed staining patterns in concordance with the ISH results of SPARC mRNA. Stromal SPARC expression continuously increased during PTs progression from benign through borderline to malignant PTs at both the mRNA (using ISH) ($P = 0.044$) and the protein (using IHC) ($P = 0.000$). The percentage of recurrence was higher in the SPARC mRNA or protein-positive group than in the SPARC-negative group, however, the difference was not statistically significant. SPARC mRNA and protein expression showed statistically significant correlation with MMP-2 ($P < 0.05$ for both).

**Conclusions:** SPARC expression at both mRNA and protein was associated with PTs grade, and correlated with MMP-2 expression. These results indicate that SPARC-mediated degradation of the extracellular matrix, and its possible association with MMPs, may contribute to the progression of PTs.

**No conflicts of interest**

**432** Poster

**hsa-miR-195 attenuates breast cancer cell migration, invasion & proliferation via targeting key enzymes of the de novo lipogenesis pathway**

V. Yadav[1], R. Singh[1], S. Kumar[1], N. Saini[1]. [1]*Institute of Genomics & Integrative Biology- Delhi- India, Functional Genomics Unit, Delhi, India*

**Introduction:** Breast cancer is currently the leading cause of cancer death among women worldwide. Metastasis of the primary tumors towards distant sites is the preliminary cause of death among breast cancer patients. Recently micro RNAs (miRNAs) have emerged as key therapeutic agents against cancers and sufficient evidences show that dysregulation of miRNAs leads to drug resistance in different cancers and correction of these miRNAs using miRNA mimics/antagomiRs provide exciting opportunities for cancer therapy.

**Material and Methods:** We performed gene expression profiling after overexpression or deletion of hsa-miR-195 in MCF-7 and MDA MB-231 cells. Data was analyzed using Ingenuity Pathway Analysis and validated using various molecular biology techniques.

**Results:** Ingenuity pathway analysis revealed mitochondrial dysfunction, fatty acid metabolism and xenobiotic metabolism signalling among the top processes being affected. Our findings further provide evidence that hsa-miR-195 plays a key role in regulating the de novo lipogenesis through targeting its key enzymes such as ACACA, FASN, HMGCR, CYP27B1. Changes in the basal levels of hsa-miR-195 in MCF-7 and MDA-MB-231 cells not only altered cellular cholesterol and triglyceride levels significantly but also inhibited proliferation, migration and invasion.

**Conclusion:** Altogether our findings highlight a novel and important role of hsa-miR-195 in targeting the genes of de novo lipogenesis, potentially opening new avenues for the treatment of breast cancer.

**No conflicts of interest**

**433** Poster

**High Ki67 levels are significantly correlated with 21-gene assay recurrence scores**

C. Uras[1], D. Eren Böler[1], H. Kara[2], G. Başaran[3], L. Balci[1], F. Tokat[4], N. Cabıoglu[5], U. Ince[6]. [1]*Acıbadem University Medical Faculty, General Surgery Department, Istanbul, Turkey;* [2]*Acıbadem Maslak Hospital, General Surgery Department, Istanbul, Turkey;* [3]*Acıbadem University Medical Faculty, Medical Oncology Department, Istanbul, Turkey;* [4]*Acıbadem Maslak Hospital, Pathology Department, Istanbul, Turkey;* [5]*Istanbul University Medical Faculty, General Surgery Department, Istanbul, Turkey;* [6]*Acıbadem University Medical Faculty, Pathology Department, Istanbul, Turkey*

**Background:** Oncotype DX breast cancer assay has been used to predict the chemotherapy benefit and the likelihood of breast cancer recurrence from the expression of a panel of 21 genes in early stage breast cancer. Ki67 has recently emerged as a prognostic and predictive marker for both endocrine therapy and chemotherapy in breast cancer. This single institutional study was designed to analyze any correlation between Oncotype DX scores and conventional histopathological and molecular markers including Ki67 scores.

**Materials and Methods:** Between September 2010 and June 2015, paraffine sections of the tumors retrieved from early stage estrogen receptor positive breast cancer patients were studied by Genomic Health (Redwood City, CA, USA) to assess the Oncotype DX recurrence score as suggested by our institutional multidisciplinary tumor board. Bivariate correlation analyses were done for recurrence scores and age, tumor size, histological grade, nuclear grade, histological type of the tumor, presence of lymphovascular invasion, progesterone receptor status, sentinel lymph node positivity, and different cut-off values of Ki67 scores (>10%, $\geqslant$15%, $\geqslant$20%, $\geqslant$25%).

**Results:** A total number of 103 patients with stage I-II breast cancer (stage I, n = 65; stage II, n = 38) were included in the study. The median age was 48 (29−75). Seventy-eight patients (75.7%) underwent breast-conserving surgery while mastectomy (simple mastectomy or nipple/skin sparing mastectomy) was performed in 25 patients (24.3%). Sentinel lymph node biopsy was positive in 19 patients (17.5%) and 14 of these were isolated tumor cells or micrometastases. Sixty-four patients (62.1%) had low Oncotype DX score whereas 32(31.1%) and 7(6.8%) patients had intermediate and high Oncotype DX scores, respectively. No significant correlations were found between Oncotype DX scores and age, tumor size, invasive ductal carcinoma type, lymphovascular invasion, sentinel lymph node positivity and cut-off values of Ki67 scores (>10%, $\geqslant$15% and $\geqslant$20%) except $\geqslant$25%. High nuclear grade ($p = 0.01$; $p < 0.05$), high histological grade ($p = 0.005$; $p < 0.05$), absence of progesterone receptor ($p = 0.02$; $p < 0.05$) significantly correlated with intermediate/high Oncotype DX scores. In bivariate correlation analysis Ki67 $\geqslant$25% significantly correlated with high Oncotype DX score ($p = 0.04$; $p < 0.05$) and there was a positive correlation between them as shown by linear regression analysis ($p = 0.015$). Twenty-one patients (20.3%) received chemotherapy based on the Oncotype DX results.

**Conclusion:** Patients with progesterone negative tumors, high nuclear and histological grade or with Ki67 score $\geqslant$25% are likely to have intermediate or high Oncotype DX recurrence scores. Considering the high cost of genetic assays, careful selection of patients is needed to determine whether they offer significant benefit to justify their use.

**No conflicts of interest**

**434** Poster

**Shifts in miRNA expression profile may affect epithelial cell polarity, adhesion and mitotic spindle orientation during breast carcinogenesis**

V. Halytskiy[1]. [1]*Palladin Institute of Biochemistry of the National Academy of Sciences of Ukraine, Molecular Immunology Department, Kiev, Ukraine*

**Background:** Impaired adhesion, loss of cell polarity and aberrant orientation of mitotic spindle are typical for cancer cells. Moreover, alterations in cell polarity and in normal asymmetry of stem cell division may also contribute to the early stages of carcinogenesis. This research aims to identify in what way the shifts in expression of non-coding RNAs, especially miRNAs, can lead to these abnormalities and contribute thereby to breast cancer.

**Material and Methods:** MiRNA targets within gene transcripts were predicted in silico using TargetScan software.

**Results:** MiRNAs, hyperexpression of which is essential for abnormal proliferation and surviving of breast cancer cells, can silence genes responsible for the establishment of epithelial cell polarity. MiRNAs miR-18, miR-23, miR-27, miR-181, and miR-375 can silence CRB1 gene. Transcripts of MPP5 and INADL genes encoding PALS1 and PATJ, the components of CRB complex, carry targets of miR-21, miR-23, miR-155, miR-181, miR-223, miR-375 and, respectively, miR-18, miR-23, miR-155, miR-181. MiRNAs miR-19, miR-21, miR-23, miR-29 can silence DLGL1 gene coding protein DLG − component of the SCRIB complex. MiRNAs miR-27 and miR-153 can silence gene PARD3 coding PAR3 − main element of PAR complex. At the same time, down-regulation of miR-15/16, miR-125 and, respectively, miR-122 allows hyperexpression of PARD6A, PRKCZ and PRKCI genes encoding other components of PAR complex − PAR6 and atypical protein kinase C.

Adherens and tight junctions also participate in the establishment and maintenance of cell polarity as well as in normal orientation of mitotic spindle. Therefore, overexpressed miRNAs (miR-18, miR-19, miR-21, miR-23, miR-27, miR-29, miR-155, miR-181, miR-206, miR-210, miR-221/222, miR-375) can affect cell polarity also indirectly, due to silencing of genes responsible for cell-cell adhesion − JAM-A/JAM-C, CLDN1 (claudin 1), TJP1/2 (tight junction proteins ZO-1 and ZO-2), OCLN (occludin), PVRL1 (nectin 1), CADM1 (nectin-like molecule 2), CDH1 (E-cadherin), CTNNA1 (alpha-catenin) and CTNND1 (p120-catenin), CGN (cingulin). In addition, some overexpressed miRNAs can silence other genes involved in mitotic spindle orientation − VHL, APC, PROX1.

**Conclusions:** Shifts in miRNA expression profile can contribute to deregulation and disintegration of protein complexes responsible for cell polarity. Loss of epithelial cell polarity complexes as well as loss of adhesion molecules leads also to randomized mitotic spindle orientation and to symmetric division of cells, despite the normal asymmetric division. These abnormalities can be early events in carcinogenesis. As a result, normal microarchitectonics of epithelial tissue is disordered, cells evade differentiation and accumulate in tissue, undergoing further alterations and forming a tumour with time.

**No conflicts of interest**

**435** Poster

**Determination of methylation status of RASSF1A, APC and ITH5 as diagnostic and prognostic biomarkers in tissue samples of breast cancer patients from Saudi population**

S. Bin Amer[1], E. Barhoush[1], H. Instabli[1], C. Eltabache[1], A. Eldali[1], A. Yaqinuddin[1], A. Tulbach[1], T. Al Twegieri[1], A. Qattan[1]. *[1]King Faisal Specialist Hospital and Research Center, Molecular Oncology, Riyadh, Saudi Arabia*

**Background:** Breast cancer remains one of the most frequent cancers among women around the world. Most common epigenetic modification of the DNA in cancers is "DNA methylation". Modifications in methylomes are an early event in cancers and remain involved throughout the process of oncogenesis.

**Materials and Methods:** In this study we analysed the DNA methylation status of CpGs located in the promoters of 5 genes (RASSF1A, APC, ESR1, DKK3 and ITH5) in 38 breast cancer tissues and compared it to 38 paired adjacent normal breast tissue samples from the same patient. The DNA methylation analysis at these loci was performed using Methyl Light PCR.

**Results:** The results showed hypermethylation of 71%, 84%, 42%, 7.8% and 5.2% in DNA derived from breast cancer tissues for RASSF1A, ITH5, APC, DKK3 and ITH5 loci respectively. Further, Mann–Whitney U-test showed statistically significant difference between Methylation Index at RASSF1A ($p < 0.0001$), ITH5 ($p < 0.001$), APC ($p < 0.006$), DKK3 ($p < 0.029$) and ESR ($p < 0.029$) loci between breast cancer tissues and normal adjacent breast cancer tissues from the same patients. However, we found that DNA from normal adjacent tissue from these breast cancer patients was also methylated at these loci but at lower a frequency (RASSF1A 6.5%, DKK3 1.3%, ESR-1 1.3%, APC 3.9% and ITH5 32%).

**Conclusion:** Taken together these data suggest that hypermethylation of DNA at RASSF1A, APC and ITH5 loci can be used as biomarkers to detect breast cancer. In-addition, hypermethylation of these loci in normal adjacent tissues suggests epigenetic field effect which should be further investigated to develop biomarkers to detect pre-cancerous stage of breast cancer.

**No conflicts of interest**

**436** Poster

**Functional and human pharmacokinetic similarity of ABP 980 and trastuzumab**

V. Hanes[1], T. Born[1], V. Chow[1], M. Coon[1], N. Zhang[1], A. Rohrbach[1], J. Crouse-Zeineddini[1], R. Markus[1]. *[1]Amgen Inc., Biosimilars, Thousand Oaks, USA*

**Background:** ABP 980 is being developed as a biosimilar to trastuzumab, a monoclonal antibody (mAb) that binds human epidermal growth factor receptor 2 (HER2), resulting in proliferation inhibition (PI) and induction of antibody-dependent cell-mediated cytotoxicity (ADCC). Biosimilar mAbs are expected to be similar to the reference product not withstanding minor differences in analytical attributes due to variances in expression systems, bioprocesses and purification; demonstration of analytical, pharmacologic and pharmacokinetic (PK) similarity is the foundation for biosimilarity.

**Objectives:** To demonstrate functional and PK similarity between ABP 980 and EU-authorized trastuzumab reference product.

**Materials and Methods:** The functional activity of ABP 980 and EU-authorized trastuzumab reference product was compared by measuring PI and ADCC activity in HER2-overexpressing cell lines. PI activity was evaluated using BT-474 cells; ADCC was assessed using HCC2218 as target cells. Antitumor activity was compared in two mouse xenograft models: BT-474 breast tumor model and N87 gastric tumor model.

PK similarity was evaluated in a randomized, single-dose (6 mg/kg IV) study in healthy adult men. Primary endpoints were area under the serum concentration-time curve from time 0 to infinity ($AUC_{inf}$) and maximum observed serum concentration ($C_{max}$). Secondary endpoints were safety, tolerability, and immunogenicity.

**Results:** ABP 980 displayed comparable PI and ADCC activities to EU-authorized trastuzumab reference product. The range of relative potency by PI was 96–107% for ABP 980 and 88–117% for trastuzumab; relative ADCC activity was 79–114% for ABP 980 and 72–123% for trastuzumab. Antitumor activity of the two test products was similar in both BT-474 and N87 tumor xenograft models.

PK similarity was demonstrated between ABP 980 and EU-authorized trastuzumab reference product; the geometric mean (GM) ratios for $C_{max}$ and $AUC_{inf}$ were 0.99 (90% CI [0.95, 1.03]) and 1.00 (90% CI [0.95, 1.06]) with both CIs within the standard pre-specified bioequivalence criteria of 0.80 to 1.25. After 6 mg/kg intravenous infusion, the GM of $C_{max}$ and $AUC_{inf}$ were 135.90 μg/mL and 34061.43 μg.h/mL for ABP 980 and 136.85 μg/mL and 33947.00 μg.h/mL for trastuzumab. Treatment-emergent adverse events (TEAEs) occurred in 84% subjects in ABP 980 and 78% subjects in trastuzumab reference product groups; the incidence of TEAEs was comparable between both treatment groups. There were no deaths or TEAEs leading to study discontinuation; one subject in the trastuzumab treatment group experienced a grade 3 SAE of infusion-related reaction with hypoxia. No subjects developed anti-drug antibodies.

**Conclusions:** ABP 980 has been shown to be similar to EU-authorized trastuzumab reference product in functional tests and in a phase 1 human PK study.

**Conflict of interest:** Corporate-sponsored Research: This study was sponsored by Amgen inc. Other Substantive Relationships: a. V. Hanes, T. Born, V. Chow, N. Zhang, A. Rohrbach, J. Crouse-Zeineddini, R. Markus are Amgen employees and stockholders; b. At the time this work was done, M. Coon was a consultant at Amgen.

**437** Poster

**Breast cancer care for older patients in the Netherlands: a population based study 2005–2013**

K. De Ligt[1], R. Bretveld[1], C. Smorenburg[2], E. Bastiaannet[3], G.J. Liefers[3], M. Van der Sangen[4], S. Siesling[1]. *[1]Comprehensive Cancer Centre The Netherlands IKNL, Department of Research, Utrecht, Netherlands; [2]Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital, Department of Oncology, Amsterdam, Netherlands; [3]Leiden University Medical Center, Department of Surgery, Leiden, Netherlands; [4]Catharina Hospital, Department of Radiotherapy, Eindhoven, Netherlands*

**Background:** Due to an aging population and an increase in life expectancy in the Netherlands, a considerable part of the breast cancer patients is among older women. The objective of this study is to give insight in diagnosis and treatment of older breast cancer patients, by examining breast cancer care of the recent years.

**Materials and Methods:** Patients newly diagnosed between 2005 and 2013 with invasive breast cancer or ductal carcinoma in situ (DCIS) were selected from the Netherlands Cancer Registration (NCR) (n = 145,949). Patients aged 75 years and older were classified as older patients. Incidence, tumour characteristics and treatment methods were compared between young and older women. Relative Survival (Ederer II method) was compared between young and older patients.

**Results:** In 2013, one in six (2.933 in 18.184) new breast cancers was diagnosed in older patients; a total of 145 older patients were diagnosed with DCIS. In 2013, very few older patients (n = 215) were diagnosed in an academic hospital compared to younger patients (n = 1.840), 6% vs 4%. Older patients tend to have a higher stage of breast cancer at the time of diagnosis compared to younger patients (stage I: 51% vs 31%). Compared to younger patients, older patients receive more often a non-surgical treatment (4% vs 27%), with over 80% of the non-surgical treated older patients receiving hormonal treatment only. Older HER2-positive tested patients were treated less often with an anti-HER2-therapy (81% vs 13%). Older patients receive far less breast conserving surgery (BCS) as younger patients (64% vs 38%), but application of BCS for older patients increased over the past years (31% in 2005, 38% in 2013). Application of radiotherapy for invasive breast cancer after BCS is lower for older patients (98% vs 87%). Survival did not increase over the past years (2005–2013) for both groups, but younger patients have a higher survival than older patients.

**Conclusion/Discussion:** Older breast cancer patients are often treated differently from younger patients. A part of this variation is desirable, since treatments for elderly are adapted to their frailty and preferences. The reasons of both desirable and undesirable variation are probably multifactorial and should be studied in more detail.

**No conflicts of interest**

**438** Poster

**Mammographic characteristics and very low mammographic breast density are associated with high numbers of M2-like (CD163-positive) tumor associated macrophages**

A. Masarwah[1], S. Tiainen[2], M. Sudah[1], A. Sutela[1], S. Oikari[3], V.M. Kosma[4], R. Vanninen[1], P. Auvinen[2]. [1]*Kuopio University Hospital, Clinical Radiology, Kuopio, Finland;* [2]*Kuopio University Hospital, Oncology, Kuopio, Finland;* [3]*University of Eastern Finland, Biomedicine, Kuopio, Finland;* [4]*Kuopio University Hospital, Pathology, Kuopio, Finland*

**Purpose:** Very low percentile mammographic density (VLD) and high amounts of tumour-associated macrophages (TAMs) separately correlate with tumour aggressiveness in breast cancer, but the relationship between these parameters is yet to be explored. The aim of this study was to assay the numbers of TAMs in 270 human breast cancer cases, and their correlations with mammographic parameters, with special emphasis on mammographic breast density and patient outcome.

**Materials and Methods:** The immunoreactivities for CD163 and CD68 were considered as indicators for M2-like and all TAMs, respectively. The numbers of TAMs were counted in at least four hot spots, and averaged to represent the numbers of TAMs in each section. In the statistical analyses, the numbers were graded as either low or high according to the median. Mammographic characteristics of 270 patients were analysed according to the BI-RADS 5$^{th}$ edition lexicon and mammographic breast density (MBD) was classified according to percentile density with densities of <10% classified as VLD. Mammographic features and density were then compared with TAMs.

**Results:** Patients with VLD breasts had a bigger percentage of high CD163 values compared to the remaining patients (62.2% vs 42.9%, $p = 0.002$), while density showed no correlation with CD68 levels ($p = 0.831$). TAMs showed no relation to calcifications or tumor location. Tumors presenting as masses had higher values of CD163 compared to non-masses (54.1% vs 25.6%, $p = 0.001$) while tumors with spiculated margins had higher CD163 values in 55.6% of cases vs 41.7% for the remaining patients ($p = 0.02$). Patients' overall survival decreased to 59.0% for patients who were both VLD and high in CD163 staining, while patients who were negative for both had an overall survival of 89.7% after an average 8 year follow up.

**Conclusion:** Our findings suggest a strong reciprocal relationship between high numbers of TAMs and breasts with low density. The increased relative fat content in the environment provided by VLD seems to facilitate macrophage infiltration and inflammatory responses during human breast cancer progression.

**No conflicts of interest**

**439** Poster

**Relation between DNA mutator APOBEC3B and chemo-resistant associated genes in Japanese breast cancer patients**

T. Miki[1], Y. Takehiko[2], H. Jun[3], Y. Arito[2], K.I. Reika[4], Y. Shinji[4], O. Hiroki[5], T. Hideaki[3], O. Tetsunari[6], T. Izumi[3], N. Masahiko[2]. [1]*Gunma University Graduate School of Medicine, Department of Thoracic Visceral Organ Surgery-Depertment of Molecular Pharmacology and Oncology, Maebashi, Japan;* [2]*Gunma University Graduate School of Medicine, Depertment of Molecular Pharmacology and Oncology, Maebashi, Japan;* [3]*Gunma University Graduate School of Medicine, Department of Thoracic Visceral Organ Surgery, Maebashi, Japan;* [4]*Gunma University, Initiative for Advanced Research, Maebashi, Japan;* [5]*Toho Hospital, Department of Surgery, Kasakake-machi, Japan;* [6]*Gunma University Graduate School of Medicine, Diagnostic Pathology, Maebashi, Japan*

**Background:** The members of AID/APOBEC protein family converts cytidine residue to uridine on DNA and RNA, and APOBEC3B (A3B) has been suggested to induce driver and passenger mutations in several types of cancer including breast cancer. Previously, we reported the overexpression of A3B expression is associated with cancer progression in Japanese breast cancer patients (Breast Cancer 2015 accepted). However, the expression was not related to the mutation of TP53 and PIK3CA, polymorphic A3B deletion allele, HPV infection, DFS and OS. To elucidate the clinical significance of A3B, we examined the relation of A3B expression to chemo-resistant associated gene expression, along with subgroup analysis in our cohort.

**Methods:** Ninety-three primary breast cancer tissues (74 estrogen-receptor (ER) positive, 3 ER and HER2 positive, 6 HER2 positive, and 10 triple negative) were assessed for the expression of A3B by quantitative real-time RT-PCR. We additionally performed the subgroup analysis in this cohort, and clarified the relationships between A3B expression and the expression levels of several chemo-resistant associated genes including TYMS, DPYD, ERCC1, ABCB1, ABCC1, ABCC2, ABCG2-BCRP, TOP1, TOP2A, GSTP1, TUBB3, VEGFA, UBE2S, and HIF1A.

**Results:** We re-evaluated the association with survival time and A3B expression according to the cutoff points calculated by ROC curves, and confirmed that overall survival time and disease free survival time in the breast cancer patients with high A3B expression were significantly shorter than those with low expression groups (Wilcoxon test, $p < 0.05$). The results were concordant with the findings obtained by the database analysis on 4,000 breast cancer patients in Western countries, However, in the expression levels, none of the relationship between A3B and 14 chemo-resistant genes examined could be observed in our cohort.

**Conclusion:** The expression levels of A3B in breast cancer were associated with survival times, but did not relate to the expression of 14 chemo-resistant genes in our cohort. Further studies will be needed using large numbers of cases to clarify the prognostic significance and association with chemo-sensitivity of A3B expression in Japanese breast cancer patients.

**No conflicts of interest**

**440** Poster

**Surviving gene expression in the primary tumor and circulating tumor cells in breast cancer**

Y. Shlyakhtunou[1]. [1]*Vitebsk State Order of Peoples' Friendship Medical University, Oncology, Vitebsk, Belarus*

Breast cancer is a leader in the structure of morbidity and mortality of the female population from malignant tumors. Distant metastases are the main cause of death of patients, a substrate for the development of which are circulating tumor cells (CTCs). However, only one-search ethics cells is not sufficient to form a complete picture of the nature and course of the tumor process in individual patients. Determination of the expression of tumor-genes responsible for the different processes of tumor progression allows a more complete picture. Such genes include the gene survivin (BIRC5) family of inhibitors of apoptosis (IAP).

**Objective:** To study the expression of the gene survivin in the tumor tissue of breast carcinoma, as well as CTCs in the peripheral blood of patients with breast cancer.

**Material and Methods:** Using real-time PCR was investigated expression of the gene survivin in 16 samples of primary invasive ductal carcinoma of the breast, three samples of benign tumors − fibroadenoma of the breast, as well as 26 samples of peripheral blood of patients with breast cancer at various stages of tumor and stage specific treatment, and 3 healthy people are controlled. After homogenization of frozen tumor samples was extracted RNA, followed by cDNA synthesis and determination of expression of survivin. Were isolated from peripheral blood using CTCs microspheres carrying antibodies to EpCAM, after several stages passed as tumor RNA extraction followed by standard stages real-time PCR.

**Results:** In primary breast carcinoma was determined by high expression of survivin gene in all 16 samples with the average value (M±m) 1.40±0.49 (min − 1.21; max − 3.41). The highest figures were determined expression in tumors of medium and high grade (G II-III) with lymphovenous invasion (LVSI +). In samples of benign tumor in 2 of 3 expression of survivin was not determined, and one was 0.015. In CTCs, isolated from peripheral blood of breast cancer patients, all 26 samples as determined by the gene expression of survivin with an average value (M±m) 0.90±0.19 (min − 0.26; max − 3.90). The level of expression of the control samples did not exceed 0.003. It should be noted that the maximum volume of expression obtained in samples of tumor patients with stage N+, and especially M1, on TNM classification. Any legitimate expression of survivin, depending on the size of the tumor had been received. In patients, receiving chemotherapy observed average expression of survivin gene, but never approached the indicators of control.

**Conclusions:** Determination of expression of the gene survivin in primary tumor and the CSC may be treated to one of the most promising markers of tumor progression and monitoring of breast cancer therapy.

**No conflicts of interest**

**441** Poster

**Managing microarray technical variations and data processing in the large randomized MINDACT trial**

L. Jacobs[1], A. Witteveen[2], I. Goossens-Beumer[2], J. Van den Akker[2], L. Delahaye[2], T. Speed[3], L. Van 't Veer[2], A. Glas[2]. [1]*CNRS, Paris, France;* [2]*Agendia, R&D, Amsterdam, Netherlands;* [3]*University of California at Berkeley, Statistics, Berkeley, USA*

**Background:** The MINDACT study enrolled 6694 breast cancer patients between 2007 and 2011. For each patient, gene expression levels were measured using full-genome microarrays. Unlike most clinical trials or

research datasets, sample analysis took place over a long period of time − during which reagents and other factors changed and may have introduced noise and technical variation. Standard techniques may not be sufficient to remove these unwanted effects. A challenging but crucial task is to remove unwanted variation without affecting the biological signals in order for (un)supervised analysis of the data to acquire (new) biological insights.

**Material and Methods:** 6694 MINDACT samples were processed using full-genome microarrays (Agilent Technologies) that contain >40,000 probes targeting >28,000 transcripts. All samples were dye normalized using a linear lowess approach. Variation in the data was analyzed using a global multivariate analysis and principal component analysis (PCA). Unwanted noise/technical variation (but not biological information) was removed by a RUV (remove unwanted variation) normalization technique.

**Results:** We performed a comprehensive analysis of the full genome MINDACT dataset and identified sources of technical variation that were not removed using standard (within sample) full genome normalization techniques: reference RNA used, labeling yield, and the use of manual versus automated RNA processing steps. After applying a RUV normalization technique, we were able to verify that the technical variation was removed while expected biological signals such as expression of ER and ERBB2 genes were preserved. These known biological signals were not used for normalization purposes and persist after correction for unwanted factors. We expect that other, yet unknown biological signals are preserved as well. Removal of unwanted technical variation and preservation of biological signals was further verified using a PCA.

**Conclusion:** We present a high-quality full-genome dataset of 6694 MINDACT samples that is ready to use for data mining. The presence of technical variation in gene expression measurements is expected given the length and complexity of MINDACT and were explained by a small number of well identified factors. More importantly this unwanted variation does not hide expected biological signals. Prior to the accompanying clinical data being released, it can be used for unsupervised analysis such as tumor clustering or inference of gene regulatory networks. Once the clinical data is released, it will be possible to use the dataset for supervised analysis such as prognosis prediction and identification of differentially expressed genes.

**Conflict of interest:** Other Substantive Relationships: Anke Witteveen, Ines Goossens-Beumer, Leonie Delahaye, Laura Van 't Veer and Annuska Glas are employees of Agendia that performed the microarray experiments.

**442** Poster

**Optimizing the use of Ki67 in breast cancer**

M. Sundquist[1], E. Holmberg[2], A. Kovacs[3], L. Mellblom[4], R. Olofsson Bagge[5]. *[1]County Hospital Kalmar, Surgery, Kalmar, Sweden; [2]Sahlgrenska University Hospital, RCC, Gothenburg, Sweden; [3]Sahlgrenska University Hospital, Pathology, Gothenburg, Sweden; [4]Blekinge Hospital, Pathology, Karlskrona, Sweden; [5]Sahlgrenska University Hospital, Surgery, Gothenburg, Sweden*

**Background:** Proliferation rates of tumour cells provide important prognostic and therapy predictive information. Mitotic Index (MI) and Ki67 Labelling Index/MIB-1 are commonly used assays of proliferation. MI is an integrated part of histological grading and assessed as the number of mitotic figures per standardized high-power fields and scored as 1=few mitoses, 2=intermediate and 3=high number of mitoses. The nuclear protein Ki67 is increased during the cell cycle. The percentage of mitotically active cells is assessed by immunostaining. Consensus of cut-points of Ki67 in breast cancer is lacking. Cut-offs vary from 1% to 30%, most units discriminating only in high and low score. In the St Gallen guidelines the cut-point was changed from 14% to 20% in 2013. Comparative studies of the assays are rare.

**Material and Methods:** Two cohorts of patients were used to compare the assays. Mitotic counts were performed according to the procedure of the NHG and different cut-offs of Ki67 were explored. (1) In approximately 1500 cases from 3 different hospitals the correlation between Ki67 and MI was explored. (2) In 403 consecutive patients from one hospital (SU) MI, Ki67/MIB-1 and 4-year follow up data were investigated.

**Results:** (1) Using a cut-point of 25%, stratifying Ki67 in high and low, 9.5% of tumours of the low MI 1 score and 50% of the intermediate MI 2 tumours were assigned to be of high Ki67 score. Further, 20% of MI 3 tumours were assigned low Ki67.

(2) In the SU cohort MI and Ki67 were both significantly correlated to early recurrence, $p < 0.001$. When Ki67 cut-off of 25% was applied 6.6% of patients with low score had early distant recurrence and 19% with high Ki67. When Ki67 was scored in 3 categories with cut-off values for Ki67 of 10% and 30% the association with prognosis was almost identical to that of MI. Ki67 added prognostic information in a small subgroup of 9 pts with NHG 2, MI 2 and Ki67 >30%. Three of these pts had early distant recurrence.

| | N | Distant recurrence | % | OR | p-value |
|---|---|---|---|---|---|
| Ki67 | 394 | | | | <0.00001 |
| <10% | 144 | 2 | 1.4 | 1 | |
| 10−30% | 182 | 22 | 12.1 | 3.1 | |
| >30% | 68 | 15 | 22.1 | 9.3 | |
| MI | 403 | | | | <0.00001 |
| 1 | 182 | 3 | 1.6 | 1 | |
| 2 | 99 | 11 | 11.1 | 3.4 | |
| 3 | 118 | 25 | 21.2 | 11.6 | |

**Conclusion:** Ki67 dichotomized in High and Low does not provide as good prognostic information as Mitotic Index. When Ki67 is stratified in 3 groups the assay performs equally well as the Mitotic Index as a prognostic indicator. Ki67 might add information to MI in a subgroup.

**No conflicts of interest**

**443** Poster

**Assessment of programmed death-ligand 1 (PD-L1) expression in different breast tumor subtypes**

M. Sobral-Leite[1], K. Van de Vijver[2], K. Kersten[3], D. Peters[4], M. Kok[5], A. Broeks[4], K.E. De Visser[3], M.K. Schmidt[1]. *[1]Netherlands Cancer Institute, Molecular Pathology, Amsterdam, Netherlands; [2]Netherlands Cancer Institute, Division of Pathology, Amsterdam, Netherlands; [3]Netherlands Cancer Institute, Division of Immunology, Amsterdam, Netherlands; [4]Netherlands Cancer Institute, Core Facility Molecular Pathology and Biobanking- Division of Molecular Pathology, Amsterdam, Netherlands; [5]Netherlands Cancer Institute, Division of Medical Oncology, Amsterdam, Netherlands*

**Background:** The recent breakthrough of cancer immunotherapy initiated a new era in the treatment of cancer. In particular, immune checkpoint inhibitors are very effective in certain cancer types, which PD-L1 expression is associated with the treatment response. It is yet largely unknown, which breast cancer patients benefit from immune checkpoint inhibitors. Breast cancer is a heterogeneous disease, and therefore we set out to assess the PD-L1 expression profiles of different subtypes of breast cancers. Clinical data with patient survival were assessed. We also compared the validity of PD-L1 scores using tissue microarray (TMA) with those of whole slides.

**Material and Methods:** We randomly selected in total 193 tumor samples of different subtypes from a consecutive breast cancer patient cohort of all ages treated between 1990 and 2000 with surgery, with or without systemic adjuvant therapy. Subtypes were defined by estrogen receptor (ER), progesterone receptor (PR) and HER2 status as follows: luminal 1 (ER+ and/or PR+ and HER2−); luminal 2 (ER+ and/or PR+ and HER2+); HER2-like (ER−, PR− and HER2+); and triple negative (TN) (ER−, PR− and HER2−). PD-L1 was stained using the E1L3N XP® antibody (Cell Signaling). A pathologist scored PD-L1 tissue staining based on the percentage of positive (tumoral and/or immune) cells; as grade 0 if <1%, 1 if 1−5%, 2 if 5−10%, or 3 if $\geqslant$10%. PD-L1 grade 2 and 3 were considered positive in the analyses. Survival analysis according PD-L1 expression was performed using univariate Cox models. Adjusted analyses with additional samples are ongoing.

**Results:** PD-L1 staining was positive in 76 cases (41.7%) of the 182 breast tumors scored using whole slides. The interface between malignant cells and tumor-infiltrating immune cells was the most common location for PD-L1 expression. Tumors with high differentiation grade were more likely to have PD-L1 expression; grade 3: 58.7%; grade 2: 25.5% and grade 1: 11.1% ($p < 0.001$), considering all the subtypes. PD-L1 positive cells were more frequently found within the TN subgroup (70.9%) compared with non-TN (29.1%; $p < 0.001$). PD-L1 positivity was associated with a statistically significant decreased risk of distant metastasis and better overall survival in the group of 92 patients with ER-negative tumors (HR = 0.47; 95% CI 0.24–0.89 and HR = 0.45; 95% CI 0.23–0.92, respectively) in univariate analyses, but not in luminal tumors. The comparison of 115 whole slides scores versus TMAs showed an agreement of 53.9% (kappa = 0.171): a large proportion of TMAs having a false negative PD-L1 score.

**Conclusion:** PD-L1 expression is most prevalent in tumors associated with poor outcome variables, as high tumor differentiation grade and TN subtype. PD-L1 expression analysis using whole slides should be taken into account in future immunotherapy studies determining the predictive capacity of PD-L1.

**No conflicts of interest**

**444** Poster

**Breast cancer versus Alzheimer: does the neuropeptide CGRP play a key role in the inverse incidence of the above diseases?**

V. Papantoniou[1], P. Valsamaki[1], S. Marinopoulos[2], Z. Delichas[1], I. Papantoniou[1], M. Tsiouma[1], A. Papadimitriou[3], D. Loutradis[2]. [1]*Alexandra Hospital, Nuclear Medicine Department, Athens, Greece;* [2]*Alexandra Hospital- Athens University Medical School, 1st Department of Obstetrics and Gynecology, Athens, Greece;* [3]*Errikos Dynan Clinic, Neurology Department, Athens, Greece*

**Background:** To assess if the variation of serum CGRP expression contributes in two different pathological entities such as breast cancer (BC) and Alzheimer disease (AD). The presence of each one seems to be unlikely to the incidence of the other.

**Material and Methods:** Serum CGRP concentrations were measured by RIA method and compared (t-test) between a group of AD patients (n = 17) and a group of patients with breast cancer (n = 17) of different histological subtypes (IDC n = 7, IDC+DCIS n = 5 and DCIS n = 5). Patients with AD and BC were compared with a group of healthy controls (n = 10).

**Results:** Serum CGRP concentration in AD, BC and healthy controls was (mean±SD: pg/mL): 179.7±50.4, 438.3±448.1 and 90.2±32.1, respectively. CGRP levels in patients with IDC were 213.1±50.1 pg/mL and in DCIS lesions 172.2±95.1 pg/mL. Statistical analysis by t-test revealed that BC patients presented significantly higher CGRP levels as compared to AD patients (P = 0.04) and the controls (P = 0.09). Between the subgroups of BC patients, only mixed DCIS+IDC lesions (1130±881.4 pg/mL) showed statistically significant difference as compared to AD patients (P = 0.00013). Patients with AD presented significantly higher CGRP levels as compared to the controls (P = 0.001). Non-significant difference was found between AD vs IDC (P = 0.16) and AD vs DCIS (P = 0.8).

**Conclusions:** The results of this study suggest that there is a close relationship between CGRP upregulation and a specific subtype of BC patients (mixed DCIS+IDC). In contrast, downregulation of CGRP expression seems to exhibit a critical role in AD progression. Based on the wide range of CGRP properties − activities as concerned to its high or low expression, the underlying pathophysiological mechanism probably involves hypoxia-induced angiogenesis at high levels in BC versus β-amyloid formation and deposition at lower levels in AD. These findings warrant further investigation and clarification, with potentially major impact in both diagnosis and anti-CGRP-peptide treatment of these disorders.

**No conflicts of interest**

**445** Poster

**Exploring and characterizing circulating exosomes in metastatic breast cancer patients**

L. Gerratana[1,2], B. Toffoletto[3], M. Bulfoni[3], D. Cesselli[1,3], A.P. Beltrami[1,3], C. Di Loreto[1,3], M. Bonotto[1,2], M. Cinausero[1,2], M. Isola[1], S. Marzinotto[1,3], A.M. Minisini[2], R. Sottile[2], M. Mansutti[2], G. Fasola[2], F. Puglisi[1,2]. [1]*University of Udine, Department of Medical and Biological Sciences, Udine, Italy;* [2]*University Hospital of Udine, Department of Oncology, Udine, Italy;* [3]*University Hospital of Udine, Institute of Pathology, Udine, Italy*

**Background:** Exosomes are nanovesicles secreted by different type of living cells. Their molecular "cargo" could influence signaling pathways and tumor microenvironment.

Aims of the study are to characterize circulating exosomes and to explore their possible association with clinicopathological features of metastatic breast cancer (MBC).

**Material and Methods:** Blood samples from 56 MBC patients (pts), treated at the University Hospital of Udine between 2013 and 2015, were collected. Circulating exosomes were first enriched from plasma fraction through ExoQuick® kit and then conjugated with anti-CD63 coated beads to assess their protein expression profiles by flow cytometry. The fluorescence intensities of different antibodies were tested on single bead-exosomes decorated with CD63 and CD9 antibodies. Demographic and clinico-pathological data were extracted from electronic medical records. The differences in exosomal subpopulation distribution between controls and MBC patients and their association with clinicopathological features were explored by Wilcoxon rank-sum test or Kruskal–Wallis test, as appropriate.

**Results:** 23 controls matched by demographic characteristics of the enrolled patients were analyzed as first step in order to determine any possible differences in exosomes subpopulations distribution. Expression of CD44 (P = 0.0372), HGFR (P = 0.0311), CXCR4 (P = 0.0094), CD49D (P = 0.0441), E-cadherin (P = 0.0003) and HER2 (P < 0.0001) were higher in MBC pts.

In addition, among MBC pts, some significant differences were observed between specific exosomes subpopulations. About pathological features, exosomes positive for CXCR4 characterized pts affected by luminal or HER2 positive disease (P = 0.0199 and P = 0.0227, respectively), and among the latter subgroup a lower expression of E-cadherin (P = 0.0137) was also observed. A disease with KI67 >14% was associated with higher expression of CD49D (P = 0.0487). Pts with multiple metastatic sites had a higher fraction of HER2 (P = 0.0376) and marginally of KDR-positive exosomes. About metastatization spread, visceral localizations were associated with higher expression of KDR (P = 0.041) and, in particular, lung involvement was associated with a lower expression of CD49D (P = 0.0438). Of note, liver localizations were marginally associated with higher expression of CXCR4 and KDR. About treatment history, pts beyond 1st line of treatment showed a higher proportion of CD44 positive exosomes (P = 0.0379), whereas a marginally lower expression of EGFR was observed in pts beyond the 3rd line.

**Conclusions:** Distinct subpopulations of exosomes were defined according to tumor biology, disease burden and therapeutic history of MBC pts. Accrual is ongoing and updated data will be presented at the meeting.

**No conflicts of interest**

**446** Poster

**P53 expression & Ki-67 labeling index as predictors for recurrence in ER positive breast cancer postmenopausal patients treated with adjuvant aromatase inhibitor**

I. Abdelhalim[1], W. Elsadda[1], M. Elebrashi[1]. [1]*Mansoura University, Clinical Oncology, Dakahlia, Egypt*

**Background:** Endocrine therapy has become the most important systemic treatment for women with estrogen receptor (ER) positive breast cancer. The third generation aromatase inhibitors such as anastrozole & letrozole are superior to tamoxifen in the treatment of postmenopausal women with early stage breast cancer. Characterization of the risk of recurrence for patients who receive AI is important for selection of treatment. We examined expression of P53, ER, PR, HER2 and Ki-67 using immunohistochemistry postmenopausal ER +ve positive breast cancer patients who were treated with AI as adjuvant endocrine therapy toxicity the predictive value of the P53 & ki-67 for recurrence and the efficacy of AI.

**Patients and Methods:** A total of 200 postmenopausal women with stage II&III breast cancer treated with AI between 2008–2015. All patients had undergone mastectomy or lumpectomy. Immunohistochemical analysis for ER, PR, HER2, P53 and Ki-67on tumor sample obtained after surgery and we study the relationships between P53 expression, Ki-67 labeling index and clinicopathological characteristics among patients with recurrence.

The cut off points for P53 expression & Ki-67 were at 10% & 14% respectively. All patients received AI (anastrozole or letrozole) as adjuvant endocrine therapy. The median foolow up period was 70 months (range 1−84 months).

**Results:** In the 200 tumors patients that were analyzed for P53 expression, no expression was detected in 100 patients (50%), of the remaining patients, 40 (20%) had >10% P53 positive cells, 30 (15%) <1% and 30 (15%) 1−9%; 130 patients (65%) had Ki-67 <14%, 70 patients (35%) had Ki-67 >14%. High P53 & Ki-67 were positively correlated with tumor grade (P = 0.001, P < 0.0001, respectively) and negatively correlated with age. Univariate analysis demonstrated significant associations between DFS, tumor size, number of positive lymph nodes, and expression of P53 & Ki-67 (P < 0.0001, P < 0.0001, P = 0.001, P < 0.0001, respectively). High expression of Ki-67 >14% was significantly associated with decreased DFS (P = 0.0007). High expression of P53 >10% was significantly associated with decreased DFS (P < 0.0001).

**Conclusion:** P53 expression and Ki-67 labeling index are a strong predictor for recurrence in ER positive breast cancer postmenopausal patients treated with AI.

**No conflicts of interest**

**447** Poster

**An evaluation of discordance in primary tumour and lymph node response following neoadjuvant therapy in breast cancer**

C. Fleming[1], A. McCarthy[2], T.J. Browne[3], M. O'Sullivan[1], H. Redmond[1], M. Corrigan[1]. [1]*Cork University Hospital, Breast Research Centre, Cork, Ireland;* [2]*Cork University Hospital, Department of Histopathology, Cork, Ireland;* [3]*Cork University Hospital, Histopathology, Cork, Ireland*

**Background:** Neoadjuvant therapy (NAT) offers a unique opportunity to assess tumour response to systemic agents. However a discrepancy may exist between the response of the primary tumour & involved nodes. This study sought to assess the frequency of response discordance following NAT.

**Methods:** All consecutive node positive patients receiving NAT in a breast cancer regional referral unit from 2009–2014 (inclusive) were

identified through prospectively collected data. Basic demographics, and radiological & pathological features were tabulated. Tumour response was estimated using MRI. Lymph node (LN) response were estimated from pathological response to treatment measurements. Statistical analysis was performed using SPSS.

**Results:** A total of 108 node positive patients were eligible for inclusion. Median age was 51.73years (range 20−87), all patients underwent axillary clearance and 62% underwent mastectomy. Statistical significance was seen in improvement of tumour grade following NAT ($p < 0.01$) with a 40% average reduction in tumour size. There was an overall positive correlation between tumour and LN response following NAT (Spearman correlation coefficient $r = 0.46$, $p < 0.001$). Twenty one patients achieved a LN complete pathological response (ypCR) with 81% having an ypCR in tumour also. An ypCR in the tumour occurred in 20 patients and predicted complete nodal response in 85% of cases.

**Conclusion:** Fifteen percent of primary tumours with ypCR had persistently positive LN's. This represents a significant discordance between the primary tumour and the LN, representing a concern for the potential lack of response of occult systemic metastasis due to potential heterogeneity.

**No conflicts of interest**

**448** Poster

**Exome sequencing of primary breast cancers with paired metastatic lesions reveals metastasis-enriched mutations in the A kinase anchoring protein family (AKAPs)**

U. Kjällquist[1], R. Erlandsson[2], J. Hartman[1], A. Alkodsi[3], N. Tobin[1], T. Hatschek[1], J. Bergh[1], S. Linnarsson[2]. *[1]Karolinska Institute, Dpt. Oncology and Pathology, Stockholm, Sweden; [2]Karolinska Institute, Dept of Medical Biochemistry and Biophysics, Stockholm, Sweden; [3]University of Helsinki, Institute of Biomedicine & Genome-Scale Biology Research Program, Helsinki, Finland*

**Background:** Genomic heterogeneity in primary solid tumors has been extensively studied using deep sequencing technologies during the last decade and the heterogeneity of cancer tumors is today a well-established concept. Most available data however, relates to the primary breast cancer tumors and little has been described about the mutational profiles of the metastatic lesions and their relation to its original malignant cell population.

Here, we report that mutations in A-kinase anchoring proteins are enriched in metastatic lesions. AKAPs are members of a protein family acting as anchors for Protein Kinase A (PKA) by specifically associate PKA regulatory subunits to cellular organelles and direct its active signal transduction spatially and temporally. Several AKAP members have been associated to cancer development and metastatic potential in vitro.

**Materials and Methods:** We sequenced the exomes from paired primary tumors and their corresponding metastatic lesion from two available clinical cohorts, in total 30 breast cancer patients. Exome capture and sequencing was performed using SureSelect (Agilent Technologies) and Highseq 2000 platform (Illumina). Data processing was performed with either Casava or BWA-mem, realignment using GATK and somatic variant detection Varscan 2 and MuTect.

**Results:** We found a marked heterogeneity of somatic mutations as well as chromosomal aberrations in the metastatic lesions. A number of mutated genes were enriched in the metastases including, significantly, members of the A-kinase anchoring protein family (AKAPs). The enrichment of AKAP mutations in metastatic lesions was confirmed in an independent cohort containing 20 patients with paired primary and metastatic lesions, which showed the same mutational pattern. Most somatic mutations were found in the metastatic lesion and in case of available multiple relapses, showed an increasing allele frequency. The frequency of mutation in the AKAP gene family was 10% in the primary breast cancer tumors while 40% of the metastatic lesions carried a somatic AKAP mutation. Several copy number variations (CNV), mostly deletions in regions containing AKAP genes were detected. For example, the down-regulation of AKAP12 is often associated with promoter hypermethylation or loss of its locus 6q24–25.2 and has been associated with tumor progression and metastasis. In our data deletion of the AKAP12 locus is present in six out of thirty patients.

**Conclusions:** Our findings indicate that in metastatic lesions, the primary tumor genome is extensively transformed, with enrichment of mutations in a distinct set of genes, A-kinase anchoring proteins. Together, these findings suggest the involvement of AKAPs in the metastatic process and provide a potential avenue for targeted therapy directed at metastatic breast cancer.

**No conflicts of interest**

**449** Poster

**Assessing genetic variants in young onset breast cancer towards clinical integration in south India**

J. Thumsi[1], R.V. L[2], H.K. Prasad[2], S. Suresh Jadhav[3], M. Natraj[1]. *[1]Global Cancer Institute- BGS Global Hospital, Breast oncology, Bangalore, India; [2]Medgenome Labs pvt ltd, Genomics, Bangalore, India; [3]Global Cancer Institute- BGS Global Hospital, Hematology- Bone marrow transplant, Bangalore, India*

**Introduction:** Knowledge of cancer genetics is rapidly improving our understanding of cancer biology, helping to identify at-risk individuals, early detection, prevention and provide insights into newer treatment modalities. Breast cancer accounts for 31% of all women cancers in urban India. However, information about genetic variations significant to cancer in the Indian population is very scarce. In this study we assess the applications of Next Generation Sequencing based screening for genetic predisposition to breast cancer in our patients and attempt to understand the feasibility of incorporating genetic screening and educative counselling into patient management.

**Materials and Methods:** The patients for screening were selected in accordance with the American College of Medical Genetics and genomics (ACMG) guidelines for breast cancer predisposition. 362 patients had undergone treatment for breast cancer in our institute in 3 years, 185 patients were eligible for genetic testing, based on age of onset, breast cancer pathology and family history of cancer. Blood samples were collected from 26 patients who consented to genetic screening and tested for mutations in 350 selected genes related to hereditary cancer. Sequencing was carried out at a depth of 80–100X on Illumina platform. These were aligned to the GRCh37/hg19 human reference genome and analysed. Clinically relevant mutations were annotated using published variants in literature and clinical databases.

**Results:** 11 cases had no clinically significant variants. Five patients who were identified with significant variants as per ACMG guidelines had highly penetrant genes like BRCA1 (n = 2), BRCA2 (n = 2) and TP53 (n = 1) with protein truncating variants, frameshift or nonsense. The 185delAG founder mutation in BRCA1 was identified in one patient. 4 patients had two variants potentially associated with cancer predisposition. Amongst 15 variants of uncertain significance, four novel missense variations of uncertain significance were identified in BRCA1 and BRCA2 genes. Frameshift or splice-site variants were detected in low or moderate penetrance genes such as CHEK2, RAD51B and ATM. Protein truncating variations were detected in the MSH2 and MSH6 genes, commonly associated with colon cancer may represent a novel finding.

**Conclusion:** Comprehensive molecular screening for genetic predisposition can provide valuable understanding in disease pathology, help patient management and educate other high-risk individuals from the family, Understanding of genetic risk factors in Indian population, establishing testing modalities and indigenous clinical guidelines are required for optimum integration of genomic information into clinical practice. Genomics based precision medicine can be realized with a concerted effort in partnering scientific knowledge and clinical expertise to holistic management of the patient.

**No conflicts of interest**

**450** Poster

**A small molecule mediated modulation of autophagy flux down-regulated the angiogenesis and pro-survival pathway in aggressive breast cancer cells leading to non-apoptotic cell death**

F. Malik[1]. *[1]Indian Institute of Integrative Medicine, Pharmacology and Cancer Research, Jammu, India*

**Background:** In Heterogenic Breast cancer, Triple Negative (TNBC) subtype including Basal and Claudine-low are highly aggressive with no available target based therapy. It has been found that TNBC cells have higher basal autophagy levels compared to other subtypes. Although autophagy have paradoxical roles in promoting both cell survival and cell death, its exploitation to target TNBC could be promising strategy to design effective therapies. In order to understand role of autophagy on the cell fate and exploit it for effective therapeutics against TNBC, we used a potent chemical derivative of natural product "maganalol" (MI) to trigger autophagy in basal and Luminal breast cancer cells. Our studies demonstrate the autophagy flux induced by MI caused downregulation of wnt/β-catenin and inhibition of angiogenesis leading to non-apoptotic autophagy cell death.

**Material and Methods:** MTT for cell growth, Protein expression by western and IF. FACS analysis, western and microscopy for studying autophagy and apoptosis. Microvessel sprouting, aortic ring assays for angiogenesis.

**Results:** Our data demonstrated that MI treatment in breast cancer cells triggered robust autophagy by targeting AKT/mTOR axis leading to

activation of ATG13. MI triggered autophagy flux in MDAMB232 and T47D caused repression of Wnt/β-catenin signaling, inhibition of angiogenesis culminating into non-apoptotic autophagic cell death. Blocking autophagy by 3-methyladenine and siRNAs against LC3 and Beclin-1 significantly reversed the β-catenin signaling repression and cell death in MI treated cells. The combined knockdown of LC3 and Beclin-1 dramatically reversed the effect of MI on autophagic cell death and β-catenin signaling. It was further observed that autophagy induced by MI downregulates the angiogenesis using in vitro and ex vivo models. expression of angiogenic factors like VEGFR2, HIFα and HIFβ was downregulated with the MI triggered autophagy that however was restored in the presence of autophagy inhibitors. Furthermore, co-immunoprecipitation and co-localization results displayed enhanced interaction between β-catenin and LC3 at endogenous and physical level respectively. Further studies suggest that MI triggered autophagy and its interaction with ubiquitin system negatively regulates beta-catenin signaling leading to breast cancer cell death.

**Conclusions:** Serval studies have suggested that inhibition of basal autophagy in TNBCs can be a promising approach to target breast cancer. However, our study demonstrated that overburdening of autophagy can redirect the survival mechanism of autophagy towards death (type-II) in aggressive TNBCs or Luminal cancers with dysfunctional or resistant pro-apoptotic machinery. These studies further elaborate that novel therapeutic agents capable of triggering robust autophagy can be promising approach in targeting aggressive TN breast cancers.

**No conflicts of interest**

**451** Poster

**Optimizing the recurrent breast cancer treatment by detecting transformed molecular phenotype**

G. Botiralieva[1]. [1]*Pathologist, Pathology, Tashkent, Uzbekistan*

**Background:** Breast cancer is the first most common cancer among women in Uzbekistan with the highest mortality rate that made up 21%. In addition to these, the rate of recurrences constitute 79%. Among women with relapsed or metastatic breast cancer, the sites of cancer recurrence might have an estrogen-receptor (ER)/progesterone-receptor (PR) and/or HER2 status that is different from the primary tumor phenotype. Due to this, it is very important to take biopsies of relapsed sites for the determining optimal treatment options.

**Methods:** The research included examination and analysis of 128 samples of relapsed/metastatic breast cancer tumors and compared the ER/PR and HER2-receptor status with the status of the original tumor, using a large population-based database in the period from 2010 to 2014. All patients underwent special treatment at National Cancer Research Center of Uzbekistan.

**Results:** Overall, 87 of the 128 samples (68%) showed no change in either hormone-receptor or HER2 status. However, the remaining 41 tumor samples (32%) did exhibit changes in receptor status. Fourteen (11%) of these were local recurrences and 27 (21%) were regional or distant relapses. Among the 27 regional/distant relapses: 9 changed from ER/PR positive to ER/PR negative, 12 changed from ER/PR negative to ER/PR positive, 2 changed from HER2 negative to HER2 positive, 4 changed from HER2 positive to HER2 negative.

**Conclusion:** Our findings revealed that the changes in molecular phenotype between the primary and relapsed breast cancer are obvious. And the assessment of these changes in molecular phenotype routinely from the obtaining biopsies of recurrent sites could be an important factor in optimizing treatment.

**No conflicts of interest**

**452** Poster

**The level of apoptosis, proliferation and the adhesive properties of MCF-7 cells in 3D cultures in terms of its non-contact co-culture with T lymphocytes**

V. Nikulina[1], L. Garmanchuk[2], T. Nikolaienko[2]. [1]*Taras Shevchenko National University of Kyiv, Research Department, Kiev, Ukraine;* [2]*Taras Shevchenko National University of Kyiv, Institute of Biology, Kiev, Ukraine*

**Background:** Tumours in vivo represent heterogeneous cell population, which is regulated by humoral factors produced by cells into microenvironment. The most adequate models in vitro, which reflect processes in vivo, are 3 dimensioned (3D) cultures of tumor cells. Multicellular spheroids being the known model of avascular state of tumor development were compared with monolayer culture. The research aim was to investigate the effect of T lymphocytes on tumor cells MCF-7 via the system of cytokines, released by cells into cultural medium.

**Material and Methods:** MCF-7 cells (mammalian gland adenocarcinoma) were incubated in DMEM medium with 10% FBS, 2mM L-glutamine and 40 mg/ml gentamicin. Cells were non-contact co-culture with T cells for 48 hours at the standard conditions at 37ºC in humidified atmosphere with 5% $CO_2$. To generate spheroids, we added 0.24% carboxymethylcellulose to the cells of the total confluent and incubated them in 12-well low-adhesion plates. Cell cycle parameters and apoptosis were assessed by flow cytometry, survival in fractions was analyzed by counting in trypan blue, and adhesive potential was inferred from the percent of attached cells stained with crystalviolet.

**Results:** In the research there have been established strong paracrine effect of T cells on the level of apoptosis, proliferation and the adhesive properties of MCF-7 cells in 3D cultures in terms of its non-contact co-culture with T cells. It has been found that depending on the growth type of cells (in spheroids or in monolayer), their proliferation, apoptotic and adhesive levels have being affected by K-medium humoral factors significantly differ. In 2D culture system increase aforementioned characteristics was revealed: apoptosis (5.78 vs. 11.23%), adhesion level (in 1.5 fold) and proliferative G2/M+S pool (52.68 vs. 67.97), in comparison with corresponding control. In 3D culture system decrease was detected: apoptosis (7.46 vs. 4.11%), adhesion level (180 thous. vs. 120 thous. cells) and proliferative G2/M+S pool (56.69 vs. 47.31) ($p < 0.05$).

**Conclusions:** Thus, the reactivity of MCF-7 cells in response to humoral effect of K-medium depends on the culturing model (monolayer or spheroids). In vitro model of tumor micro-node on avascular stage of growth and the system of indirect humoral effect of immune cells on survival and proliferation of tumor cells have quite the opposite pattern of influence that can be applied in preclinical studies.

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**No conflicts of interest**

**453** Poster

**Tumor subtypes among breast cancer patients with diabetes**

H. Bronsveld[1], V. Jensen[2], J. Sanders[3], P. Vahl[2], S. Cornelissen[1], I. Hofland[1], I. De Rink[4], M. De Bruin[5], P. Vestergaard[6], M. Schmidt[1]. [1]*The Netherlands Cancer Institute, Division of Molecular Pathology, Amsterdam, Netherlands;* [2]*Aarhus University Hospital THG, Department of Pathology, Aarhus, Denmark;* [3]*The Netherlands Cancer Institute, Division of Pathology, Amsterdam, Netherlands;* [4]*The Netherlands Cancer Institute, Microarray and sequencing facility, Amsterdam, Netherlands;* [5]*Utrecht University, Division of Pharmacoepidemiology & Clinical Pharmacology, Utrecht, Netherlands;* [6]*Aalborg University, Departments of Clinical Medicine and Endocrinology, Aalborg, Denmark*

**Background:** Diabetes mellitus (DM) and insulin treatment have been associated with increased breast cancer (BC) risk. DM itself and/or insulin treatment might be associated with the development of specific BC subtypes and subsequent differential survival. Our aim is to investigate whether DM patients develop specific BC subtypes compared to non-DM patients.

**Materials and Methods:** This retrospective study randomly selected, through the Danish Breast Cancer Cooperative Group, invasive BC patients diagnosed in 2000–2010. 43,701 women with incident BC were identified, of whom 3,047 had DM (7.0%). Selection was stratified by age (⩽50, >50 years) at BC diagnosis and for each BC case with DM, 2 non-DM patients were matched on year of birth and 10-years age of BC diagnosis categories, in order to select 300 patients.

Tissue Micro Arrays (TMA) were stained by immunohistochemistry (IHC) for; ER, PR, HER2, Ki67, CK5/6, CK14, p63, and for IHC markers in proliferation versus glucose metabolism pathways; EGFR, AR, p-Erk, p-ER, p-Akt, p-mTOR. A pathologist scored all TMAs and revised tumor histological type and grade. Associations between DM and IHC markers were analyzed using multivariate logistic regression. RNA sequencing is being performed for tumors with tumor nuclei% ⩾40; and data will be analyzed by hierarchical and supervised by DM status clustering.

**Results:** Patients with DM (n = 211) had developed more breast tumors with grade 3 compared to non-DM patients (n = 101, 44.1% vs 30.0%, p = 0.03), while no significant differences were observed between tumor size (median: 20 mm), number of positive lymph nodes and the histology type. DM patients with a BC diagnosis ⩽50 years had more often ER-negative (25.2% vs 11.8%, p = 0.05), PR-negative (38.1% vs 17.7%, p = 0.01), HER2-negative (89.0% vs 74.5%, p = 0.02) and CK5/6 positive (17.8% vs 5.9%, p = 0.04) tumors than their non-DM counterparts. After adjustment for BMI, the association between DM and PR-negative or HER2-negative tumors in women with a BC diagnosis ⩽50 years was still significant (p = 0.02, p = 0.04). No association was found between any of the tumor markers and DM in women diagnosed with BC >50 years. The proliferation/glucose metabolism markers are stained and scored, results

will be available at the conference, as well as RNA sequencing results. Preliminary results show that DM patients with a BC diagnosis ⩽50 years had more often AR-negative tumors (35.8% vs 16.3%, p = 0.01).

**Conclusions:** DM patients diagnosed with BC ⩽50 years tend to develop breast tumors that do not express hormonal receptors, which are typically associated with poor prognosis, as compared to their non-DM counterparts. Subtyping by other markers and gene expression profiles might elucidate more subtle differences within pathway activation of the tumor. Our results warrant further investigation, including the use of insulin analogues, and BC survival.

**Conflict of interest:** Other Substantive Relationships: The research leading to the results of this study has received funding from the European Community's Seventh Framework Programme (FP-7) under grant agreement number 282526, the CARING project. The funding source had no role in study design, data collection, data analysis, data interpretation or writing of this abstract.

**454** Poster

**In vitro 3D growth breast cancer system as a model for antitumor drugs screening**

T. Nikolaienko[1], L. Garmanchuk[1], Y. Stupak[1]. [1]*Taras Shevchenko National University of Kyiv, Institute of Biology, Kiev, Ukraine*

**Introduction:** Gene expression profiles in spheroid cultivated cells are more similar to natural tumors, than profiles of the same cells in monolayer culture. Tumor spheroids are heterogeneous cellular aggregates that, when greater than 500 μm diameter, are frequently characterized by hypoxic regions and necrotic centers. Architecture of three-dimensionally (3D) propagated cells is very similar to avascular tumor areas. The gradient of diffusion in cell aggregates leads to reduced proliferation rates and increased drug resistance. The purpose of the work was to conduct a comparative study between 3D and monolayer growth systems of MCF-7 cells, and prove the value of spheroid model.

**Materials and Methods:** The standard method was used for multicellular spheroid generation. MCF-7 cells proliferation activities were measured by MTT-test, and in flow cytometry. Cells were cultivated in 2D and 3D growth. Two variants culture media were used: complete (with 10% FBS), and incomplete (without serum).

**Results:** MCF-7 cells growth parameters differ significantly in 2D and 3D growth systems. Cells in 2D system are more sensitive to serum starvation then 3D cultures. Cell viability increases dramatically in 3D system. The level of apoptotic and necrotic cells for 2D growth in serum starvation conditions (39.2±7.3% and 33.5±2.8% respectively) were twice increased in comparison with conditions of complete culture medium (19.0±1.3% and 11.4±1.7% respectively), whereas incomplete medium have no detectible effects on 3D cultured cells. However, the 3D cells percentage in $G_0/G_1$ phase of the cell cycle was increased in 1.6 times in serum free conditions, whereas it was not changed in complete medium that can indicate similarity to natural tumors.

**Conclusions:** Three-dimensional (3D) spheroids are therefore considered valid models to recapitulate tumor features due to increased spheroid survivability.

**No conflicts of interest**

## Friday, 11 March 2016

**POSTER SESSION**

# Follow up

**455** Poster

**The use of a brochure to enable CAM-with-chemotherapy patient education**

P. Smith[1,2], A. Clavarino[1], J. Long[2], K. Steadman[1]. [1]*The University of Queensland, School of Pharmacy, Brisbane, Australia;* [2]*Nambour General Hospital, Sunshine Coast Cancer Care Services, Nambour, Australia*

**Background:** This study aimed to find if the availability of a purpose-designed complementary and alternative medicine (CAM) brochure within a cancer service aided doctors' discussions with their patients on the effects of CAM, helped patients understand the effects of CAM during their chemotherapy treatment and saved doctor consultation time.

**Methods:** Cancer-care doctors consulting in an adult day unit completed a structured post-intervention feedback survey form. Cancer patients receiving chemotherapy treatment were provided the brochure and completed the local health service consumer testing feedback form.

**Results:** All cancer care doctors (n = 17) perceived a need for the brochure, and recommended the brochure to their patients. All doctors thought the brochure made it easier for them to discuss CAM with their patients and 59% answered it saved them time during patient consultations. 90% of cancer patients (n = 30) reported the brochure had enough information to answer their CAM questions and all patients thought the brochure's information easy to read and understand.

**Conclusions:** An evidence-based CAM-with-chemotherapy patient brochure enabled cancer-care doctors to discuss CAM with their patients, answered patients' CAM questions and may save consultation time.

**No conflicts of interest**

**456** Poster

**Long term results of prognostic factors of regional recurrence in node negative breast cancer**

T. Mehmood[1]. [1]*Shaukat Khanum Memorial Cancer Hospital and Research Centre, Radiation Oncology, Lahore, Pakistan*

**Background:** The aims of this study is to evaluate long-term clinical results of node-negative breast cancer and predicting factor of regional recurrence of node-negative breast cancer such as axillary or supraclavicular lymph node recurrence.

**Methods:** A total 619 node-negative breast cancer patients who received breast cancer surgery such as breast conserving therapy (BCT) or total mastectomy with sentinel lymph node biopsy (SLNB) from January 1995 to December 2010 were enrolled in this study. The enrolled patients were divided into two group, non-recurrent group and recurrent group. Their medical records were retrospectively reviewed including clinico-pathological characteristics and Memorial Sloan Kettering Cancer Center (MSKCC) sentinel lymph node metastasis nomogram score.

**Results:** Mean age of study patients were 53 years and median follow up period was 69 months (range 0–144 months). All patients had received SLNB and confirmed node-negative breast cancer. 5-years and 10-years disease-free survival were 94.1% and 91.7% respectively. A total 5.3% of the patients were detected to have relapsed. Regional recurrence in 1.9% patients, local recurrence in 1.4% patients, and systemic recurrence in 2.0% of the patients. Lymphovascular invasion 25.3% vs 54.5% (p = 0.029)] and MSKCC nomogram score [37.10±22.25 vs 57.36±26.84 (p = 0.031)] were significant higher in regional recurrent group than non-recurrent group.

**Conclusion:** Lymphovascular invasion and MSKCC nomogram score will be helpful in predicting the regional recurrence of node-negative breast cancer.

**No conflicts of interest**

**457** Poster

**Triple negative breast cancer: A single center experience**

T. Mehmood[1]. [1]*Shaukat Khanum Memorial Cancer Hospital and Research Centre, Radiation Oncology, Lahore, Pakistan*

**Background:** Triple-negative breast cancer (TNBC) represents a heterogeneous group of breast cancers that do not express estrogen receptor, progesterone receptor and human epidermal growth factor receptor 2 receptors. Generally, these tumors are aggressive and more common in younger women, in which an association of TNBC with mutations in the BRCA1 gene was documented. The aim of our study was to create a representative group of patients with TNBC, which could be analyzed and the data gathered to build basic epidemiological, molecular and clinical characteristics of TNBC.

**Methods:** We retrospectively studied 516 patients diagnosed and/or treated for TNBC at our institute between 1995 and 2010. Some clinical-pathologic/molecular correlations were performed to identify different subsets of TNBC and groups of patients who may potentially benefit from different modes of anticancer therapy.

**Results:** The median age of patients with TNBC was 56 years (range 25−88 years). A total of 18% of TNBC cases were diagnosed in patients under the age of 34, another 44.5% and 37.5% of cases were in the age group of 35 to 44 years and up to 70 years, respectively. 'Basal-like' carcinomas accounted for 75% of TNBC. We confirmed the aggressive nature of this disease: in the median follow-up period of 7.7 years, we observed a relapse in 27.2% of patients: 71% of deaths due to disease progression occurred within 2 years after diagnosis of the disease. Treatment strategies include chemotherapy, in most cases (88.9%). Chemotherapy was mostly based on regimens with anthracyclines or in combination with taxanes. 7 year OS and DFS were 51% and 40% respectively. The most important negative prognostic factors in relation to disease specific OS were: higher clinical stage and 381 pT (both-p < 0.0001), pN-positive status (p < 0.001), absence or early withholding

of chemotherapy ($p < 0.001$) and minimal disease response to neoadjuvant treatment ($p = 0.005$).

**Conclusion:** TNBC is an aggressive form of breast cancer, which may occur in patients of all ages, but more frequently in younger patients. Early detection and intensive treatment of these tumors gives a high chance of cure. BCL2 expression analysis could facilitate decision making on adjuvant treatment in TNBC patients. Better therapeutic results can be expected from targeted therapy.

**No conflicts of interest**

**458** Poster

**Retrospective analysis of factors affecting survival in Egyptian patients aged ⩾65 years with non metastatic breast cancer**

M. Kamal[1], A. Nagy[1], M. Kelany[1]. *[1]Ain Shams University, Clinical Oncology Department, Cairo, Egypt*

**Background:** The management of the elderly patient with breast cancer (BC) is a challenge for several reasons. Elderly women have been underrepresented in clinical trials despite that the incidence of BC increases with age and the section of elderly women in the population continue to enlarge. This study assessed the effect of clinicopathological characteristics on the outcome of elderly patients with BC.

**Material and Methods:** This study conducted in Department of Clinical Oncology, Ain Shams University, Egypt. Medical records of women aged ⩾65 years with BC between January 2010 and December 2012 were reviewed. Survival outcome was described using Kaplan–Meier curves and the association of clinico-pathological characteristics with overall (OS) and disease free survival (DFS) was assessed.

**Results:** A total of 103 patients were analyzed. Median age was 70 years (SD ±5.490, Range 65−88). About 87.4% of the tumors were invasive ductal carcinoma (IDC), 7.8% were invasive lobular carcinoma (ILC) and 3.8% were of other pathologies. About 1.9%, 67% and 31.1% of the tumors were grade I, II and III respectively. Median tumor size was 3.5 cm (SD ±1.414, Range 1−7). Median number of positive axillary lymph nodes (ALN) was 3 (SD ±4.836, Range 0−19). Median ratio of positive ALN to removed LN (LNR) was 0.3 (SD ±0.397, Range 0−1). Regarding receptor expression, 14.6% were HER-2+, 71.8% were ER+ and about 24% were triple negative. About 19.4% of the patients received taxanes with anthracyclines as adjuvant combination regimen.

Median DFS was 18 months (SD ±12.124, Range 1−60) and the median OS was 30.5 months (SD ±13.972, Range 2−60). DFS was 19 months (95% CI 17.239–20.671) in patients with IDC versus 12 months (95% CI 10.326–13.674) in patients with other pathologies ($p = 0.008$). DFS in patients with >3 positive ALN was 13 months (95% CI 9.079–16.921) but in those with ⩽3 was 19 months (95% CI 16.301–21.699) ($p = 0.038$). DFS in patients with LNR >0.3 was 13 months (95% CI 9.463–16.537) but was 19 months (95% CI 16.581–21.419) in those with LNR ⩽0.3 ($p = 0.041$).

OS was 31 months (95% CI 27.840–34.160) in patients with IDC versus 19 months (95% CI 14.474–23.526) in patients with other pathologies ($p = 0.013$). OS in patients with >3 positive ALN was 26 months (95% CI 19.882–32.118) but in those with ⩽3 was 32 months (95% CI 27.970–36.030) ($p = 0.005$). OS in patients with LNR >0.3 was 25 months (95% CI 17.449–32.551) but was 32 months (95% CI 28.124–35.876) in those with LNR ⩽0.3 ($p = 0.007$).

**Conclusion:** This study highlights the importance of contribution of elderly patients in clinical trials. The elderly patients with BC could present with high lymph nodes burden which significantly affects the OS and DFS.

**No conflicts of interest**

**459** Poster

**Study of serum interleukin 18 and nitric oxide levels as prognostic markers in breast cancer patients, and their relation to different treatment modalities**

M. Eldeeb[1], A. Nomair[1], G. Khedr[2], R. Rashidy[3], H. Nomair[4]. *[1]Lecturer Medical Research Institute, Chemical Pathology, Alexandria, Egypt; [2]Lecturer Faculty of Medicine, Oncology, Alexandria, Egypt; [3]Alexandria University Student Hospital, General Surgery Department, Alexandria, Egypt; [4]Faculty of Medicine, Medical Biochemistry Department, Alexandria, Egypt*

**Background:** Etiology of breast cancer is mostly hormonal related with other modifying risk factors. The molecular mechanisms linking inflammation and tumorigenesis remained elusive. The role of IL-18 in cancer progression and metastasis remains controversial with insufficient data in the Egyptian population. Thus we aimed to study the rule of IL-18 as a prognostic marker in a group of Egyptian females with breast cancer and its relation to different treatment modalities.

**Material and Methods:** Case–control study was carried on 29 cancer breast female patients and comparable 15 controls. Follow up of patients were done at three and six months after completion of their planned treatment, assessments were done including: clinical, radiological examinations (if needed) and laboratory work-up (IL-18, CA 15-3, Nitric oxide).

**Results:** IL18 had significant higher values in patients preoperatively than controls ($p < 0.001$) and no significant differences between the different time intervals. IL18 had negative significant correlation with CA15.3 ($r = -0.433$, $p = 0.019$) at three months post treatment, and negative correlation with NO both in three and six months post treatment ($r = -0.436$, $p = 0.018$ and $r = -0.433$, $p = 0.019$) respectively. IL18 had significant negative correlations with CA 15.3 in relapsed cases ($r = -0.821$, $p = 0.023$). Both NO and CA15.3 had the highest overall performance to predict relapse six months post treatment ($p = 0.039$).

**Conclusion:** IL18 could have a possible role as a prognostic marker in breast cancer patients with a larger scale and a longer period of follow up needed.

**No conflicts of interest**

Table (abstract 459).

| | Cases | | | Controls |
|---|---|---|---|---|
| | Preoperative | After 3 months | After 6 months | |
| IL18 (pg/ml) | 163.47 (60.02–1187.23) | 163.96 (5.47–704.38) | 188.89 (44.70–902.57) | 112 (40.05–400.78) |
| P [a] | – | – | – | <0.001* |
| $P_1$ [b] | – | 0.496 | 0.112 | – |
| CA 15.3 (U/L) | 33.50 (0.03–80.80) | 22.50 (8.50–80.30) | 20.80 (1.60–47.30) | 12.60 (1.56–32.40) |
| P [a] | – | – | – | <0.001* |
| $P_1$ [b] | – | 0.567 | 0.013* | – |
| NO (μmol/L) | 290.45±126.28 | 3962.42±1722.82 | 54057.59±23503.67 | 62.5±23.2 |
| P [a] | – | – | – | <0.001* |
| $P_1$ [b] | – | <0.001* | <0.001* | – |

[a] P: Statistical significance of difference between patients preoperatively and controls.
[b] $P_1$: Statistical significance of difference between patients preoperatively and three and six months postoperatively.
*Statistically significant − $p \leqslant 0.05$.

**460** Poster

**Using oral chemotherapy regimen for increasing patient outcome and resources utilization in metastatic breast cancer patients: Cost-effectiveness study**

A. Abotaleb[1]. [1]*Health Economist & Technical Advisor, Ministry of Health, Cairo, Egypt*

**Background:** The interest of oral drugs in the management of cancer patients is growing. The rationale intended for this study is to determine the cost effectiveness of vinorelbine oral plus capecitabine oral against docetaxel IV plus capecitabine oral in metastatic breast cancer in the Egyptian patients from the national fund perspective over a time horizon of 3 years.

**Objective:** The main objective behind conducting this study was to evaluate echonomic evaluation and increasing patients outcomes with resources utilization through the cost-effectiveness study of vinorelbine oral capsule plus oral capecitabine versus docetaxel iv plus oral capecitabine in treatment of metastatic breast cancer, in the Egyptian patients previously treated with anthracycline, from the national fund perspective over a time horizon of 3 years.

**Methods:** A cost-effectiveness analysis from the perspective of the Ministry of Health and Population was conducted. A Markov model was applied with three health states. Utility data were incorporated in the model to make adjusted results. Costs used were the local ones according to the national fund list. Discounting was applied at 3.5% annually both on costs and benefits. The results obtained were in term of ICER and number of QALYs. Robustness of our findings was checked using sensitivity analyses. Results are expressed in QALYs.

**Results:** During the three-year time horizon, for vinorelbine oral 2015 exchange rate: 0.13 with a 2.46QALY gained. Versus 0.84 QALY gained for docetaxel IV. That yields a difference of 1.62 in QALY. Vinorelbine oral is economically dominating the docetaxel strategy, producing more benefit at a lower cost.

The one-dimensional sensitivity analysis indicated that the overall survival medians of both drugs had the largest impact on the results. When conducting sensitivity analysis using plausible ranges, Vinorelbine oral remained economically dominant in all cases.

**Conclusions:** The introduction of oral chemotherapy regimen in metastatic breast cancer vinorelbine oral to the national fund Pay-at-The-Expense-of-the-State (PTES) system was likely be cost saving based strictly from its perspective and saving for budget will lead to resources subsidization and better patients outcomes.

The clinical data were derived from Campone, 2013 and adjusted for quality of life.

**No conflicts of interest**

**461** Poster

**Nipple-sparing mastectomy in breast cancer patients − predictors of postoperative complications and reconstruction outcomes**

M. Ranisavljević[1], Z. Radovanović[1], A. Golubović[1], F. Vicko[1], M. Đurić[1], D. Lukić[1]. [1]*Oncology Institute of Vojvodina, Operative Oncology, Novi Sad, Serbia*

**Introduction:** Nipple spearing mastectomy (NSM) and immediate breast reconstruction improve aesthetic outcomes and quality of life after mastectomy. Aim of our study was to analyze outcomes of immediate breast reconstruction with silicone implants after NSM and to identify risk factors for surgical complications.

**Materials and Patients:** This single institutional retrospective study included 435 patients with 441 procedures during nine years (2004–2012). Median follow-up was 79 (IQR 34–141, SD 28) months. Surgery was the primary treatment for breast cancer in 252 (57.93%) patients. 117 (26.90%) primary reconstructions were made after neoadjuvant chemotherapy while 66 (15.17%) patients previously had breast conserving surgery followed by adjuvant radiotherapy. Patients were regularly followed and all early and late complications after surgery were recorded.

**Results:** The overall early complication rate was 63 (14.3%), and included: major skin flap necrosis 13 (2.9%), minor skin flap necrosis 11 (2.5%), nipple necrosis 1 (0.2%) and epidermolysis 2 (0.5%), infection 16 (3.6%), prolonged seroma formation 12 (2.7%), hematoma 3 (0.7%) and prosthesis transposition in 5 (1.1%) cases. Capsular contracture as a late complication was identified in 33 (7.5%) cases. In 26 (5.9%) reconstruction procedures explantation of prosthesis was done due to early surgical complications. Preoperative chemotherapy, diabetes mellitus and increased body mass index were associated with higher rate of complications ($p \leqslant 0.05$). Preoperative radiotherapy, smoking, higher volume of silicone implants ($\geqslant$500 cc) and previous breast operations were not associated with higher rate of complications.

**Conclusion:** Nipple-sparing mastectomy with primary silicone implant reconstructions has a low rate of complications. Preoperative chemotherapy, diabetes mellitus and increased body mass index are predictors of complications.

**No conflicts of interest**

**462** Poster

**Communication in oncology: Is there ageism?**

S. Schroyen[1], P. Missotten[1], S. Adam[1], G. Jerusalem[2], A.L. Giraudet[3], M. Marquet[1]. [1]*Université de Liège, Psychology of Aging Unit, Liège, Belgium;* [2]*CHU, Department of Medical Oncology, Liège, Belgium;* [3]*Université de Liège, Faculty of Speech Therapy, Liège, Belgium*

**Background:** "Elderspeak" (or "baby talk") is a kind of speech characterized by speaking slower and/or louder, using simplified sentences, a patronizing tone etc., when talking to an elderly individual (Caporael, 1981). It is not without consequences for older people: they can feel powerless and experience lower self-esteem. This study has two objectives: (1) to analyze if more characteristic of elderspeak is observed when participants have to explain a treatment to older patients in comparison to younger ones; (2) to observe if elderspeak is linked to aging view: our hypothesis is that participants with a negative vision of aging will speak with more characteristics of elderspeak.

**Material and Methods:** Participants were 20 physicians and 20 students in medicine. They have to record a podcast where they explain hormonotherapy to a fictional patient, suffering from a breast cancer. On this aim, they receive two clinical vignettes: the clinical situation is similar but in one case the patient is 40 years old and in the other case 70 years old. Then, they complete some anamnestic information and two scales to assess their aging vision (the FSA-R and the Aging Semantic Differential). We then analyze several measures of speech, as verbal fluency, grammatical complexity, semantic content and vocal analysis.

**Results:** First of all, concerning characteristics of elderspeak, paired t test show that the number of words is smaller ($p = 0.048$), the mean length of utterance (MLU) is shorter ($p = 0.003$), the debit is slower ($p = 0.027$) and there is more repetitions ($p = 0.003$) when participants talk to older patients in comparison to younger ones. By contrast, the number of sentences is the same ($p = 0.23$), there is no difference concerning grammatical complexity ($p = 0.44$), lexical diversity ($p = 0.57$) and of the highest, lowest and mean pitch (all $p > 0.06$). Secondly, concerning aging view, results show that participants with a positive aging view made a bigger difference of MLU and debit between a 40- and a 70-year-old patient, in comparison to participants with a more negative aging view.

**Conclusions:** Participants with a positive aging view seem to adjust their speech to older patients. In this way, we can talk about "benevolent ageism": basis on their stereotypes of aging, participants speak slower and reduced their sentences. These changes had certainly a good intention: it's expecting to enhance speech comprehension. However, previous studies has shown that such adjustments have negative consequences for elderly: it brings negative self-assessments of communicative competence (Kemper and Harden, 1999).

**No conflicts of interest**

**463** Poster

**Changes in cardiovascular risk profiles among young Chinese patients with breast cancer after adjuvant chemotherapy**

W. Yeo[1], F. Mo[1], J. Suen[2], E. Pang[1], C. Yip[1], K. Lee[1], G. Liem[1]. [1]*Chinese University of Hong Kong, Clinical Oncology, Hong Kong, Hong Kong;* [2]*Prince of Wales Hospital, Clinical Oncology, Hong Kong, Hong Kong*

**Background:** Adjuvant chemotherapy improves survival of patients with Early Stage Breast Cancer (ESBC). However, it may be associated with long term toxicities. Among young Asian women with ESBC, there is limited data on the incidence of changes in cardiovascular risk profiles after having received adjuvant chemotherapy.

**Patients and Methods:** Premenopausal Chinese patients with ESBC were recruited into this cross-sectional study. Eligibility criteria include breast cancer (BC) patients of stage I-III, younger than 45 years at diagnosis of BC, having received adjuvant chemotherapy, within 3−10 years after the diagnosis of BC. The data on body mass index (BMI) and blood pressure were collected from the report in patients' files at diagnosis and measured at recruitment. The Lipid Profiles were determined by fasting blood test at recruitment.

**Results:** A total of 286 patients were recruited; the median time from breast cancer diagnosis to study entry was 5.0 years. With regards to BMI, the proportions of patients who were underweight vs. normal vs. overweight vs. obese at BC diagnosis were 12% vs. 72% vs. 14 vs. 2%; the corresponding figures at study recruitment were 4% vs. 66% vs. 25%

vs. 5%. For patients who had increased BMI vs. those who maintained their BMI at study recruitment, % with hypercholesterolaemia were 91% vs. 9% (p = 0.002), and % with hypertriglycidaemia were 96% vs. 4% (p = 0.006). Similar trends were observed for % with abnormal LDL (86% vs. 14%, p = 0.44) and abnormal HDL (90% vs. 10%, p = 0.12), although the differences were not statistically significant. With regards to the relationship between BMI and hypertension, there were significantly more patients with hypertension in patients who became overweight and obese than those with normal BMI (47% vs. 29%, p = 0.02).

**Conclusion:** At a median of 5 years after BC diagnosis and adjuvant chemotherapy, there was a higher % of patients who became overweight or obese. When compared with patients who maintained their BMI after adjuvant chemotherapy, the lipid profiles revealed that there were significantly more hypercholesterolaemia and hypertriglyceridaemia among those who had increased BMI. More patients with higher BMI developed hypertension when compared with those of normal BMI. Further research is needed to assess possible associated factors such as changes in lifestyle and menopausal status in addition to age.

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**No conflicts of interest**

**464** Poster

### Is breast ultrasonography required for follow-up after breast-conserving therapy for breast cancer?

T. Sato[1], I. Muto[1], M. Kira[2], T. Miyazaki[2]. *[1]Niigata Prefectural Central Hospital, Surgery, Joetsu City- Niigata, Japan; [2]Niigata Prefectural Central Hospital, Clinical Laboratory, Joetsu City- Niigata, Japan*

**Background:** Although an annual mammogram (MMG) is recommended for follow-up after breast-conserving therapy (BCT) for breast cancer (BC), whether breast ultrasonography (US) is required to detect ipsilateral breast tumor recurrence (IBTR) or new primary BC remains to be determined.

**Materials and Methods:** In 238 BC patients after BCT, annual US (486 times: once, 53 patients; twice, 122 patients; three times, 63 patients) in addition to MMG was performed by trained medical technologists (MT) from January 2013 to September 2015. The patients' characteristics were as follows: age 32−91 (mean 62.3, median 63); BCT breasts, 248; intact breasts, 221; node positive, 42 (17.6%); non-invasive carcinoma, 39 breasts; margin status negative, 74.2%; close (up to 5 mm), 18.1%; positive (exposed), 7.7%; breast irradiation, 94%; systemic therapy, 89.1%.

**Results:** The average period from the BCT operation to the first US was 41.8 months (6–159, median 38 mo). After the first US, two patients developed distant metastases. One died of another cause. US detected only one non-palpable axillary lymph node recurrence, but there was no IBTR among the patients during the period. Among the 486 US, abnormal findings were detected 52 times by the MT; however, in 43 of these 52 times, the findings were diagnosed as benign by breast surgeons. Breast needle biopsies were performed 9 times in these 52, but no malignancy was diagnosed.

**Conclusions:** Breast US for follow-up after BCT did not detect any IBTR or new primary BC, but increased unnecessary biopsies; therefore, US is not required for follow-up after BCT for BC.

**No conflicts of interest**

**465** Poster

### Comparison of treatment variations in old age breast cancer in two units of a metropolitan city in the United Kingdom

L. Romics[1], G. Bentley[2], D. Kipgen[3], E. Mallon[3], S. Stallard[4], J. Doughty[4]. *[1]New Victoria Hospital, Surgery, Glasgow, United Kingdom; [2]Managed Cancer Network, Breast Cancer, Glasgow, United Kingdom; [3]Queen Elizabeth University Hospital, Pathology, Glasgow, United Kingdom; [4]Gartnavel General Hospital, Surgery, Glasgow, United Kingdom*

**Background:** Treatment of patients with old age breast cancer is widely varied and depends on numerous factors including tumour biology and stage, comorbidity, frailty, patients' choice and surgeons' preference. We retrospectively compared the management of old age patients with breast cancer in two neighbouring breast units in a metropolitan city in the United Kingdom.

**Methods:** Management of patients diagnosed with old age breast cancer between 2009 and 2013 were compared. All data were collected prospectively within the West of Scotland Managed Cancer Network. Pathological characteristics and treatment provided within each unit were analysed focusing on hormonal therapy only or surgery as part of the management. Results were compared using two-tailed Z-test.

Table 1. Comparison of management of old age breast cancer in two neighbouring units in a UK metropolitan city

| | | Hormone only | Surgery |
|---|---|---|---|
| Unit 1 | 2009 | 97/17 (17.5%) | 97/77 (79.4%) |
| Unit 2 | 2009 | 101/38 (37.6%) | 101/60 (59.4%) |
| P-value | | **0.00158** | **0.00236** |
| Unit 1 | 2010 | 95/15 (15.8%) | 95/74 (77.9%) |
| Unit 2 | 2010 | 101/38 (37.6%) | 101/60 (59.4%) |
| P-value | | **0.00058** | **0.00544** |
| Unit 1 | 2011 | 97/20 (20.6%) | 97/74 (76.3%) |
| Unit 2 | 2011 | 90/29 (32.2%) | 97/58 (59.8%) |
| P-value | | 0.07186 | **0.0139** |
| Unit 1 | 2012 | 111/28 (25.2%) | 111/77 (69.4%) |
| Unit 2 | 2012 | 92/29 (31.5%) | 92/59 (64.1%) |
| P-value | | 0.32218 | 0.42952 |
| Unit 1 | 2013 | 87/14 (16.1%) | 87/69 (79.3%) |
| Unit 2 | 2013 | 87/27 (32.5%) | 87/52 (59.8%) |
| P-value | | **0.01242** | **0.00512** |

**Results:** 3850 patients were treated with breast cancer in the two units during this five-year period of time. 954 patients were 70 years or older at the time of diagnosis. 718 patients (75.3%) had ER positive/Her-2 negative combination of cancer, with no significant differences within the two units. Similar number of patients with old age breast cancer was treated in the units (487 and 471). Unit 1 treated significantly lower proportion of old age breast cancer patients with hormonal therapy only (94; 19.3%) than Unit 2 (161; 34.2%) (p = 0) (Table 1). Unit 1 operated on significantly more patients with old age breast cancer (371; 76.2%) than Unit 2 (289; 61.3%) (p = 0). When patients underwent surgery, mastectomy rates were almost identical (50.1% and 51.2%; p = 0.944).

**Conclusion:** Significant variation of treatment in old age breast cancer was found in two neighbouring breast units. Since these two units work in close geographical proximity it is unlikely that comorbidity, frailty or deprivation would be significantly different, although these need to be looked at. Decision-making on the multidisciplinary meetings should be examined in the future.

**No conflicts of interest**

**466** Poster

### Conditional disease-free survival among patients with breast cancer

H.J. Paik[1], S.K. Lee[1], J.M. Ryu[1], S. Park[1], H.W. Yi[1], S.Y. Bae[1], J. Yu[1], J.E. Lee[1], S.W. Kim[1], S.J. Nam[1]. *[1]Samsung Medical Center, Department of Surgery, Seoul, South Korea*

**Background:** Conditional disease-free survival (CDFS) reflects changes in progress over time. As traditional disease-free survival is estimated from the date of diagnosis, it has a limitation to measure the risk of recurrence in patients who have already been disease-free for a period of time. In this study, we determined CDFS of breast cancer patients and estimated the prognostic factors of disease-free survival (DFS) in these patients.

**Material and Methods:** The study retrospectively reviewed clinical data of 7,587 consecutive patients who underwent curative surgery for breast cancer between January 2004 and December 2013 at Samsung medical center. Univariate and multivariate analysis were done for risk factors of DFS. DFS was computed by Kaplan–Meier method. CDFS rates were based on cumulative DFS estimates.

**Results:** Median DFS was 19.14 months (range, 0.33–110.56 months) and 3-year DFS at baseline was 93.46%. 3-year CDFS survival estimates for patients who had already been disease-free for 1, 2, 3, 4 and 5 years after treatment, were calculated as 92.84%, 92.37%, 93.03%, 89.41% and 79.64%, respectively. In the hormone receptor (HR) negative group, after 1 year of DFS, 3-year CDFS continuously increased each year. However, in the HR positive group, 3-year CDFS continuously decreased each year.

**Conclusions:** HR positive patients require a continuous care during surveillance period and metastases workup can be considered after 2-year of disease-free, which is not recommended in current guidelines. On the other hand, saving social cost can be possible in HR negative patients by stretching the surveillance period. Also further study is still required to find prognosis indicator of DFS in breast cancer.

**No conflicts of interest**

**467** Poster

**Acute coronary events after breast irradiation based on planned mean heart dose**

B.D.P. Ta[1], A.B. Bouma[1], A.M.H. Middag[1], E.J. Bantema-Joppe[1], L.V. Van Dijk[1], F.B.J. Van Dijk-Peters[1], G.H. De Bock[2], A.J. Berendsen[3], J.A. Langendijk[1], J.H. Maduro[1], A.P.G. Crijns[1]. *[1]University Medical Center Groningen, Radiation Oncology, Groningen, Netherlands; [2]University Medical Center Groningen, Epidemiology, Groningen, Netherlands; [3]University Medical Center Groningen, General Practice, Groningen, Netherlands*

**Background:** The prevalence of breast cancer (BC) survivors has increased due to early detection and improved treatment modalities including radiotherapy (RT). Consequently, acute coronary events (ACEs) attributable to cardiac irradiation will become increasingly relevant. Darby et al found a linearly increased ACE rate of 7.4%/Gy mean heart dose (MHD). In this study we compared the observed versus the expected number of ACEs based on planned MHD.

**Material and Methods:** Stage I−III BC patients, treated with three-dimensional conformal RT with a simultaneous integrated boost after breast-conserving therapy between 2005–2008, were included. Primary endpoint was the occurrence of an ACE, i.e. unstable angina, myocardial infarction, coronary revascularization and death due to ischemic heart disease (IHD). Observed events were extracted from hospital and general practitioners' records. The expected number of ACEs following RT was calculated, based on the individual patient's age, risk factors (RF) for IHD and MHD at baseline, according to Darby's tables. Chi-square and logistic regression analyses were used to identity prognostic factors for an ACE.

**Results:** The analysis included 1031 BC patients. Median age was 59 years (range 27−98). Median follow-up was 6.5 years (0.1–10.2). The median MHD was 3.5 Gy (0.4−27). Median MHD was 6.7 Gy (1−27) for left-sided and 1.9 Gy (0.4–10.6) for right-sided BC. The observed and expected ACEs are shown in Table 1. Thirty-three (3.2%, 95% CI 2.2−4.2) patients had $\geqslant$1 ACE, whereas 21.25 (2.0%) were expected ($p < 0.05$). Median time to the first ACE was 4.6 years (0.4−9.8). Nineteen (58%) patients had their first ACE <5 years following RT. Prognostic factors were higher age per year (HR 1.08, 95% CI 1.05–1.13, $p < 0.001$) and $\geqslant$1 RF at baseline (HR 5.97, 95% CI 1.8–19.9, $p = 0.004$).

Table 1. Observed versus expected number of ACEs in 1031 patients

| | Number of ACEs |
|---|---|
| Expected events at 10 years following RT | |
| expected without RT | 20.58 |
| expected due to RT based on Darby's model | 0.67 |
| total expected | **21.25** |
| Observed events at medium 6.5 years follow-up | **33** |

**Conclusions:** The observed number of ACEs following RT was significantly higher than expected among BC survivors. This may be explained by better survival outcome after BC in this cohort compared to that in the Darby cohort. This could be due to less competitive risks or more cardiotoxic effects of systemic agents.

**No conflicts of interest**

**468** Poster

**The development of an on-line decision tool for health care professionals to aid collaborative decision making with older women with breast cancer**

M. Burton[1], F. Armitage[2], K. Collins[1], P. Richards[3], A. Nettleship[4], K. Lifford[5], L. Wyld[2]. *[1]Sheffield Hallam University, Centre for Health and Social Care Research, Sheffield, United Kingdom; [2]University of Sheffield, Surgical Oncology, Sheffield, United Kingdom; [3]University of Sheffield, Health Economics and Decision Science, Sheffield, United Kingdom; [4]University of Sheffield, EpiGenesys, Sheffield, United Kingdom; [5]Cardiff University, Institute of Primary Care and Public Health, Cardiff, United Kingdom*

**Background:** This paper focuses on the development and preliminary field-testing of an on-line decision tool to aid UK clinicians during collaborative decision making with older women (70 years and older) with breast cancer who are being considered for chemotherapy or PET versus surgery.

**Material and Methods:** This tool is based on a statistical model which estimates the risk of breast cancer and non-breast cancer death over time, conditional on individual covariates and treatment modality. The model was developed using UK Cancer Registry data, with information on co-morbidity derived from linked records from inpatient Hospital Episode Statistics. Published data on the effects of Activities of Daily Living on survival derived from the US Longitudinal Study of Ageing were incorporated using Bayesian methods. The on-line decision tool is designed to facilitate ease of use, limited need for data input and the facility to generate personalised outcomes and patient friendly printouts of this information to share with the patient and their family, friends and carers.

**Results:** The tool has been piloted with surgeons, oncologists and specialist nurses across six UK breast cancer units. All found the tools quick, easy and intuitive to use. The option of providing patients with printed information about personal risk and survival was agreed to be potentially useful but this would need to be used with discretion. All thought the inclusion of comorbidities and frailty was beneficial. Surgeons were less familiar with this type of tool however viewed it as potentially useful in supporting or confirming treatment decisions. The oncologists were positive about the development of a tool underpinned by data from older UK women and were keen to understand the provenance of the data and the modelling methods employed.

**Conclusions:** The decision tool was well received by clinicians. Based on the feedback, further amendments have been made to the tool and a 'frequently asked questions' document developed to answer questions related to the underpinning data and the modelling. This tool will be enhanced by data from our prospective cohort study; currently underway. This tool will now be tested as part of a randomised control trial.

**No conflicts of interest**

**470** Poster

**Accuracy of serum HER2 and CA 15-3 together in early detection of breast cancer recurrence. A preliminary case−control study**

F. Lumachi[1], G.B. Chiara[2], R. Tozzoli[3], L. Foltran[4], S.M.M. Basso[2]. *[1]University of Padova, School of Medicine Department of Surgery-Oncology & Gastroenterology, Padova, Italy; [2]S. Maria degli Angeli Hospital, Surgery 1, 33170 Pordenone, Italy; [3]S. Maria degli Angeli Hospital, Department of Laboratory Medicine, 33170 Pordenone, Italy; [4]S. Maria degli Angeli Hospital, Clinical Oncology, 33170 Pordenone, Italy*

**Background:** Breast cancer is the most common female cancer worldwide, and the 5-year recurrence rates range from 7% to 13%, according to the stage (I-III) of the disease. Because late detection of metastases can contribute to the failure of primary treatment, their early identification has a substantial impact on adequate therapy and prognosis. In this setting, several serum tumor markers (TM) and tissue-extracting prognostic factors have been tested. Unfortunately, none has shown such a sensitivity to be recommended as a routine test. Human epidermal growth factor receptor 2 (HER2) is a transmembrane glycoprotein with intracellular tyrosine kinase activity, that can also be measured in the blood. The monoclonal antibody of the cancer antigen (CA) 15−3 assay recognizes an epitope localized in a mucine glycoprotein encoded by the gene MUC1, and this protein is overexpressed in BC cells and shed into the bloodstream. The purpose of this study was to evaluate the usefulness of HER2 and CA 15-3 serum levels measurements in the early detection of cancer recurrence in women who underwent curative surgery for stage I-II BC invasive ductal carcinoma of the breast.

**Materials and Methods:** Nineteen women (median age 62 years, range 38−74) who underwent curative surgery for stage I-II BC and developed distant metastases during follow-up (cases) were enrolled in the study. Controls were 21 age- and stage-matched patients at the time of surgery, in whom a recurrence was excluded by whole body 18F-FDG-PET/CT. All patients had undergone serum HER2 and CA 15-3 measurements using two-site sandwich immunoassay and direct chemiluminescent technology. The cut-off limit was 32 U/mL and 15 ng/mL for CA 15-3 and HER2, respectively. The chi-squared test was used to compare results.

**Results:** The results (HER2 vs CA 15-3) were the following: sensitivity 52.6% vs 36.8% ($p = 0.022$), specificity 81.0 vs. 76.2% ($p = 0.39$), positive predictive value 71.4% (95% CI 45.3–88.3) vs. 58.3% (95% CI 31.9–80.7) ($p = 0.054$), negative predictive value 65.4% (95% CI 46.2–80.6) vs. 57.1% (95% CI 39.1–73.5) ($p = 0.19$), accuracy 67.5% vs. 57.5% ($p = 0.14$). The prevalence was the same (47.5%). With the combination of CA 15-3 and HER2, the sensitivity, specificity and accuracy reached 63.1% ($p = 0.15$), 85.7% ($p = 0.34$), and 75.0% ($p = 0.21$), respectively.

**Conclusions:** In the early detection of distant metastases in patients with BC, the sensitivity of both serum HER2 and CA 15-3 was low. HER2 was more sensitive than CA 15-3 (52.6% vs. 36.8%, $p = 0.02$), but the combination of HER2 and CA 15-3 did not improved significantly (p=NS) the results, and thus is not recommended.

**No conflicts of interest**

**471** Poster

**Clinical characteristics & prognosis of diffuse large B cell lymphoma of the breast, a review of 20 cases from a single center**

R. Bano[1], M. Mir[1], W. Zafar[2]. [1]*Shaukat Khanum Memorial Cancer Hospital & Research Centre Lahore Pakistan, Breast surgery- Surgical Oncology, Lahore, Pakistan;* [2]*Shaukat Khanum Memorial Cancer Hospital & Research Centre Lahore Pakistan, Department of Cancer registry and data management, Lahore, Pakistan*

**Background:** Primary breast lymphoma is very rare entity. It is a subtype of Non Hodgkin's lymphoma constitute 0.5% of all the breast tumors. Amongst them Diffuse Large B cell Lymphoma is the commonest subtype constitutes up to 50% of primary breast lymphoma. Our aim was to review clinical presentation, demographics and prognosis of DLBCL of breast treated at our institute outcome according to stage.

**Materials and Methods:** Data was extracted from the cancer registry, 20 cases of DLBCL breast were registered during 1995 to January 2014. We reviewed medical records of the patients, clinical notes, and medical reports. Demographics studied were age at diagnosis, gender, clinical presentation, immunohistochemistry, stage at presentation, treatment details, time to local and distant relapse and final outcome.

**Results:** A total of 31 cases of breast lymphoma patients were treated in our institute. Amongst them 20 cases were Diffuse Large B cell Lymphoma (DLBCL) constituting 64.5% of breast lymphoma. Primary breast lymphoma (PBL) were 45% (n = 9), while 55% (n = 11) were Secondary breast lymphoma (SBL) based on Wiseman & Liao criteria. Majority were female patients 90% (n = 18) whereas only 2 were males. Median age was 35 years (range 22−63). Left side predominance was seen in our population 45% (n = 18). B symptoms were present in 55% (n = 11) cases. All patients underwent whole body computed tomography, bone marrow biopsy. Bone marrow was positive in 20% (n = 4). Main stay of treatment was Chemotherapy CHOP and RCHOP (Rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisolone). Radiotherapy to the breast was offered in 40% (n = 8) patients. Complete response was achieved in 11 cases (55%). Surgery was performed in progressive disease. Local relapse was seen in 2 patients whereas 3 developed distant relapse. Follow up period was from 1 to 177 months. Lymphoma specific deaths were 35%.

**Conclusion:** Patients of DLBCL should be treated aggressively with combination of chemotherapy and radiation therapy. Role of surgery is limited for diagnosis and palliation only.

**No conflicts of interest**

**472** Poster

**Analysis of breast cancer drug treatment in Russia**

E. Derkach[1], M. Avxentyeva[1], A. Tarakanov[2], V. Bogin[3]. [1]*The Russian Presidential Academy of National Economy and Public Administration, Centre for Health Technology Assessment, Moscow, Russian Federation;* [2]*Cromos Pharma, Russian office, Moscow, Russian Federation;* [3]*Stand Up to Cancer, Scientific Group, Los Angeles, USA*

**Background:** According to the state legislature all cancer patients in Russia should receive free medical care and drug treatment, both as in-patients and in the framework of state reimbursement programs (SRP). Still the differences in healthcare spending between Russian regions may result in unequal access to treatment.

**Objectives:** To evaluate the access to drug therapy among BC patients in the framework of SRP in different Russian regions.

**Methods:** Prescription data for antineoplastic and endocrine therapy in the framework of SRP during 2013 was collected from regional health care authorities. The number and the international nonproprietary names (INN) of drugs prescribed to BC patients were defined in each region. Consumption was measured in daily defined doses (DDD)/ 1000 population/day for endocrine medications and in mg/1000 population/ day for antineoplastic agents as DDD were unavailable in the latter case.

**Results:** Prescription data was collected from 42 regions of the Russian Federation that covers 56.6% of country's total population. The number of drugs prescribed to BC patients varied from 3 to 39 INN between regions. The most commonly used antineoplastic drugs were capecitabine and trastuzumab (both prescribed in 92.9% of regions), when anastrozole, tamoxifen and letrozole were used most often among endocrine medications (95.2–100%). Consumption of drugs also varied significantly between the regions. The highest levels of consumption were noted for anastrozole [median 0.10 DDD/1000/day; interquartile range 0.05–0.17), tamoxifen [0.08 (0.05–0.13)] and letrozole [0.05 (0.02–0.10)]. The consumption for capecitabine was [20.12 mg/1000/day (7.24–34.82)], and for trastuzumab [0.23 mg (0.11–0.40)]. The use of other antineoplastic agents was identified, but their comparison could not be made because of the lack of DDD.

**Conclusions:** There exist significant discrepancies in access and utilization of drug therapy among BC patients in different regions of Russian Federation in the framework of SRP.

**No conflicts of interest**

**473** Poster

**Metaplastic carcinoma of the breast: 10 years clinical experience of Kuwait Cancer Control Center**

S. Fayaz[1], G. Demian[1], H. Eissa[1], S. Samir[1], S. Abuzallouf[1], A. Ali[2]. [1]*Kuwait Cancer Control Center, Radiation Oncology, Kuwait, Kuwait;* [2]*Kuwait Cancer Control Center, Surgical Pathology, Kuwait, Kuwait*

**Background:** Metaplastic breast carcinoma (MBC) is a histologically diverse category of breast malignancy that accounts for less than 1% of all mammary tumors and seems to have different characteristics from infiltrating duct carcinoma (IDC). This study aimed to analyze the clinico-pathological features and treatment outcome for MBC patients presented to the Kuwait Cancer Control Center (KCCC).

**Patients and Methods:** Twenty-eight cases were retrieved from our surgical pathology registry between Jan. 2005 and Dec. 2014. Medical records were revised regarding the clinico-pathological features and treatment outcome. Analysis of overall survival (OS) and progression free survival (PFS) were estimated using Kaplan Meir method.

**Results:** MBC represented 1% of 2970 patients diagnosed with breast cancer in the 10 year period. The median age was 50 years (32−70 years). Two patients presented with metastatic disease and Twenty-one patients presented with locally advanced T stage disease. Mastectomy was needed in 21 while conservative surgery was feasible in seven. The median tumor size at the time of surgery was 5.5 cm (1.5−12 cm). Axillary clearance was done in 57% of the patients while 43% underwent sentinel lymph node biopsy. Histopathological evaluation revealed 68% N0, 21% were N1 and 10% were N2. Three subtypes were detected: carcinosarcoma (5 cases), squamous cell carcinoma/squamous differentiation (14 cases) and high grade IDC with metaplastic differentiation (9 cases). Hormone receptor status was negative in 23 cases and positive in 5, all were negative for HER2neu. Chemotherapy was given to all patients, twelve of them in the neoadjuvant setting. Adjuvant radiotherapy was administered in 19 patients. The median follow-up was 24 months (1−99 months), six patients lost follow-up. The OS at 2 years was 65% and the PFS was 61%.

**Conclusion:** MBC is a rare entity among breast carcinoma in Kuwait. They often present with advanced T stage, lack of expression of ER, PR and HER2neu and less frequent nodal involvement. Further molecular studies are needed to develop molecular targeted therapy.

**No conflicts of interest**

**474** Poster

**Sentinel lymph node detection in breast surgery using indocyanine green vs technetium-99: A comparison among different diagnostic protocols**

F. Cattin[1], T. Fogacci[1], G. Frisoni[1], L. Fabiocchi[1], L. Dellachiesa[2], G. Semprini[1], D. Samorani[1]. [1]*Ospedale "Franchini" − Santarcangelo di Romagna RN, General Surgery- Breast Unit, Santarcangelo di Romagna, Italy;* [2]*University of Ferrara, General Surgery, Ferrara, Italy*

**Background:** Equivalence in sensitivity and specificity between $^{99}$Tc and ICG (indocyanine green) in sentinel lymph node detection for breast cancer is nowadays demonstrated. The radioactive medium of contrast needs to be injected a Nuclear Medicine Department. On the contrary, ICG can be injected directly in the operatory theatre. This implies that, using $^{99}$Tc, Patients must undergo two travels instead than the one required using ICG.

Aim of our study is to determine the economic expenses linked to the two possible ways to detect sentinel lymph nodes in breast surgery.

**Materials and Methods:** 291 Patients (01/2013–07/2014) of the Breast Unit of the Santarcangelo di Romagna Hospital underwent both a $^{99}$Tc injection and a ICG injection during the validation study of the ICG technique. Patients received $^{99}$Tc in the Nuclear Medicine of the Cesena Hospital (the nearest to the Santarcangelo one). The cost for each kilometer has been calculated (considering a 0.2788 € refund for kilometer), as well as the carbon footprint (considering a mean $CO_2$ emission of 118.2 g/km). $^{99}$Tc injection has a cost, all considered, of 1500 € for one patient, and just 100 € are due to the tracer itself. ICG costs 302 € each patient, which become 102 € after the first 250 patients, considering the infrared detecting machine amortization.

**Results:** An overall number of 49,778.5 km has been required when using $^{99}$Tc, on the contrary IDG has required 18,861.7 km. This implies a carbon footprint of 5.88 tons of $CO_2$ when using $^{99}$Tc and of 2.22 tons of $CO_2$ when using ICG.

The overall amount of costs of the $^{99}$Tc pathway has been 450,363.62 €. Considering the same patients, the overall cost of the ICG pathway has been 84,883.39 €. This means that ICG costs are 18.84% of the $^{99}$Tc costs.

| | $^{99}$Tc | ICG |
|---|---|---|
| Overall kilometers | 49,778.5 | 18,861.7 |
| Overall carbon footprint (tons of $CO_2$) | 5.883 | 2.229 |
| Overall cost of patients' travels (€) | 13,863.62 | 5,249.39 |
| Overall costs of clinical pathway (€) | 436,500 | 79,634 |
| Overall costs (€) | 450,363.62 | 84,883.39 |

**Conclusions:** ICG is a safe tracer, as it has a sensibility and specificity equal to the radioactive one. It is cheaper as the traditional radioactive techniques as well, especially if surgery is performed in peripheric centres or in hospitals which do not own a Nuclear Medicine Department.

Considering our results, we can suggest the use of ICG for the sentinel lymph node detection in breast surgery, not only as safe technique, but also as cost-effective one.

**No conflicts of interest**

**475** Poster

**Impact and risk factors for lymphoedema after axillary clearance for breast cancer**

P. Daskalakis[1], I. Flessas[1], E. Karopoulou[1], D. Korfias[1], I. Papanagiotou[2], V. Kalles[2], T. Mariolis-Sapsakos[2], A. Tsikkinis[1]. *[1]General Hospital "Elena Venizelou", Surgical Department of Breast Diseases, Athens, Greece; [2]National and Kapodistrian University of Athens Faculty of Nursing, Department of Anatomy, Athens, Greece*

**Background:** Lymphoedema after breast cancer is characterised by regional swelling, typically in one or both arms, due to excess accumulation of protein-rich fluid in body tissues. The adverse consequences of lymphoedema are well known, and cause much morbidity. Arm lymphoedema, and its associated symptoms, such as pain, heaviness, tightness, and decreased range of motion, experienced especially by breast cancer survivors, impede daily function and adversely affect gross and fine motor skills, with negative impact for work, home, and personal care functions, as well as recreational and social relationships.

Despite the clear symptoms of this clinical condition, mechanisms and risk factors do remain unclear. Axillary lymph node dissection (ALND) and axillary radiation therapy have been cited as the most important risk factors for lymphoedema. However, approaches to breast cancer diagnosis and treatment have evolved, and the impact of these changes on risk of lymphedema is not known.

**Material and Methods:** The aim of this study was to study the incidence of lymphoedema in patients undergoing axillary lymph node clearance for breast cancer while simultaneously studied the potential risk factors for its occurrence. This is a retrospective study, during the period 2007–2013, in which 486 patients were evaluated.

The criteria under which the patients where included were:

1. Increment of the circumference of the ipsilateral limb surgery for >2 cm, as measured 15 cm centrally from epicondyle and/or 10 cm distally and clinically evident lymphoedema on wrist.
2. Patients with primary non metastatic invasive breast cancer.

The main demographic characteristics of the patients studied were age, body mass index, as calculated from height and weight, history of diabetes mellitus and hypertension and other.

**Results:** From 486 cases of axillary lymph nodes clearance that were performed, 51 patients developed lymphoedema, corresponding to 10.4%. 2/3 of those developed in the first year after surgery, and 90% within the first 24 months. The majority of the patients who developed lymphoedema were between 40 and 60 years old (34 patients). Twenty-nine patients who developed lymphoedema underwent a level III axillary clearance and 38 postoperative radiotherapy and 22 patients axillary radiotherapy, while 31 patients were stage II.

**Conclusion:** In our study the risk factors that are strongly connected with the formation of lymphoedema are, level III axillary clearance, radiation in the breast and the axilla and the stage of the disease, while potential complications are increased BMI. Of great importance is the prospective registration and evaluation of lymphoedema formation factors in the future. Also, the evaluation of the quality of life of the people who underwent lymphoedema is going to provide us with important and useful information.

**No conflicts of interest**

**476** Poster

**Lipofilling and breast cancer conservative surgery (BCS): State of the art in 2015**

I. Jeanjot[1], D. Hertens[1], B. Carly[2], B. Beier[1], L. Vandermeeren[3], F. Liebens[1]. *[1]CHU St Pierre, Gynecology, Bruxelles, Belgium; [2]CHU St Pierre, Surgery, Bruxelles, Belgium; [3]CHU St Pierre, Plastic surgery, Bruxelles, Belgium*

**Introduction:** Breast cancer conservative surgery BCS is a standard treatment for early breast cancers (BC) and has similar results equivalent as mastectomy in terms of outcomes. Nevertheless, surgical and radiation-induced sequelae after BCS are common. In such cases, lipofilling, a reconstructive and aesthetic technique, is increasingly being used, although concerns have been raised regarding its safety when using it in BC patients.

**Aim:** Up to date review of literature.

**Material and Methods:** We conducted an online search of Medline and Cochrane Library from January 2004 to December 2014. Studies included were original articles of lipofilling use in BCS with description of radiographic changes and local breast cancer recurrence.

**Results:** Only 7 studies were found. But two studies of them could not be analyzed because patients who had undergone they a mastectomy or a conservative treatment were grouped. We therefore analyzed only 5 studies, of which 3 were prospective and 2 retrospective. Radiologic changes were assessed in 1 studie totalizing 21 BCS patients and local recurrence risk was assessed in 4 studies of which only three were prospective totalizing 259 BCS patients.

After lipofilling for correcting BCS sequelae, radiographic changes occurred in 12 patients out of 21 patients (57%). These changes included microcalcifications (4/21, 19%); oil cysts (12/21, 57%); complex cysts (4/21, 19%) and liponecrosis (4/21, 19%). Local recurrence of BC after lipofilling in BCS patients occurred in 6/259 (2.3%).

**Conclusion:** Lipofiling induced radiological changes in 57% of the patients, most of which were benign and should not affect radiological follow up after BCS. Although data are scares, there was no evidence of an increased local recurrence risk. Nevertheless the potential risk of local 'dormant' tumour cells being stimulated to induce a local recurrence should be assessed in large prospective studies.

**No conflicts of interest**

**477** Poster

**Comparisons of anxiety and depression between premenopausal women who received tamoxifen and goserelin versus tamoxifen alone to manage breast cancer: A 12-month prospective randomized study**

H.W. Yi[1]. *[1]Samsung Medical Center, General Surgery, Seoul, Korea*

**Background:** Tamoxifen is an estrogen receptor antagonist used to prevent recurrence of breast cancer continuously for 5−10 years after surgery. We compared anxiety and depression symptoms in premenopausal women with breast cancer who received add-on goserelin, a gonadotropin-releasing hormone (GnRH) analogue, to tamoxifen with those who received conventional tamoxifen alone therapy.

**Methods:** Sixty-four premenopausal women with hormone receptor-positive early-stage breast cancer were included and were assigned randomly to receive either tamoxifen and goserelin or tamoxifen alone for 12 months. The participants were evaluated blindly using the Hamilton Depression Rating Scale, the Hamilton Anxiety Rating Scale, the Beck Depression Rating Scale, and the Albany Panic and Phobia Questionnaire. Brain-derived neurotrophic factor (BDNF) and follicle-stimulating hormone (FSH) levels were assessed at baseline and 6 and 12 months.

**Results:** No significant differences for age, tumor grade, body mass index, or family history were found at baseline between the two groups. The tamoxifen and goserelin group showed significantly less of an increase in agoraphobia and a greater decrease in FSH than those in the tamoxifen-alone group from baseline to 12 months of treatment, whereas no significant time-group differences in depression were observed between the groups. A time-dependent ascending trend was detected in anxiety, genital, intellectual, somatosensory, and autonomic symptoms, as well as serum and platelet BDNF levels in both groups. A multiple linear regression analysis revealed that lower baseline FSH level was a significant predictor of increased anxiety ($\beta = 0.22$, $P = 0.02$).

**Conclusions:** Our results suggest that the tamoxifen and goserelin treatment resulted in less agoraphobia than that of the tamoxifen alone treatment in premenopausal women with breast cancer, but no change in depression was detected between the two groups.

**No conflicts of interest**

**478** Poster

**Single centre loco-regional recurrence rate over a 5 year follow up period**

V. Pegna[1], L. Hanna[1], E. Shah[1]. [1]*East Sussex Healthcare Trust, Breast Surgery, Hastings, United Kingdom*

**Background:** To assess the loco regional recurrence (LRR) of early operable breast cancer over a 5 year follow up period at a single centre.

**Materials and Methods:** Retrospective cohort study of breast cancer operations; single centre; single surgeon between 2008–2015. Treatment and outcome of 734 patients were reviewed; primary outcome was LRR. LRR was defined as first site of tumour recurrence involving the ipsilateral breast tissue or chest wall and/or regional lymph node(LN) area. Histopathology of tumour recurrence was compared with that of the primary. Patients' notes and electronic records were used to obtain data. Multiple factors were assessed, including age, grade, tumour size and LN status. Exclusion criteria were primary surgery carried out at a different centre or by a different surgeon, and patients who declined surgery and were treated by primary hormonal therapy alone. All patients had a minimum of 1 year follow up, with some having had follow up for 5+ years, ie all patients were followed up until the end of the study date, Dec 2015, enabling relapse-free survival for periods of up to 5 years from the date of diagnosis to be calculated. Median follow-up: 4 years.

**Results:** 734 patients were identified as operated on between 2008–2014. 9/734 patients had LRR so 5+ year follow up LRR rate: 1.21%. 33% (3/9) had DCIS, with the remaining 66% (6/9) having IDC. The total size range was between 5−40 mm. 5/7 invasive cancers were grade 3. 77% (7/9) were ER +ve, and 2/9 were triple negative. None of the LRR patients had positive lymph nodes. 77% (7/9) had axillary staging, 2/9 did not have axillary staging as had DCIS only. 44% (4/9) had lymphovascular invasion (LVI) and 22% (2/9) had close margins (both were DCIS cases). All LRR received some form of adjuvant therapy, 33% (3/9) received chemo, 66% (6/9) received hormonal therapy and 44% (4/9) had radiotherapy. 2/9 patients were treated for DCIS, of which 1 recurred as invasive disease.

356 out of 734 had a full 5 year follow up, and these accounted for 5/9 LRR cases; resulting in a 1.4% LRR rate. 1/9 had evidence of simultaneous distant metastases.

**Conclusions:** Our LRR compares favourably with other studies. It reiterates the importance of adequate margins in DCIS. LN negativity is not necessarily indicative of a lower LRR. This study shows that other factors such as grade and LVI besides LN positivity play an important role in LRR. However it would be worth following up all these patients for the full 5 years.

**No conflicts of interest**

**480** Poster

**The maxSUV in tumor and lymph node by $^{18}$F-FDG PET/CT as prognostic value in patients with node positive breast cancer**

S.H. Kang[1]. [1]*Keimyung University Hospital, General Surgery, Daegu, South Korea*

**Background**: We aimed to evaluate the prognostic value of maximum standardized uptake value (SUVmax, determining by $^{18}$F-FDG PET/CT) of primary tumor and metastatic node in pathologic node positive breast cancer.

**Material and Methods:** Between January 2007 and November 2011, eighty patients performed $^{18}$F-FDG PET/CT before treatment for invasive breast carcinoma. All patients underwent curative surgery and confirmed axillary node metastasis by pathologic report. We retrospectively reviewed medical records of all patients and analyzed clinicopathologic features, including age, tumor size, number of metastatic node, stage, estrogen receptor (ER), human epidermal growth factor receptor 2 (HER2) status, primary tumor SUVmax, nodal SUVmax and ratio of nodal SUVmax to tumor SUVmax. We compared recurrence rate according to stage, SUVmax of tumor and lymph node. We used one-way ANOVA, Kaplan–Meier method and Cox proportional hazard ratio, and the receiver-operating-characteristic (ROC) curve to determine the optimal cutoff value of SUVmax for recurrence by SPSS software.

**Results:** All patients were women and mean age was 52 years old (range, 30−84). Median follow up period of total patients was 58 months (range 11−95), and 23 patients had recurrence (median follow-up, 21 months). Five years overall survival (OS) rate was 90.9% and 5 years disease free survival (DFS) rate was 72.8%. The mean value of tumor SUVmax, nodal SUVmax and ratio of nodal SUVmax to tumor SUVmax were 8.15 (range, 1.0–26.5), 5.06 (range, 0.9–27.8) and 0.77 (range, 0.06–12.0). The tumor SUVmax had more a significant difference from T stage ($p = 0.021$) and nodal SUVmax had more a significant difference from N stage ($p < 0.0001$). The advanced breast stage, ER negative, triple negative breast carcinoma (TNBC) and recurrence groups had higher SUVmax. The ROC curve determined a tumor SUVmax of 8.3 (sensitivity, 65%; specificity, 68%; area under the curve 0.659) and nodal SUVmax of 4.4 (sensitivity, 69%; specificity, 68%; area under the curve 0.672) to identify the optimal cutoff value about predicting recurrence. Univariate analysis showed that stage ($p = 0.017$), cut off value of tumor SUVmax ($p = 0.009$) and nodal SUVmax ($p = 0.003$) influenced to disease free survival (Table). However, multivariate analysis showed these factors did not have statistical significance.

| | 5Y DFS (%) | p-value |
|---|---|---|
| Tumor SUVmax | | |
| <8.3 | 82.4 | 0.009 |
| ⩾8.3 | 58.3 | |
| Lymph node SUVmax | | |
| <4.4 | 83.5 | 0.003 |
| ⩾4.4 | 58.7 | |
| Stage | | |
| II | 81.9 | 0.017 |
| III | 42.1 | |

**Conclusions:** The tumor and nodal SUVmax on $^{18}$F-FDG PET/CT may be prognostic factors in patients with node positive breast cancer.

**No conflicts of interest**

**481** Poster

**Influence of phenotype and breast density on recurrences, disease-free and overall survival of screen detected and interval breast cancer**

I. Torá-Rocamora[1], L. Domingo[1], M. Baré[2], T. Barata[3], C. Carmona[4], F. Macià[1], X. Castells[1], M. Sala[1]. [1]*IMIM Hospital del Mar Medical Research Institute. Research Network on Health Services in Chronic Diseases REDISSEC, Department of Epidemiology and Evaluation, Barcelona, Spain;* [2]*Parc Taulí University Hospital. Research Network on Health Services in Chronic Diseases REDISSEC, Clinical Epidemiology and Cancer Screening, Sabadell, Spain;* [3]*General Directorate of Health Care Programmes, Canary Islands Health Care, Las Palmas de Gran Canaria, Spain;* [4]*Hospital Dr. Josep Trueta, Epidemiology and Register of Cancer of Girona, Girona, Spain*

**Background:** Interval cancers (IC) have a worse prognosis and survival than screen-detected cancers (SDC), and it has been reported that differences remain after taking into account clinical and biological characteristics. However little is known about the role of phenotype and breast density, when considering the different subtypes of IC: true interval cancers (TIC) and false negative cancers (FNC). We aimed to evaluate the influence of phenotype and breast density on recurrences, disease-free and overall survival on overall IC, TIC and FNC vs. SDC.

**Material and Methods:** Retrospective cohort of women participants in a population-based breast cancer screening program in Spain 2000–2006, and diagnosed as SDC or IC, and followed up until August 2014 (CAMISS Project). Complete clinical and radiological information was obtained allowing classify interval cancers into subtypes. To assess the risk of recurrence, disease-free and overall survival, Cox regression models were computed to estimate crude Hazard Ratios (HR) and 95% confidence intervals (95% CI), and adjusted by prognostic and predictive factors as age, TNM stage, tumor size, phenotype and breast density.

**Results:** 1,086 cancer cases (741 SDC and 345 IC) were included. 27% of IC were TIC and 13% FNC. Occult tumors and minimal signs were not included due to low numbers. IC had a higher proportion of more advance TNM stages, larger tumors, triple negative phenotype, and dense breast. Crude models showed that IC had higher risk of recurrence, disease-free and overall survival than SDC [HR (95% CI); 2.16 (1.58–2.95), 1.84 (1.38–2.46), 2.53 (1.84–3.46), respectively]. When adjusting by age, TNM stage, tumor size, and phenotype the association with survival remained [HR (95% CI); 2.03 (1.31–3.13)] but when adjusting simultaneously by breast density the risk decreased and was not statistically significant (1.55; 0.82–2.93). The adjusted risk of survival without taking into account breast density was higher for TIC (1.88; 1.02–3.46) than for FNC (1.78; 0.79–4.05), but differences disappeared when adjusting by breast density.

**Conclusion:** Breast density and phenotype could explain the differences observed in free-disease and overall survival between different subtypes of IC, specially TIC and FNC, and SDC. Our results reinforce the need to identify women with higher risk of TIC to tailor screening and follow up strategies.

**No conflicts of interest**

**482** Poster

**Validity of Adjuvant! Online program in Spanish women with breast cancer participating in the CAMISS cohort**

A. Romero[1], S. Garcia[2], U. Aguirre[2], T. Barata[3], L. Domingo[1], M. Bare[4], J. Ferrer[5], A. Rivero[6], T. Tellez[7], C. Sarasqueta[2], M. Orive[2], C. Valcarcel[6], M. Redondo[7], I. Zarcos[7], X. Castells[1], M. Sala[1]. *[1]IMIM Hospital del Mar Medical Research Institute − Research Network on Health Services in Chronic Diseases REDISSEC, Epidemiology and Evaluation, Barcelona, Spain; [2]Hospital Galdakao-Usansolo- Research Network on Health Services in Chronic Diseases REDISSEC, Research Unit, Galdakao, Spain; [3]Canary Islands Health Service, General Directorate of Health Care Programmes, Las Palmas de Gran Canaria, Spain; [4]Parc Taulí-University Hospital − Research Network on Health Services in Chronic Diseases REDISSEC, Clinical Epidemiology and Cancer Screening, Sabadell, Spain; [5]Hospital Santa Caterina, Radiology Unit, Girona, Spain; [6]Canary Health Service − Research Network on Health Services in Chronic Diseases REDISSEC, Canary Foundation for Health Research, Tenerife, Spain; [7]Hospital Costa del Sol- University of Málaga − Research Network on Health Services in Chronic Diseases REDISSEC, Research Unit, Málaga, Spain*

**Background:** Several prediction methods are used to aids in decision making for oncologists in patients diagnosed with breast cancer. These prediction methods present some limitations, mainly due to the rapid improvement in breast cancer diagnosis and treatment. Moreover, traditional prediction methods do not include invidivual information, such as comorbidities or general health status. One of the best known prediction methods is Adjuvant! Online: an online, open-access prediction program that predicts 10-year breast cancer recurrence and breast cancer mortality. Adjuvant! predictions are based on six clinical factors, including comorbidity. It has been validated in Canada, the US, and in several Asian and European studies, but it has not been validated in Spain. Our aim was to validate Adjuvant! Online in a cohort of Spanish women diagnosed with breast cancer.

**Material and Methods:** A retrospective cohort of women participating in population-based cancer screening programs in Catalonia and Canarias, diagnosed with breast cancer between 2000–2009, and followed up until August 2014 (CAMISS cohort). Clinical and epidemiological variables were collected. A Cox regression model was computed, being the dependant variable the 10-year survival, and the independent variables those included in the Adjuvant! program: age, comorbidities (minor/major), oestrogen receptor status (positive/negative), tumor size, tumor stage, tumor grade and number of positive nodes. A logistic regression model was also performed, and the area under de curve (AUC) of the receiver-operator curves was estimated for the Adjuvant! program. All the analyses were performed in SAS version 9.4.

**Results:** 1,086 women were included in the cohort, with a mean age of 58.43 [standard deviation (SD): 5.46]. The mean time of survival was 8.52 years (SD: 2.89). A total of 291 women (26.80%) presented more than 2 comorbidities, 147 (13.80%) were diagnosed with advanced stages (III and IV), and 280 (29.98%) tumors were grade III. The presence of more than 2 comorbidities, advanced stage, tumor grade III and 10 or more positive nodes were associated to women's survival. The AUC computed was 0.70.

**Conclusions:** Although the Adjuvant! Online program shows an acceptable predictive ability, it should be improved. Prediction risks methods of death and recurrence in breast cancer patients need to be updated in the Spanish population.

**No conflicts of interest**

**483** Poster

**Risk of contralateral breast cancer in BRCA1 and BRCA2 mutation carriers: impact of adjuvant systemic treatment**

M. Hooning[1], A. Jager[1], L. Koppert[2], C. Van Deurzen[3], M. Collée[4], A. Hollestelle[1], C. Seynaeve[1]. *[1]Erasmus MC Cancer Institute, Medical Oncology, Rotterdam, Netherlands; [2]Erasmus MC Cancer Institute, Surgical Oncology, Rotterdam, Netherlands; [3]Erasmus MC Cancer Institute, Pathology, Rotterdam, Netherlands; [4]Erasmus MC Cancer Institute, Clinical Genetics, Rotterdam, Netherlands*

**Background:** BRCA1/2-associated breast cancer (BC) patients are at increased risk of contralateral BC (CBC) compared to sporadic patients. Younger age at primary BC (PBC) is associated with increased risk of CBC, while adjuvant chemo- and endocrine therapy have been reported to reduce risk of CBC.

Aim of the study was to assess the potential risk reducing effect of adjuvant chemo- and/or endocrine therapy on the occurrence of CBC in BRCA1/2-associated BC patients, taking into account ER-status, age at PBC and risk-reducing salpingo-oophorectomy (RRSO).

**Material and Methods:** Data were collected for 646 BRCA1 and 226 BRCA2 mutation carriers with PBC treated at the Erasmus MC between 1980 and 2012, and analyzed using Cox regression.

**Results:** In BRCA1 mutation carriers, chemotherapy was associated with decreased risk of CBC (adjusted HR, 0.45; 0.23–0.86); HR for endocrine therapy was 0.39 (0.08–1.72). In BRCA2 mutation carriers, univariate HR for chemotherapy was 0.15 (0.03–0.85) and for endocrine therapy 0.31 (0.06–1.67). Combining BRCA1/2 mutation carriers, both chemo- and endocrine therapy were associated with decreased CBC risk: adjusted HR for chemotherapy, 0.45 (0.26–0.80); for endocrine therapy, 0.35 (0.12–1.00). In premenopausal patients opting for RRSO before age 50, adjusted HR for chemotherapy was 0.36 (0.15–0.87) and for endocrine therapy 0.16 (0.02–1.19).

**Conclusions:** Adjuvant chemotherapy reduces CBC risk by half and for adjuvant endocrine therapy the risk reduction was even larger but this last finding needs further validation.

For a more accurate personalized risk assessment of CBC, one should take into account not only mutation status and age at PBC, but also adjuvant systemic treatment administered for PBC.

**No conflicts of interest**

**484** Poster

**Early detection of secondary lymphedema after cancer treatments**

L. Vandermeeren[1], J.P. Belgrado[1], S. Vankerckhove[1], J.B. Valsamis[2], B. Carly[3], D. Hertens[3], I. Jeanjot[3], M. Fastrez[3], B. Beier[3], F. Liebens[3]. *[1]CHU St-Pierre, Lymphology clinic, Brussels, Belgium; [2]Université libre de Bruxelles, BEAMS- école polytechnique, Brussels, Belgium; [3]CHU St-Pierre, ISALA Breast clinic, Brussels, Belgium*

**Introduction:** Axillary lymph node dissection for breast cancer may in some cases affect the lymphatic drainage of the arm, increasing the risk for the patient to develop a secondary lymphedema, shorter or longer after surgery. Efficient treatments exist, but lymphedema is a chronic disease which needs repeated and continued treatments. The later the treatment of the lymphedema begins, the heavier it is. Currently, a lymphedema is diagnosed after it has clinically developed. Near-infrared (NIR) fluorescence imaging after intradermal injection of Indocyanine Green shows that some oncologic patients, operated and free of apparent secondary lymphedema, present abnormalities of the lymphatic network. The study aims to confirm that it is now possible to detect secondary lymphedema at a subclinical stage. Detection may be performed using NIR fluoroscopy that allows to realize a mapping of the superficial lymphatic network and to identify the characteristics of the secondary lymphedema in the group of patients at risk to develop lymphedema after lymph node dissection.

**Material and Methods:** Breast cancer patients are recruited before surgery. They undergo fluoroscopy imaging before surgery, and 10 days, 3 months, 6 months, 1 year and 2 years after surgery. Images of the different videos are then compared in order to detect any decrease in lymphatic drainage of the operated arm. Clinical examination of the arm is performed at each session. Patients gave their written informed consent before inclusion (NCT02415725).

**Results:** 13 patients have been recruited to date in this study. Two patients have been controlled after 6 months from surgery, three patients after 3 months from surgery, and 8 patients after 10 days from surgery. No patient show for the moment any sign of developing lymphedema, nor clinically, or according to lymphofluoroscopy imaging.

**Conclusion:** As patients sometimes develop lymphedema many years after breast cancer surgery, and taking account that we have diagnosed several subclinical lymphedema thanks to NIR fluoroscopy, we have good reasons to think that it is possible to detect lymphedema in the patients of this study before the lymphedema is clinically visible. Additional results will be obtained in the next weeks.

**No conflicts of interest**

**485** Poster

**Clinicopathological features of neuroendocrine carcinoma of the breast: A rare cancer with an excellent outcome**

M. Ilhan[1], O.C. Cücük[1], N. Cabioglu[1], E. Ozkurt[1], S. Onder[2], M. Tukenmez[1], H. Karanlık[3], M. Muslumanoglu[1], V. Ozmen[1], A. Dinccag[1], A. Igci[1]. *[1]Istanbul University Faculty of Medicine, Department of Surgery, Istanbul, Turkey; [2]Istanbul University Faculty of Medicine, Department of Pathology, Istanbul, Turkey; [3]Istanbul University Institute of Oncology, Department of Surgical Oncology, Istanbul, Turkey*

**Background:** Primary neuroendocrine carcinoma of the breast (NECB) is a rare distinct type of breast carcinoma. Therefore, there is still

unsufficient knowledge about the optimal management, treatment, and clinical outcome. In this study, we investigated the clinicopathological characteristics and management and the clinical outcome of this rare breast carcinoma.

**Materials and Methods:** Patients diagnosed as NECB between July 2008 to February 2014 were included into the study. Medical records were retrospectively reviewed to obtain the demographic features of patients, clinicopathologic factors, treatment modalities, and outcomes of NECB. Tumors were stained by immunohistochemistry for NE markers, synaptophysin and/or chromogranin A along with estrogen and progesterone receptors, HER-2 neu expression, Ki-67 levels.

**Results:** All 14 patients were female (100%). The median age was 65 (range, 30−82 years). The majority of patients with NECB were postmenopausal (71%). Three (21%) patients underwent mastectomy whereas 11 (79%) patients had lumpectomy. All patients had sentinel lymph node biopsy, and axillary lymph dissection was performed in 6 of them with a positive SLNB. All cases were diagnosed with solid neuroendocrine (NE) carcinoma. Four patients had stage 1 disease (29%) and 10 patients had stage II disease (71%). The majority of NECB were grade 2 tumors (12 of 14, 86%) whereas the remaining 2 tumors were grade 3 (14%). Lymphovascular invasion was identified in 3 of 14 (21%) cases.

Thirteen (93%) patients were ER-positive, and 11 (79%) were PR-positive. All patients were found to be HER-2 negative, whereas 13 (93%) cases had low Ki67 expression (<20%). Furthermore, synaptophizin and chromogranin-A expressions were found to be positive in all specimens.

The median follow-up for patients with NEC of the breast was 44 months (range 13−80 months). Ten patients received chemotherapy whereas all patients had appropriate hormonotherapy as tamoxifen in premenopausal women, and anastrazol in postmenopausal patients. All patients with breast conservation had radiotherapy. Five-year disease specific and disease free survival rates were 100% and 100%, respectively.

**Conclusion:** NECB is a rare different subtype of breast carcinoma. Our resuts indicate NECBs are morelikely to be ER/PR positive and HER-2 negative as luminal A subtype. Therefore, the excellent clinical outcome might be due this good tumor biology profile despite a substantial number of patients with axillary lymph node positivity.

**No conflicts of interest**

**486** Poster/Poster Spotlight

**Towards personalized breast cancer follow-up: Prediction model for recurrence and allocation of visits during 10 years of follow-up**

A. Witteveen[1,2], J.W. Ruiter[1], R. Bretveld[3], C.G.M. Groothuis-Oudshoorn[1], I.M.H. Vliegen[4], M.J. IJzerman[1], S. Siesling[1,3]. *[1]University of Twente, Health Technology and Services Research HTSR- MIRA institute for Biomedical Technology and Technical Medicine, Enschede, Netherlands; [2]Mayo Clinic, Robert D. and Patricia E. Kern Center for the Science of Health Care Delivery, Rochester, USA; [3]Netherlands Comprehensive Cancer Organisation IKNL, Research, Utrecht, Netherlands; [4]University of Twente, Industrial Engineering and Business Information Systems IEBIS- Centre for Healthcare Operations Improvement & Research, Enschede, Netherlands*

The aim of this nationwide population based study was to analyze recurrence patterns and define predictive factors for locoregional recurrence (LRR) and subsequent recurrences up to ten years after the primary tumor. In the Netherlands, follow-up takes place for five years after primary treatment with a yearly mammography. Using risk thresholds, follow-up visits can be reallocated based on risk over the ten years following primary treatment.

Women diagnosed with primary invasive breast cancer in 2003 with no distant metastasis, previous or synchronous tumors and curatively treated with surgery were selected from the Netherlands Cancer Registry (N = 8,035). Survival analysis was performed to identify predictive factors for LRR. Predictors for the second and third recurrence after a LRR were assessed as well. Based on the current follow-up, the lower risk boundary and quantiles for intervals were determined. With these thresholds redistribution of the visits was established for a low, middle and high risk group, over ten years of follow-up.

During ten years of follow-up 509 (6.3%) of the 8,035 patients developed a LRR as a first event. Predictive factors for first LRR can be found in Table 1. The chances of developing a second and third event after a LRR were 41% and 48% respectively. Most important predictors for all types (LRR/second primary/metastasis) of second recurrence were tumor size, surgery type and radiotherapy, with the effect of the last two reversed compared to the first recurrence (Table 1). The predictors for second LRR and third recurrence were all non-significant.

The cumulative hazard of the population after five year was 0.0448, resulting in a hazard interval of 0.00896 per visit. The hazard after five years was 0.0068, which constituted the lower boundary for follow-up. Given the used thresholds, the medium (<50, hormone therapy) risk group should receive two follow-up visits and the high group (>50, no hormone therapy) seven during the follow-up period of ten years. The low risk group (>50, hormone therapy) remained below the threshold for all the ten years.

Table 1. Hazard rates from the Cox regression analyses [a]

| | First recurrence (LRR) | Second recurrence (all types) |
|---|---|---|
| Age (⩽50 / >50) | − / **0.70** | − / 0.78 |
| Size (⩽2 cm / >2 cm) | − / **1.47** | − / **1.45** |
| Grade (I / II / III) | − / **1.12** / **1.77** | − / 0.74 / 0.79 |
| Lymph nodes (0 / 1−3 / >3) | − / **1.65** / **3.29** | − / 0.78 / 0.65 |
| Hormone status (non-negative / negative) | − / 1.16 | − / 1.21 |
| Surgery type (breast conserving / mastectomy) | − / **0.61** | − / **1.75** |
| Radiotherapy (yes / no) | − / **1.92** | − / **0.51** |
| Hormone therapy (yes / no) | − / **2.07** | − / 1.01 |
| Chemotherapy (yes / no) | − / **1.69** | − / 1.00 |

[a] Values in Bold indicate a significant difference.

This study developed a prediction model for LRR risk for up to ten years of follow-up. The model can be used to identify patients with a low or high risk to personalize follow-up after breast cancer, develop a decision support tool and allocate resources efficiently.

**No conflicts of interest**

**487** Poster

**Patterns and risk of first and subsequent recurrences in women within ten years after primary invasive breast cancer**

Y. Geurts[1], R. Bretveld[1], P. Poortmans[2], G. Sonke[3], L. Strobbe[4], S. Siesling[1]. *[1]Comprehensive Cancer Centre The Netherlands IKNL, Research, Enschede, Netherlands; [2]Radboud university medical center, Radiation Oncology, Nijmegen, Netherlands; [3]Netherlands Cancer Institute, Medical Oncology, Amsterdam, Netherlands; [4]Canisius-Wilhelmina Hospital, Surgical Oncology, Nijmegen, Netherlands*

**Background:** Previous studies suggest a distinct pattern and a number of predictive factors for breast cancer recurrence. However, only few studies include data on recurrence site and no study provides data regarding second and third breast cancer recurrence after local and regional recurrence. The aim of this study was to analyse the occurrence, timing and predictive factors of first and subsequent local (LR), regional (RR) or distant (DM) recurrence during the first 10 years after treatment for primary invasive breast cancer in women.

**Methods:** Women with stage I-III invasive breast cancer diagnosed in 2003 and treated with curative intent were selected from the Netherlands Cancer Registry (N = 9797). Median follow-up was 10 years. Multivariable cox proportional hazards regression was used to model the hazard of recurrence over time for site-specific first recurrence and for subsequent recurrences after LR or RR. Predictive factors were identified for first and for subsequent recurrences. All tests were two-sided and probability values of <0.05 were considered statistically significant.

**Results:** In total 379 patients had LR, 156 patients had RR and 1412 patients had DM as first recurrence. The risk of first recurrence was highest around 2 years post-diagnosis (HR 0.040 95% CI 0.036–0.044) with a similar pattern for LR, RR and DM. Multivariable analysis showed that lower age and negative estrogen-receptor (ER) status were predictive factors for first LR. Tumour size >2 cm, grade III and negative ER were predictive factors for first RR and tumour size >2 cm, grade II or III, increasing number of involved lymph nodes and negative progesterone-receptor (PR) status were predictive factors for first DM. After a LR 109/379 patients (28.7%) developed subsequent recurrence: 11 patients had another LR (2.9%), 13 patients had RR (3.4%) and 85 patients (22.4%) had DM. Median time to second recurrence was 1.1 year (IQR 0.3−2.5 year). Tumour size >2 cm, grade III, primary tumour histology (other vs invasive ductal), >3 positive lymph nodes and negative PR-status were predictive factors for a second recurrence after LR. After a first RR 79/156 patients (50.6%) developed subsequent recurrence: 8 patients had LR (5.1%), 3 patients had RR (1.9%) and 68 patients (43.6%) had DM. Median time to second recurrence was 1.1 year (IQR 0.5−2.1 year). In multivariable analysis, no predictive factor for a second recurrence after RR was identified. After previous LR or RR a third subsequent recurrence occurred in 18 patients (9.6%).

**Conclusions:** The pattern of first recurrence was similar for LR, RR and DM. To improve personalized follow-up, predictive factors could be taken into account. However, this study showed no explicit predictive factor for site specific recurrence and subsequent recurrences after LR and RR. Future studies that take treatment characteristics into account are needed.

**No conflicts of interest**

**489** Poster

**Long-term risks of specific cardiovascular diseases associated with contemporary breast cancer treatment in combination with cardiovascular risk factors: A large Dutch cohort study**

N. Boekel[1], J. Jacobse[1], M. Schaapveld[1], J. Gietema[2], M. Hooning[3], C. Seynaeve[3], M. Baaijens[4], G. Sonke[5], E. Rutgers[6], N. Russell[7], B. Aleman[7], F. Van Leeuwen[1]. *[1]Netherlands Cancer Institute, Psychosocial research and Epidemiology, Amsterdam, Netherlands; [2]University Medical Center Groningen, Medical Oncology, Groningen, Netherlands; [3]Erasmus MC − Cancer Institute, Medical Oncology, Rotterdam, Netherlands; [4]Erasmus MC − Cancer Institute, Radiation Oncology, Rotterdam, Netherlands; [5]Netherlands Cancer Institute, Medical Oncology, Amsterdam, Netherlands; [6]Netherlands Cancer Institute, Surgery, Amsterdam, Netherlands; [7]Netherlands Cancer Institute, Radiation Oncology, Amsterdam, Netherlands*

**Background:** With the growing number of breast cancer (BC) survivors it is increasingly important to understand the cardiovascular disease (CVD) risks associated with contemporary BC treatment in order to identify patients at increased risk of developing treatment induced CVD.

**Methods:** We have constructed a large cohort of 1-year survivors of in situ and stage I-IIIa BC, diagnosed from 1970–2009 at two Dutch Cancer Institutes. Data on BC characteristics, treatment modalities, recurrences, subsequent malignancies, CVD, and CVD risk factors (i.e. hypertension, hypercholesterolemia, diabetes, smoking) were collected using hospital registries, medical files, and questionnaires to patients' general practitioners and cardiologists.

BC treatment was classified time-varyingly, taking into account treatment for primary BC, locoregional recurrences, and second BC. CVD risks were compared with general population rates and estimated using Cox proportional hazards regression models. We will specifically report on the interactions between treatment regimens and CVD factors at BC diagnosis and during follow-up.

**Results:** Total analytic cohort comprised of 14,819 patients. Mean age at BC was 46 years (range 19−61). 68% of the cohort was treated with radiotherapy (breast only: 35%, chest wall only: 9%, at least the internal mammary chain field (IMC): 48%), and 30% with adjuvant chemotherapy, consisting of an anthracycline-containing regimen in 55%.

After a median follow-up of 15 years (25% was followed for $\geqslant$20 years), 2,210 patients had been diagnosed with CVD. First CVD was coronary heart disease (CHD) in 639 patients (incl. 332 myocardial infarctions), heart failure (HF) in 252 patients, and valvular heart disease (VHD) in 277 patients. Overall 20-year cumulative CVD incidence was 19% for patients diagnosed 1970–1989 and 17% for 1990–2009.

At BC diagnosis, 2,753 patients had at least one CVD risk factor (most frequent: smoking (2,251 patients) and hypertension (576 patients)). During follow-up, 3,087 more patients developed a CVD risk factor. CVD risk factor at BC diagnosis was associated with a HR of 2.1 for CHD (95% CI 1.4−3.2).

First preliminary results show a HR of 4.4 for HF as first CVD in patients treated with anthracyclines at age $\leqslant$50 years (95% CI 2.5−7.8, compared to no chemotherapy), that remained increased until at least 15 years after treatment.

Compared to right-sided tangential breast irradiation, IMC field irradiation increased the risks of VHD (HR=1.7 95% CI 1.1−2.7) and CHD (HR=2.6 95% CI 1.8−3.6) as first event. IMC field irradiation in combination with a CVD risk factor at BC diagnosis increased the CHD risk to 4.0 (95% CI 2.7−6.0).

**Conclusion:** Radiotherapy and chemotherapy increase the risk of CVD, also in patients treated after 1990. Caregivers should be aware of the increased risks, especially after treatment with anthracylines and irradiation of the IMC field.

**No conflicts of interest**

**490** Poster

**Trastuzumab-induced cardiotoxicity in patients over 70 years of age: A single institution retrospective analysis**

M. Sousa[1], P. Winckler[1], L. Pereira[1], E. Gouveia[1], M. Brito[1], P. Maria José[1], A. Moreira[1]. *[1]IPO Lisboa, Medical Oncology, Lisbon, Portugal*

**Background:** Breast cancer (BC) is the most common cancer in women. Almost one-third presents with an aggressive form characterized by increased expression of the human epidermal growth factor receptor 2 (HER2) proteins (HER2+). Trastuzumab is a monoclonal antibody against HER2 expression that improves survival in BC but is also associated with a degree of cardiotoxicity.

**Material and Methods:** Retrospective analysis of all HER2+ BC pts, older than 70 years of age ("over-70"), treated with trastuzumab in our institution from December 2004 to April 30th 2014. All pts had sequential cardiologic evaluation by echocardiogram (pre and during treatment).

**Results:** Seventy-one pts "over-70" with proven HER2+ BC by Fluorescence In Situ Hybridization (FISH) or immunohistochemistry (IHC) were treated with Trastuzumab: 70 women (99%) and 1 man (n = 1%); median age of 74.2 years [70.1–89.8].

Treatment was done for a median of 12 months [3−20] in neoadjuvant (n = 3, 4%), adjuvant (n = 54, 76%) and metastatic (n = 14, 20%) therapeutic schemes.

A reduction in left ventricular ejection fraction (LVEF) ($\geqslant$10% from basal values or LVEF <50%) and/or clinical suspicion of Trastuzumab-related cardiotoxicity (reduction in NYHA cardiac function) was detected in 8 pts (11%) and treatment was interrupted. Half restarted treatment after clinical improvement and recovery of LVEF to basal values by clinical and echocardiographic revaluation.

During treatment, 6 pts (8%) discontinued Trastuzumab permanently, all after adjuvant chemotherapy with anthracyclines and breast radiotherapy. One patient (1%) also had documented pulmonary toxicity. Half of these patients (n = 3) had a history of hypertension treated with a median of 2 anti-hypertensive drugs [1−3], 1 had dyslipidemia, 1 isquemic cardiopathy, 1 non-specific miocardiopathy and 2 had type 2 diabetes; none were smokers or had alcohol habits. None died of treatment toxicity.

At the end of analysis, 17 pts had died (n = 24%) of disease progression (n = 10, 14%), other tumors (n = 2, 3%) or of unknown cause (n = 5, 7%); 5 pts were lost to follow up (7%).

**Conclusions:** Estimated Trastuzumab-induced cardiotoxicity in HER2+ BC treatment varies from 8 to 30% (Onitilo et al, 2014). In patients "over-60" with similar characteristics to our population cardiotoxicity can be as high as 32% (Tarantini et al, 2012) and 11% in patients "over-70" but this subgroup was under represented (9% of patients in the study by Neuget et al, 2014). Cardiovascular risks are also frequent in this specific population and can potentiate this toxicity. Little information currently exists with these patients and more studies are needed. In our series, although Trastuzumab cardiotoxity was detected and limited treatment duration, it was not responsible for any of the deaths.

**No conflicts of interest**

## Friday, 11 March 2016

**POSTER SESSION**

# Optimal Diagnosis II

**491** Poster/Poster Spotlight

**Between-lab variability in Ki67 scoring by a standardised method in core-cuts has little impact on risk estimates by the IHC4+Clinical (IHC4+C) Score. A study presented on behalf of the International Ki67 in Breast Cancer Working Group of the Breast International Group**

A. Dodson[1,2], L. Zabaglo[3], V. Martins[2], B. Yeo[4], D. Hayes[5], L. McShane[6], S. Leung[7], T. Neilsen[7], M. Dowsett[1,2]. *[1]The Royal Marsden Hospital, Academic Department of Biochemistry, London, United Kingdom; [2]Institute of Cancer Research, Breast Cancer Research, London, United Kingdom; [3]Institute of Cancer Research, The BreakThrough Toby Robins Breast Cancer Research Centre, London, United Kingdom; [4]The Royal Marsden Hospital, Department of Medicine, London, United Kingdom; [5]University of Michigan, Comprehensive Cancer Center, Michigan, USA; [6]National Cancer Institute, Cancer Therapy Evaluation Program, Bethesda, USA; [7]University of British Columbia, Pathology and Laboratory Medicine, Vancouver, Canada*

**Background:** immunohistochemical (IHC) assessment of proliferation using Ki67 in breast cancer has been shown to associate with prognosis, surrogate luminal A/B calling (with progesterone receptor, PgR) and is a marker of residual risk of recurrence (RR) for ER+ cases treated with endocrine therapy. Much attention has been paid to Ki67's analysis and reporting but until recently modest progress made. The International Ki67 Working Group has reported that a standardised "Global" scoring method can reduce inter-observer variability when assessing Ki67 in breast cancer core biopsies but despite meeting pre-specified success criteria, inter-laboratory variability remained with potential for clinically significant discordance between risk categorisation based on single cut-points. Integration of Ki67 with other prognostic factors into a single molecular-clinicopathologic algorithm leads to a risk-predictor less sensitive to variability in any single component. In particular, combination with ER, PgR, HER2 and clinicopathological (C) parameters in the IHC4+C algorithm produces RR scores with analytical and clinical validity for aiding

in chemotherapy decision making. We determined the effects of between-lab variability in use of the Global method on IHC4+C reproducibility and in defining luminal subtypes according to St Gallen consensus definitions.

**Material and Methods:** Ki67 data were derived from Phase 3 of the International Ki67 in Breast Cancer Working Party program of standardisation. Core biopsies from 20 ER+, HER2− breast cancers were centrally stained and scored for Ki67, ER and PgR at Royal Marsden Hospital (RMH) using established standardised methods. The Ki67 stained sections were circulated to 21 labs in 11 countries, and scored using the Global method, comprising selection of 4 fields representative of overall heterogeneity (where present) and scoring of 100 cells in each field. Intraclass correlation (ICC) was calculated for RR scores. RR scores were categorised as low/intermediate/high risk and analysed for agreement between RMH (reference centre) and other centres for risk-category assignment. Local Ki67 and central PgR data were combined in agreement tables to examine luminal A/B calling.

**Results:** ICC for the Phase 3 Global method Ki67 scores was 0.88 (95% CI: 0.81–0.93). When integrated into the IHC4+C algorithm ICC for RR was 0.99 (95% CI: 0.99–1.00); risk category agreement level was 414/420 (98.6%), both indicating almost perfect agreement. Agreement for intrinsic subtype calls varied between 347/399 (87.0%) and 381/418 (91.1%) dependent on definition and archetype used.

**Conclusions:** Residual inter-lab variability in Ki67 when scored by the Global method has negligible effect on estimates of RR when integrated into the IHC4+C algorithm.

**Conflict of interest:** Ownership: Torsten Neilsen, proprietary/patent interest in Bioclassifier LLC. Advisory Board: Mitch Dowsett, Genoptix. Other Substantive Relationships: Torsten Neilsen, consultancy with NanoString.

**492** Poster/Poster Spotlight

**Diagnostic performance of standard breast MRI to exclude extensive nodal disease in breast cancer patients**

T. Van Nijnatten[1], E. Ploumen[1], B. Goorts[1], R.J. Schipper[1], S. Vanwetswinkel[2], M. Schavemaker[2], P. Nelemans[3], E. Heuts[4], R. Beets-Tan[5], M. Smidt[4], M. Lobbes[2]. *[1]Maastricht University Medical Centre, Radiology and Nuclear Medicine/Surgery, Maastricht, Netherlands; [2]Maastricht University Medical Centre, Radiology and Nuclear Medicine, Maastricht, Netherlands; [3]Maastricht University Medical Centre, Epidemiology, Maastricht, Netherlands; [4]Maastricht University Medical Centre, Surgery, Maastricht, Netherlands; [5]The Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital, Radiology, Amsterdam, Netherlands*

**Background:** According to recent studies, limited axillary nodal disease (pN1) in breast cancer patients does not affect prognosis compared to node negative patients (pN0). As a result, excluding extensive axilary nodal disease (pN2−3) at initial diagnosis is becoming more and more important. Therefore, the purpose of this study was to evaluate the diagnostic performance of standard breast MRI in breast cancer patients to exclude pN2−3, in case pN0 or pN1 is predicted.

**Material and Methods:** All patients diagnosed with primary invasive breast cancer who underwent standard breast MRI prior to surgery in our hospital between 2009 and 2014 were included. Exclusion criteria were neoadjuvant systemic therapy and previous axillary surgery or radiotherapy. Two dedicated breast radiologists independently reassessed all breast MRIs and scored each axillary lymph node on a confidence level scale of 0 to 4. Results were compared to the gold standard of histopathology. Diagnostic performance was analysed by calculating false negative percentages and negative predictive values (NPV) for respectively pN0 and pN1. Quadratic weighted kappa measured interobserver agreement.

**Results:** A total of 200 patients were included. In case pN0 was predicted by the radiologists, pathology showed pN2−3 in 1.2% and 1.4%, with a NPV of 98.8% (95.3–99.8%) and 98.7% (94.7–99.8%) respectively. When pN1 was predicted by the radiologists, pathology showed pN2−3 in 13.0% and 10.2%, with a NPV of 87.0% (65.3–96.6%) and 89.8% (77.0–96.2%) respectively (Table 1). Interobserver agreement between both radiologists was considered good (weighted kappa = 0.624).

Table 1. Diagnostic performance of nodal staging on standard breast MRI

| | Reader 1 | | | Reader 2 | | |
|---|---|---|---|---|---|---|
| | pN0 | pN1 | pN2−3 | pN0 | pN1 | pN2−3 |
| pN0 (n = 153) | 140 | 9 | 4 | 127 | 26 | 0 |
| pN1 (n = 38) | 24 | 11 | 3 | 18 | 18 | 2 |
| pN2−3 (n = 9) | 2 | 3 | 4 | 2 | 5 | 2 |

**Conclusion:** A negative preoperative breast MRI can exclude extensive nodal disease in breast cancer patients. Furthermore, breast MRI differentiates more accurately between limited and extensive axillary nodal disease, compared to current conventional imaging.

**No conflicts of interest**

**493** Poster

**True false negative rate of benign histology after stereotactic vacuum-assisted biopsy for BI-RADS IV calcifications in the breast**

F.E.M. Dams[1], P.J. Westenend[2,3], H.S. Roodenburg-Kooij[1], M.C. Rozendaal[1], M.C.J.M. Kock[1,3]. *[1]Albert Schweitzer Hospital, Radiology, Dordrecht, Netherlands; [2]Laboratory For Pathology, Pathology, Dordrecht, Netherlands; [3]Bevolkingsonderzoek Zuid-west, Rotterdam, Netherlands*

**Background:** Currently there are no uniform guidelines in the Netherlands regarding the necessity and timing of follow-up after stereotactic vacuum-assisted biopsy of Breast Imaging-Reporting and Data System (BI-RADS) IV breast calcifications with benign histology. To determine whether follow-up is indicated for these benign lesions we wanted to know the true false negative rate after stereotactic vacuum-assisted biopsy.

**Materials and Methods:** In our hospital stereotactic vacuum-assisted biopsy is performed since august 2004, consecutively with 10 Gauge en 9 Gauge needles. Retrospectively we identified the number of BI-RADS IV breast calcifications with benign histology for which a stereotactic vacuum-assisted biopsy was performed between August 2004 and May 2014 and for which a follow-up period of at least one year is available. Subsequently we determined in which of these lesions a malignancy or ductal carcinoma in situ (DCIS) developed and if so, after what interval. We retrospectively revised the biopsies of the cases in which later a malignancy or DCIS was diagnosed in the biopsied area.

**Results:** In the study period for 744 BI-RADS IV breast calcifications a stereotactic vacuum-assisted biopsy was performed with a benign histology. Patient age varied from 27 to 87 years, with a median of 53 years. In six lesions a malignancy or DCIS developed, with patient age varying from 40 to 72 years and with a median of 53 years. In three lesions a ductal type adenocarcinoma developed (two T1 and one T2, all three N1). In one lesion a tubular carcinoma with DCIS grade I developed and in two lesions DCIS grade III developed. The interval between stereotactic biopsy and detection of DCIS or breast carcinoma was 21 to 88 months, with an average of 47 months. In two cases at revision of the biopsies DCIS was identified, corresponding to the type of DCIS which was later diagnosed.

**Conclusions:** According to our database the true false negative rate (including cases with an interval of more than three years) after stereotactic vacuum-assisted biopsy of BI-RADS IV breast calcifications is 0.81%. In our opinion, in hospital follow-up is not necessary for woman in the age group of the nationwide breast cancer screening programme. For younger patients we suggest in hospital mammographic screening once every two years.

**No conflicts of interest**

**494** Poster

**The role of radiologic evaluation for detection of axillary lymph node metastasis in early breast cancer**

C.H. Shin[1], J.I. Kim[1], J.Y. Lee[2]. *[1]Inje University College of Medicine-Ilsan Paik Hospital, Department of Surgery, 170- Juhwa-ro- Ilsanseo-gu- Goyang-si- Gyeonggi-do- Korea, Korea; [2]Inje University College of Medicine- Ilsan Paik Hospital, Department of Radiology, 170- Juhwa-ro- Ilsanseo-gu- Goyang-si- Gyeonggi-do- Korea, Korea*

**Background:** Axillary lymph node metastasis (ALNM) is a key prognostic factor of breast cancer, thus, diagnostically accurate methods for determining ALNM are very important.

The purpose of this study was to evaluate the availability of preoperative breast ultrasonography (US), contrast-enhanced magnetic resonance imaging (MRI), and $^{18}$F-fluorodeoxyglucose positron emission tomography-computed tomography (PET-CT) for detection of ALNM in early breast cancer (tumor size $\leqslant$5 cm).

**Material and Methods:** The medical records of patients with breast cancer who underwent sentinel lymph node biopsy or axillary lymph node dissection after preoperative breast US, MRI and PET-CT between January 1, 2012 and October 31, 2014, were retrospectively reviewed. We analyzed positive predictive value (PPV), negative predictive value (NPV), sensitivity and specificity of each radiologic modality.

**Results:** Of 105 patients with early breast cancer underwent axillary surgery, 71 patients evaluated all radiologic modalities preoperatively.

The mean age of patients was 50.7±11.0 years (range 30−80 years). 55 patients underwent planned sentinel lymph node biopsy (SLNB), and 16 patients underwent planned axillary lymph node dissection (ALND).

8 patients underwent SLNB needed additional ALND after frozen biopsy. 28.2% (20/71) of patients exhibited ALNM on pathologic report.

The PPV was 52.2%, 61.9%, and 92.3%, and the NPV was 83.3%, 86.0%, and 86.2%, respectively. The sensitivity was 60.0%, 65.0%, and 60.0%, and specificity was 78.4%, 84.3%, and 98.0%, respectively.

**Conclusion:** There are no definitive modalities for detecting ALNM in early breast cancers to replace SLNB. However, PET-CT seems to be a predictive radiologic modality for detection of axillary LN metastasis considering higher PPV and specificity. If ALNM is suspected based on PET-CT, ALND without SLNB might be a better option.

**No conflicts of interest**

**495** Poster

**Outcomes of incidental breast nodules, overview of imaging and histopathology**

S.Y. Ham[1], B.K. Ko[2], S.B. Park[2]. *[1]Korea University Anam Hospital, Department of Radiology, Seoul, Korea; [2]Ulsan University Hospital, Department of Surgery, Ulsan, Korea*

**Background:** An increasing number of breast lesions are noted in chest CT scan, for the purpose of screening or follow evaluation for malignancy evaluation detected. The aim of this study was to review the rate of referrals to the breast section for assessment of lesions identified on CT and to evaluate the imaging findings and histopathology in case of biopsy, excision.

**Materials and Methods:** A retrospective review was undertaken of CT examinations conducted over a period of 7 years. All patients (with no previous history of breast cancer) whose report contained the keyword "recommand breast U or mammogrpahy"and who were referred to a specialist breast center for assessment were reviewed. CT lesion morphology and enhancement pattern were identified and compared with the final diagnostic outcome. The imaging findings were classified into to three groups, mass, asymmetry, calcifications. The site, location and extent or mass size were recorded.

**Results:** 61 patients were identified by retrospective analysis, incidental breast lesions, of which 11 (18%) were malignant. This gave a positive predictive value (PPV) for malignancy of 14.7%. The histopathology types were invasive ductal carcinoma (7), ductal carcinoma in situ (1), phyllodes tumor (1), medullary carcinoma (1), lymphoma (1). The best morphological predictor of malignancy was spiculation (PPV, 68%) and enhancement (PPV, 48%), whereas calcification patterns (PPV, 27%). Malignant lesions were likely to be larger (mean, 21.5 mm) than benign lesions (mean, 17.2 mm). As an associated findings, axillary nodes enlargement and regional parenchymal retraction are more common in malignancy. Combined malignancy were colon cancer (5), hepatocellular ca (2), lymphoma (1), thyroid ca (2), lung cancer (3). Two of them were triple cancer, lung, thyroid, breast and breast, lung and colon cancers.

**Conclusions:** In conclusion, 18% of incidental breast lesions in this large series of patients proved to be as breast cancers, particularly irregular spiculated masses with enhancement. Careful evaluation for incidentally detected breast lesions are should be followed, especially in cancer follow up patients.

**No conflicts of interest**

**496** Poster

**Breast cancer diagnosis and subtyping by analysing exhaled breath: A pilot study using a portable electronic nose (Aeonose®)**

J. Timmer-Bonte[1], S. Grosfeld[1], N. Seelen-Janssen[1], L. Veenendaal[2], F. Zijlstra[3]. *[1]Alexander Monro Breast Cancer Hospital, Medical Oncology, Bilthoven, Netherlands; [2]Alexander Monro Breast Cancer Hospital, Surgery, Bilthoven, Netherlands; [3]Alexander Monro Breast Cancer Hospital, Radiology, Bilthoven, Netherlands*

**Background:** Analysing exhaled breath is a rapidly emerging field of medical diagnostics. Growing evidence suggests pathological conditions can cause metabolic changes in the body resulting in deviations in volatile organic compounds (VOC's) in exhaled breath. The hand-held electronic nose used in this pilot study is convenient to use and has already proven to be capable of distinguishing patients (pts) suffering from lung cancer and head and neck cancer from healthy controls. Advantages include non-invasiveness and fast results. The objective of the current study is to investigate if exhaled-breath patterns from breast cancer (BC) pts can be distinguished from pts with benign breast pathology or healthy controls.

**Methods:** Female pts referred to our breast cancer hospital for screening or on suspicion of BC, were subjected to standard diagnostic procedures as per protocol (with a minimum of clinical examination, mammography and in case of BIRADS >2 biopsy). All pts were asked written informed consent for performing an additional breath test. Pts had to breathe into the Aeonose® device (made available for this pilot study by The eNose Company, Zutphen, The Netherlands) for a period of 5 minutes. Collected measurement data were compressed using a Tucker3 algorithm followed by neural network analysis. In this way, the electronic nose has been trained to distinguish between healthy and affected pts.

**Results:** 185 pts were eligible; the majority was referred because of a palpable lesion or abnormal findings on mammography in the Dutch national screening program. In 56 pts BC was confirmed (biopsy or surgery). In the remaining 129 pts no or benign (e.g. cysts or fibroadenoma) breast disease (noBC) was diagnosed. Based on the measurement data of the VOC's in exhaled breath, a ROC (Receiver Operating Characteristic)-curve has been created showing only a fair sensitivity and specificity of 68% and 64%, respectively. However, BC is a heterogeneous disease. Therefore, explorative analyses were performed. Indeed, noBC (n = 119) compared to either Invasive Ductal Carcinoma (IDC) (n = 38) or to Invasive Lobular Carcinoma (ILC) (n = 11) showed an improved sensitivity and specificity (IDC 71% and 55%; ILC 100% and 81% respectively). All analyses were cross-validated using a leave-one-out method.

**Conclusion:** The high sensitivity and specificity values found for (the relatively homogeneous) ILC indicates this technology has potential for convenient, quick, and non-invasive screening of (a)symptomatic patients. Based on our experience we expect the ROC-curve to improve for IDC when increasing numbers in several pathological subtypes can be included. Based on these results we intend to perform a larger multicentre trial as the Aeonose electronic nose could be a convenient and cost-effective screening test for both patient and staff.

**No conflicts of interest**

**497** Poster

**Hybrid PET-MR imaging for accurate nodal staging prior to neoadjuvant chemotherapy in breast cancer patients − preliminary results**

B. Goorts[1], T. Van Nijnatten[2], S. Voo[3], F. Mottaghy[3], J. Wildberger[2], M. Lobbes[2], M. Smidt[4]. *[1]MUMC, Surgery and Radiology, Maastricht, Netherlands; [2]MUMC, Radiology, Maastricht, Netherlands; [3]MUMC, Nuclear Medicine, Maastricht, Netherlands; [4]MUMC, Surgery, Maastricht, Netherlands*

**Purpose:** To assess the clinical value of hybrid FDG PET-MR imaging for nodal staging prior to neoadjuvant chemo- and immunotherapy (NAC) in breast cancer patients.

**Materials and Methods:** In this prospective study, patients with primary invasive breast cancer with at least cT2 and/or a histopathologically confirmed lymph node metastasis undergoing NAC were included. A hybrid PET-MR breast protocol was performed before NAC. MR images were evaluated independently by one dedicated breast radiologist, PET images independently by one dedicated nuclear physician. Afterwards a combined PET-MR report was made. The number and localization of lymph nodes suspicious for metastases on PET-MR was compared to conventional nodal staging methods, i.e. ultrasound with core needle biopsy and MRI-only. The percentage of patients with a modified treatment plan based on PET-MR was studied.

**Results:** In this ongoing study, 25 patients were included. In 16% (4/25) of the included cases, treatment plan altered based on PET-MR findings. In two patients, PET-MR showed an enlarged internal mammary lymph node with high FDG-uptake. One patient had five axillary lymph nodes suspicious for metastases on PET-MR, whereas initially only two where seen on ultrasound and none on MRI-only. For these three patients radiotherapy plan was extended. One patient had three axillary lymph nodes suspicious for metastases on PET-MR compared to more than three on ultrasound and MRI-only, resulting in a reduced radiotherapy plan.

**Conclusion:** Pre-NAC hybrid PET-MR changed treatment plan in 16% of patients. Consequently, PET-MR might be more accurate for nodal staging, compared to conventional imaging.

**No conflicts of interest**

**498** Poster

**Molecular determination of the clonal relationship between multiple tumors in BRCA1/2 patients has clinical importance**

W. Geurts-Giele[1], V. Van Verschuer[2], C. Van Deurzen[1], P. Van Diest[3], R. Pedrosa[1], J. Collee[4], L. Koppert[2], C. Seynaeve[5], W. Dinjens[1]. *[1]Erasmus MC Cancer Institute- University Medical Center Rotterdam, Pathology, Rotterdam, Netherlands; [2]Erasmus MC Cancer Institute-University Medical Center Rotterdam, Surgical Oncology, Rotterdam, Netherlands; [3]University Medical Center Utrecht, Pathology, Utrecht, Netherlands; [4]Erasmus MC Cancer Institute- University Medical Center Rotterdam, Clinical Genetics, Rotterdam, Netherlands; [5]Erasmus MC Cancer Institute- University Medical Center Rotterdam, Medical Oncology, Rotterdam, Netherlands*

**Background:** Female BRCA1/2 mutation carriers commonly develop breast cancer and ovarian cancer. If multiple tumor localizations are present, it is of utmost importance to know the clonal relationship between the lesions (multiple primaries or metastasized disease), since prognosis and treatment differ between these tumors and their metastases. We evaluated the value of targeted Next Generation Sequencing (NGS) in the diagnostic workup of BRCA1/2 mutation carriers with $\geqslant$2 tumor localizations and uncertain tumor origins.

**Materials and Methods:** Fourteen BRCA1/2 mutation carriers with $\geqslant$2 tumor localizations were selected, median age at first cancer diagnosis was 41.5 years (range 33−59). Four patients with inconclusive tumor origin after histological and immunohistochemical analyses were 'cases'; 10 patients with certain tumor origin of $\geqslant$3 tumors served as 'controls'. Tumors of cases and controls were analyzed by targeted NGS using a panel including CDKN2A, PTEN and TP53, hotspot mutation sites for 27 different genes and 143 single nucleotide polymorphisms for detection of loss of heterozygosity (LOH). Based on prevalence of identical or different mutations and/or LOH patterns, tumors were classified as 'multiple primaries' or 'one entity'.

**Results:** In 44 tumors, 48 mutations were found; 39 (81%) concerned TP53 mutations. In all 10 controls and all 4 cases, the intrapatient clonal relationships between the tumors could be unequivocally identified by molecular analysis. In all controls, tumor origins based on molecular outcomes matched the conventional histopathological diagnosis.

**Conclusions:** In most BRCA1/2 mutation carriers with multiple tumors routine pathology work-up is sufficient to determine tumor origins and relatedness. However, in 10% of cases conventional pathology is inconclusive. Molecular analysis using NGS can reliably determine clonal relationships between tumors, facilitating appropriate treatment of individual patients.

**No conflicts of interest**

**499** Poster

**Concomitant breast carcinoma and phyllodes tumour: A case series**

E. Sin[1], B. Tan[1], T. Puay Hoon[2]. *[1]Singapore General Hospital, General Surgery, Singapore, Singapore; [2]Singapore General Hospital, Pathology, Singapore, Singapore*

**Background:** Phyllodes tumours (PT) are rare fibroepithelial breast neoplasms, accounting for merely 0.3−1% of all primary tumours of the breast. Malignant transformation of the epithelial component is rare, and only reported in literature as sporadic cases of carcinoma associated with PTs. We report the clinico-pathological characteristics of in-situ and invasive carcinoma co-existing with PT in 10 patients treated in our institution over an 11-year period.

**Methods:** From 1992 to 2012, all patients who were found to have PT associated with an in-situ or invasive carcinoma on histology were included in the study. Patient demographics, clinical presentation, surgery, histology, treatment and follow-up were recorded and analysed.

**Results:** Ten patients with co-existing PT and in-situ or invasive carcinoma were identified from our records. Six of them had carcinoma found within the PT. All were female and their median age was 47 (range 43−72) years. One patient had a history of PT in the same breast while another had a history of PT in the same breast as well as IDC in the contralateral breast. The rest did not have any risk factors of breast cancer. Five patients had a pre-operative core needle biopsy performed with the report of a fibroepithelial lesion. The rest of the patients had surgery upfront for their breast masses. Two patients who had ER/PR positive invasive carcinoma received adjuvant hormonal therapy. Patients were followed-up for a mean of 3.6 years (9 months to 10 years) and all patients were alive and recurrence-free.

**Conclusion:** PT associated with carcinoma is a rare entity, and we present a series of cases that add to the limited current literature. It is often difficult to detect the presence of the carcinomatous component pre-operatively. Hence, close examination of resected PT specimens must be carried out to allow prompt detection of any associated carcinomas, however rare, such that adequate treatment can be given.

*Please note that tables were not included in this abstract because it exceeded the size allowed by the submitting software.

**No conflicts of interest**

**500** Poster

**Variation in the use of FDG-PET/CT in staging of node positive breast cancer**

L. Veneklaas[1], L.F. De Geus-Oei[2], J. Verloop[1], J. Klaase[3], C. Ticheler[2], C. Bavelaar-Croon[4], S. Siesling[1]. *[1]Netherlands Comprehensive Cancer Organisation, Research, Utrecht, Netherlands; [2]Leiden University Medical Centre, Radiology, Leiden, Netherlands; [3]Medisch Spectrum Twente, Surgery, Enschede, Netherlands; [4]Ziekenhuis Gelderse Vallei, Nuclear Medicine, Ede, Netherlands*

**Background:** To prevent ineffective treatment and unnecessary costs correct staging information is needed to choose the best treatment plan in breast cancer patients having positive axillary lymph nodes or a tumour with direct extension to chest wall and/or skin. Recommendations within the Dutch national NABON-guideline concerning the use of FDG-PET/CT in staging of breast cancer are limited. The primary objective of the present study was to get insight in the application of imaging techniques and the use of FDG-PET/CT for breast cancer staging in hospitals in the Netherlands.

**Material and Methods:** In this retrospective multi-institutional study, patients diagnosed with lymph node positive breast cancer in 2011 and 2012 were selected from the Netherlands Cancer Registry (NCR). Data about applied initial staging imaging techniques (conventional imaging by bone scan, chest x-ray, ultrasonography of the liver or abdominal/chest CT-scan versus whole body FDG-PET/CT) and additional imaging techniques in case of inconclusive results by initial imaging were collected from the patient files from eight participating hospitals.

**Results:** The study population consisted of 262 patients. In 19 patients no staging by imaging was performed. Initial FDG-PET/CT was performed in 68 patients and conventional imaging in 175 patients. In 97 patients (39.9%) additional imaging was required. Additional imaging seemed to be more often requested after initial conventional imaging (42.3%) as compared to FDG-PET/CT based staging (33.8%), however this was not significant ($\chi$2: p = 0.16). Timing of staging (pre- or postoperatively) differed between the two imaging methods and between different hospitals however not statistically significantly, $\chi$2: p = 0.87.

**Conclusions:** Our study shows that eight Dutch hospitals greatly vary in the number, frequency and timing of the different staging imaging techniques. Further research is needed to explore the factors explaining the variance on the one hand, and accuracy and efficiency of the staging imaging techniques on the other hand to support the development of evidence based recommendations for the guideline.

**No conflicts of interest**

**501** Poster

**Digital pattern recognition can aid H&E based breast histopathological diagnosis**

M. Balkenhol[1], B. Ehteshami Bejnordi[2], R. Holland[2], M. Hermsen[1], N. Timofeeva[1], N. Karssemeijer[2], G. Litjens[3], P. Bult[1], J. Van der Laak[1]. *[1]Radboud University Medical Centre, Pathology, Nijmegen, Netherlands; [2]Radboud University Medical Centre, Radiology and Nuclear Medicine, Nijmegen, Netherlands; [3]University of Heidelberg, Hamamatsu Tissue Imaging and Analysis Center, Heidelberg, Germany*

**Background:** Breast cancer incidence keeps rising and with the advent of personalized medicine, there is an increasing demand for high level pathological diagnostics. Protocols for microscopic inspection of tissue slides have to focus equally on efficiency and accuracy to address this adequately. Digitizing microscopic tissue sections at high resolution by means of whole-slide scanning systems provides new opportunities for breast histopathology. Application of advanced pattern recognition techniques on these so called 'whole slide images' (WSI) can aid pathologists by detecting clinically relevant regions or sections, allowing them to optimize their workflow.

Where conventional digital pattern recognition relied on computerized extraction of features that resemble those used by humans, this field has recently shifted dramatically to 'deep learning' algorithms. In this work, we studied the feasibility of using digital pattern recognition techniques to fully automatically detect lesions in WSI of haematoxylin and eosin (H&E) stained tissue sections. We focused on two clinically relevant applications:

detecting DCIS in resection specimens and detecting metastases in sentinel lymph nodes.

**Material and Methods:** DCIS detection A set of 150 WSI of H&E stained tissue sections (75 benign/normal, 75 annotated DCIS) was used to develop an algorithm that automatically identifies regions containing epithelium and classifies these as DCIS or benign/normal. The performance of this system was evaluated on an independent test set.

Sentinel lymph node metastasis detection From a set of 173 annotated WSI of H&E stained tissue sections, small prototype image regions were extracted to train a convolutional neural network to detect cancer areas. After training and optimization, the network was used to predict presence of metastases in an independent test set.

**Results:** DCIS detection The proposed system detected all slides containing DCIS at an average of 2.6 false positive detections per WSI. On lesion level, 80% of all DCIS lesions in an abnormal slide were detected at an average of 2 false positive detected regions per WSI.

Sentinel lymph node metastasis detection Of all individual micro- and macro-metastases, 90% could be identified at the cost of 1 false positive detection per normal WSI. Including isolated tumor cell clusters, 71% was found with 1 false positive detection per normal WSI. In the independent test set, 40% of the WSI containing benign and normal tissue could be identified without missing a cancer case without the use of any additional staining or human intervention.

**Conclusions:** Our results show that advanced digital pattern recognition is capable to fully automatically identify and characterise lesions in WSI. We therefore expect these techniques to have the potential to substantially aid the pathological diagnostic process in the near future.

**No conflicts of interest**

**502** Poster

**Concordance between PAM50 and clinico-pathological prognostic markers when deciding on adjuvant chemotherapy in early breast cancer**

K. Van Asten[1], P. Neven[2], V. Puthod[3], N. Ghali[4], A. Lintermans[2], L. Jongen[1], P. Moerman[5], E. Van Limbergen[6], A. Smeets[7], I. Nevelsteen[7], H. Wildiers[8], G. Floris[5]. *[1]KU Leuven, Gynaecological Oncology, Leuven, Belgium; [2]UZ Leuven, Gynaecology and Obstetrics, Leuven, Belgium; [3]NanoString Technologies- Inc., Cancer Research, Paris, France; [4]NanoString Technologies- Inc., Cancer Research, Seattle, USA; [5]UZ Leuven, Imaging and Pathology, Leuven, Belgium; [6]UZ Leuven, Radiotherapy, Leuven, Belgium; [7]UZ Leuven, Surgical Oncology, Leuven, Belgium; [8]UZ Leuven, General Medical Oncology, Leuven, Belgium*

**Background:** In early estrogen receptor-positive (ER+) HER2-negative (HER2−) breast cancer (BC), multigene signatures (MGS) are prognostic and may guide clinical decisions on adding adjuvant chemotherapy (CT). The Prosigna® test (PAM50) is a commercially available MGS from Nanostring Technologies which identifies intrinsic molecular BC subtypes and provides a risk of recurrence score based on the expression level of 50 BC-related genes. Here, we calculated how frequent Prosigna® changed our decision based on clinico-pathological data to add CT in a cohort of 51 patients.

**Patients and Methods:** In UZ Leuven, all early primary operable ER+ HER2− BCs are assigned a surrogate BC subtype (Luminal A (LumA)-like or Luminal B (LumB)-like) using tumor grade, progesterone receptor status and Ki-67 according to the St-Gallen 2013 guidelines. Adjuvant CT indication is discussed weekly by a multidisciplinary team (MT), based on 'clinical parameters' (demographic and prognostic clinico-pathological data). In this prospective study, Prosigna® was proposed by the MT when the 'clinical decision' to add CT was unclear. Given the lack of a reimbursement for MGS in Belgium, a specific consent of patients was collected, and their tumor samples were analyzed with Prosigna® test in the Institute für Pathologie und Zytologie in Viersen, Germany. We assessed how Prosigna® changed our CT decision.

**Results:** From 01-2014 till 10-2015, 531 consecutive patients with ER+ HER2− operated BC were discussed by the MT for the indication of adjuvant CT, and in 51 patients, a Prosigna® test was performed. According to clinical decision by the MT, 25/51 (49%) would have received CT. However, after including Prosigna® 10/25 (40%) were determined to not receive CT. Out of the 26/51 (51%) deemed to not receive CT based on clinical factors, 11/26 (42%) were switched to receiving CT according to Prosigna® results. In total, Prosigna® results resulted in a switch in CT decision in 21/51 (41%) of cases.

According to standard histopathology, 17/51 (33%) were categorized in the surrogate LumA-like subtype. All these cases were also Prosigna® LumA, except for 2 that were Prosigna® LumB (12%). The surrogate LumB-like subtype was assigned in 34/51 (67%) based on standard histopathology. Of these, 13 were LumB (38%), 18 LumA (53%), 2 basal-like (6%) and 1 HER2-enriched (3%) according to Prosigna®.

Table: Changes in decision of CT based on Prosigna®

| Decision of CT by MT | Decision of CT by Prosigna® | | |
|---|---|---|---|
| | CT | No CT | Total |
| CT | 15 | 10 | 25 |
| No CT | 11 | 15 | 26 |
| Total | 26 | 25 | 51 |

**Conclusion:** As compared to standard histopathology, the Prosigna® test reclassified 12% of surrogate LumA tumors and 62% of the surrogate LumB tumors. We observed discrepancy between the clinical decision by a MT to administer CT and the Prosigna® test in 41% of the cases. About half of these discordant cases switched from no CT to CT by performing the Prosigna® analysis.

**No conflicts of interest**

**503** Poster

**Lymphomas of the breast: A single tertiary center experience**

C. Lord[1], C. Desbiens[2], S. Laberge[3], L. Provencher[2], B. Poirier[2], E. Poirier[2], G. Cantin[1], J. Lemieux[1], J.C. Hogue[2], C. Doyle[1]. *[1]CHU de Québec − Université Laval, Hemato-oncology, Quebec City, Canada; [2]CHU de Québec − Université Laval, Center for Breast Diseases, Quebec City, Canada; [3]CHU de Québec − Université Laval, Pathology, Quebec City, Canada*

**Background:** Lymphomas of the breast are rare, and there is no consensus for their management.

**Materials and Methods:** Retrospective study of breast lymphomas diagnosed between January 1993 and December 2011 at the Deschênes-Fabia Center for Breast Diseases (Quebec City, Canada). Clinical and radiological presentation, patients' characteristics, treatments, histological characteristics and outcomes were examined.

**Results:** Frequency of breast lymphoma was 0.43% (n = 30). Fourteen cases were primary breast lymphomas. Mean age was 66.4±13.6 years in 29 women and one man. A palpable mass was present in 15 patients. Mammography was abnormal in 20 patients. Percutaneous biopsy was performed in all patients. Thirteen patients underwent surgery, and biopsy/surgery correlated in 69.2% of these 13 cases. Six mucosa-associated lymphoid tissue (MALT), 9 follicular (FL), 10 diffuse large B-cell (DLBCL), 3 mantle cell, one small cell lymphocytic (SCLL) and one plasmoblastic lymphomas were diagnosed. Using a variety of therapeutic approaches, a complete response was achieved in 77.8% of DLBCL cases, and in 70.0% of indolent cases. Median follow-up was 3.06 (0.37–11.16) and 3.14 (0.72–7.20) years in DLBCL patients and in indolent cases, respectively, and median disease-free survival was 10.4 years and 5.0 years, respectively (P = 0.34). There were 6 lymphoma-related deaths (1 plasmoblastic, 0.91 years after diagnosis; 1 mantle cell, 2.36 years; 1 FL, 6.58 years; 2 DLBCL, 0.72 and 11.16 years, 1 MALT, 0.72 years).

**Conclusion:** Breast lymphomas are rare and include different subtypes. Clinical presentation may be similar to breast cancer. Core needle biopsy may allow avoiding surgery in most cases. Treatment should be tailored to each specific histology.

**No conflicts of interest**

**504** Poster

**Value of geriatric screening tools in the prediction of undertreatment in older patients with breast cancer**

F. Osorio[1], J. Urbano[2], A.R. Barradas[1], A. Magalhães[1], J.L. Fougo[1]. *[1]Sao Joao Hospital − Medical School Univ. Oporto, Breast Center, Oporto, Portugal; [2]Sao Joao Hospital − Medical School Univ. Oporto, Internal Medicine, Oporto, Portugal*

**Background:** Undertreatment is a real problem in older patients with breast cancer (BC). Our purpose was to identify the most practical and useful screening tool of geriatric frailty that predicted a higher risk of undertreatment.

**Material and Methods:** We studied a consecutive series of BC patients, aged 70yo or higher, treated from January to December 2014. Concurrent with the traditional functional evaluation we applied 3 screening scales of geriatric risk (G8, Flemish version of the Triage Risk Screening Tool and Groningen Frailty Indicator) in an additional hospital visit, before the MDT meeting or immediately after the start of treatment. We also assessed the socio-psychological status and evaluation of social, economic

and familial support. Clinical and oncologic characteristics and treatment options were recorded. Undertreatment was defined as: 1) non-completion of the age-independent MDT treatment protocol; 2) when patient refused MDT treatment proposal; 3) when in the presence of physiological frailty. Data analyses were performed using SPSS v23; statistical significance $p < 0.05$.

**Results:** We analysed 92 patients, corresponding to 26.1% of our patients in 2014. Median age was 78.1 (70−94) yo. There was only one male patient. The diagnosis was predominantly clinical, 73.9% by self-detection and 2.2% by symptomatic bone disease, and only in 23.9% was made by routine image detection. Most predominant stages were IIA (30.4%) and IA (23.9%). Eight patients presented in stage IV (8.7%). Immunohistochemical evaluation showed 83.1% of patients oestrogen receptor (ER) positive, 73.5% progesterone receptor positive and 16.4% were HER2 positive. We found that 58.7% of our patients were undertreated. Undertreatment was more frequent in stages IIA and superior; this is also pronounced in ER positive patients. Increasing age (a median age of 79.9 years had a higher risk) and pN+ correlates significantly ($p < 0.001$) with undertreatment. Other assessed variables, such as sense of being older, living alone, non-pleasing life and depression, correlated strongly (but not significantly) with undertreatment. ECOG-PS grade 2−3 and risk G8-scale also correlated with undertreatment (non-significantly); there was no such correlation with the Karnofsky, Flemish or Groninger scales. The multivariate analysis showed statistical significance ($p < 0.033$) between increasing age and undertreatment; there was correlation (without statistical significance) with TNM stage, non-pleasing life and ECOG PS and G8 scales.

**Conclusion:** The attempt to add a geriatric risk screening tool that improved the patient functional assessment before the therapeutic decision in MDT has shown us that, beyond increasing age itself, the risk identified by G8 geriatric scale equal our traditional evaluation with ECOG PS to predict an stronger likelihood of undertreatment in the elderly patient with breast cancer.

**No conflicts of interest**

**505** Poster

**Breast MRI in invasive lobular carcinoma: A useful investigation in surgical planning?**

A. Parvaiz[1], P. Yang[2], E. Razia[2], M. Mascarenhas[2], C. Deacon[2], P. Matey[2], B. Isgar[2], T. Sircar[2]. [1]*Peterborough City Hospital, Oncoplastic Breast Surgery, Peterborough, United Kingdom;* [2]*New Cross Hospital, Breast Surgery, Wolverhampton, United Kingdom*

**Background:** Breast magnetic resonance imaging (MRI) is highly sensitive in detecting invasive lobular carcinoma (ILC) of the breast. We investigate the use of breast MRI in ILC and in what proportion of patients it influences a change in the management.

**Materials and Methods:** A prospective cohort study over a 58-months period, including all consecutive patients with ILC having breast MRI scans.

**Results:** A total of 334 bilateral breast MRI scans were performed. 72 (21.5%) of these were for the assessment of histologically confirmed ILC and were eligible for evaluation. All these MRI scans were carried out within 2 week of patients given the diagnosis (median 5.5 days). Age range of these patients was 24−83 (median 56.5) years. 19 out of 72 patients in ILC group (26.4%) had change in their planned operation from wide local excision (WLE) to a different operation based on the MRI. This included 7 patients with multifocal cancers, 10 patients with significantly larger size of the cancer shown on the MRI than mammogram/ultrasound and 2 patients with contralateral malignancy. Instead of simple WLE, different operations in these 19 patients included 15 mastectomies, 1 double wire guided WLE, 1 therapeutic mammoplasty and 2 bilateral operations.

With regard to the size of cancers, MRI (median 25 mm) correlated significantly better with histopathology (median 23 mm) than mammogram (median 17 mm) and ultrasound scans (median 14.5 mm). Over a median 37 months follow up (range 20−78), 2.7% mortality rate (2/72) was observed with no loco-regional recurrence or distant metastases.

**Conclusions:** One out of every four patients (26.4%) with ILC had a change in planned operation, including 20.8% needing mastectomies instead of planned WLE due to MRI findings, hence proving its usefulness in ILC.

**No conflicts of interest**

**506** Poster

**MammaPrint in large clinical studies (MINDACT) and in diagnostics; how similar are they?**

I. Goossens-Beumer[1], A. Witteveen[1], L. Delahaye[1], M. Snel[1], J. Zheng[1], L. Van 't Veer[1], A.M. Glas[1]. [1]*Agendia, R&D, Amsterdam, Netherlands*

**Background:** MammaPrint is an FDA cleared microarray-based test that uses the expression levels of 70 genes to assess the risk of recurrence in early stage breast cancer (independent of receptor status) to help guide physicians make treatment decisions. The clinical validity of MammaPrint has been shown in a multitude of retrospective and prospective studies, including RASTER where it was shown that MammaPrint accurately predicts that Low Risk patients can safely forgo chemotherapy. This finding will be confirmed in the MINDACT trial comprising 6694 patients. While diagnostic testing is performed on custom designed diagnostic arrays, large clinical trials like MINDACT and I-SPY 2 may be performed on arrays covering the whole genome. This enables full genome analyses and development of new signatures alongside the primary study aim. The objective of the current study is to demonstrate the similarity and stability of the MammaPrint test between the diagnostic and full genome arrays, between FFPE and FF tissues, and for control samples over time.

**Material and Methods:** Both the full genome arrays and the diagnostic MammaPrint arrays contain the same 70 signature probes and the same normalization and control genes in multiple replicates. The MammaPrint algorithm was applied and MammaPrint indices were calculated for all breast cancer samples that were hybridized to both a diagnostic and a full genome array ($n = 1897$ pairs). In addition, MammaPrint indices were calculated for all samples that had both FFPE and FF tissues hybridized to either a diagnostic or full genome array ($n = 552$ pairs), and for all control samples ($n > 11{,}000$). We evaluated the concordance of MammaPrint indices between the diagnostic versus full genome arrays and between FF versus FFPE tissues, and assessed stability of control samples over time.

**Results:** For the diagnostic versus full genome array comparison, Lin's concordance correlation coefficient (CCC), a measure for both precision and accuracy, was 0.99 (95% CI 0.989–0.991), indicating an almost perfect concordance. For paired FF and FFPE samples the CCC indicated very high concordance of 0.91 (95% CI 0.90–0.92). Control samples that were taken along with each batch of MammaPrint were plotted over time (>10 years) and showed highly stable repeated measurements.

**Conclusions:** Results confirm that MammaPrint and MammaPrint FFPE are robust, equivalent and stable tests. Moreover, MammaPrint results on full genome arrays, as used in the MINDACT trial show an excellent concordance to MammaPrint results obtained from the regular diagnostic array. The combination of the outstanding equivalence between FF and FFPE, excellent concordance between different array types, and profound stability over time demonstrate that results from clinical trials are similar to the current MammaPrint FFPE and fresh diagnostics and can be used interchangeably.

**Conflict of interest:** Other Substantive Relationships: All authors are current employees of Agendia. In addition LvV is listed as one of the inventors on the MammaPrint 70 gene patent.

**507** Poster

**Determining HER2 status on one-day accelerated core needle biopsy specimen: A consecutive case series of breast lesions**

J. Bulte[1], A. Halilovic[2], L. Strobbe[1], P. Bult[2], J. De Wilt[3]. [1]*Canisius Wilhelmina hospital, General surgery, Nijmegen, Netherlands;* [2]*Radboudumc, Pathology, Nijmegen, Netherlands;* [3]*Radboudumc, General surgery, Nijmegen, Netherlands*

**Background:** In breast cancer diagnosis, there are high demands on both accuracy and speed. Also, the initial biopsy should ideally provide reliable information on prognostic and predictive parameters. This includes histologic type, Bloom-Richardson grading, Estrogen and Progesterone Receptor status (ER and PR), and human epidermal growth factor receptor 2 (HER2) status. This is particularly crucial in cases where neo-adjuvant systemic therapy is considered. To meet these demands our clinic adopted the accelerated core needle biopsy (aCNB) procedure. This procedure utilises microwave irradiation to shorten the required formalin fixation time. The results of the diagnostic accuracy have been published previously. The accuracy of the HER2 status assessment in aCNB specimen is presented in this study.

**Methods:** The HER2 status of 69 consecutive cases from our breast clinic that underwent aCNB and subsequent resection was determined on both the aCNB and the resection specimen. Immunohistochemistry (IHC) was used as the primary test. HER2 is scored as 0, 1+, 2+ or 3+. 0 and 1+ are considered negative, 2+ equivocal and 3+ a positive result. In accordance with Dutch breast cancer guidelines, whenever results were equivocal, fluorescence in situ hybridization (FISH) was performed as an additional test. The final HER2 status of aCNB and resection specimen was then compared, and related to the correlation for regular CNB- and resection specimen in the literature.

**Results:** The absolute correlation between aCNB and resection for IHC data alone is 37/69 cases (54%). This is mostly due to cases with equivocal (2+) results on aCNB that had a negative (1+) result on the resection. The results IHC combined with FISH testing of equivocal results raises the absolute correlation to 66/69 cases (96%). When this result is corrected for

chance correlation using the cohens kappa statistic, kappa is 0.86 (which is generally considered to be a good correlation). A recent meta-analysis shows a raw correlation of 98%.

**Conclusion:** The correlation between HER2 status of aCNB and resection specimen is high, and similar to correlation of HER2 status for regular CNB and resection specimen as reported in the literature. Therefore HER2 status can reliably be determined on accelerated processing Core Needle Biopsy specimen.

**No conflicts of interest**

**509** Poster

**Improved detection rate of invasive breast cancers with tomosynthesis compared to 2D mammography in a screening program context**

J.C. Hogue[1], M. Julien[2], Y. Loisel[3], L. Provencher[1], C. Diorio[1]. [1]*CHU de Québec, Center for Breast Diseases, Québec, Canada;* [2]*Laval University, Radiology, Quebec City, Canada;* [3]*CHU de Québec, Radiology, Québec, Canada*

**Background:** Recall rate of the breast cancer screening population-based program with 2D digital mammography (2D DM) in Quebec, Canada, is high (11.4%) and positive predictive value (PPV) of recalls is low. The purpose of this study was to determine if screening with digital breast tomosynthesis (DBT) in addition to 2D DM could reduce the recall rate and improve the positive predictive value of the recalls, while keeping an adequate cancer detection rate.

**Material and Methods:** We reviewed all 50−69 years old women who had a screening 2D DM between Nov 1st 2012 and Oct 31st 2013 and those who had a DBT with their screening 2D DM between Nov 1st 2013 and Oct 31st 2014. We compared recall, PPV of recalls and cancer detection rates between these two groups. Type of cancers diagnosed after screening was assessed.

**Results:** 2716 screening DBT with 2D DM were performed between Nov 1st 2013 and Oct 31st 2014 and were included. In the group with 2D DM alone, 11.4% of patients were recalled and cancer detection rate was 5.2/1000, compared to 13.1% (n = 355) recall rate and 16.2/1000 (n = 44) cancer detection rate for the group with 2D DM+DBT. PPV was 12.4% for 2D DM+DBT, compared to 5.9% for 2D DM alone group. Proportion of in situ cancers was 15.7% for 2D DM group and 10.9% for 2D DM+DBT group.

**Conclusions:** These results suggest that using DBT with 2D DM for screening greatly improves PPV of the recalls. Cancer detection rates are also higher when using DBT. We detected less in situ cancers in proportion when combining 2D DM+DBT, which means not only we detected more cancers, but also the cancers were more frequently invasive cancers. However, recall rates are slightly higher with DBT compared to 2D DM alone. DBT might be integrated in population-based screening in order to improve program performance.

**No conflicts of interest**

**510** Poster

**Serum tumor biomarkers in breast cancer: PAB1 and PAB2**

J.S. Lee[1], J. Na[1], I. Yoon[2], K. Suh[3], J. Kim[1]. [1]*Chungnam National University, General surgery, Daejeon, Korea;* [2]*CNC M&Y surgical Clinic, General surgery, Chung-Ju, Korea;* [3]*Paichai Unuiversity, Department of Biochemistry, Daejeon, Korea*

**Background:** For many malignancies, serum tumor markers play an important role in patient management. The elevation of serum markers in breast cancer may be helpful in early diagnosis, determining prognosis, predicting response or resistance to specific therapies, surveillance after primary surgery, and monitoring therapy in patients with advanced disease. Clinician has been need for a diagnostic marker and a method for breast cancer that allows the accurate diagnosis of early breast cancer and allows the prognosis of breast cancer to be made. Simple and selective diagnosis of breast cancer using blood, which is a relatively easily obtainable specimen for healthy persons and patients affected with breast cancer. The aim of this study was to assess the clinical significance of serum tumor marker PAB1 and PAB2.

**Material and Methods:** This study enrolled 92 subjects undergoing diagnostic biopsy for breast cancer and 88 normal controls. We measured the serum levels of PAB1 and PAB2 using an ELISA and investigated its associations with tumor clinicopathologic characteristics and diagnostic power.

**Results:** At the cut-off point 9.59 ng/ml on the receiver operating characteristic curve (ROC) PAB1 could well discriminate breast cancer from normal controls with a sensitivity of 85.6%, specificity 79.6% and area under the ROC(AUC) 0.87±0.03. Also cut-off point on ROC PAB2 is 2.59 ng/ml with a sensitivity of 93.8%, specificity 83.7% at AUC 0.94±0.18. Combination analysis of PAB1 or PAB2 for detection of breast cancer shows the superior diagnostic capacity than CA15−3.

**Conclusions:** Overall, we conclude the serum PAB1 and PAB2 is useful serum marker for diagnosis of breast cancer therefore these marker has a valuable use as a diagnostic marker and companion marker to conventional breast tumor markers.

**No conflicts of interest**

# Friday, 11 March 2016

**POSTER SESSION**

# Rehabilitation/Survivorship

**511** Poster

**Predictors of post traumatic growth among breast cancer patients in Nepal**

A. Sharma[1], J. Zhang[2]. [1]*Janamaitri Foundation Institute of Health Sciences, School of Nursing, Lalitpur, Nepal;* [2]*Central South University, School of Nursing, Changsha, China*

**Background:** Living with highly adverse experiences like breast cancer has both negative and positive consequences. There has been found increasing evidence that there are some aspects of having cancer that patients view as positive or beneficial termed as post traumatic growth (PTG). It has been found that total PTG score is significantly positively associated with global quality of life and physical functioning.

**Method:** A cross-sectional descriptive design was used. Structured form for socio-demographic and disease related information, Hospital Anxiety and Depression Scale (HADS) and Post traumatic growth Inventory (PTGI) were used to collect information from 120 participants from Bhaktapur cancer hospital, Nepal from May 2013 to August 2013.

**Result:** The mean age of respondents was 51.92 (SD = 10.1783). Mean post traumatic growth (PTG) score was 54.62 (SD = 13.66). 19.2% of respondents had no or low level of PTG and 80.8% had moderate to high levels of PTG. Among the factors of PTG, majority of respondents (85%) shown growth in relating to others, followed by appreciation of life (74.2%), spiritual change (67.5%), personal strength (63.3%), and new possibilities (45.8%). Post traumatic growth was found to be significantly positively correlated with educational status of respondents ($r = 0.220$, $P = 0.016$) and negatively correlated with year since diagnosis ($r = -0.253$, $P = 0.005$), anxiety level of respondents ($r = -0.286$, $P = 0.002$) and depression level of respondents ($r = -0.200$, $P = 0.029$). Age of respondents ($P = 0.003$, $B = -0.331$ and Beta = −0.247) and depression level of respondents ($P = 0.000$, $B = -1.968$ and Beta = −0.401) accounts for 25.1% of variance in post traumatic growth of respondents. Depression level ($P = 0.001$, $B = -0.600$ and Beta = −0.296), occupation ($P = 0.007$, $B = -1.517$ and Beta = −0.228) and age of respondents ($P = 0.016$, $B = -0.113$ and Beta = −0.204) accounted for 23% of variance in growth in relating to others. Depression level ($P = 0.000$, $B = -0.482$ and Beta = −0.371) and age ($P = 0.004$, $B = -0.086$ and Beta = −0.241) accounted for 22.3% of variance in growth in new possibilities. Depression level ($P = 0.001$, $B = -0.346$ and Beta = −0.291) and age ($P = 0.001$, $B = -0.90$ and Beta = −0.277) accounted for 18.5% of variance in growth in personal strength. Depression level ($P = 0.001$, $B = -0.226$ and Beta = −0.282), occupation ($P = 0.021$, $B = -0.509$ and Beta = −0.194) and age of respondents ($P = 0.003$, $B = -0.055$ and Beta = −0.194) accounted for 23.1% of variance in appreciation of life.

**Conclusion:** Screening for psychological morbidity in oncology patients is very important. Growth (positive psychological changes) was observed in various factors of PTG among breast cancer patients. Finding suggests negative correlation between anxiety and depression with PTG. Thus for the holistic treatment plan of cancer patient prompt screening along with psychological rehabilitation is required.

**No conflicts of interest**

**512** Poster

**Time-dependent risk of depression, anxiety and stress-related disorders in patients with breast cancer**

H. Yang[1], J. Brand[1], F. Fang[1], F. Chiesa[1], A. Johansson[1], P. Hall[1], K. Czene[1]. [1]*Karolinska Institutet, Department of Medical Epidemiology and Biostatistics, Stockholm, Sweden*

**Introduction:** Despite the known concerns about mental health of breast cancer patients, little is known regarding the risk of common mental

disorders among these patients. This study was to describe the time-dependent risk patterns of depression, anxiety and stress-related disorders among breast cancer patients, overall and by patient, tumor and treatment characteristics.

**Material and Methods:** We estimated standardized incidence ratios (SIRs) of mental health outcomes (extracted from the Swedish Patient Registers) in a Swedish nationwide cohort of 40,879 women with breast cancer (2001–2010, median follow-up = 4.5 years). Impact of patient, tumor and treatment characteristics was analyzed using flexible parametric survival models in a regional cohort of 7,940 breast cancer patients (2001–2013, median follow-up = 7.5 years).

**Results:** Women with breast cancer showed increased risk of depression, anxiety and stress-related disorders [overall SIR (95% CI) = 1.58 (1.47–1.70), 1.56 (1.44–1.69) and 1.78 (1.61–1.97), respectively]. SIRs were highest shortly after diagnosis, but remained increased up to five years after diagnosis. Younger age at diagnosis, comorbidities, higher histological grade, positive lymph node status and chemotherapy were all associated with an excess risk of depression and anxiety in breast cancer patients. Among these factors, higher histological grade and chemotherapy mostly contributed to the short-term risk increase, whereas comorbidities to the long-term risk increase (Table 1). No clinical risk factors were identified for stress-related disorders except for a greater risk increase associated with younger age.

Table 1. Relative risks of depression, anxiety and stress-related disorders in breast cancer patients

| | Hazard ratio (95% CI) of | | |
|---|---|---|---|
| | Depression | Anxiety | Stress-related disorders |
| Age at diagnosis | | | |
| 23−44 years | 1.00 (REF) | 1.00 (REF) | 1.00 (REF) |
| 45−54 years | 0.69 (0.52–0.91) | 0.49 (0.38–0.64) | 0.70 (0.48–1.02) |
| 55−64 years | 0.34 (0.25–0.47) | 0.27 (0.21–0.36) | 0.20 (0.13–0.33) |
| 65−80 years | 0.27 (0.19–0.38) | 0.19 (0.13–0.26) | 0.09 (0.05–0.18) |
| Comorbidities | | | |
| No | 1.00 (REF) | 1.00 (REF) | 1.00 (REF) |
| Yes | 1.38 (1.01–1.89) | 1.66 (1.25–2.22) | 1.48 (0.91–2.41) |
| Histological grade | | | |
| Low | 1.00 (REF) | 1.00 (REF) | 1.00 (REF) |
| Moderate | 1.53 (0.99–2.36) | 1.64 (1.07–2.52) | 0.74 (0.44–1.25) |
| High | 1.62 (1.02–2.58) | 1.89 (1.20–2.99) | 0.73 (0.41–1.31) |
| Lymph nodes | | | |
| Negative | 1.00 (REF) | 1.00 (REF) | 1.00 (REF) |
| Positive | 1.42 (1.13–1.79) | 1.40 (1.12–1.75) | 1.07 (0.75–1.52) |
| Chemotherapy | | | |
| No | 1.00 (REF) | 1.00 (REF) | 1.00 (REF) |
| Yes | 1.36 (1.07–1.73) | 1.59 (1.26–2.01) | 0.81 (0.56–1.18) |

**Conclusions:** Women with breast cancer are at increased risks of depression, anxiety and stress-related disorders. The time-dependent risk profiles may guide the health care professionals in providing timely psychosocial interventions for specific patient groups.

**No conflicts of interest**

**513** Poster

**The effect of cognitive behaviour therapy on resilience and quality of life in women suffering from breast cancer**

J. Srivastava[1], H. Shukla[2], S. Kaushik[3], M. Tewari[2]. *[1]Institute of Medical Sciences, Surgical Oncology, Varanasi, India; [2]Institute of Medical Sciences- Banaras Hindu University, Surgical Oncology, Varanasi, India; [3]Mmv- Banaras Hindu University, Psychology, Varanasi, India*

**Background:** Resilience is an important factor which helps women with breast cancer to fight against their disease and various treatments related stressors which ultimately lead them to have a better quality of life. Several empirical studies have confirmed that psychotherapies may improve quality of life but only a few studies have focused on the effect of these therapies for improving resilience in cancer patients. The main objective of this study was to find out the effect of Cognitive Behaviour Therapy (CBT) on resilience and quality of life in women suffering from breast cancer.

**Material and Methods:** The study comprised of 72 women diagnosed of early stage of breast cancer, taken after surgery and undergoing chemotherapy. The mean age was 47.2 (SD= 10.5) years. CBT (6 sessions, 45 minutes each) was adopted for experimental group (n = 38). The control group (n = 34) consisted of women awaiting psychotherapy. Before and after intervention and at 3 months follow-up, study participants were individually assessed for level of resilience and quality of life using Connor Davidson Resilience Scale (Indian adaptation) and European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire (QLQ) 30 and its breast cancer supplementary measure QLQ BR-23 respectively.

**Results:** A significant improvement in resilience level ($p < 0.05$) was observed in the period following the therapy among CBT patients in comparison with the control group. Higher resilience to cancer treatment stressors in CBT group was related to the fact that patients were more able to cope with the traumatic experiences of treatment process during and after therapy. The analysis of result in relation to the quality of life also showed significant improvement ($p < 0.01$) in the functional and global health status dimensions, which resulted from participation in the therapy. The CBT patients reported lower intensification of somatic symptoms as well.

**Conclusion:** CBT has a clinical relevance in improving resilience and quality of life in breast cancer survivors. It may also be used as a support method for enhancing standard oncological treatment and improving physician-patient relationship.

**No conflicts of interest**

**514** Poster

**Impact of spiritual training on mental health and quality of life among women suffering from breast cancer**

S. Kaushik[1]. *[1]Banaras Hindu University, Psychology, Varanasi, India*

**Background:** National Surveys consistently support the idea that spirituality is important to most individuals in the general population. More than 90% of adults express a belief in God, and slightly more than 70% of the individuals surveyed identified religion as one of the most important influences in their lives. Researchers have shown positive psychological changes due to effects of meditation, chanting and spiritual readings. The practice has been growing around the world in 192 countries. The objective of the study was to find out the impact of spiritual training on mental health dimensions (depression and anxiety) in women suffering from breast cancer so they can be used as complementary therapies.

**Material and Methods:** The sample consisted of 112 women of age 40−65 years (mean age= 48.3 years), who were breast cancer survivors taken after screening to meet the inclusion and exclusion criteria. The experimental group (N = 58) was provided with some spiritual practices (Chanting, Spiritual Readings and Meditation) for 4 weeks (1 hour daily), while the control group (N = 54) was not given any such practices. Before and after spiritual training, study participants were individually assessed and compared on pre and post scores using Depression Anxiety and Stress Scale developed by Lovibond & Lovibond (Indian adaptation) and European Organization for Research and Treatment of Cancer (EORTC) Quality of life Questionnaire (QLQ) 30 (Indian Adaptation).

**Result:** The results revealed that the practitioners (the experimental group) scored significantly lower on anxiety and depression scales after spiritual practices when compared with non-practitioners (control group) ($p < 0.05$) and with pre-treatment scores ($p < 0.01$), while Quality of life scores were found to be significantly improved when compared with non practitioner group ($p < 0.05$) as well as with their pre-treatment scores ($p < 0.01$). Descriptive statistics and t-test were used to analyze the data.

**Conclusion:** Spiritual training/practices can be effective dealing with the side effects of medical treatment related most common psychological problems like depression and anxiety and therefore ultimately lead to have good mental health, better quality of life and wellness. Therefore, they can be used as adjunct therapies along with medical treatment for better outcome.

**No conflicts of interest**

**516** Poster

**Adherence to adjuvant endocrine therapy in oestrogen receptor-positive breast cancer patients, who had participated in psychoeducational groups. A five year prospective study**

I. Schou Bredal[1], E.M. Sørensen[1]. *[1]Oslo University Hospital, Breast and Endocrine Surgery, Oslo, Norway*

**Background:** Adjuvant endocrine therapy is usually recommended for a 5-year period for women with hormon-sensitive breast cancer. Both tamoxifen and aromatase inhibitors (AI) have shown to reduce recurrence and mortality. However, rates of adherence to endocrine therapy are low and fall progressively with each year from the date of diagnosis. Reports indicate that only 40−60% of the women finish their recommended courses of endocrine therapy. Adherence to endocrine therapy in adjuvant breast cancer settings is a substantial clinical problem. The aim of the present study was to investigate the adherence to adjuvant endocrine therapy in women diagnosed with early-stage breast cancer, who had participated in psychoeducational groups in 2007–2010. Adjuvant endocrine therapy was one of the topics for group discussion.

**Patients and Methods:** Of the 367 women participating in the psychoeducational groups intervention, 255 women had hormon-sensitive breast cancer. Of the 255 women, 107 were prescribed tamoxifen and 65

were prescribed AI for five years. Eigthy three women were prescribed tamoxifen as initial hormonal theraphy, then swtiched to AI after 2 years. The intervention consisted of 3 to 5 weekly 2-hour sessions, were free of charge and started 1 to 8 weeks after surgery (usually before or just after patients started adjuvant treatment). The women filled out questionnaire at time of diagnosis, one, three and five years after surgery. In addition to the questionnaire, data was also collected from their medical journals.

**Results:** At one year only one woman had prematurely discontinued tamoxifen. At three and five years follow-up the adherence rate was 96%, and 90% respectively. During the five years follow-up, six patients died, two patients were prescribed Zoladex instead of AI, eigth patients discontinued because of extrem side effects, after consulting the doctor. Only 14 patients prematurely discontinued tamoxifen or AI without consulting the doctor. The most frekvent side effect reported was hot flushes. At baseline 19% reported that they had "quite a bit/very much" hot flushes, compared to 57% at one year, 57% at three years and 45% at five years.

**Conclusion:** The adherence to endocrine therapy was good (>80%) among women who had participated in the psychoeducational groups.

**No conflicts of interest**

**517** Poster

**Acupuncture for chemotherapy-induced peripheral neuropathy in breast cancer patients: Pilot trial**

S.H. Park[1], Y.J. Jeong[1], M.A. Kwak[2]. *[1]College of Medicine- Catholic University of Daegu, Department of Surgery, Daegu, South Korea; [2]College of Oriental Medicine- Daegu Haany University, Department of Oriental Internal Medicine, Daegu, South Korea*

**Background:** Some chemotherapy drugs can cause peripheral neuropathy which results in severe neuropathic pain or gait impairment. Recent studies suggest that acupuncture may be a useful treatment for chemotherapy-induced peripheral neuropathy (CIPN). The purpose of this study was to assess the feasibility and the safety of acupuncture for the treatment of peripheral neuropathy following chemotherapy in Korean breast cancer patients.

**Material and Methods:** Ten breast cancer patients presenting with CIPN were enrolled in a prospective, pilot study. Acupuncture interventions were given three times a week for 4 consecutive weeks. The primary outcome measure was Neuropathic Pain Symptom Inventory (NPSI) assessed by a self-administered questionnaire, and Nerve Conduction Velocity (NCV). The secondary outcome measure was quality of life assessed by the SF-36 Questionnaire.

**Results:** Acupuncture significantly reduced the severity of CIPN assessed by NPSI score. 4 weeks after the last treatment the symptoms were not aggravated. According to the NCV assessment, 3 participants showed improvement of sensory neuropathy. SF-36 scores significantly increased for variables including physical functioning, role limitations due to physical health, social functioning, and general health status.

**Conclusions:** Acupuncture appeared to provide effective improvement of CIPN among Korean women with breast cancer, and the effects lasted for at least 1 month after the treatment. A randomized controlled prospective study with a larger sample size is required to clarify the role of acupuncture in the management of CIPN in breast cancer patients.

**No conflicts of interest**

**518** Poster

**Complications and persistent pain after breast cancer treatment in a cohort of women participating in four population-based screening programs: the CAMISS cohort**

A. Romero[1], I. Torà-Rocamora[1], M. Baré[2], T. Barata[3], L. Domingo[1], J. Ferrer[4], C. Carmona[5], N. Torà[2], J.M. Reyes[3], I. Collet[1], I. Díez[3], M. Comas[1], F. Macià[1], X. Castells[1], M. Sala[1]. *[1]IMIM − Hospital del Mar Medical Research Institute − Research Network on Health Services in Chronic Diseases REDISSEC, Epidemiology and Evaluation, Barcelona, Spain; [2]Parc Taulí-University Hospital − Research Network on Health Services in Chronic Diseases REDISSEC, Clinical Epidemiology and Cancer Screening, Sabadell, Spain; [3]Canary Islands Health Service, General Directorate of Health Care Programmes, Las Palmas de Gran Canaria, Spain; [4]Hospital de Santa Caterina, Radiology Department, Girona, Spain; [5]Hospital Dr. Josep Trueta, Epidemiology and Register of Cancer of Girona, Girona, Spain*

**Background:** The onset of complications and, specifically, of persistent pain after breast cancer treatment has not been evaluated within the context of population-based screening programs. The main objective of this study was to investigate whether the diagnostic route (screening or interval) is related to the complications rate, and, specifically, to the persistent pain prevalence in women participating in four population-based breast cancer screening programs. A secondary objective was to identify risk factors to the onset of persistent pain.

**Material and Methods:** Our study population comprises a sample of 1,057 women, coming from four population-based screening programs. These women were diagnosed with breast cancer and treated surgically between 2000 and 2008, and were followed up to August 2014. In 732 women (69.3%) the breast cancer was detected during the routine screening mammograms, and in 325 women (30.7%) it emerged as interval cancer. The prevalence of overall complications, as well as the prevalence of persistent pain, and its 95% confidence intervals (CI) were estimated. The risk for developing persistent pain was estimated through multivariate logistic regression analysis.

**Results:** A total of 313 women (29.6%, 95% CI 27.4–33.0) experienced at least one complication during all the follow up. Persistent pain was present in 117 women (11.4%, 95% CI 9.4–13.3). Although women who were diagnosed in routine screening reported a higher prevalence of persistent pain (12.9%, 95% CI 10.4–15.3) than those women with tumours that emerged as interval cancers between two screening rounds (7.5%, 95% CI 4.6–10.3) ($p = 0.010$), in the multivariate logistic regression analysis other variables associated to persistent pain were found. Having developed lymphedema was identified as a main risk factor for developing persistent pain. Women that had lymphedema showed an OR of 20.7 (95% CI 7.0–61.2), comparing with women who had not. Women with anxiety showed an OR of 17.4 (95% CI 5.4–55.6), comparing with women without. A Charlson index $\geqslant 3$ was identified also as a risk factor for persistent pain, with an OR of 8.8 (95% CI 1.5–52.6) compared with having an index of 0.

**Conclusions:** In our study population, prevalence of persistent pain is not very high (11.4%). The diagnostic route (screening or interval) is not related to the onset of persistent pain. The presence of lymphedema, anxiety and having a Charlson index equal or higher than 3 are shown as associated factors to the onset of persistent pain.

**No conflicts of interest**

**520** Poster

**"It is up to the patient whether they experience a few kilos more as a problem". A qualitative study exploring perceptions of health care professionals on weight changes of women with breast cancer during and after chemotherapy**

A. De Kruif[1], M. Scholtens[1], J. Van de Rijt[1], M. Derks[2], R. Winkels[2], M. De Boer[1], M. Visser[3], E. Kampman[2], M. Westerman[1]. *[1]Vrije Universiteit Amsterdam, Health Sciences, Amsterdam, Netherlands; [2]Wageningen University, Human Nutrition, Wageningen, Netherlands; [3]Vrije Universiteit Amsterdam/Vrije Universiteit Medical Center, Health Sciences/Internal Medicine- Nutrition and Dietetics, Amsterdam, Netherlands*

**Background:** Yearly, more than 60% of the 14,000 Dutch women newly diagnosed with breast cancer will receive chemotherapy (CT). Since CT is used prominently and survival rates are increasing, long-term negative side effects of CT, such as increases in weight, changes in body composition and loss of muscle strength, become increasingly important. These changes have a profound influence on self-esteem and quality of life (QoL) in breast cancer survivors, but may also increase the risk of co-morbidities such as cardio-vascular disease, diabetes, functional limitations and breast cancer recurrence. Studies suggest that paying more attention to weight changes and its psycho-social impact, may lead to an improved QoL. Furthermore, women with breast cancer desire more information about nutrition and physical activity, especially related to weight gain, but generally do not receive this from their health care professionals.

It is unclear whether health care professionals observe and act upon changes in weight and whether they consider providing information about dietary intake and physical activity during treatment as part of their role.

**Material and Methods:** A qualitative explorative study using semi-structured interviews with health care professionals involved in breast cancer care. Oncologists, nurses and dieticians ($n = 18$) working in five Dutch hospitals, and General Practitioners (GP) ($n = 16$) participated in this study. Interviews were audiotaped and transcribed verbatim. A thematic content analysis approach was used.

**Results:** Although many women asked questions about nutrition and weight gain during CT, oncologists and specialized nurses provided concise information based on generally applicable recommendations for obesity prevention. GPs also indicated to provide women with information and support, but not with information regarding weight gain, nutrition or physical activity. Most of the health care professionals said not to be concerned about the health risks of weight gain during and after CT. They considered it not important or not relevant to discuss it with women throughout therapy. Dieticians were not routinely involved in the treatment of breast cancer. When consulted it was mostly about weight loss, they experienced no possibilities to support women with weight gain. To curb the weight

increases all professionals suggested that possible interventions should focus on encouraging women to be more physically active.

**Conclusions:** Weight gain as a side effect of CT is no high priority for health care professionals. Interventions need to focus on adapting existing guidelines and cultivation of more awareness among health care professionals about the health risks associated with weight gain during and after chemotherapy in order to raise quality of life for women with breast cancer.

**No conflicts of interest**

**521** Poster

**The musculoskeletal consequences of breast reconstruction using the latissimus dorsi muscle: A focus group study**

N. Blackburn[1], J. McVeigh[1], E. McCaughan[2], I. Wilson[1]. [1]*Ulster University, Life and Health Sciences, Belfast, United Kingdom;* [2]*Ulster University, Life and Health Sciences, Coleraine, United Kingdom*

**Background:** Breast reconstruction using the latissimus dorsi (LD) flap following mastectomy is an important management option in breast cancer. However, one common, but often ignored, complication following LD flap reconstruction is shoulder dysfunction. The aim of the study, therefore, was to explore the musculoskeletal consequences of this surgery and their impact on function and quality of life as perceived by patients and the healthcare professionals who manage this client group.

**Materials and Methods:** An integrated methodology was used in this study. Five focus groups were conducted; three with women who had undergone reconstructive surgery (n = 15) and two with the healthcare professionals (n = 11). The women also completed a demographics questionnaire, and their shoulder movement was assessed. All focus groups were audio and video recorded. Inductive content analysis was used to analyse transcripts and to develop core themes and sub-themes.

**Results:** The over-arching theme to emerge from the women's focus groups was 'Resilience', sub-themes were 'preparation and awareness', 'coping' and 'self-management'. Women reported a change in their musculoskeletal ability post-surgery but gradually returned to 'new normal' function, stating that they could now carry out their daily activities albeit for shorter periods of time, with assistance, or by adapting how they performed the task. The women recognised their lack of awareness regarding the potential long-term musculoskeletal implications of surgery, acknowledging pre and post-operative care to be mainly concerning wound healing and aesthetic outcome. This was reflected in the healthcare professionals group, whereby the breast care nurses demonstrated a varying awareness of the musculoskeletal impact of surgery, anticipating full recovery between three to twelve months. It was evident from the groups that the relative importance of overcoming the cancer and recovering from the adjuvant treatments was of higher priority than the potential of reduced function of the shoulder, following surgery.

**Conclusions:** LD breast reconstruction has an impact on function and activities of daily living to varying extents, with women facing on-going challenges at least one year post-operative. As a result of the musculoskeletal implications of surgery women are adjusting to a 'new normal', demonstrating resilience in their approach to coping with this adaptive way of living. There is a lack of awareness regarding the long-term musculoskeletal consequences of surgery, with short-term follow up mainly regarding wound healing and aesthetic outcome, this has clinical implications for physiotherapists and breast care nurses in this area.

**No conflicts of interest**

**522** Poster

**The development of a mobile application for self-management of arm and shoulder exercises after breast cancer treatment**

H. Harder[1], V. Jenkins[1], L. Burkinshaw[1], P. Watten[2], P. Holroyd[2], A. Good[3], P. Harris[3], C. Zammit[4]. [1]*University of Sussex, Sussex Health Outcomes Research and Education in Cancer SHORE-C- Brighton and Sussex Medical School, Brighton, United Kingdom;* [2]*University of Sussex, School of Engineering and Informatics, Brighton, United Kingdom;* [3]*University of Sussex, School of Psychology, Brighton, United Kingdom;* [4]*Brighton & Sussex University Hospitals NHS Trust, Cancer Services, Brighton, United Kingdom*

**Background:** Upper-limb dysfunction (ULD) is common after axillary surgery or radiotherapy for breast cancer. Symptoms include impaired function, pain, decreased muscle strength and lymphoedema, and frequently have an adverse effect on activities of daily living and quality of life. Post-operative arm and shoulder exercises have proven to be an effective and safe intervention for ULD. Standard of care in the UK for arm mobility is information provision on functional exercises (including written information). However, adherence and self-management of exercise routines at home is often sub-optimal. Smartphone and tablet computer applications are promising new strategies in the provision of health care and have the potential to support the delivery of an easily accessible intervention. The aim of this pilot study was to develop an evidence-based application supported by user preferences to optimise self-management of arm and shoulder exercises after breast cancer treatment.

**Materials and Methods:** Existing literature (including clinical guidelines) was reviewed to develop an exercise program and to explore the health behaviour change techniques for the application. Two focus groups were conducted with 9 breast cancer patients (time since diagnosis 3−18 months; aged 47−58 years). The group discussions centred on patients' experiences with arm and shoulder exercises, their opinion about the content and requirements of the application, and their general impression and feedback on a prototype of the application. The focus groups were recorded, transcribed and analysed using thematic analysis techniques.

**Results:** Patients' experience with arm and shoulder exercises varied widely. They suggested including the following content: education (information about breast cancer/exercises, clear instructions, reassurance about different levels/ability), demonstration (videos with audio of individual exercises, including a class), motivation (ability to set reminders to prompt practise), and self-monitoring (ratings and graph plotting, diary function for self-evaluation of symptoms). An evidence-based rehabilitation program was developed in consultation with a physiotherapist with exercises for passive and active mobilisation, stretching and strengthening. The arm and shoulder exercises were demonstrated by a breast cancer survivor and filmed; videos were included in the application.

**Conclusions:** A novel mobile application (iOS) was developed for smartphone and tablet use by breast cancer patients, health care professionals and academics. Several tools including videos, reminder and self-monitoring features were included. The innovative and easily accessible nature of this application called $A^4BC$ ® (Arm exercises 4 Breast Cancer), has the potential to improve clinical care by encouraging self-management of ULD. A usability study in breast cancer patients is underway.

**No conflicts of interest**

**523** Poster

**The efficacy of psychosocial interventions among women following surgical treatment for breast cancer: A systematic review and meta-analysis**

H. Matthews[1], B. Grunfeld[1], A. Turner[1]. [1]*Coventry University, Centre for Technology Enabled Health Research CTEHR, Coventry, United Kingdom*

**Background:** Breast cancer is the most commonly diagnosed cancer in women across the world. It is estimated that one out of every nine women will develop breast cancer at some point in their lives and nearly all undergo surgery. The aim of this meta-analysis was to identify the efficacy of psychosocial interventions for women following breast cancer surgery.

**Materials and Methods:** A comprehensive literature search was undertaken using keyword and subject searching with seven databases from 1974–2015. Included studies employed a quantitative methodology presenting empirical findings focusing on interventions for female breast cancer patients following surgery. A meta-analysis was undertaken and the following descriptors were used to classify the results: strong, moderate, limited and conflicting.

**Results:** 32 studies were included and strong evidence emerged for the efficacy of psychosocial interventions in promoting improvements in anxiety (Hedges g=0.31), depression (0.38), quality of life (0.40), mood disturbance (0.31), distress (0.27) and sleep disturbance (0.67). Moderate evidence emerged for the efficacy of psychosocial interventions in relation to body image (0.40) and self-esteem (0.35). Limited evidence was reported in relation to sexual functioning (0.22). Strong evidence emerged for the efficacy of cognitive behavioural therapy in promoting improvements in anxiety, depression and quality of life.

**Conclusion:** This is the first meta-analysis to report the efficacy of psychosocial interventions following breast cancer surgery. The meta-analysis highlighted the time period following breast cancer surgery as an appropriate time to implement psychosocial interventions. The findings demonstrated cognitive behavioural therapy was consistently the most effective psychosocial intervention promoting improvements in anxiety, depression and quality of life.

**No conflicts of interest**

**524** Poster

**Information needs and decision-making preferences: Perspective of Pakistani breast cancer patients**

N.A. Jadoon[1], M. Hussain[2], F.U. Sulehri[2], M. Zubair[2], N.A. Shair[2]. *[1]Ittefaq Trust Hospital, Medicine, Lahore, Pakistan; [2]Nishtar Medical College Hospital, Medicine, Multan, Pakistan*

**Background:** Due to insufficient data regarding patient needs and preferences, health professionals remain concerned about correct the amount, type and extent of information to be communicated to cancer patients. The study intended to explore whether and to what extent patients want to participate in treatment decision making if provided with complete diagnostic and treatment information and clearly defined goals.

**Aim:** The objective of this study was to assess the needs and preferences of breast cancer patients for information regarding their disease and to explore preferences for involvement in treatment decision making among patients with cancer.

**Methods:** The study was carried out at a regional cancer centre and a tertiary care hospital in Multan. Patients were interviewed using a structured pretested questionnaire to determine their desire and preferences for information about their illness, selected from a heterogeneous sample of 232 individuals visiting Multan Institute of Niuclear Medicine and Radiotherapy and Nishtar Medical College Hospital, Multan.

**Results:** Two hundred thirty two patients having a mean age of 44.44±17.24 years participated in the study. About two third of the patients (71.9%) wanted to know all the information about their condition regardless of its nature, good or unfavorable. Information about prognosis of disease and chances of cure was desired by 94.3% of the respondents. Most of the patients wanted to know about all the possible treatments (68.7%), about the action of treatment in body (57.6%) and its side effects (68%). Majority of the patients interviewed were likely to let the physician make decisions regarding their disease management. The overall proportion of patients preferring active, collaborative and passive roles were 35.4%, 2.6% and 62% respectively. Majority of the patients thought that cancer patients should be involved in decisions regarding their treatment, although paradoxically 75% were of the view that all the cancer patients do not have the ability to get involved in deciding about their treatment. Half of the patients (50.4%) opined that if a patient does not want to be involved in deciding about treatment, the physicians should nevertheless try to involve him in deciding about his treatment.

**Conclusions:** Majority of the patients with cancer want to know about their diagnosis, effect of illness on daily functioning, prognosis and examples of cases in which treatment they are receiving was effective. The results of the study suggest that oncologists should individually assess each patient to determine the type of role they prefer in making decisions about their treatment.

**No conflicts of interest**

**525** Poster

**Hospital services utilization among 5- and 10-year breast cancer survivors**

L. Monfil Herrera[1], I. Torá-Rocamora[2], M. Comas[2], M. Sala[2]. *[1]IMIM (Hospital del Mar Medical Research Institute), Department of Epidemiology and Evaluation, Barcelona, Spain; [2]IMIM (Hospital del Mar Medical Research Institute), Research Network on Health Services in Chronic Diseases (REDISSEC), Department of Epidemiology and Evaluation, Barcelona, Spain*

**Background:** Breast cancer survival has greatly increased during the last years, which may have an impact on the utilization of health services among long-term survivors. The aim of this study was to assess the use of hospital acts and to compare between 5- and 10-year breast cancer survivors.

**Material and Methods:** A retrospective cohort of 695 breast cancer survivors treated in Hospital del Mar (Barcelona, Spain) between 2000 and 2005 was analyzed.

A total of 49,152 hospital services provided from 2005 to 2015 were included in the analysis. Date, hospital act type and specialty were considered for each hospital service.

Frequencies and visits rates per woman according to age and cancer characteristics at diagnosis, treatment, and other cancer diagnosis were computed at 5 and 10 years of survival. For comparisons between periods Chi-square, Fisher and Wilcoxon tests were performed (significance level: $\alpha$=0.05).

**Results:** Overall, 5,100 and 5,086 hospital services were performed at 5-year and 10-year survival, respectively. Each woman had a median of 5 (Percentile 25 and 75: 3−9) and 3 (2−8) visits each year respectively ($p < 0.001$). The visits were concentrated among few women, resulting in both years that less than 20% of women received more than 50% of hospital services.

At 5 and 10 years: Younger women (⩾49) had more outpatient visits ($Rate_{5th} = 4.6$, $Rate_{10th} = 4.8$) and tests performed (2.6; 3.1), than older women (⩾70) (3.8, 2.5; and 2.5, 1.9 respectively). Older women had more emergencies ($Rate_{5th} = 0.3$; $Rate_{10th} = 0.4$) than younger women. Advanced stages at diagnosis were associated to a higher use of outpatient visits and Day hospital. Use of outpatients visits and tests were higher in women who received chemotherapy. Women with another cancer diagnosed after breast cancer, visited the hospital near twice than women who only had breast cancer.

According specialities, most of the visits were performed at oncology (5th: 25.6%, 10th: 27.1%), radiology (6.9%, 14.4%) and mammography (11.0%, 10.2%). Intern medicine, Gynaecology/Obstetrics, Rehabilitation, General surgery, psychiatry and plastic surgery services were also highly used through patients.

Statistical differences in frequency were found among 5- and 10-year survival in Hospitalization and Day hospital between stage at diagnosis, treatment, and speciality. Day hospital also differs by cancer histology. In test there were only differences by specialty.

**Conclusion:** Hospital services uses were distributed irregularly through breast cancer survivors. There were differences between the number of visits per women at 5-year and 10-year survival, with a decreasing trend. The ones more used continued being the ones related to diagnosis and treatment cancer. Women's age and stage at diagnosis, treatment received for cancer and if were diagnosed with a posterior cancer determined the use of hospital services.

**No conflicts of interest**

**526** Poster

**Sexual dysfunction in breast cancer patients: About 78 Tunisian women**

F. Mohamed Aymen[1], Y. Atef[1], B.A. Fethi[1], G. Majed[1], R. Hedi[1]. *[1]Tunis Maternity Hospital, Department B of Gynecology and Obstetrics, Tunis, Tunisia*

**Background:** Breast cancer is the most common female cancer. The study of sexual function in women treated for breast cancer and the treatment of sexual dysfunctions represents a new perspective in improving the quality of life after treatment of breast cancer.

**Methods:** This is a descriptive retrospective study of 78 women treated for breast cancer in department B of gynecology and obstetrics of the Tunis maternity center. To study the sexuality of these patients, the female sexual function index (FSFI) was used. Patients were asked to complete the form FSFI twice, before and after discovering the breast cancer.

**Results:** Between January 2008 and December 2012, 100 women with breast cancer were assessed and treated in Department B of gynecology and obstetrics of Tunis maternity center. Of these 100 patients we had 78 patients who agreed to talk about their sexuality. The average age of patients at the time of the discovery of the disease was 42 years. 14 patients were menopausal. All these patients underwent surgical treatment. 48 had radical surgery (mastectomy and axillary lymph node dissection) and 30 had conservative treatment.

Sexual dysfunction is found in 16 patients before discovering breast cancer. However, 72 patients reported a sexual dysfunction after the management of the disease. All patients who underwent radical surgery (48 patients) reported sexual dysfunction. All of menopausal patients (14 patients) reported sexual dysfunction (a cessation of sexual activity).

The patient age at the time of breast cancer discovery, the type of surgical treatment and the intellectual level seem to be the determining factors of sexual dysfunction in breast cancer patients.

**Conclusions:** Sexual dysfunction is observed frequently in women treated for breast cancer. This disease is multifactorial; it may be secondary to chemotherapy, hormone therapy and surgery especially in case of radical surgery. Body image is deeply damaged in these patients. A special care by sexologists or onco-sexologists is necessary to improve the quality of life of these patients.

**No conflicts of interest**

**527** Poster

**Planned and unplanned pregnancy in breast cancer survivors**

J. Mansi[1]. *[1]Guy's and St Thomas NHS Foundation Trust, Oncology, London, United Kingdom*

**Background:** At least 25% of women presenting with breast cancer are of reproductive age. There are numerous studies highlighting the importance of offering fertility preservation to such women with early breast cancer. However, information on fertility intention and outcome in these women after treatment is sparce. This study was established to gain a greater understanding of this in terms of desire to become pregnant and success rate.

**Materials and Methods:** A questionnaire regarding fertility intention, pregnancies achieved, and desire to have children was conducted between July 2011 and December 2013 in a tertiary breast cancer centre in South-East London. Only women under the age of 45 at the time of diagnosis were included. Voluntary completion of the questionnaire was taken as consent to participate. Results were merged and analysed using SPSS 18.

**Results:** 282 women completed the questionnaire at a mean time of 6.9±3.1 years from the time of diagnosis. Mean age of women at the time of cancer diagnosis was 37.2±3.9 years. 75% (212) received systemic chemotherapy and 44% (124) had endocrine therapy. 136 (48%) women were childless at the time of cancer diagnosis.

At the time of the survey, 51% had completed their family, 6% did not wish to have children, and 32% (90) reported that they would like to have children (9% did not answer the question and 2% were unable to have children). Of these 90 women, 28 (31%) actively tried to conceive, of whom 15 had a live birth. However, there were also 11 pregnancies reported among those who did not plan to conceive. The majority of these pregnancies (7) were terminated with only 2 resulting in live birth. Among patients who reported no intention to conceive 76% (146/192) were not using any contraception.

**Conclusion:** These data demonstrate that at least one third of patients with breast cancer diagnosed before the age 45 would like to have one or more children. At the time of this survey 54% (15/28) of those who actively tried were successful. There was also a 6% unintentional pregnancy rate, with only 25% of women using contraception while not planning to have any children. This highlights the need for healthcare professionals to focus more on providing contraceptive advice to women who may be oligo/amenorrheic and who do not wish to conceive.

**No conflicts of interest**

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