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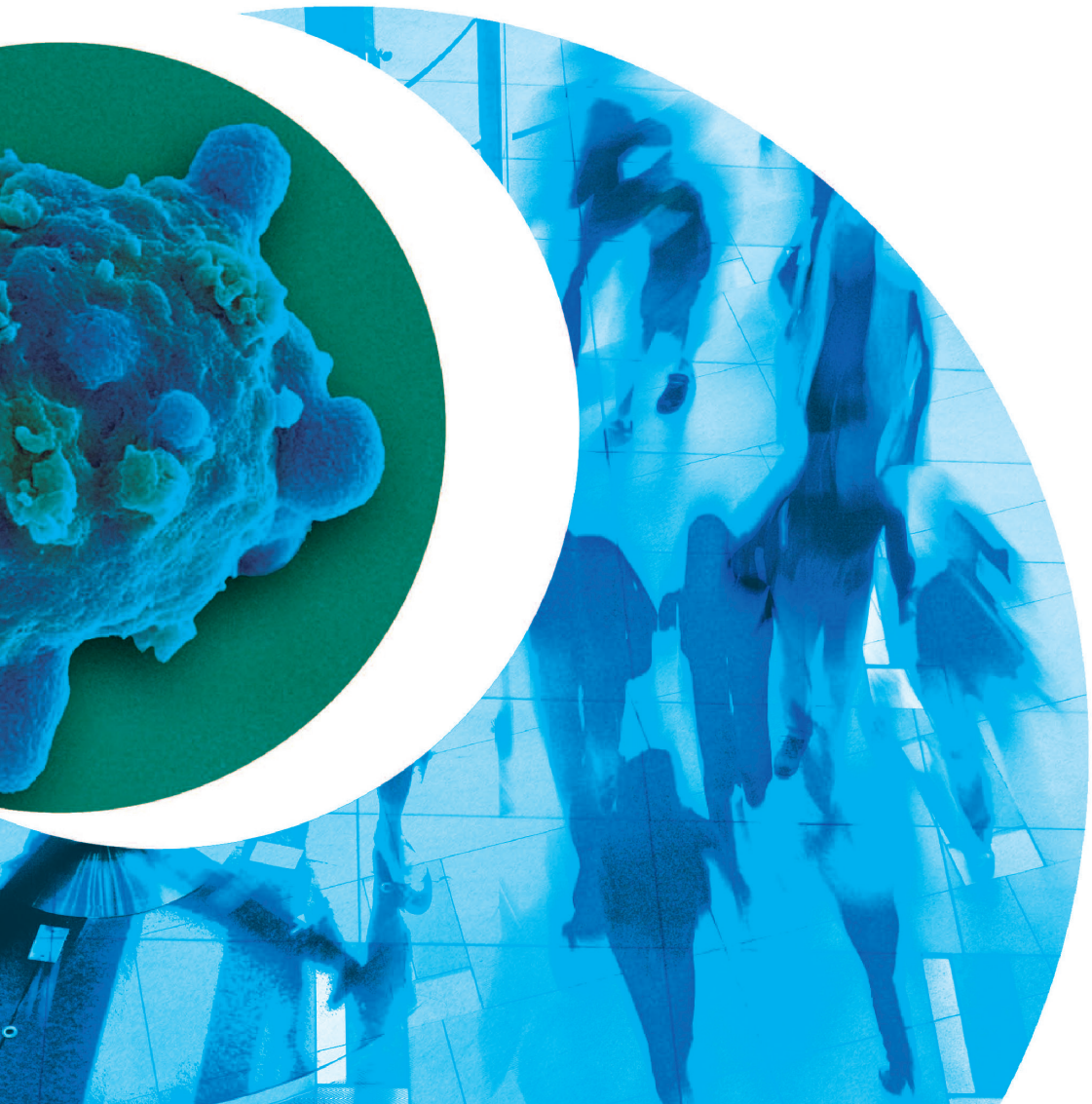
12th European Breast Cancer Conference (EBCC-12)

2–3 October 2020
Virtual Conference

ABSTRACT BOOK



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Abstract Book

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Aims and Scope

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PLENARY SESSION

Keynote Lecture, Best and Late Breaking Abstract Presentations

1LBA

Differential impact of prognostic parameters in hormone receptor-positive lobular early breast cancer in the WSG PlanB trial

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Background: Invasive lobular breast cancer is the second most common breast cancer (BC) subtype. Clinicopathological parameters associated with lobular BC and their prognostic implications are still controversial.

Material and Methods: Prognostic parameters (tumor stage, nodal stage, histological grade, Oncotype DX recurrence score [RS], PR status, Ki67) were retrospectively studied in a large prospective clinical trial encompassing 2585 hormone receptor-positive early BCs (WSG PlanB trial). All BCs were centrally reviewed and classified as lobular (n = 353, 14%) and non-lobular (n = 2232, 86%). Median follow-up time was 60 months. Five-year disease-free survival (DFS) estimates were obtained by the Kaplan-Meier method. Prognostic parameters were evaluated using Cox proportional hazard models.

Results: Lobular BC was associated with higher tumor stage, higher nodal stage, lower histological grade, lower Ki67, and low/intermediate RS. The prevalence of high recurrence scores (RS 26–100) was 3-fold lower in lobular compared to non-lobular BC (8% versus 24%, P < 0.001). Five-year DFS estimates for lobular and non-lobular BC, however, were similar (92.1% and 92.3%, P = 0.673). In multivariate analyses, prognostic parameters for DFS in lobular BC included histological grade G3 (hazard ratio [HR] = 5.06; 95% confidence interval [CI]: 1.91–13.39) and nodal stage pN3 (HR = 12.16, 95% CI 3.87–38.24), but not RS. By contrast, prognostic parameters in non-lobular BC included histological grade G3 (HR = 1.65; 95% CI: 1.11–2.44), nodal stage pN3 (HR = 3.68; 95% CI: 1.60–8.46), and high RS (HR = 2.49; 95% CI: 1.69–3.68).

Conclusions: In summary, lobular BC is associated with low/intermediate RS, although five-year DFS is similar to non-lobular BC. The prognostic impact of RS in the lobular subtype appears to be distinct from that in non-lobular BC. For risk assessment, RS thus needs to be complemented by clinicopathological parameters for therapy decision making.

Conflict of interest:

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PROFFERED PAPER SESSION

Proffered Paper Session

2LBA

High likelihood of actionable pathogenic variant detection in breast cancer genes in women with very early onset breast cancer, but low rate of additional panel genes

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Background: Early age at onset of breast cancer is a known risk factor for hereditary predisposition. The likelihood of *BRCA1*, *BRCA2* and *TP53* pathogenic variants (PVs) increases with earlier age at diagnosis, but little is known about the age distribution of PVs in other predisposition genes. Here, we assessed the contribution of known breast cancer-associated genes to very early onset disease.

Methods: Sequencing of the *BRCA1*, *BRCA2*, *TP53* genes and *CHEK2*-c.1100delC was carried out alongside tests for copy number variants on women with breast cancer diagnosed ≤30 years. Those testing negative were screened for PVs in a panel of a minimum of 8 additional breast cancer-associated genes.

Results: Testing of 370 women with breast cancer aged ≤30 years identified 72 PVs in *BRCA1* (19.5%), 35 in *BRCA2* (9.5%), 22 in *TP53* (5.9%) and 2 in *CHEK2*-c.1100delC (0.54%). Extended screening of 178 women testing negative only identified 7 additional actionable PVs (*PALB2* = 3, *CHEK2* = 1, *ATM* = 2, *PTEN* = 1). *BRCA1/2* PVs were more common in women aged 26–30 than in younger women (p = 0.008), whereas *TP53* PVs showed the reverse trend (p = 0.06). The Manchester score was highly predictive of PV detection, with only 8/104 (7.7%) of those with scores <15 having a PV compared to 31/31 (100%) of those with a score ≥40. Surprisingly 10/26 (38.5%) with ductal carcinoma *in situ* (DCIS) alone had a PV (*TP53* = 6), almost as common as *BRCA1/2* PVs in early onset triple-negative breast cancer (TNBC) 54/120.

Conclusions: Rates of *BRCA1*, *BRCA2* and *TP53* PVs are high in very early onset breast cancer, with limited benefit from testing of additional breast cancer-associated genes. Pathologies such as DCIS and TNBC are strongly predictive of particular gene associations.

No conflict of interest.

3LBA

Fatigue among long-term breast cancer survivors: a controlled cross-sectional study

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Background: Fatigue is the most common and persistent symptom among women in the first five years after a breast cancer diagnosis. To compare fatigue experienced by long-term breast cancer survivors with that in a reference population, and to evaluate the determinants of that fatigue.

Material and methods: A cross-sectional cohort study of 350 breast cancer survivors 10 years (median) after diagnosis, and a reference population of 350 women matched by age and general practitioner. Fatigue was measured using the Multidimensional Fatigue Inventory (MFI-20), and a sum score of >60 was the primary outcome. Logistic regression was applied to compare the prevalence of multidimensional fatigue between the survivor and reference populations, adjusted for body mass index (BMI), for cardiovascular and psychological variables. Odds ratios (ORs) and 95% confidence intervals (95%CIs) were estimated. Logistic regression was applied to evaluate the determinants of multidimensional fatigue among the survivors.

Results: Breast cancer survivors more often experienced multidimensional fatigue than the reference population (26.6% versus 15.4%; OR, 2.0 [95%CI, 1.4–2.9]), even after adjusting for confounders. The odds of multidimensional fatigue were also higher among survivors with symptoms of depression (32.2% versus 2.7%; OR, 17.0 [95%CI, 7.1–40.5]) or anxiety (41.9% versus 10.1%; OR, 6.4 [95%CI, 3.6–11.4]).

Conclusions: One in four breast cancer survivors experience multidimensional fatigue up to 10 years after diagnosis and fatigue occurs more frequently than in women of the same age and general practitioner. This fatigue appears to be associated with symptoms of depression and anxiety.

No conflict of interest.

CLINICAL SCIENCE SYMPOSIUM

Advances in Imaging

4LBA

Cost-effective strategies according to the first randomized trial comparing MRI breast cancer screening with mammography in women with a familial risk: FaMRIsc

M. Tilanus-Linthorst[1], A. Geuzinge[2], A.I.M. Obdeijn[3], E. Rutgers[4], R. Mann[5], S. Saadatmand[6], D. de Roy van Zuidewijn[7], R. Tollenaar[8], M. Lobbes[9], M. Ausems[10], M. van 't Riet[11], M. Hooning[12], E. Luiten[13], C. Loo[14], J. Wesseling[15], C. Verhoef[1], J.G. Oosterwijk[16], E. Heijnsdijk[2], H. de Koning[2], The Famrisc Study Group. *[1]ErasmusMC, Surgery, Rotterdam, Netherlands; [2]ErasmusMC, Public Health, Rotterdam, Netherlands; [3]ErasmusMC, Radiology, Rotterdam, Netherlands; [4]Netherlands Cancer Institute, AVL, Surgery, Amsterdam, Netherlands; [5]Radboud University Hospital, Radiology, Nijmegen, Netherlands; [6]ErasmusMC, Anaestesiology, Rotterdam, Netherlands; [7]Medical Centre Leeuwarden, Surgery, Leeuwarden, Netherlands; [8]Leiden University Medical Centre, Surgery, Leiden, Netherlands; [9]Academic Hospital Maastricht, Radiology, Maastricht, Netherlands; [10]University Medical Centre Utrecht, Medical Genetics, Utrecht, Netherlands; [11]Reinier de Graaf Gasthuis, Surgery, Delft, Netherlands; [12]ErasmusMC, Medical Oncology, Rotterdam, Netherlands; [13]Amphia Ziekenhuis, Surgery, Breda, Netherlands; [14]Netherlands Cancer Institute, AVL, Radiology, Amsterdam, Netherlands; [15]Netherlands Cancer Institute, AVL, Pathology, Amsterdam, Netherlands; [16]University Medical Centre Groningen, Human Genetics, Groningen, Netherlands*

Background: Women with ≥20% lifetime risk for breast cancer because of their family history, but without a BRCA1/2 mutation are advised to have screening with yearly MRI in the USA, but with mammography in Europe. We recently published in Lancet Oncology how much earlier MRI screening can detect the breast cancers compared with mammography, but at the cost of more false-positive results, in a randomized trial in twelve Dutch hospitals.

Here we want to present based on these results some effective strategies.

Methods: From January 2011 until December 2017, 1355 women aged 30–55 years with a cumulative lifetime risk (CLTR) of ≥20% without a *BRCA1/2* mutation were randomized into two groups; in the MRI-group women were screened yearly with MRI, clinical breast examination (CBE), and mammography every other year; in the Mx-group with yearly mammography and CBE. We will assessed cost per group as well as per detected cancer in both groups, also by breast density. The modelled benefit and cost of several strategies will be compared in the presentation.

Results: In the MRI-group (N = 674) compared to the Mx-group (N = 680) more breast cancers were detected (40 versus 15, $p < 0.002$), invasive cancers were smaller (median size 9 versus 17 mm, $p = 0.01$) and less often node positive (17% versus 63%, $p = 0.023$). In incident rounds (on average 3.3 inc. rds.) fewer large or node positive cancers were detected with MRI, reducing the cost for adjuvant therapy, but there remained more false positive results and biopsies with MRI. The total cost of MRI screening was nearly twice as high as for mammography-screening. Per detected cancer MRI screening was cheaper than mammography, especially >50 yr. and at density A-C. Screening with only yearly MRI is expected to reduce most breast cancer deaths in this risk category, but at rather high cost. Strategies affordable according to NICE criteria and still effective, like screening with only MRI every 18 months, will be discussed.

Table 1. Participants and cost

Participants	MRI 675	Mx 680	p-value
Mean age – yr ± SD	44.7 ± 6.3	44.7 ± 6.3	
BI-RADS density category[a]			
A entirely fat	13%	14%	
B scattered densities	37%	34%	
C heterogeneously dense	35%	36%	
D extremely dense	15%	15%	
Invasive breast cancers – no. DCIS – nr.	24 16	8 7	0.0017
Median size invasive cancers mm	9	17	0.01
Node positive	4/24 (17%)	5/8 (63%)	0.023
Biopsy nr.	149	54	<0.0001
Total screening cost in FaMRIsc	€1,094,241	€516,440	
Cost per detected cancer	€32.340	€42.384	
Cost per detected ca. BIRADS A-C	€28.945	€39.964	

Conclusions: MRI-screening can be cost-effective in groups with ≥20% lifetime risk for breast cancer, in which the advantage of the earlier cancer detection outweighs the disadvantage of more additional investigations, overdiagnosis and cost.

No conflict of interest.

5LBA

Determinants of non-participation in population-based breast cancer screening: a systematic review and meta-analysis

L. Ding[1], J. Wang[1], M. Greuter[1], M. Goossens[2], G. van Hal[3], G.H. de Bock[1]. *[1]University of Groningen- University Medical Center Groningen, Department of Epidemiology, Groningen, Netherlands [2]Center for Cancer Detection- Flanders- Belgium, Center for Cancer Detection- Flanders- Belgium, Brugge, Belgium [3]University of Antwerp, Department of Social Epidemiology and Health Policy, Antwerp, Belgium*

Background: Breast cancer (BC) screening can be performed in a screening program (BCSP) or an opportunistic screening. The existing reviews on determinants associated with the non-participation in BC screening including self-reported screening non-participation and studies from the two screening strategies were combined in these reviews. To find determinants associated with the non-participation in BCSP with meta-analyses.

Methods: PubMed, Embase, and Web of Science were searched for observational studies examining quantified factors associated with non-participation in BCSP in a general population. Studies on the non-participation in an opportunistic screening setting, and/or including self-reported data on non-participation were excluded. A random-effect model was used to calculate pooled odds ratios (ORs) and 95% confidence intervals (CIs). Potential sources of heterogeneity were explored by stratification of the results.

Results: Thirty-three studies with a total of 20,786,944 women were included. Being unmarried, having low education, being an immigrant, living far from an assigned screening unit and having low income was associated with a higher non-participation in screening (OR: 1.44, 95%CI: 1.18-1.75, OR: 1.19, 95%CI: 1.05-1.35, OR: 1.17, 95%CI: 1.09-1.27, OR: 1.17, 95%CI: 1.06-1.30, and OR: 1.10, 95%CI: 1.07-1.14, respectively). Reminder sent to non-attendees or not and reporting adjusted estimates or not partly explained the substantial heterogeneity.

Conclusions: In this meta-analysis excluding studies on the non-participation of opportunistic screening, or with self-reported data on non-participation, the well-known determinants for non-participation are still significant, but less strong. This analysis supports the relevance of meta-analysis including only studies with registered non-participation in a BCSP.

No conflict of interest.

CLINICAL SCIENCE SYMPOSIUM

The Axilla: How to Reduce Overtreatment

1A Oral

The generalisability of randomised clinical trials: An interim external validity analysis of the ongoing SENOMAC trial in sentinel lymph node-positive breast cancer

J. De Boniface[1], J. Ahlgren[2], Y. Andersson[3], L. Bergkvist[3], J. Frisell[4], D. Lundstedt[5], R. Olofsson Bagge[6], L. Rydén[7], M. Sund[8], SENOMC Trialists' Group. *[1]Karolinska Institutet and Capio St. Göran's Hospital, Department of Molecular Medicine and Surgery, Stockholm, Sweden; [2]Cancer Center Uppsala Örebro, Dept. of Oncology, Örebro, Sweden; [3]Uppsala University, Center for Clinical Research Västerås, Västerås, Sweden; [4]Karolinska Institutet, Department of Molecular Medicine and Surgery, Stockholm, Sweden; [5]Sahlgrenska University Hospital, Dept of Oncology, Gothenburg, Sweden; [6]Sahlgrenska University Hospital, Dept of Surgery, Gothenburg, Sweden; [7]Lund University, Department of Clinical Sciences and Division of Surgery, Lund, Sweden; [8]Umeå University, Department of Surgical and Perioperative Science/Surgery, Umeå, Sweden*

Background: None of the key randomized trials on the omission of axillary lymph node dissection (ALND) in sentinel lymph node (SLN)-positive breast cancer have reported external validity, though results indicate selection bias. Our aim was to assess the external validity of the ongoing randomised SENOMAC trial by comparing characteristics of Swedish SENOMAC trial participants with non-included eligible patients registered in the Swedish National Breast Cancer Register (NKBC).

Material and Methods: The non-inferiority SENOMAC trial (NCT 02240472) is open for recruitment in six European countries and randomises clinically node-negative T1-T3 breast cancer patients with up to two sentinel lymph node macrometastases to completion ALND or SLN biopsy only. Both breast-conserving surgery and mastectomy are eligible interventions. The primary endpoint is 5-year breast cancer-specific survival and the target accrual 3500 patients, more than 1600 of whom had been included by October 2019. Data from NKBC were extracted for the years 2016 and 2017, and patient and tumour characteristics compared with Swedish trial participants from the same years.

Results: Overall, 306 NKBC cases from non-participating and 847 NKBC cases from participating sites (excluding SENOMAC participants) were compared with 463 SENOMAC trial participants. Patients belonging to the middle age groups ($p = 0.015$), with smaller tumours ($p = 0.013$) treated by breast-conserving therapy (50.3 versus 47.1 versus 65.2%, $p < 0.001$) and less nodal tumour burden (only 1 macrometastasis in 78.8 versus 79.9 versus 87.3%, $p = 0.001$) were over-represented in the trial population. Time trends indicate, however, that differences may be mitigated over time.

Conclusions: This interim external validity analysis specifically addresses selection mechanisms during an ongoing randomised trial, potentially increasing generalisability by the time full accrual is reached. Similar validity checks should be an integral part of prospective clinical trials.

No conflict of interest.

1B Oral

Omitting completion axillary lymph node dissection after sentinel node micrometastases in breast cancer – first results from the Swedish prospective SENOMIC trial

Y. Andersson[1], L. Bergkvist[2], J. Frisell[3], J. de Boniface[3]. *[1]Västmanland Hospital, Department of Surgery, Vasteras, Sweden; [2]Uppsala University, Center for Clinical Research Uppsala University, Västmanland County Hospital, Västerås, Sweden; [3]Karolinska Institutet, Department of Molecular Medicine and Surgery, Stockholm, Sweden*

Background: The therapeutic role of completion axillary dissection (ALND) has been increasingly questioned in breast cancer patients with limited axillary lymph node metastases. Several studies have suggested non-inferior axillary recurrence and survival rates in patients with or without completion ALND. Patients undergoing mastectomy, however, are under-represented, and there are indications of selection bias in key trials.

Material and Methods: Since October 2013, breast cancer patients with sentinel lymph node (SLN) micrometastases are prospectively enrolled into the single-arm SENOMIC trial, thereby avoiding completion ALND. For the present analysis, patients treated by breast conservation or mastectomy until March 2017 and not receiving nodal irradiation were selected; the SENOMIC trial, however, is still selectively open for patients treated by mastectomy. Patients are followed by annual mammography and clinical examination for five years. Here, we present the first results on event-free survival, calculated by Kaplan-Meier survival estimates, and subsequently adjusted for by multivariable Cox regression analyses, taking the type of surgery performed into special consideration.

Results: Some 493 patients were included by 23 Swedish centres. Median follow-up was 38 (range 7–67) months. Three-year event-free survival was 94.0% after mastectomy and 97.9% after breast conservation (log rank $p = 0.010$). After adjustment for competing factors by multivariable analyses, including adjuvant systemic therapy and irradiation to the chest wall or remaining breast tissue, however, the survival difference between mastectomy and breast conservation did not persist (HR 2.181, 95% C.I. 0.52–9.09). Isolated axillary recurrences were diagnosed in 3 of 184 (1.6%) patients undergoing mastectomy and 1 of 309 (0.3%) patients after breast-conserving surgery, resulting in estimated five-year axillary recurrence-free survival rates of 94.5% and 99.7%, respectively (log rank $p = 0.086$).

Conclusions: After three years, event-free survival was excellent in breast cancer patients with SLN micrometastases despite omission of ALND. Of notice, axillary recurrences were somewhat more frequent in mastectomy patients; this, however, may be a chance finding, as events are still scarce. Long-term follow-up is therefore of utmost importance, as is the continued inclusion of these patients in the SENOMIC trial.

No conflict of interest.

2 Oral

Tailored axillary treatment after neoadjuvant systemic therapy in clinically node-positive breast cancer patients is safe: 3-year follow-up of the MARI protocol

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Background: More than one-third of clinically node positive (cN+) breast cancer (BC) patients currently show a pathologic complete response (pCR) of the axilla after neoadjuvant systemic therapy (NST). In patients with pCR, axillary lymph node dissection (ALND) is considered as overtreatment. The MARI procedure (Marking Axillary lymph nodes with Radioactive Iodine seeds) combined with pre-NST FDG-PET/CT (MARI protocol) is an accurate method to restage the axilla after NST. Here, we present 3-year follow-up results of BC patients treated according to the MARI protocol.

Methods: All cN+ BC patients with pre-NST FDG-PET/CT and the MARI procedure between July 2014–Nov 2017 were selected. Exclusion criteria were history of BC, synchronous metastasis and non-FDG-avid BC. Patients were divided in two groups based on the number of FDG-avid axillary lymph nodes (ALNs) on PET/CT pre-NST: <4 (cN < 4) or ≥4 (cN4+). Patients received tailored axillary treatment according to the response in the MARI node (Table 1).

Table 1 MARI protocol

Procedure	cN+ patients			
FDG-PET/CT pre-NST	<4 ALNs		≥4 ALNs	
MARI node post-NST	pCR	no pCR	pCR	no pCR
Treatment axilla	None	ART	ART	ALND +ART

Results: A total of 257 patients were identified. Tumors were HR+/HER2– in 43%, HER2+ in 33% and triple negative in 24% of patients. There were 184 (72%) cN < 4 patients and 73 (28%) cN4+ patients. After NST, pCR of the MARI node was seen in 78/184 (42%) cN < 4 patients and in 34/73 (47%) cN4+ patients. A positive MARI resulted in ALND in all cN4+ patients (n = 39) and in 2/106 cN < 4 patients, both with extensive disease recognized intraoperatively. The 104/106 cN < 4 patients with a positive MARI received ART only as well as cN4+ patients with a negative MARI (n = 34). The 78 cN < 4 patients with a negative MARI received no further axillary treatment. Overall, ALND was omitted in 216/257 patients (84%).

After a median follow-up of 3.0 years (IQR 2.3–4.0), 28/257 patients (11%) had disease recurrence of whom 16/184 (9%) were cN < 4 and 12/73 (16%) cN4+. Most recurrences occurred in patients who had ALND (n = 11, 27%) compared to ART (n = 13, 9%) or no treatment (n = 4, 5%) (p = 0.002). One (1%) patient had local recurrence only and 1 (1%) had local plus distant metastasis, 10 (4%) patients had locoregional recurrence (LRR) (3 LRR only, 7 LRR and distant) and 16 (6%) had solely distant metastases. Only 1/10 patients with LRR had not received further axillary treatment (5 patients ART, 4 ALND and ART). Three-year BCS survival, RFS and LR control were 94% (95%CI: 91%–97%), 88% (95%CI: 84%–93%) and 96% (95%CI: 93%–99%).

Conclusion: Tailored axillary treatment after NST according to the MARI protocol has resulted in an 84% reduction of ALNDs for cN+BC patients. Three-year follow-up shows an acceptable LR control rate of 96%, with only one axillary recurrence in patients who did not receive any further axillary treatment.

No conflict of interest.

CLINICAL SCIENCE SYMPOSIUM

Metastatic Breast Cancer

3 Oral

Panel-guided personalized medicine in metastatic breast and gynecological cancer: First experiences at the Comprehensive Cancer Centre Munich and clinical relevant changes over time

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Background: Recent advances in the understanding of malignant diseases have shown that some tumorigenic genomic alterations associated with the hallmarks of cancer can be therapeutically addressed by molecularly targeted agents. Comprehensive genomic profiling identifying such actionable alterations aims to offer personalized treatment to cancer patients. With the ongoing approval of many targeted therapies, the growing field of precision medicine is constantly expanding and requires optimization. Here, we report first experiences of the Comprehensive Cancer Center Molecular Tumor Board (CCCM) in breast and gynecological malignancies. The aim of this analysis was to retrospectively measure the impact of recommendations made by a multidisciplinary tumor board on the outcome of patients with breast or gynecologic cancers, who had progressed under standard treatment.

Material and Methods: 95 patients diagnosed with metastatic breast or gynecologic malignancies underwent molecular diagnostic multigene- and/or TMB (tumor mutational burden) testing using the Oncomine system (Ion Torrent). From May 2017 through March 2019, our Molecular Tumor Board (MTB) reviewed the clinical cases carefully considering tumor profile and discovered molecular aberrations providing further diagnostic and therapeutic recommendations. All patients were part of a prospective registry (Der informative Patient).

Results: 95 patients with metastatic breast or gynecologic tumors were discussed in the MTB (68% breast cancer, 20% ovarian cancer, 5% cervical cancer, 3% endometrial cancer and 4% others). The genes with the highest rates of abnormality were PI3KCA, KRAS, FGFR1 and CCND1. Overall, 34 patients (36%) received a biomarker based targeted therapy recommendation. Recommended treatments included various drugs such as protein-kinase inhibitors (45%), combination therapies (24%), or clinical trials (20%). Therapeutic recommendations were implemented in 9 cases; 4 patients experienced clinical benefit with a partial response or stabilization lasting over 4 months, including 3 of them receiving off-label treatment. In spring 2019, the FDA approved the PIK3CA inhibitor alpelisib in combination with endocrine therapy for patients with HR-positive metastatic breast cancer and PIK3CA mutations, which could have resulted in 5 further therapy recommendations.

Conclusions: In the setting of a multidisciplinary molecular tumor board, a small but clinically meaningful group of breast and gynecologic cancer patients derives benefit from comprehensive genomic profiling. Main problems of precision cancer medicine include patient referral only at late stage disease and limited access to targeted agents as well as continuously updated therapeutic algorithms.

No conflict of interest.

4 Oral

Contemporary picture of metastatic breast cancer: Characteristics and outcomes of 22,000 women from the ESME cohort 2008–2016

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Background: Real-world data help identify current medical needs, and inform future therapeutic developments. We aimed to describe the full characteristics and outcomes in the ESME cohort, a large national contemporary observational database of patients with metastatic breast cancer (MBC).

Material and Methods: ESME-MBC cohort is a population-based registry, which has been collecting individual data on all consecutive patients treated for MBC in 18 French Comprehensive Cancer Centers. Women aged ≥18 years with newly diagnosed MBC and who initiated MBC treatment between January 2008 and December 2016 (n = 22109) were included. We assessed full patients' characteristics, first-line treatments, Overall survival (OS) and first-line progression free survival (PFS), as well as updated prognostic factors in the whole cohort and among the three major subtypes: hormone receptor positive and HER2-negative (HR+/HER2–, n = 13656), HER2-positive (HER2+, n = 4017) and triple-negative (n = 2963) tumors.

Results: The median OS of the whole cohort was 39.5 months (95%CI, 38.7–40.3). 5-year OS was 33.8%. Median OS differed significantly between HR+/HER2– (43.3 months; 95%CI, 42.5–44.5), HER2+ (50.1 months; 95% CI, 47.6–53.1) and triple-negative subtypes (14.8 months; 95%CI, 14.1–15.5) (p < 0.0001). The following variables had a constant significant negative prognostic impact on OS in the whole cohort and among subtypes: worse performance status, older age at diagnosis of metastases (except for the triple-negative subtype), metastasis-free interval between 6 and 24 months, presence of visceral metastases, number of metastatic sites >3.

The median first line PFS (all treatments included) was 9.7 months for the whole population (95% CI, 9.4–9.9), 10.7 months (95% CI, 10.5–11.0) in the HR+/HER2–; 11.3 months (95% CI, 10.7–11.8) in the HER2+ and 4.8 months (95% CI, 4.6–5.1) in the triple negative subgroups respectively (p < 0.0001).

Conclusions: These data provide a full picture of current characteristics and outcomes of MBC patients. Areas of major uncovered medical need can be identified.

Database registration: clinicaltrials.gov Identifier NCT032753.

Conflict of interest:
Other Substantive Relationships:
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The other authors declare that they have no conflict of interest to disclose.

CLINICAL SCIENCE SYMPOSIUM

Latest Practices in Follow up of Patients

5 Oral

Trends in incidence, mortality, survival and treatment of primary invasive breast cancer in the Netherlands for women diagnosed between 1989–2017

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Background: During three last decades, the breast cancer (BC) landscape has changed considerably e.g. due to early-detection by screening and the more widespread use of (neo) adjuvant systemic treatments. The effects of these developments have influence on stage and treatment management, and trends in core epidemiological indicators and clinical management have hardly been studied. The aim of this study was to provide a comprehensive overview of the trends in incidence, mortality, survival and treatment of invasive BC, according to age, stage, and hormone receptor (HR)- and HER2 receptor-subtype in the Netherlands between 1989–2017.

Material and Methods: We selected all women aged ≥18 years diagnosed with primary stage I–IV BC between 1989–2017 from the nationwide population based Netherlands Cancer Registry (N = 320,249). BC mortality and reference population data were retrieved from Statistics Netherlands. Age-standardized incidence and mortality rates were calculated and joinpoint regression analysis was used to estimate average annual percentage changes. To estimate BC-specific survival, relative survival was calculated using the Ederer II method.

Results: BC incidence increased from 126 to 153 per 100,000 person-years between 1989 and 2017, but decreased annually for women aged ≥75 since 1998 with −1.2% (95% confidence interval [CI]:−1.3, −1.1). For the total population, BC incidence decreased annually with −0.8% (95%CI: −1.1, −0.5) between 2013–2017. The incidence of stage I BC increased from 36 to 72 per 100,000 person-years between 1989–2017, whereas it decreased for stage II and III BC since 2004. Stage IV BC incidence remained stable around 8 per 100,000 person-years. Subtype-specific analyses showed that the incidence of HR+/HER2− and HR+/HER2+ BC increased annually with 0.7% (95%CI: 0.5, 0.9) and 1.0% (95%CI: 0.8, 1.3), respectively, between 2006–2017. The use of any (neo)adjuvant systemic treatment increased from 41.8% in 1989–1992 to 71.1% in 2013–2017, and combinations were provided more frequently. The use of breast conserving surgery and radiotherapy increased from 37.1% and 53.9% in 1989–1992, respectively, to 57.2% and 68.6% in 2013–2017. Mortality rates decreased from 57 to 35 per 100,000 person-years and relative survival improved for all ages, tumour stages and receptor-subtypes between 1989–2017. The five- and ten-year relative survival rates were 76.8% and 55.9% in 1989–1999, respectively, and increased to 92.0% and 84.8% in 2010–2017.

Conclusions: In the Netherlands, the incidence of primary invasive BC has steadily increased for most women since 1989, but the latest trends show promising declines. The use of (neo) adjuvant systemic treatments has increased considerably. Meanwhile, the mortality of invasive BC has decreased substantially and the survival has improved for all age groups, stages and receptor-subtypes.

No conflict of interest.

PLENARY SESSION

Keynote Lecture, Best and Late Breaking Abstract Presentations

6 Oral

Clinical utility of MammaPrint testing in Invasive Lobular Carcinoma: Results from the MINDACT phase III trial

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Background: Chemotherapy-treatment (CT) decision for patients (pts) diagnosed with Invasive Lobular Carcinoma (ILC) remains controversial. We investigated the clinical utility of MammaPrint in pts diagnosed with early-stage ILC enrolled in MINDACT.

Material and Methods: MINDACT enrolled 6693 women with early-stage breast cancer and demonstrated the clinical utility of MammaPrint for adjuvant CT decision. This exploratory subgroup analysis includes pts with centrally-reviewed histologic data classified as IDC or ILC. Pts were categorized into risk groups based on MammaPrint for genomic risk (g-risk) and modified Adjuvant!Online for clinical risk (c-risk). Pts with c-low/g-low risk were spared CT, while pts with c-high/g-high risk received CT. Discordant cases were randomized to receive CT based on the c- or g-risk.

Results: 5313 pts were included and centrally-classified as ILC (n = 487, including 255 classic ILC and 232 ILC variants) or IDC (n = 4826). 60.3% (395/654) of ILC cases by local assessment were confirmed by central pathology. 92 ILC cases by central review were classified differently by local assessment.

Compared to IDC, ILC tumors were larger (>2 cm, 41.1% vs 27.1%), more often ER+ (98.8% vs 87.7%) and less often HER2+ (3.5% vs 10.6%). 29.0% of ILC pts and 36.3% of IDC pts were premenopausal. Nodal status was balanced between groups (N1-3, 18.5% and 21.5% of ILC and IDC). 30.6% of ILC and 45.1% of IDC were treated with CT.

The C-risk classified 48.3% of ILC and 51.5% of IDC as c-high risk (cH). MammaPrint classified 16.2% of ILC and 39.1% of IDC as g-high risk (gH). In the subset of ILC, c- and g-risk were discordant in 6% cL/gH and 38% cH/gL and concordant in 45.8% cL/gL and 10.3% cH/gH.

MammaPrint classified 10.2% of classic ILC and 22.8% of ILC variants as gH. 5-yr DFS estimates was 93.0% (88.7; 95.7) for classic ILC and 88.4% (83.1; 92.1) for ILC variants.

		IDC		ILC	
		N	5-year KM estimate	N	5-year KM estimate
All	DMFS	4826	94.9% (94.2; 95.5)	487	95.5% (92.9; 97.1)
	DFS		90.4% (89.5; 91.2)		90.8% (87.6; 93.2)
gH	DMFS	1888	92.3% (90.9; 93.5)	79	89.4% (78.5; 94.9)
	DFS		87.1% (85.3; 88.6)		84.6% (73.5; 91.3)
gL	DMFS	2938	96.5% (95.7; 97.2)	408	96.6% (94.0; 98.1)
	DFS		92.5% (91.4; 93.4)		92.0% (88.6; 94.4)

Conclusions: Compared to IDC, ILC tend to have higher tumor size, were more often ER-positive and less often HER2+. ILC and IDC had a similar distribution of c-risk, while 16% of ILC were high g-risk, with unfavorable survival outcomes. 38% ILC pts classified as c-high/g-low risk.

Higher rates of gH and lower DFS rate were observed in ILC variants than in classic ILC.

DMFS and DFS estimates were similar for ILC and IDC classified as either low or high-g-risk, suggesting that MammaPrint also has prognostic value in ILC and may be a clinically useful tool for adjuvant treatment decision making in ILC.

Conflict of interest:
Ownership:
Laura van 't Veer: Agendia NV, The Netherlands.
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7 Oral

The risk of cardiovascular disease in irradiated breast cancer patients: The role of cardiac calcifications and adjuvant treatment

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Background: (Neo) adjuvant treatments including anthracyclines, trastuzumab and (left-sided) radiotherapy (RT) are associated with an increased risk of cardiovascular disease (CVD). Breast cancer patients with pre-existing CVD risk factors have the highest risk of treatment induced cardiotoxicity. Coronary artery calcium (CAC) is a strong independent CVD risk factor and can be quantified on dedicated radiotherapy planning CT scans of the chest. Automated assessment of CAC scores in breast cancer patients planned for RT may be helpful in detecting patients at increased CVD risk. In the Bragatston study, we evaluate the association between automated CAC measurement on RT planning CT scans and the risk of CVD in breast cancer patients treated with RT.

Methods: In this multicenter retrospective cohort study, CAC scores of breast cancer patients receiving RT between 2005 and 2016 were automatically calculated in planning CT scans using an deep learning algorithm and classified into Agatston categories (0, 1–10, 11–100, 101–399, >400 units). Tumor and treatment characteristics were obtained from the Netherlands Cancer Registry. Data on CVD occurrence were obtained from Dutch Hospital Data and the National Cause of Death Register. Cox proportional hazard regression models were used to evaluate the association between CAC scores and CVD risk. Stratification for left- vs right-sided RT and treatment with vs without anthracyclines was performed.

Results: Data from 14,002 patients with a mean age of 58 years (SD = 11) were included. Twenty-nine percent of the patients had a CAC score of >0 (Table). At a median follow-up of 52 months (IQR: 27–82), 8% of the patients (n = 1138) were admitted to the hospital for CVD and 93 patients (1%) died from CVD. After adjustment for age and calendar year at planning CT, the risk of CVD increased with higher CAC, from 5% for patients without CAC to 28% of patients with a CAC score >400. The association between a high CAC score and CVD was strongest in patients treated with anthracyclines ($HR_{CAC\ >400}$ = 5.4, 95%CI = 2.6–11.3).

Table

CAC score	N (%)	Patients with CVD, N (% within CAC group)	HR (95%CI)*
0	9982 (71)	498 (5)	1.0
1–10	1378 (10)	122 (9)	1.3 (1.0–1.5)
11–100	1565 (11)	210 (13)	1.7 (1.5–2.1)
101–400	669 (5)	117 (18)	2.2 (1.8–2.7)
>400	408 (3)	114 (28)	3.6 (2.9–4.5)

*Adjusted for age and calendar year at planning CT.

Conclusion: CAC detected on the RT planning CT is strongly associated with CVD risk. This finding is relevant for breast cancer patients since early identification of high risk patients enables switching to less cardiotoxic breast cancer treatment (e.g. adaptation of RT target volumes or technique, chemotherapy dose reduction). Also, patients can adopt targeted cardio-preventive interventions (e.g. lifestyle changes, pharmaco-prevention, close monitoring for early detection).

No conflict of interest.

8A Oral

Impacts of omission of breast cancer surgery in older women with ER+ early breast cancer. A risk stratified analysis of survival and quality of life outcomes

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Background: In breast cancer (BC) management, age related practice variance is widespread with older women having lower rates of surgery, based on the premise of poor tolerance and reduced treatment benefit. Primary endocrine therapy (PET) may be appropriate in those who are unfit for surgery or with a limited life expectancy. This prospective multi-center study aimed to determine co-morbidity and frailty thresholds beyond which surgery is no longer beneficial.

Methods: A multi-center, prospective observational study with propensity score matched analysis to determine thresholds for optimal allocation of surgery or PET in women over age 70 with operable breast cancer. Baseline comprehensive geriatric assessment was performed. Cancer stage, grade and biological subtype were recorded as were treatment details. Outcome measures (overall and breast cancer specific survival, quality of life and adverse events) were recorded at 6 monthly intervals for 2 years. Propensity score matching was performed in Stata.

Results: The study recruited 3416 women from 56 UK breast units between 2013 and 2018.

Of these, 2979 (88%) had ER+ BC, of whom 2354 had surgery and 500 PET. The median age was 77 (range 69–102), varying by treatment allocation: surgery: 76 years (69–94) versus PET: 84 years (70–102). Similarly Charlson co morbidity score (CCI) differed (median CCI surgery group: 4 (interquartile range IQR: 3–5) versus 6 (IQR 4–7)) and activities of daily living (ADL) scores differed by treatment allocation (median ADL surgery 100 (IQR 100–100) versus PET 95 (IQR 95–100). Un-adjusted all cause mortality (median 2 years) was 135/486 (28%) for PET and 212/2307 (9%) for surgery (P < 0.001). Un-adjusted BC specific mortality was 5% for PET patients, 3% for surgery patients. There were no deaths due to surgery

and significant systemic surgical adverse events were rare (~2%) although wound complications were relatively common (19%).

Baseline variation in health status (age, CCI, ADL and tumor stage) was propensity score adjusted yielding a matched cohort of 426 surgery and 240 PET patients with similar levels of age, fitness and frailty. Matched all cause mortality was 20.8% for PET versus 16.3% for surgery (NS). Breast cancer specific mortality was 5.3% for PET versus 5.4% for surgery (NS). Survival outcomes in the matched cohort remained similar up to 4 years after which divergence occurred, suggesting that 4 years predicted life expectancy is the cut off for PET having non inferior survival outcomes compared to surgery. In this frailer, less fit, matched group, quality of life and functional outcomes deteriorated after surgery.

Conclusion: PET is unlikely to be inferior for women (with ER+ BC) who are unfit for surgery or have a life expectancy of <4 yrs, and this can be used to inform treatment decision-making with older women with BC about their appropriate treatment choice.

No conflict of interest.

8B Oral

Cluster randomised trial to evaluate the clinical benefits of decision support interventions for older women with operable breast cancer

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Introduction: Breast cancer (BC) survival in older women is inferior to younger women partly due to reduced rates of surgery, chemotherapy and radiotherapy. Some treatment variance may be appropriate to minimise complications in the least fit older women, but there are no guidelines to aid decision-making regarding the level of fitness where such tailored approaches are appropriate. This cluster-randomised controlled trial (cRCT) has evaluated the impact of two decision support tools (DESIs) in older women with BC. One supports decisions about surgery (+ adjuvant endocrine therapy) or primary endocrine therapy (PET); the second concerns choosing adjuvant chemotherapy or not. Both DESIs allow treatment tailoring for fitness & frailty, based on validated outcome models derived from UK registry data. The two DESIs each have an on-line tool with down-loadable outcome print-outs, booklets & brief decision aids to support fitness tailored decision-making in older women between surgery or PET or, in the post-surgical setting, between chemotherapy or no chemotherapy. The aims were to compare quality of life (QoL) & a range of secondary outcomes including measures of decision quality & treatment choice between clusters.

Methods: A multicentre cluster RCT comparing use of two DESIs versus usual care in treatment decision-making in older women (≥70 years) with operable BC. Breast units (clusters) were randomised to usual care (UC) or access to both DESI interventions. The primary outcome was QoL (EORTC C30 tool). Secondary outcomes included decision quality measures, patient knowledge levels and treatment choices.

Results: The study recruited 1339 women across 46 sites, (21 intervention, 25 UC), median age 77 (range 70–102 years), (670 intervention, 669 UC). There was no difference in global QoL at 6 months post-baseline on intention to treat (ITT) analysis [difference = −0.20, 95% CI −2.69 to 2.29, p = 0.90). Treatment choices were altered with 21% (123/591) of patients with an ER+ tumour undergoing PET at intervention sites compared with 15% (88/570) at UC sites (difference = 5.5%, 95% CI 1.1% to 10.0%, p = 0.02). Uptake of adjuvant chemotherapy was lower among intervention sites than UC sites 10% (64/647) v 16% (103/642); difference = −6.2%, 95% CI −10.0% to −2.5%, p = 0.001).

Patient knowledge about treatments was greater in the intervention arm, with 94% vs 74% aware of treatment options (p = 0.003) & with greater awareness of treatment risks & benefits (91% vs 79%, p = 0.054). Feedback about the value & implementation of the DESIs, from patients and clinicians, was favorable.

Interpretation: Use of older age specific BC DESIs increases knowledge of treatment options to facilitate shared decision-making. Their use alters treatment selection & enhances patient knowledge. Longer term follow-up is required to establish if survival outcomes are affected.

No conflict of interest.

PROFFERED PAPER SESSION

Proffered Paper Session

9 Oral

Predictors of efficacy in patients (pts) with hormone receptor–positive/human epidermal growth factor receptor 2–negative advanced breast cancer (HR+/HER2− ABC): Subgroup analyses of PALOMA-3

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Background: In PALOMA-3, endocrine therapy (ET)-sensitive (ie, documented clinical benefit from prior ET or 2 y adjuvant ET before recurrence) pts with HR+/HER2− ABC and disease progression on prior ET derived overall survival (OS) benefit from palbociclib (PAL) + fulvestrant (FUL) vs placebo (PBO)+FUL. In pts who received prior chemotherapy (CT) for ABC, median (m)OS was similar between treatment arms, suggesting that prior CT impacts the benefit of PAL+FUL. This post hoc analysis reports OS and progression-free survival (PFS) in the ITT and ET-sensitive populations from PALOMA-3 with/without prior CT for ABC and by menopausal status.

Material and Methods: Pts were randomized 2:1 to receive PAL (125 mg; 3/1 schedule)+FUL (500 mg IM, q2w for 3 injections, then q4w) or matching PBO+FUL. Data cutoff dates were Apr 13 2018 (OS) and Oct 23 2015 (PFS). mOS/PFS were estimated using the Kaplan-Meier method. Hazard ratios and CIs were calculated using an unstratified Cox proportional hazards model.

Results: In total, 521 pts were randomized in PALOMA-3 (Table). There were minimal differences in the characteristics of pts treated with/without prior CT; in both ITT and ET-sensitive populations, fewer pts without vs with prior CT in ABC had visceral disease (56% vs 68%; 57% vs 67%), 3+ involved sites (35% vs 46%; 34% vs 44%), or 3+ prior systemic therapies (31% vs 58%; 33% vs 62%). Pts without prior CT in ABC in the ITT or ET-sensitive populations had higher mPFS and mOS regardless of treatment, favoring PAL vs PBO. ET-sensitive premenopausal pts had prolonged OS with PAL.

Conclusion: In this exploratory analysis, improved OS benefit was observed with PAL+FUL vs PBO+FUL in the subset of pts without prior CT for MBC as well as in the ET-sensitive cohort. Pts may derive greater clinical benefit from early use of PAL to treat HR+/HER2− ABC.

Pfizer (NCT01942135).

Conflict of interest:
Ownership:
K. Theall, X. Huang, L. McRoy, and E. Bananis are employees of and stockholders in Pfizer Inc.
Advisory Board:
Y.H. Park reports consultancy or advisory board member roles for AstraZeneca, Pfizer, Eisai, and Novartis.

Table (abstract 9)

	PAL+FUL	PBO+FUL	PAL+FUL	PBO+FUL
	Prior CT	**No Prior CT**		
ITT, n	**113**	**64**	**234**	**110**
mOS (95% CI), mo	25.6 (21.4–30.1)	26.2 (20.0–37.5)	39.7 (34.9–44.4)	29.5 (23.8–37.9)
Hazard ratio (95% CI)	0.91 (0.63–1.32)	0.75 (0.56–1.01)		
mPFS (95% CI), mo	9.5 (7.3–11.3)	3.5 (1.9–5.4)	12.9 (11.0–15.0)	5.5 (3.6–7.6)
Hazard ratio (95% CI)	0.53 (0.37–0.77)	0.49 (0.37–0.65)		
ET sensitive, n	**86**	**54**	**188**	**82**
mOS (95% CI), mo	27.6 (22.8–42.0)	28.0 (18.9–39.1)	42.3 (38.0–48.3)	32.1 (24.6–41.4)
Hazard ratio (95% CI)	0.84 (0.54–1.28)	0.68 (0.48–0.96)		
mPFS (95% CI), mo	9.5 (5.7–12.7)	3.5 (1.9–5.4)	13.6 (11.3–16.6)	5.5 (3.5–9.2)
Hazard ratio (95% CI)	0.50 (0.33–0.76)	0.46 (0.33–0.64)		
	Premenopausal	**Postmenopausal**		
ITT, n	**72**	**36**	**275**	**138**
mOS (95% CI), mo	38.0 (24.4–NE)	38.0 (22.2–NE)	34.8 (28.8–40.1)	27.1 (22.8–32.1)
Hazard ratio (95% CI)	1.07 (0.61–01.86)	0.73 (0.57–0.95)		
ET sensitive, n	**51**	**25**	**223**	**111**
mOS (95% CI), mo	48.3 (27.7–NE)	34.6 (20.3–NE)	38.8 (32.0–43.5)	29.7 (23.5–37.5)
Hazard ratio (95% CI)	0.73 (0.37–1.46)	0.72 (0.54–0.97)		

NE = not estimable.

Board of Directors:
N/A.
Corporate-sponsored Research:
H.S. Rugo reports sponsored research to her institution from Eisai, Roche/Genentech, Eli Lilly, Macrogenics, Merck, Novartis, OBI Pharma, Odonate, Immunomedics, Daichi, and Pfizer. M. Cristofanilli reports sponsored research from Pfizer, Novartis, Merus, Eli Lilly, and G1 Therapeutics. S. Loibl reports research fees to her institution from AbbVie, Amgen, AstraZeneca, Celgene, Novartis, Pfizer, Roche, Teva, and Vifor. A. DeMichele reports sponsored research from Pfizer, Novartis, Menarini Biosystems, Calithera, Incyte, and Genentech. N. Turner reports sponsored research from Pfizer, Eli Lilly, and Novartis. Y.H. Park reports sponsored research from AstraZeneca, Eisai, Merck, Pfizer, Novartis, and Roche.
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10 Oral

Chemoprevention for breast cancer: A survey of the views of Australian women and clinicians

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Background: Chemoprevention for women at elevated risk of breast cancer is endorsed by international guidelines. This study examined the uptake of chemoprevention by Australian women at increased risk and aimed to identify modifiable barriers and facilitators for both patients and clinicians.

Material and Methods: 1,113 participants enrolled in the Kathleen Cuningham Foundation Consortium for Research into Familial Breast Cancer Follow-Up Study (kConFab FUS) and at ≥16% lifetime risk of BC (≥1.5 times the average population risk) were mailed a 68-item survey. 130 currently practising breast surgeons and 394 family doctors (FDs) who reportedly provided care for kConFab-FUS participants were sent a 49-item survey. Surveys were developed based on the theoretical domains framework.

Results: 725 participants (65%) and 221 (42%) clinicians responded (147 (37%) FDs, 74 (57%) breast surgeons). The median age of participants was 55 years. Most (84%) were at moderately increased risk (<3 times population risk). Ten women (1.4%) had taken chemoprevention. Possible side effects, lack of information and preferring the adoption of a healthy lifestyle alone were the three strongest barriers. The 20-year reduction in BC risk with tamoxifen was the most important facilitator, followed by desire to stay healthy for their family and having an abnormal breast biopsy. Most patients preferred to get information from a cancer genetics centre (CGC) (38%) followed by their FD (33%).

Most surgeons knew about chemoprevention (97%), but 35% of FDs did not; 7% and 74%, respectively, were not confident in providing chemoprevention information. The majority of FDs (75%) and breast surgeons (89%) thought discussing chemoprevention should be part of their role. For FDs the strongest barriers were insufficient knowledge and lack of confidence. For breast surgeons, the strongest barriers were medication side-effects and lack of consultation time. Clear guidelines and strong family history were facilitators for both clinician groups. FDs identified that availability of better tools to select suitable patients would be a strong facilitator.

Conclusions: Chemoprevention uptake is low in Australia by international standards. This study identified barriers and facilitators not previously noted in the literature and that could suggest interventions. However, as in other studies, improving both clinician and patient knowledge may be the most important driver of interventions. Upskilling FDs is important as, in Australia, moderate risk women are not generally eligible for CGC consultation (despite their preference for one). Providing FDs and patients with tailored education resources and tools (such as iPrevent- www.petermac.org/iprevent) to improve their confidence and awareness of chemoprevention may reduce the gap between evidence and implementation.

Conflict of interest:
Other Substantive Relationships:
KAP has a patent "System and Process of Cancer Risk Estimation" (Australian Innovation Patent) issued regarding iPrevent.

11 Oral

Screen-detected breast cancers have different tumor biology and better prognosis compared to interval breast cancers

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Background: Studies have shown that screen-detection by national screening programs is independently associated with better prognosis of breast cancer. This association can not only be explained by clinical-pathological prognostic factors. Previously, we showed there was a significantly higher proportion of breast cancers with a high risk tumor biology according to the 70-gene signature (70-GS) among interval cancers compared to screen-detected cancers. The aim of this study is to evaluate the association between tumor biology and survival for screen-detected and interval breast cancers.

Material and Methods: All Dutch breast cancer patients enrolled in the MINDACT trial (EORTC 10041/BIG3-04) accrued 2007–2011, who participated in the national screening program (biennial screening, ages 50–75) were included (n = 1102). We evaluated differences in Distant Metastasis Free Interval (DMFI) for high, low and ultralow risk biology tumors according to the 70-GS for patients with screen-detected (n = 754) and interval cancers (n = 348) using Kaplan Meier curves and Cox regression models.

Results: The median follow-up of the cohort was 8.6 years and 83 events occurred. Within the screen-detected cancers, 36% received no adjuvant systemic treatment (AST), 33% endocrine therapy (ET) only and 30% chemotherapy (CT) with or without ET. Within the interval cancers, 17% received no AST, 35% ET only and 47% CT with or without ET. For patients with screen-detected cancers a 8-year DMFI rate of 98.2% (95% CI: 95.7-100) was seen for those with 70-GS ultralow risk tumors (n = 118), 94.6% (95% CI: 92.3-97.0) for low risk tumors (n = 398) and 93.8% (95% CI: 90.7-97.0) for high risk tumors (n = 238; p = 0.4). Among the interval cancers a 8-year DMFI rate of 97.4% (95% CI: 92.4-100) was seen for patients with ultralow risk tumors (n = 39), 92.2% (95% CI: 87.6-97.0) for low risk tumors (n = 143) and 85.2% (95% CI: 79.9-90.9) for high risk tumors (n = 166; p = 0.023). Within the patients with 70-GS high risk tumors, a significant difference in DMFI was seen between screen-detected and interval cancers (p = 0.002) with a HR of 2.4 (95% CI: 1.3-4.6) for interval cancers compared to screen-detected cancers after adjusting for clinical risk (Adjuvant! Online) and AST.

Conclusions: Both screen-detected and interval breast cancers show very good 8-year DMFI rates. Among patients with 70-GS high risk tumors, a significant difference in DMFI was seen between screen-detected and interval cancers, suggesting that method of detection is an additional prognostic factor in this subgroup and should be taken into account when deciding on adjuvant treatment strategies.

Disclosures: Dr. F. Cardoso: Advisory role for: Amgen, Astellas/Medivation, AstraZeneca, Celgene, Daiichi-Sankyo, Eisai, GE Oncology, Genentech, GlaxoSmithKline, Macrogenics, Medscape, Merck-Sharp, Merus BV, Mylan, Mundipharma, Novartis, Pfizer, Pierre-Fabre, prIME Oncology, Roche, Sanofi, Seattle Genetics, Teva.

Dr. L.J. van 't Veer: Co-founder, part-time employee and stock-holder of Agendia N.V.

Conflict of interest:
Ownership:
Dr. L.J. van 't Veer: Co-founder, part-time employee and stock-holder of Agendia N.V.
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Dr. F. Cardoso: Advisory role for: Amgen, Astellas/Medivation, AstraZeneca, Celgene, Daiichi-Sankyo, Eisai, GE Oncology, Genentech, GlaxoSmithKline, Macrogenics, Medscape, Merck-Sharp, Merus BV, Mylan, Mundipharma, Novartis, Pfizer, Pierre-Fabre, prIME Oncology, Roche, Sanofi, Seattle Genetics, Teva.

CLINICAL SCIENCE SYMPOSIUM

Preoperative Systemic Therapy: How do we Respond to the Response?

12 Oral

Minimally Invasive Complete Response Assessment of the breast after neoadjuvant systemic therapy (MICRA trial): Interim analysis of a multicenter observational cohort study

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Background: Improvements in neoadjuvant systemic therapy (NST) for breast cancer (BC) patients have led to increasing rates of pathologic complete response (pCR). In patients with an excellent response, imaging alone is not accurate enough to identify patients with pCR, in whom surgery could be considered overtreatment. In the MICRA trial (NTR6120) a combination of MRI and minimal invasive biopsies of the breast is used to identify patients with pCR after NST.

Methods: The MICRA trial is a multi-center prospective cohort study. BC patients with a pre-NST placed marker and radiologic complete response (rCR) or partial response (rPR; i.e. ≥30% decrease and <2 cm longest diameter) on MRI are eligible for inclusion. Exclusion criteria are histopathological confirmed DCIS pre-NST, history of ipsilateral breast surgery and/or radiotherapy, and metastatic disease. Post-NST, 8 ultrasound-guided 14G core biopsies of the marked tumor area are obtained in the OR, preceding surgery. Pathology results of the biopsies and surgical specimens are compared. The primary endpoint is the false-negative rate (FNR) of biopsies identifying pCR. A FNR ≤8% is considered clinically acceptable. Here, we report the results of the interim analysis.

Results: 219 patients were enrolled between April 2016 and June 2019; 202 patients fulfilled eligibility criteria. Post-NST biopsies were successfully obtained in 167 patients, of whom 135 had rCR and 32 rPR. Tumors were HR+/HER2– in 26%, HR+HER2+ in 24%, HR–/HER2+ in 14% and TN in 36% of patients. In 89 (53%) patients a pCR was found in the surgical specimen, all correctly identified by post-NST biopsies. Biopsies missed residual disease in 29/78 patients (FNR = 37%) (Table 1). The FNR was higher in patients with rCR (26/55 = 47%) compared to patients with rPR (3/23 = 13%). Patients with FN biopsies compared to true-positive biopsies had smaller tumors pre-NST (25 mm, IQR: 20–31 vs. 32 mm, IQR: 23–58, p = 0.03), higher grade (66% vs 33% gr. 3, p = 0.006), smaller residual tumors in the specimens (4 mm, IQR:1–7 vs. 13 mm, IQR: 6–21; p < 0.001), differed in subtype (27% vs. 53% HR+, p = 0.03), and were more often ypTis only (21% vs. 4%, p = 0.009). Univariable predictive for false-negative biopsies were smaller residual tumor in the specimen (OR 0.90, 95%CI: 0.84–0.96) and HR-negative subtype (HR+, OR: 0.24, 95%CI: 0.09–0.63). The conditional power estimating the probability of the FNR being ≤8% at final analysis was <1%.

	Residual Disease in Surgical Specimen						
		No			Yes		
MICRA biopsies	rPR	rCR	Overall	rPR	rCR	Overall	Total
Negative	9	80	**89**	3	26	**29**	118
Positive	0	0	**0**	20	29	**49**	49
Total	9	80	**89**	23	55	**78**	167

Conclusions: The interim results of the MICRA trial demonstrate that 8 ultrasound-guided core-biopsies of the breast in patients with excellent response on MRI after NST are not accurate enough in identifying patients with pCR for omission of surgery.

Conflict of interest:
Other Substantive Relationships:
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CLINICAL SCIENCE SYMPOSIUM

Implants

13 Oral

Safety of pre-pectoral breast reconstruction followed by post mastectomy radiotherapy

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Background: Implant-based breast reconstruction (IBBR) after mastectomy either with TE or DTI in pre-pectoral position has been widely accepted. The pre-pec breast reconstruction, in fact, spares muscles, preserving the natural anatomy and reduces post-operative pain. Moreover, the pre-pec approach is associated to a decreased risk of capsular contracture and animation deformities. An increasing number of women, who undergo IBBR, will require post mastectomy radiotherapy (PMRT), since the meta-analysis of Early Breast Cancer Trialists' Collaborative Group (EBCTCG) confirmed a significant reduction of both local recurrence and breast cancer mortality in patients with pathological nodal involvement and locally advanced cancer.

Methods: Between January 2013 and December 2018, 521 pre-pectoral IBBR were performed and prospectively recorded at University of Florence Careggi teaching hospital, Italy. Two hundred and eight were two-stage pre-pectoral TE IBBR and 313 cases were DTI. In both cases, a titanium-coated polypropylene synthetic mesh (Ti-LOOP Bra, pfm medical Cologne, Germany) was used to cover the prosthesis and create a pre-pectoral pocket in a subcutaneous plane. Seventy three cases underwent PMRT, which was performed 10 to 20 weeks after surgery and in between first and second surgical stage in case of TE reconstruction. In case of adjuvant chemotherapy, PMRT was delivered at the end of medical treatment. We analysed short term complications of PMRT and reconstruction failure rate in pre-pectoral IBBR. In case of DTI we observed complications whithin 6 months after PMRT. In case of TE we considered complications both after PMRT and 6 months after second stage procedure.

Results: The most frequent complication was seroma, which occurred in 8 cases (10.9%). Infection rate was 5.4% (4 cases) and in only two cases (2.7%) the implant was removed and replaced with a retro-pectoral TE: in both cases the patients were active smokers and with BMI > 30.

Patients characteristics			
	Total 73	TE 40	DTI 33
Age, mean (range)	53.3 (28–75)	52.5 (28–70)	54.0 (29–75)
BMI, mean (range)	23.5 (18–36)	22.8 (18–35)	23.9(19–36)
Active smokers (%)	9 (12.3%)	5 (12.5%)	4 (12.1%)
Previous breast surgery (%)	4 (5.4%)	3 (7.5%)	1 (3.0%)
Comorbidities (%)	6 (8.2%)	4 (10%)	2 (6.1%)
Surgical complications			
	Total 73	TE 40	DTI 33
Infection (%)	4 (5.4%)	1 (2.5%)	3 (9.1%)
Seroma (%)	8 (10.9%)	3 (7.5%)	5 (15.1%)
Failure (%)	2 (2.7%)	1 (2.5%)	1 (3.0%)

Conclusions: This is the most numerous series of PMRT in pre-pec IBBR and the only one with a synthetic mesh. Currently, there are few studies, only with ADM, that analyzed pre-pectoral DTI and TE in the setting of PMRT. Our prospective series showed that PMRT in the setting of pre-pec IBBR with synthetic mesh is surgically safe, except in not-fit patients and active smokers, who shouldn't be candidate for pre-pectoral reconstruction overall.

No conflict of interest.

PROFFERED PAPER SESSION

Are your breasts still at risk?

14 Oral

Risk of subsequent in situ and invasive lesions after a primary diagnosis of ductal carcinoma in situ with follow-up time up to 28 years

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Background: Ductal Carcinoma in situ (DCIS) is considered a potential precursor of invasive breast cancer (BC) and is treated by mastectomy or breast conserving surgery (BCS) often supplemented with radiotherapy (RT). This study aimed to assess the long-term risk of ipsilateral subsequent in situ and invasive lesions after a diagnosis of primary DCIS and the association with initial DCIS treatment.

Material and Methods: The study cohort comprised all women diagnosed with DCIS between 1989 and 2004 in the Netherlands. Subsequent ipsilateral in situ (iDCIS) and/or invasive breast (iBC) lesions, and death were derived by linkage with the Netherlands Cancer Registry (NCR) and the nationwide registry of histo- and cytopathology in the Netherlands (PALGA). Information was complete until 2017. Cumulative incidence following mastectomy, BCS only and BCS supplemented with RT were assessed, with death as competing risk. Associations of DCIS treatment with risk of subsequent ipsilateral invasive and in situ lesions were studied in uni- and multivariable Cox models.

Results: Our study cohort comprised 10,051 women with a median follow-up of 15.7 years. After 20 years of follow-up cumulative incidence of iBC was 2.0% after mastectomy, 11.6% after BCS+RT and 17.5% after BCS only; 20-year cumulative incidence of iDCIS was 6.1% after BCS+RT and 12.3% after BCS only. In the first five years of follow-up, patients treated with BCS had a higher risk of developing subsequent iDCIS (HR 3.3; 95%CI 2.5–4.2) and iBC (HR 4.1; 95%CI 3.0–5.7) compared to those who also received RT. However, this risk difference between treatment with or without RT after BCS stabilized after ten years of follow-up (HR > 10 years for BCS+RT versus BCS only 0.7; (95%CI 0.3–1.3 for iDCIS and HR 1.1; 95%CI 0.9–1.4 for iBC, respectively). Influence of age, grade and method of detection will be available at EBCC.

Conclusions: In the first five years following diagnosis, patients treated with BCSonly had a higher risk of developing a subsequent in situ or invasive lesion than patients treated with BCS+RT. The favorable effect of radiotherapy for prognosis of BCS treated patients disappeared after ten years of follow-up.

Acknowledgement: This work is supported by Cancer Research UK and by the Dutch Cancer Society (ref. C38317/A24043).

No conflict of interest.

Table 1 (abstract 14): Cumulative incidence, assessed by competing risk analysis, and cox regression analysis in women treated for DCIS

		Cumulative incidence (%)		Hazard ratio (95%CI)			
Event	Treatment	5 year	10 year	20 year	0–5 year	5–10 year	>10 year - end follow-up
iBC + iDCIS	BCS RT+	4.7	9.2	17.4	1.0		
	BCS only	15.4	23.0	28.7	3.6 (3.0–4.5)	2.1(1.7–2.6)	1.0 (0.8–1.3)
iDCIS	BCS RT+	3.0	4.3	6.1	1.0		
	BCS only	9.0	11.5	12.3	3.3 (2.5–4.2)	2.2 (1.5–3.3)	0.7 (0.3–1.3)
iBC	BCS RT+	1.8	5.1	11.6	1.0		
	BCS only	6.7	12.2	17.5	4.1 (3.0–5.7)	2.0 (1.6–2.6)	1.1 (0.9–1.4)
	Mastectomy	0.7	1.2	2.0	0.4 (0.2–0.6)	0.1 (0.1–0.2)	0.1 (0.1–0.2)

15 Oral

Differences in breast cancer risk after a benign breast disease according to the screening type

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Background: Benign breast diseases (BBD) are related with an increased risk of developing breast cancer and have been proposed as a risk factor to personalize breast cancer screening strategies. This risk varies significantly depending on the pathological characteristics of the BBD. Our aim was to explore the differences in the risk of breast cancer across BBD types diagnosed at prevalent or incident screen in a population-based mammography program.

Materials and Methods: We conducted a retrospective cohort study with data from 629,087 women who underwent 2,327,384 mammographic examinations at the long-standing population-based screening program in Spain between 1995 and 2015, and followed up until 2017. Each BBD was classified according to the screening type as prevalent and incident, and according to the BBD type as non-proliferative and proliferative. We used partly conditional Cox hazard regression to estimate the adjusted hazard ratios (aHR) and we plotted the adjusted survival curves.

Results: During a mean 7.8 years of follow-up, 9,431 breast cancers and 9,184 benign breast diseases were diagnosed in the study population. There was a strong association between presence of a BBD and the risk of subsequent breast cancer. Compared with those without a BBD, women with incident BBD (aHR: 2.67) had a higher risk than those with prevalent BBD (aHR: 1.87). In addition, women with proliferative BBD had an increased risk than with those with non-proliferative BBD (aHR: 3.28 vs 1.96). The highest risk was found in women with an incident proliferative BBD (aHR: 3.92). There was no interaction between screening type and BBD type (p-value 0.83).

Conclusion: We found that classifying benign breast diseases according to screening type predicts the risk of subsequent breast cancer independently to the type of BBD. This information could be useful to design personalized breast cancer screening strategies aimed at improving the effectiveness of breast cancer screening.

No conflict of interest.

Table (abstract 15): Age and year adjusted hazard ratio for each classification and for the combined effect

	Women – year	Breast Cancer cases	Crude rate (×1000 wy)*	aHR (95%CI)**
Screening type				
No benign breast disease	4,847,709	9,184	1.89	Ref
Prevalent	34,040	121	3.55	1.87 (1.57–2.24)
Incident	21,691	126	5.81	2.67 (2.24–3.19)
BBD type				
No benign breast disease	4,847,709	9,184	1.89	Ref
Nonproliferative	44,528	177	3.98	1.96 (1.68–2.27)
Proliferative	11,203	70	6.25	3.28 (2.60–4.15)
Combined effect between screening and BBD type				
No benign breast disease	4,847,709	9,184	1.89	Ref
Prevalent nonproliferative	27,053	85	3.14	1.63 (1.32–2.02)
Prevalent proliferative	6,987	36	5.15	2.85 (2.06–3.94)
Incident nonproliferative	17,475	92	5.26	2.39 (1.95–2.94)
Incident proliferative	4,216	34	8.06	3.92 (2.80–5.48)

aHR: adjusted Hazard Ratio, 95%CI: 95% confidence interval.
*Crude rate per 1000 women year.
**Adjusted by age and year of screening.

16 Oral

Contralateral breast cancer in patients with ductal carcinoma in situ and invasive breast cancer in the Netherlands

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Background: The cumulative incidence of invasive contralateral breast cancer (CBC) for patients with first invasive breast cancer (BC) is approximately 0.4% per year. Less is known about CBC risk in patients with ductal carcinoma in situ (DCIS). We aimed to assess the CBC risk in patients with first DCIS compared to those with invasive BC, taking age, screening period, and (neo) adjuvant systemic therapy into account.

Material and Methods: From the nationwide, population-based Netherlands Cancer Registry, all women diagnosed with first DCIS (N = 28,003) or first invasive BC stage I-III (N = 275,836) between 1989 and 2017 were selected. Follow-up for second tumors and death was complete until 2018. Cumulative incidences, for invasive metachronous CBC (diagnosed ≥3 months after the first diagnosis) was calculated accounting for invasive ipsilateral BC, in situ CBC and mortality as competing risks. Cox regression models were performed to calculate the risk to develop invasive CBC for women with DCIS compared to women with BC using hazard ratios (HRs). Discrimination (c-statistic) of multivariable Cox regression models was calculated to assess the ability of the predictors routinely available in clinical practice for women with BC or DCIS to predict CBC risk.

Results: During a median follow-up of 7.8 years, 1,334 invasive CBC events occurred among DCIS patients and 12,821 among BC patients. The 10-year cumulative incidence was 4.8% in DCIS patients and 4.0% in BC patients (HR: 1.08; 95% confidence interval [CI]:1.01–1.14). The CBC risk was lower in patients with DCIS compared to patients with stage I BC not treated with (neo)adjuvant systemic therapy (N = 86,481, HR:0.87; 95% CI: 0.82–0.92). For patients at first diagnosis ≥50 years between 1989 and 1998 (implementation phase national screening program), the 10-year cumulative CBC incidences were 4.3% and 4.1% for DCIS and BC patients, respectively, and 5.1% and 3.9% between 1999 and 2017 (full screening coverage for women 50–75 years) (HR:1.18; 95% CI:1.10–1.26). For patients <50 years and diagnosed between 1989 and 1998 (no systemic treatment for part of lymph node negative breast cancers according to national guidelines), the 10-year cumulative CBC incidences were 4.6% and 5.5% for DCIS and BC patients, respectively, and 4.7% and 3.5% in 1999–2017 (HR: 1.20; 95% CI: 1.06–1.37). In the multivariable model, the c-statistic was 0.53 for patients with DCIS and 0.65 for BC patients.

Conclusions: We observed a higher CBC risk in patients with DCIS compared to invasive BC, which may be largely explained by different treatment strategies, especially systemic therapies. Overall CBC risk is low and difficult to predict especially in patients with DCIS. Improved individualized CBC risk prediction may be as important for patients with DCIS as for patients with invasive BC.

No conflict of interest.

CLINICAL SCIENCE SYMPOSIUM

Early Breast Cancer and Germline Gene Panel Results: Help!

17 Oral

Genome wide association study of acute radiation toxicity and quality of life in breast cancer patients – results from the REQUITE cohort study

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Background: Around a quarter of breast cancer patients treated by surgery and radiotherapy experience clinically significant toxicity, which may adversely affect breast cosmesis and quality of life (QoL). If patients at high risk of toxicity could be identified at diagnosis, this could be taken into account when discussing treatment options. This study was designed to identify common single nucleotide polymorphisms (SNPs) associated with acute radiation toxicity and change in QoL on completion of radiotherapy.

Methods: A genome-wide association study (GWAS) was performed in 1,838 breast cancer patients with complete clinical, treatment and toxicity data, recruited following breast-conserving surgery across eight centres in Europe and North America into the REQUITE prospective cohort study (www.requite.eu). Toxicity (CTCAE v4.0) and QoL (EORTC-QLQ-C30 and -B23) data were collected at baseline and on completion of radiotherapy. All patients were genotyped using Illumina OncoArrays. Datasets were imputed according to methods used by the OncoArray Network. A total of 7,409.901 SNP variants with minor allele frequency >0.05 were tested for association with the residuals of acute toxicity endpoints and worsening QoL (≥10 point change from baseline, dichotomised) adjusted for clinical and treatment co-variates. Worsening QoL was also adjusted for toxicity.

Results: By the end of radiotherapy, 20.8% of patients experienced ≥grade 2 erythema, 31.6% ≥grade 1 oedema, and 9.1% acute ulceration (skin breakdown). Overall QoL, fatigue, pain, and breast symptoms worsened significantly compared to baseline. Acute erythema was associated with the Chr1 rs631134 variant, 1 kb upstream of *PLA2G2F* (phospholipase A2 Group IIF, known to affect acute skin inflammation, $p = 1.89 \times 10^{-8}$). Acute ulceration was associated with the Chr 9 rs12554549 *PTPN3* intronic variant (protein tyrosine phosphatase non-receptor type 3, $p = 2.67 \times 10^{-8}$). Several previously significant SNP associations with toxicity were validated at the nominal 0.05 level in this cohort. Quantile-quantile plots for association with worsening QoL showed more associations above the $p < 5 \times 10^{-5}$ level than expected by chance. The strongest signal was for worsening arm symptoms and the Chr 11 rs4757774 variant, 5 kb upstream of *E2F8* (E2F transcription factor 8 transcript variant, involved in regulating cell cycle gene expression, $p = 5.66 \times 10^{-8}$).

Conclusions: The results of the largest GWAS of acute breast radiation toxicity to date can be used to develop clinical predictive risk models for toxicity and change in QoL after breast surgery and radiotherapy. This has the potential to provide clinicians with important information when planning breast cancer treatment, in order to reduce side-effects and optimise quality of life.

No conflict of interest.

18 Oral

Recommendations from the European Commission Initiative on Breast Cancer on multigene tests to guide the use of adjuvant chemotherapy in patients who have hormone receptor positive, HER-2 negative, lymph node negative or up to 3 lymph nodes positive invasive breast cancer

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Background: Predicting the risk of recurrence of hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative invasive breast cancer is crucial for deciding on adjuvant treatment. Several multigene tests are nowadays commercially available for predicting the risk of recurrence and avoiding overtreatment. Although some of these tests are recommended in national guidelines, there are still unanswered questions about their utility and cost-effectiveness. The European Commission Initiative on Breast Cancer (ECIBC) Guidelines Development Group (GDG) prioritized the following question for the European Guidelines on Breast Cancer Screening and Diagnosis: "Should multigene tests be used in patients who have hormone receptor positive, HER-2 negative, lymph node negative or up to 3 lymph nodes positive invasive breast cancer to guide the use of adjuvant chemotherapy?."

Methods: The ECIBC GDG, a multidisciplinary guideline panel of 27 members, developed the recommendations informed by systematic reviews conducted up to December 2018 by an external systematic review team (Cochrane Iberoamerica). Grading of Recommendations Assessment, Development and Evaluation (GRADE) Evidence to Decision (EtD) frameworks was used to assess the evidence, structure the process and minimize the influence of competing interests by enhancing transparency. Four commercially available multigene tests in patients with HR-positive, HER-2 negative, lymph node negative or up to 3 lymph nodes positive invasive breast cancer were evaluated: 21-gene recurrence score (21-RS), the 70-gene signature (70-GS), the PAM50 risk of recurrence score (RORs) and the 12-gene molecular score (12-MS).

Results: Recommendations were developed for only two of the tests (21-RS and 70-GS) because no eligible studies were identified concerning the others (PAM50 RORS and 12-MS). For the systematic review of effects, we included 5 studies (2 marker-based design randomised controlled trials (RCT), 2 treatment interaction design RCTs and 1 pooled individual data analysis from previous reported validation studies) out of an initial set of 2119 unique citations.

Conclusions: For women with hormone receptor positive, HER2 negative, lymph node negative invasive breast cancer, the ECIBC's GDG suggests the use of 21-RS to guide the use of chemotherapy (conditional recommendation, very low certainty of the evidence). It can be indirectly deduced from the evidence for the 70-GS that women with low clinical risk and high genomic risk may experience smaller or no net desirable effects by chemotherapy and thus there is no clinical utility in testing with 21-RS. The GDG suggests use of the 70-GS for women at high clinical risk who are HR-positive, HER2-negative, lymph node negative or up to 3 lymph nodes positive invasive breast cancer (conditional recommendation, low certainty of evidence).

Conflict of interest:
Other Substantive Relationships:
Members of the GDG do not receive financial compensation for their work but are reimbursed by the EC for travel-related expenses for the meetings organized by the JRC. Dr. Giorgi Rossi as former-PI of an independent study on HPV-based cervical cancer screening, funded by the Italian Ministry of Health, data owner, conducted negotiations with Roche diagnostics, Hologic-Genprobe, Abbott, Qiagen, Becton-Dickinson to obtain reagents at reduced price or for free the reagents obtained were not used in his institution. Dr. Lebeau reports grants and consulting from Roche Pharma AG, consulting from Novartis Oncology, and grants from BioNTech Diagnostics GmbH outside the submitted work. Dr. Lebeau reports grants and reimbursement for travel-related expenses related to consultancy from Roche Pharma AG, reimbursement for travel-related expenses related to consultancy from Novartis Oncology, and grants from BioNTech Diagnostics GmbH outside the submitted work. Dr. Gräwingholt is head of screening center in mammography screening center, consultant radiologist for screening programs in Switzerland, and consultant radiologist for Hellenic School of Senology. Dr. Saz-Parkinson is employed by the European Commission, coordinating the ECIBC's Guidelines Development Group. Dr. Quinn is the Chair of the European Working Group for Breast Screening Pathology (EWGBSP). Various companies have provided some sponsorship to the EWGBSP for group meetings. Authors not named here have disclosed no conflicts of interest.

CLINICAL SCIENCE SYMPOSIUM

Advances in Imaging

19 Oral

Determinants of mammographic density change

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Background: Mammographic density (MD) is a strong risk factor for breast cancer. We examined how breast cancer risk factors are associated with MD area (cm^2) change across age.

Material and Methods: We conducted a cohort study of 31 782 Swedish women ages 40–70 years at time of baseline mammogram. Lifestyle and reproductive risk factors were assessed by a web-based questionnaire. MD was measured as dense area using the STRATUS method (mean over the left and right breast). Linear regression analyses with adjustments for age, body mass index (BMI), and menopausal status at baseline were performed to assess the association between breast cancer risk factors and mean baseline MD. To investigate mean MD change across age, linear regression analyses with adjustments for age, BMI, menopausal status, and age at last mammogram were performed. All tests of statistical significance were two-sided.

Results: Except for oral contraceptive use, established lifestyle and reproductive risk factors for breast cancer were associated with baseline mean MD. The overall average annual MD change was -1.0 cm^2. BMI and physical activity were statistically significantly associated with MD change. Lean women (BMI < 20 kg/m^2) had a mean MD change of -1.13 cm^2 per year (95% confidence interval = -1.25 to -1.02) compared with -0.46 cm^2 per year (95% confidence interval = -0.57 to -0.35) for women with BMI 30 or higher. The annual MD change was -0.4 cm^2 larger in women who were very physically active compared with less physically active women.

Conclusions: Our results indicate that all risk factors for breast cancer, except oral contraceptive use, are associated with baseline MD but that only age, BMI, and physical activity are determinants of MD change.

No conflict of interest.

PROFFERED PAPER SESSION

Proffered Paper Session

20 Oral

Radiomics and Machine Learning with DWI for breast cancer diagnosis: Comparison with dynamic contrast enhanced and multiparametric MRI

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Background: Radiomics is the extraction and analysis of quantitative imaging features that are beyond the perception of the human eye and has been shown to improve diagnostic accuracy. To date radiomics coupled with machine learning (ML) has been mainly applied to dynamic contrast-enhanced MRI (DCE-MRI) but mining quantitative radiomics features extracted from DWI may further improve diagnostic accuracy. We evaluated radiomics and ML with DWI for breast cancer diagnosis and compared diagnostic accuracy with DCE-MRI.

Materials and Methods: In this IRB-approved retrospective study 90 women with biopsy-proven breast masses (41 benign, 49 malignant) were included. Three-dimensional tumor segmentation was conducted in images from first post-contrast T1-weighted, DWI and ADC maps by a dedicated breast radiologist with five years of experience in breast imaging. Lesions containing more than 40 pixels were included resulting in a total number of 77 lesions (33 benign and 44 malignant). Radiomics analysis and ML was performed using CERR software, and measures of accuracy, sensitivity,

Table (abstract 20)

Parameter class	ADC Data	DCE Data	ADC and DCE Data
First order parameters	Range		Robust Mean Abs Deviation
Gray level co-occurrence matrix	Joint Entropy		
First Inf Correlation			
Cluster Shade	Joint Variance		
Inverse Variance			
Haralick Correlation	Joint Variance		
Inverse Variance			
Cluster Shade			
Size zone matrix-based	zln		
gln Normalized	zln	zln	
gln Normalized			
Neighborhood gray level dependence matrix-based	Complexity	Contrast	Complexity
Run-length matrix		glv	
Sensitivity	95.5%	77.3%	90.9%
Specificity	66.7%	69.7%	75.8%
PPV	79.2%	77.3%	83.3%
NPV	91.7%	69.7%	86.2%
Accuracy	83.1%	74%	84.4%

specificity, negative predictive value (NPV) and positive predictive value (PPV) were estimated for DCE-MRI, DWI and multiparametric MRI.

Results: Of the 102 calculated radiomics parameters, 34 and 31 were significantly different between the two groups using ADC and DCE-MRI data respectively. After parameter reduction via correlation analysis, the parameters with the lowest AUC for any significant correlations (Spearman rank correlation coefficient >0.8 or <–0.8) were removed from consideration. Multivariate modelling for ADC, DCE-MRI and a combination of both data rendered 16, 11 and 18 parameters respectively. A final robust ML model was developed through a fine Gaussian support vector machine model with five-fold cross validation. Finally, 6 parameters from DCE-MRI data and 7 parameters from DWI and combined data were included in the ML model.

Conclusions: Radiomics and ML with DWI improves breast cancer detection compared to DCE-MRI. Radiomics and ML with multiparametric MRI yields best diagnostic accuracies.

No conflict of interest.

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Updated results of the MINDACT trial: 70-gene signature to guide de-escalation of chemotherapy in early breast cancer

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Background: The 70-gene signature MammaPrint® has been shown to identify breast cancer patients for whom adjuvant chemotherapy (CT) could be considered to be omitted even in the presence of unfavorable standard clinical-pathological criteria. In 2016 the MINDACT trial showed excellent 5-year distant metastasis-free survival of 94.7% (95%CI 92.5–96.2) in clinical high (C-High)/genomic low (G-Low) risk patients who did not receive chemotherapy. Long-term follow-up is now presented.

Methods: 693 patients were enrolled in the prospective phase III randomized MINDACT trial (EORTC 10041/BIG3–04) between 2007 and 2011. Patients were assigned to four risk groups on the basis of the 70-gene signature to determine genomic risk and Adjuvant! Online to determine clinical risk. We reassessed distant metastasis-free survival (DMFS) rate at 5 years in C-High/G-Low patients not receiving chemotherapy (n = 644) (primary analysis). We updated DMFS and overall survival in all four risk groups, including C-High/G-Low patients receiving chemotherapy or not (n = 749 and 748, respectively).

Results: At a median follow-up of 8.7 years, the updated 5-year DMFS rate for C-High/G-Low patients receiving no chemotherapy is 95.1% (95%CI 93.1–96.6), above the predefined non-inferiority boundary of 92%. The four risk groups showed excellent 8-year DMFS rates except for the C-High/G-High group despite treatment with chemotherapy. The 8-year outcome of C-High/G-Low patients shows a 2.6% (SE ± 1.6) difference for chemotherapy versus no chemotherapy (92.0% (95%CI 89.6–93.8) vs 89.4% (95%CI 86.8–91.5); HR 0.66; 95%CI 0.48–0.92), with minor differences in overall survival (95.7% (95%CI 93.9–97.0) vs 94.3% (95%CI 92.2–95.8)). The same comparisons confined to HR+/HER2- disease (91% of patients) generate different gain estimates from chemotherapy administration for DMFS according to age: 5% (SE ± 2.8%) in women ≤50 years versus 0.2% (SE ± 2.3%) in women >50 years.

Conclusion: MINDACT confirms the clinical utility of the addition of the 70-gene signature to clinical risk assessment for recurrence. We demonstrate that a low risk 70-gene signature can guide de-escalation of adjuvant chemotherapy in the presence of a high clinical risk (and up to 3 positive nodes) in women >50 years. In younger women, a clinically relevant benefit of about 5% is observed, which might be due to chemotherapy-induced ovarian function suppression, and the risk vs benefit of either treatment should be part of informed, shared decision-making.

Conflict of interest:

Ownership:

Dr. L.J. van 't Veer: Co-founder, part-time employee and stock-holder of Agendia N.V.

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Isabel Rubio: Honoraria Roche.
Gabriele Zoppoli: Patents, Royalties, Other intellectual property author AstraZeneca UK concerning methods for SLFN11 detection in cancer samples and its correlation with clinical outcome, Davide Bedognetti and Wouter Hendrickxk from SIDRA Medicine, Doha, concerning in vitro experiments with SLFN11 and cancer models, European patent no. 102019000018989 concerning a "multi-domain method for prediction of one-year mortality in senior patients diagnosed with cancer".

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Association of genetic variations for prediction of hot flushes in women taking tamoxifen for breast cancer prevention

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Background: Single nucleotide polymorphisms (SNPs) have been reported some of which increase or decrease the risk of breast cancer. However, few studies have investigated the association of SNPs and hot flushes in women taking preventive endocrine therapy for breast cancer. Here, we investigate whether SNPs are associated with hot flushes and whether multiple SNPs can be used to predict hot flush occurrence in the first International Breast Intervention Study (IBIS-I).

Materials and methods: We performed a candidate gene (n = 60) and a genome-wide association analysis (GWAS) on 350,000 SNPs in 310 women randomised to tamoxifen in IBIS-I. Using logistic regression, odds ratios and 95% confidence intervals were determined for the association of each SNP with hot flushes reported at the 6-month follow-up visit. We subsequently developed a multi-genic model for hot flushes using the 5-fold cross-validation for variable selection.

Results: No SNPs in the candidate gene analysis were significantly associated with hot flushes. Similarly, no SNP met the genome-wide significance level in the GWAS. However, six SNPs were below a univariate significance level of 5×10^{-5}, suggesting a possible association. These SNPs occur in genomic regions associated with RNA coding genes and genes coding for proteins involved in enzymatic activity. Using 5-fold cross-validation we identified a 12 SNP gene model which predicted hot flushes (Accuracy = 0.72, 95% CI 0.66–0.77) P-value < 0.01) in women on tamoxifen. SNPs included in the model differ from those identified as significant in the single-locus analysis and occur in genomic regions associated with metabolism of tamoxifen and sex hormones, oestrogen receptor proteins, vascular injury repair and DNA damage response.

Conclusions: While we did not find any genome wide statistically significant associations of SNPs with hot flushes, we identified several SNPs with suggestive associations. A multi-loci model, including 12 SNPs showed prediction of hot flushes reported at 6 months in women taking tamoxifen. We were unable to substantiate findings from previous studies, and our results need to be confirmed in other studies. Using models to predict side effects may lead to increased understanding of how an individual may respond to tamoxifen and produce new insights into biological pathways that result in hot flushes.

No conflict of interest.

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Nine-year survival outcome of neoadjuvant lapatinib with trastuzumab for HER2-positive breast cancer (NeoALTTO, BIG 1-06): final analysis of a multicentre, open-label, phase 3 randomised clinical trial.

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Background: Lapatinib (L) plus trastuzumab (T) with weekly paclitaxel significantly increased the pathologic complete response (pCR) rate (51.3%) compared with either anti-human epidermal growth factor receptor 2 (HER2) drug alone (24.7%% for L, 29.5% for T). Here, we report the results of the prespecified long-term event-free survival (EFS) and overall survival (OS) analyses by the treatment arms. In addition, we assess the relationship between pCR and survival, both in the overall study population and according to hormone receptor status and treatment arm.

Material and methods: Four hundred fifty-five patients with HER2-positive early breast cancer were randomly allocated to receive oral L 1500 mg/day (n = 154), intravenous T (4 mg/kg loading dose followed by 2 mg/kg, n = 149) or the combination (n = 152) of L (1000 mg/day) plus T (same dose as single agent) for 6 weeks, followed by the assigned anti-HER2 treatment combined with paclitaxel for 12 weeks. After surgery, patients received 3 cycles of fluorouracil, epirubicin and cyclophosphamide followed by 34 weeks of the same assigned neoadjuvant anti-HER2 therapy. The primary end-point was pCR (defined as ypT0/is ypN0 for this analysis), and the secondary end-points included EFS and OS. Median follow-up for the current analysis is 9.7 years (interquartile range, 6.6–9.9).

Results: Nine-year EFS rates were 63%, 65% and 69% with L, T and L + T, respectively (L vs T: hazard ratio [HR] 1.01, 95% confidence interval [CI] 0.66–1.52; p = 0.98; L + T vs T: HR 0.88, 95% CI 0.57–1.34, p = 0.55). Nine-year OS rates were 77%, 76% and 80% for L, T and L + T, respectively (L vs T: HR 0.96, 95% CI 0.58–1.60, p = 0.88; L + T vs T: HR 0.79, 95% CI 0.46–1.34, p = 0.38). Landmark analyses showed that women who achieved a pCR had improved EFS (77% vs 61%, HR 0.48, 95% CI 0.31–0.73, p = 0.0008) and OS (88% vs 72%, HR 0.37, 95% CI 0.20–0.63, p = 0.0004) compared with those who did not. pCR was associated with increased EFS and OS in hormone receptor negative (EFS: HR 0.43, 95% CI 0.25–0.73, p = 0.002; OS: HR 0.33, 95% CI 0.15–0.66, p = 0.002) and the L+T arm (EFS: HR 0.35, 95% CI 0.16–0.71, p = 0.004; OS: HR 0.22, 95% CI 0.07–0.58, p = 0.002). There were no new or long-term safety concerns.

Conclusions: Long-term follow up analysis confirms that patients with pCR have a significant higher survival probability than those who did not achieve pCR, supporting pCR as an early indicator of long-term outcome in HER2-positive disease. These effects were particularly seen in patients with

negative hormone receptors and dual anti-HER2 treatment. Although overall survival rates were not significantly different between arms, patients who reached pCR with L + T therapy were nearly doubled compared to the patients in the single agent arms. Additional exploratory analyses will be presented.

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Advisory Board:
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PROFFERED PAPER SESSION

Measuring Impact of COVID-19 on Breast Cancer Care

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Effects of cancer screening restart strategies after COVID-19 disruption

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Background: Many breast cancer screening programmes were disrupted due to the COVID-19 pandemic. This study aimed to estimate the effects of four restart strategies after the disruption on screening capacity and cancer burden.

Materials and methods: The Microsimulation Screening ANalyses breast cancer model (MISCAN-Breast) was used to simulate restart strategies for breast cancer screening. The model estimated required screening capacity, breast cancer incidence, and breast cancer mortality after a screening disruption of six months. Four restart strategies were simulated varying in population affected, duration of effects, and stopping age. Similar modelling was performed for cervical and colorectal cancer screening.

Results: The impact of the disruption heavily depended on the restart strategy. Immediately catching-up on missed screens after the disruption was estimated to lead to 0.13 additional breast cancer deaths per 100 000 women between 2020 and 2030 compared to undisrupted screening (table 1). This strategy minimised the impact of the disruption, but also required a surge in screening capacity. Delaying screening, resulting in one less screen for a quarter of the women, required the least capacity, but also had the largest impact on incidence and mortality (2.35 additional deaths per 100 000 individuals between 2020 and 2030 compared to undisrupted screening). A scenario with delays in screening, but still offering all screening rounds gave the best balance between required capacity, incidence, and mortality. The effects for cervical and colorectal cancer screening followed similar patterns, but the effect sizes were smaller.

Table 1 Cumulative breast cancer mortality per 100 000 individuals compared to undisrupted screening for four restart strategies

Restart strategies	Delaying all screens, resulting in one less screen for 1/4th of the women	Delaying all screens, except for first screening rounds	Delaying all screens and increasing the stopping age	Immediately catching-up on missed screens after the disruption
2020	0.02	0.02	0.02	0.01
2021	0.10	0.10	0.10	0.05
2022	0.26	0.25	0.26	0.08
2023	0.44	0.42	0.42	0.10
2024	0.66	0.61	0.61	0.12
2025	0.93	0.85	0.84	0.14
2026	1.18	1.06	1.04	0.14
2027	1.42	1.26	1.21	0.14
2028	1.72	1.51	1.43	0.14
2029	2.00	1.71	1.61	0.15
2030	2.35	1.98	1.85	0.13
2040	5.35	3.93	2.98	0.10
2050	7.99	4.74	3.16	0.06
2060	10.27	4.71	2.84	0.02

Conclusions: The strategies with the smallest loss in health effects were also the most burdensome for the screening organisations. Which strategy is preferred depends on the organisation and capacity of the breast screening programme in a cohuntry.

No conflict of interest.

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The COVID-19 outbreak may be associated to a reduced level of care for breast cancer. A comparative study with the pre-COVID era in an Italian Breast Unit

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Background: The recent COVID-19 pandemic has caused profound changes on the health-care systems as well as deleterious repercussions on the care of patients with cancer. In this comparative study, we sought to evaluate the effects the COVID-19 pandemic on the surgical management of breast cancer in a Breast Unit belonging to an Italian region with a low incidence of COVID-19 infection.

Methods: Eighty-three patients were included, of whom 41 received surgery during the heights of the pandemic (Group A-operated on in March and April 2020), and 42 during the same period (March-April) of the year 2019 (Group B). Clinicopathological characteristics and surgical outcomes were compared between the two groups

Results: There were no significant differences in the baseline characteristics of the two groups in regard to age ($p = 0.62$), tumour size ($p = 0.25$), grade ($p = 0.27$), histology ($p = 0.43$), positive lymph nodes ($p = 0.35$), ER positive status (0.35). Waiting time for surgery was slightly longer in Group A (49.11 vs 46.39,$p = 0.38$). Patients receiving immediate breast reconstruction were significantly less in patients of Group A ($p < 0.001$). Use of sentinel node biopsy was similar in the two groups ($p = 0.84$). Hospital stay was longer in patients of Group B ($p = 0.008$). Use of regional nerve blocks was lower in the Group A ($p < 0.001$).

Conclusions: Patients operated on during the height of pandemic were less likely to receive immediate reconstruction and regional nerve blocks. Health-care services should develop reliable and useful measures aiming to maintain the highest standards of care in case of new pandemic, and extraordinary events in general.

No conflict of interest.

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The impact of the COVID-19 pandemic on quality of life, physical and psychosocial wellbeing in breast cancer patients – a prospective, multicenter cohort study

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Background: The COVID-19 pandemic, and the resulting measures, are impacting daily life and medical management of patients with breast cancer. We evaluated to what extent these changes have affected quality of life, and physical and psychosocial wellbeing of patients (being) treated for breast cancer.

Materials and methods: This study was conducted within the prospective Utrecht cohort for Multiple BREast cancer intervention studies and Long-term evaluation (UMBRELLA). Shortly after the implementation of COVID-19 measures, extra questionnaires were sent to 1595 cohort participants, including standard quality of life (EORTC) questionnaires. Patient-reported outcomes (PROs) were compared to the most recent PROs collected within UMBRELLA before COVID-19. The impact of COVID-19 on PROs was assessed using mixed model analysis, adjusting for confounders.

Results: 1051 patients (66%) completed the questionnaires; 31% (n = 327) reported a higher threshold to contact their general practitioner amid the COVID-19 pandemic. A significant deterioration in emotional functioning was observed (82.6 to 77.9, $p < 0.001$), and 505 (48%, 95% CI 45–51) patients reported moderate to severe loneliness. Small improvements were observed in QoL, physical-, social- and role functioning scores. In the subgroup of 51 patients under active treatment, social functioning strongly deteriorated (69.8 to 5.0, $p = 0.03$).

Conclusion: Due to COVID-19, patients (being) treated for breast cancer are less likely to contact physicians, and experience a deterioration in emotional functioning. Patients undergoing active treatment report a strong drop in social functioning. One in two patients reports (severe) loneliness. Online interventions supporting mental health and social interaction are needed during times of social distancing and lockdowns.

No conflict of interest.

POSTER IN THE SPOTLIGHT

Poster in the Spotlight I

100 Poster Spotlight

Salivary metabolomics with artificial intelligence-based methods for breast cancer detection and subtype prediction

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Background: Saliva is an easily accessible and informative biological fluid which has high potential for the early diagnosis of various diseases. The primary aim of this study is to develop machine learning methods and to explore new salivary biomarkers to discriminate breast cancer patients from healthy controls. The secondary aim of this study is to evaluate the possibility of breast cancer subtype diagnosis by salivary metabolomics analysis.

Material and Methods: We conducted a comprehensive metabolite analysis of saliva samples obtained from 101 patients with invasive carcinoma (IC), 23 patients with ductal carcinoma in situ (DCIS) and 42 healthy controls, using capillary electrophoresis and liquid chromatography with mass spectrometry to quantify hundreds of hydrophilic metabolites. Saliva samples were collected under 9 h fasting. Conventional statistical analyses and artificial intelligence-based methods were used to access the discrimination abilities of the quantified metabolites. Multiple logistic regression (MLR) model and alternative decision tree (ADTree) – based machine learning methods were used to detect IC-specific elevation of salivary metabolites. We also compared these salivary metabolites among four breast cancer subtypes (luminal A-like, luminal B-like, HER2-positive and triple -negative) to identify subtype-specific metabolites.

Results: Among 101 patients with IC, most patients were clinical Stage I or II (44 patients and 46 patients, respectively). Forty-one patients were luminal A-like, 32 were luminal B-like, 13 were HER2-positive and 15 were triple-negative. Among quantified 260 metabolites, amino acids and polyamines showed significantly higher concentrations in breast cancer patients than controls, e.g. spermine showed the highest area under the receiver operating characteristic curves (AUC) to discriminate IC from C; 0.767 (95% confidence interval [CI]; 0.671–0.840, $P < 0.001$). The MLR yielded higher AUC to discriminate IC from C; 0.790 (95% CI; 0.699–0.859, $P < 0.001$). The ADTree with ensemble approach showed the best AUC; 0.919 (95% CI; 0.838–0.936, $P < 0.001$). Thirty-four metabolites showed significant differences in comparisons between C and IC. Among these 34 metabolites, Cadaverine, 5-Aminovalerate, gamma-Butyrobetaine, 2-Hydroxy-4-methypentanoate and Ala-Ala were significantly different between luminal A-like and luminal B-like subtypes, while N-Acetylneuraminate was the only significant different metabolites between luminal A-like and triple-negative subtypes. No metabolites were significantly different among the other subtypes.

Conclusions: Salivary metabolomics with machine learning methods is a promising technology not only to discriminate breast cancer from healthy control, but also to predict breast cancer subtypes.

No conflict of interest.

101 Poster Spotlight

Sense of coherence as predictor of quality of life in early breast cancer patients

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Background: Breast cancer and its treatments affect patients' health-related quality of life (HRQoL) both during therapy and afterwards. Variation among patients in QoL is clinically significant but the sources thereof only partially known and thereby challenging to predict.

The aim of the present study, a part of a randomised clinical trial (BREX), was to evaluate the cross-sectional and prospective associations between the sense of coherence (SOC) and the HRQoL of breast cancer survivors.

Material and Methods: 573 early breast cancer patients aged 35–68 years who participated in a prospective randomized physical exercise intervention with twelve months of supervised exercise training were followed up for five years. Those 406 participants who both participated in the 5-year follow-up and filled the SOC questionnaire were included in the final analysis. SOC was measured by the Finnish and Swedish 13-item short forms of Orientation to life Questionnaire (SOC-13) at 3 years. Cancer-specific HRQoL was measured by the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30) version 3 and general HRQoL by the 15D.

Results: Patients with lower SOC also risked to have significantly lower cancer-specific and general HRQoL after adjuvant treatment. SOC at 3 years was associated with cancer-specific and general HRQoL both at 3 years and at 5 years. The association was strongest for general HRQoL, global health/quality of life and emotional and cognitive functions.

Conclusions: Strong SOC as an inner resource may serve as a protective psychological factor in the adaptation process of breast cancer survivors. The SOC-13 questionnaire might be useful in identifying patients vulnerable to decreases in the HRQoL and in planning targeted psychosocial interventions.

No conflict of interest.

102 Poster Spotlight

Does mesh improve patient satisfaction and health-related quality of life after implant-based breast reconstruction? A multicentre prospective cohort study

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Background: The use of biological and synthetic mesh may improve outcomes for patients undergoing immediate implant-based breast reconstruction (IBBR) by facilitating one stage direct-to-implant procedures and more recently, muscle-sparing prepectoral techniques. Although these procedures have been widely adopted, there is limited high-quality evidence to support their long-term benefits. Patient reported outcome (PRO) data are particularly lacking. This study explores the impact of mesh use on the 18-month PROs of IBBR in the iBRA cohort.

Methods: The iBRA study prospectively recruited 2108 consecutive women undergoing immediate IBBR following mastectomy at 81 UK centres between February 2014 and June 2016. Demographic, operative, oncological and 3-month complication data were collected. Consent was sought from recruited patients to receive post-operative questionnaires at 3- and 18-months. The 18-month questionnaire assessed PROs using the validated BREAST-Q and asked patients to rate the overall outcome of their reconstruction on a five-point Likert scale.

The association between different methods of IBBR, BREAST-Q domain scores and overall outcome was explored using mixed-effects regression models adjusted for clinically relevant confounders and including a random effect to account for potential clustering by centre. The reference group was 2-stage submuscular reconstruction without mesh. Comparisons were also made with the 2008/9 National Mastectomy and Breast Reconstruction Audit (NMBRA) cohort.

Results: 1470 iBRA participants consented to receive the 18-month questionnaire and 891 (61%) completed it. Of these, 67 (8%) patients underwent standard two-stage submuscular reconstruction; 764 (86%)

patients received subpectoral reconstructions with biological mesh (n = 495, 56%), synthetic mesh (n = 95, 11%) or dermal sling (n = 174, 20%). A small number of patients (n = 14, 2%) underwent prepectoral reconstructions, which were introduced at the end of the study.

Compared with standard 2-stage submuscular techniques, no differences in BREAST-Q scores or overall outcome ($p > 0.05$) were seen in either biological or synthetic mesh-assisted subpectoral procedures or IBBR with dermal sling. Patients who underwent pre-pectoral IBBR, however, reported higher satisfaction with breasts scores than the submuscular group (difference = 6.63, 95% confidence interval [1.65–11.61], $p = 0.009$). Outcomes in the iBRA cohort were similar to those reported in the NMBRA which included only submuscular procedures.

Conclusions: This large, prospective, multicentre cohort study does not suggest that mesh improves the PROs of IBBR compared with standard submuscular techniques. However, it provides early data to support improved satisfaction with breasts in the prepectoral setting. Further trials are needed to robustly evaluate prepectoral IBBR before it becomes established as standard practice.

No conflict of interest.

POSTER IN THE SPOTLIGHT

Poster in the Spotlight II

103 Poster Spotlight

Characteristics and clinical outcome of breast cancer patients with asymptomatic brain metastases

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Background: Brain metastases (BM) have become a major challenge in the management of patients with metastatic breast cancer. So far, it is unclear whether an earlier detection of BM is associated with a better prognosis.

Material and Methods: The aim of this retrospective analysis from the Brain Metastases in Breast Cancer Network Germany Registry (BMBC) was to characterize patients with asymptomatic BM (n = 580) in a cohort of 2,589 breast cancer patients with BM as well as to compare the overall survival. Asymptomatic patients were defined as no neurological symptoms at diagnosis of BM. Patients were diagnosed with BM from breast cancer between 2000–2019.

Results: Patients in our cohort had a median age of 57.0 years at time of BM diagnosis. 46.4% of the patients (n = 1062) had a HER2-positive, 22.8% (n = 522) a triple-negative, 17.1% (n = 392) a luminal-A-like and 13.7% (n = 313) a luminal B-like primary breast cancer. 58.2% (n = 1347) of the patients had a G3 primary tumor.

Asymptomatic patients were significantly younger at BM diagnosis than symptomatic patients (median age: 55.5 vs. 57.0 years, $p = 0.01$), had a better performance status at BM diagnosis (Karnofsky Index 80–100%: 68.4% vs. 57%, $p < 0.001$), lower tumor grading (G1: 3.1% vs 1.4%, $p = 0.015$), lower number of BM (>1 BM: 56% vs. 70%, $p = 0.027$), a smaller diameter of BM (median: 1.5 vs. 2.2 cm, $p < 0.001$), more extracranial metastases (86.7% vs. 81.5%, $p = 0.003$), less common a meningeosis carcinomatosa (6.3% vs. 10.9%, $p < 0.001$), more frequently MRI alone than CT alone or a combination of both as detection method of BM (MRI alone: 71% vs. 64.8%, $p < 0.001$) and less intensive BM therapy (combined surgery and radiotherapy: 21% vs. 26.9%, $p = 0.001$). The breast cancer subtype did not differ significantly between the two groups ($p = 0.312$).

In a multivariate logistic regression analysis with 705 available patients only the performance status was significant (OR = 1.1, 95%-CI: 1.06–1.13; $p < 0.001$) to distinguish between symptomatic vs. asymptomatic patients. An analysis without the performance status and therefore a larger cohort with almost twice as many patients identified tumor grading, number of BM, BM therapy and diameter of BM as significant factors to differentiate the both groups of patients.

Asymptomatic patients had a significantly longer median overall survival compared to symptomatic patients (10.4 vs. 6.9 months, $p < 0.001$).

Conclusions: Our analyses indicate that asymptomatic patients have a minor severity of the metastatic disease in the brain and have a better outcome despite a less intense local BM therapy compared to symptomatic patients. This analysis is of clinical relevance in the context of prospective trials examining the benefit of BM early detection. Of course, a lead time bias of the earlier diagnosis cannot be ruled out.

Conflict of interest:
Other Substantive Relationships:

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The other co-authors have nothing to disclose.

104 Poster Spotlight

Real-world analysis of patients' clinical and geriatric characteristics aged ≥70 years with advanced breast cancer receiving palbociclib with endocrine therapy in the French cohort PALOMAGE

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Background: Due to the common exclusion of older patients with cancer from clinical trials, few specific data are available on the treatment of advanced breast cancer (ABC) in this population.

Methods: PALOMAGE is an ongoing French observational study evaluating the use of palbociclib (PAL) in a real life setting in patients aged ≥70 years with hormone receptor–positive (HR+), HER2- ABC. Inclusion criteria: patients aged ≥70 years starting PAL combined with endocrine therapy, split in 2 cohorts: patients with HR+ sensitive ABC defined as with no prior systemic treatment for ABC (cohort A), and patients with HR+ resistant ABC defined as having relapsed during or within one year from the end of adjuvant endocrine therapy, or treated from second line of systemic treatment (cohort B). Geriatric parameters and quality of life (QoL) are collected at baseline and in the follow-up: Geriatric-Core Data Set (G-CODE), G8, EORTC QLQ-C30 and ELD14. This early report describes baseline characteristics of patients enrolled in the study since its opening. For each variable reported, percentages are calculated on the total of the categories filled for the variable.

Results: From 10/2018 to 09/2019, 120 and 156 patients were included in cohort A and B respectively (total 276 patients). The median age was 78 years (70–94), 39 patients (14.6%) being older than 85 years. ECOG performance status (PS) was 0, 1, and ≥2 in 82 (32.5%), 121 (48%), and 49 (19.4%) patients respectively. Bone metastasis only and presence of visceral disease were reported in 90 (36%) and 106 (42.1%) patients, respectively. 93 patients (87.7%) in cohort A and 37 patients (24.5%) in cohort B had not been treated for ABC before entering the study. Of all patients, 192 (74.7%), 53 (20.6%) and 12 (4.7%) started PAL with a daily dose of 125 mg, 100 mg, or 75 mg respectively. Based on the baseline geriatric information already collected and available in the database, frailty suggested by a G8 score ≤14 was present in 72 patients (28.8%), 85 patients (48%) lived alone while 25 (14.6%) had no support, 56 (30.1%) had functional impairment (4-IADL score ≤3), 49 (33.6%) had limitation in mobility (TUG ≥ 20″), 33 (20.2%) had weight loss >10% during the past 6 months, 63 (36%) were at risk of cognitive disorder (3 words or clock drawing tests), and 79 (43.6%) were at risk of depression (4-GDS ≥ 2).

Conclusion: PALOMAGE is a unique study investigating specifically the use of PAL in elderly ABC patients in real life. Preliminary results show that patients aged 70 years and older are prescribed the CDK4/6 inhibitor with dose adjustment upfront in 1 out of 4 cases. Whether this is driven by potential frailty, as suggested by G8 or other geriatric defects, will need further analysis at full recruitment (787 patients planned).

Conflict of interest:
Advisory Board:
Etienne Brain, Elisabeth Carola, Elena Paillaud, Marina Pulido, Philippe Caillet, Louis Tassy, Claire Falandry have received fees from Pfizer as member of the scientific committee of this study.
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E. Brain: personal fees from Pfizer (lecture and ad board), Roche (lecture), BMS (lecture and ad board), Mylan (lecture and ad board), Clinigen (lecture and ad board), G1 Therapeutics (ad board), TLC PharmaChem (ad board), Samsung (consulting), non financial support (travel) from Roche, Pierre Fabre, Novartis, Pfizer, AstraZeneca.
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O. Guillem: Jansen (ad board).
N. Jovenin: Pfizer.
Nada Rifi and Jean-Michel Vauthier are Pfizer employees.
No COI reported by the other co-authors.

105 Poster Spotlight

Gut microbial short chain fatty acids are associated with pathological complete response (pCR) after neoadjuvant chemotherapy for breast cancer

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Background: The composition and function of the gut microbiome may influence the activity of systemic anti-cancer therapies. However, it is not yet known whether and how the gut microbiome impacts on chemo-sensitivity in breast cancer. To address this we have investigated associations between short chain fatty acids (SCFAs), key functional metabolites of the gut microbiome, and pCR.

Material and Methods: Female patients receiving neoadjuvant chemotherapy (NACT) for breast cancer at the Beatson West of Scotland Cancer Centre were recruited from Aug 2017-Mar 2019. Patient stool samples were collected at 3 timepoints: T1 before first NACT, T2) mid-point during NACT and T3) after final cycle of NACT. A healthy control (HC) population, approximately matched for age and weight, provided a sample at one timepoint. Analysis for 10 SCFAs was performed using gas chromatography. After surgery each patient was categorised as having pCR (ypT0/is ypN0) or non-pCR.

Results: 21 patients and 24 HCs were recruited. Median age and BMI of HCs were 46 (range 31–61) and 25.9 kg/m^2 (range 18–42.4) respectively. Patient median age and BMI were 56 (range 33–72) and 28.6 kg/m^2 (range 19.6–55.6) respectively. Most (n = 9, 42.9%) had HER2+ cancers whilst 8 (38.1%) had TNBC and 4 (19%) had ER+HER2–. NACT included FEC-T in 9 (42.9%), FEC-TH in 6 (28.6%) and other regimes in 6 (28.6%). pCR was observed in 5 of 20 evaluable patients (25%). SCFA results are available for 20 patients and 20 controls. SCFA concentrations were not significantly different between HCs and T1 patient samples. Mean concentrations (μmol/g) of the SCFAs acetate, propionate and butyrate are lower in pCR vs. non-pCR patients: T3) acetate 69.59 vs. 109.84 ($p = 0.005$), T1) propionate 14.5 vs. 25.3 ($p = 0.036$), T3 propionate mean 6.6 vs. 23.7 ($p = 0.027$), T1) butyrate 13.2 vs. 28.2 ($p = 0.027$) and T3 mean 7.8 vs. 20.5 ($p = 0.024$).

Conclusions: Significantly lower concentrations of butyrate and proprionate were observed in patients with pCR vs. non-pCR. These SCFAs are known to play important roles in shaping the immune environment, in particular by promoting development of regulatory T cells (Tregs). We speculate that lower proprionate and butyrate concentrations may result in a relatively lower peripheral Treg proportion, which in turn supports development of a more immune-stimulatory tumour microenvironment and improved pCR. Further investigation is warranted including immunophenotyping of patients' peripheral blood and tumour-infiltrating lymphocytes.

No conflict of interest.

POSTERS A
Follow up

107 Poster

Metachronous breast cancer: An observational study in a single institution

W.P. Lee[1], S.S. Shetty[1], C.M.J. Seah[1], J.W.C. Kam[2], S.M. Tan[1]. *[1]Changi General Hospital, Singapore, Department of General Surgery, Singapore, Singapore; [2]Changi General Hospital, Singapore, Clinical Trials and Research Unit, Singapore, Singapore*

Background: Breast cancer surgery has undergone dramatic paradigm shift from radical mastectomy to conservation surgery due to increased awareness and hence, early diagnosis. There has been an increasing acceptance of contralateral prophylactic mastectomy in the Western world which is slowly gaining popularity in the Asian society for fear of developing

metachronous breast cancer. In Southeast Asia, the prevalence of metachronous breast cancer has been assumed to be low and non-hereditary though relevant data reporting its incidence has been scarce. Our study aims to review the incidence, tumour characteristics and survival outcome of all metachronous breast cancer diagnosed and treated in a single institution.

Methods: Patients with histologically proven metachronous breast cancer were identified from a prospectively collected database in a single institution from January 2000 to June 2017. Metachronous breast cancer was defined as a second cancer affecting the contralateral breast diagnosed after 6 months from the first cancer diagnosis.

Results: There were 2840 breast cancer patients diagnosed and treated in our institution from January 2000 to June 2017. One hundred and fifty two patients had developed bilateral breast cancers, of which 58 patients (0.38%) were diagnosed with metachronous tumours. At the first cancer diagnosis, their mean age was 54.3 (range from 41.8 to 66.8) years. The median duration to the diagnosis of metachronous cancer was 4. 9 (IQR 2.9 to 8.2, range from 0.52 to 14.9) years. Nine patients (16.1%) had a family history of breast cancer. Thirty nine patients (70.9%) had presented with a lump at the first cancer diagnosis and 38 patients (69.1%) were asymptomatic and detected to have metachronous cancer on surveillance mammogram ($p < 0.001$). Thirty two patients (56.1%) were found to have invasive ductal carcinoma (NOS) at the first diagnosis. Statistical analysis showed no significant correlation of histological subtype of tumour and the pathological stage between first and the subsequent cancer ($p = 0.912$). The type of surgery performed for the first cancer was not found to have a significant influence on the patient's choice of surgery for the metachronous cancer ($p = 0.013$). The average overall survival for all patients with metachronous bilateral breast cancers was 14.7 (95% CI 13.5–15.9) years with an all-cause mortality rate of 15.5%.

Conclusion: Our study concludes that the incidence of metachronous breast cancer remains extremely low. Continued mammogram surveillance can help to detect early development of metachronous cancers. Our results also suggest that development of metachronous breast cancer was independent of the histological subtype and pathological stage of the initial cancer. Lastly, the average overall survival for all patients in this study remains optimistic at 14.7 years.

No conflict of interest.

108 Poster

Improvement of recurrent rates and survival in patients with primary breast cancer according to subtypes

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Background: Previously we reported that the survival rate of patients with the HER2 enriched breast cancer subtype who experienced recurrence after 2001 had improved with the availability of trastuzumab in Japan. Moreover, there is an increase in the variability of therapeutic agents for luminal or triple negative (TN) subtypes. The aim of this study is to demonstrate that there was a change in the recurrence rate and survival time of patients who received these new therapeutic agents after 2001, and to show the efficacy of these agents according to the different breast cancer subtypes.

Materials and Methods: Patients (n = 4539) were treated based on a multidisciplinary approach for primary breast cancer between 2001 and 2018. The patients were divided into two groups based on the year of initial diagnosis. The first group (n = 2260) received treatment from 2001 to 2010 and the second group (n = 2279) received from 2011 to 2018. Breast cancer subtypes were determined by immunohistochemistry; luminal A, luminal B, luminal-HER2, HER2 enriched and TN. The recurrence rate and the survival rate after recurrence were compared and analyzed using log rank test. Median follow up period was 10 years in the first group and 4.6 years in the second group.

Results: The recurrent rate of the second group (2011–2018) was significantly lower than the first group (2001–2010) in all of the breast cancer subtypes ($p < 0.01$). However, only the survival rate of the TN subtype after recurrence improved ($p = 0.05$). There were no remarkable changes in survival after recurrence in all of the other subtypes except TN. Moreover, an analysis of the menopausal status revealed that only the recurrence rate of postmenopausal patients with TN subtype did not decrease ($p = 0.17$). The findings also revealed that the premenopausal patients with TN subtype and any other menopausal patient with any of the other subtypes significantly decreased ($p < 0.01$). The survival rate of patients with premenopausal TN subtype after recurrence increased ($p = 0.04$).

Conclusion: The findings in this study indicate that patients with any of the subtypes improved with the target therapy except postmenopausal TN breast cancer patients. Moreover, an improvement in the survival rate after recurrence was only seen in premenopausal patients with TN subtype. Further follow up studies are needed to evaluate the true efficacy of novel molecular targeting agents for recurrent breast cancer.

No conflict of interest.

109 Poster

Characteristics of ipsilateral breast tumor recurrence after breast conserving surgery: Single center experience

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Background: Ipsilateral breast tumor recurrence (IBTR) is defined as a recurrent in situ or invasive carcinoma that occurred after breast conserving surgery (BCS) in either the skin or parenchyma of the ipsilateral breast without clinical-radiologic evidence of regional or distant disease. Incidence of IBTR after BCS is known as 5–10% during 5 years of follow-up. This study aims to analyze characteristics of IBTR after BCS in single center.

Material and Methods: We retrospectively reviewed 1130 cases who were treated with BCS between 2000. Jan and 2017. June. We analyzed the characteristics of IBTR of in situ cancer and invasive breast cancer.

Results: Follow-up period ranged from 1 to 225 months, a median of 68 months. Among the 1130 cases of BCS, 250 cases were performed for DCIS, 516 cases for stage I, 404 cases for stage II and 56 cases for stage III. The patients underwent adjuvant radiotherapy except 34 patients with IDC and 43 patients with DCIS. Among the 77 patients who didn't undergo radiotherapy, 2 patients had IBTR. Overall survival rate of total patients was 96.1%.

IBTR occurred in 33 patients, 8 in DCIS, 12 in stage I, 10 in stage II and 3 in stage III respectively. Median period to IBTR was 49 months in IDC and 62 months in DCIS.

IBTR was diagnosed by physical examination in 9 patients and by breast image during routine follow-up in 24 patients. IBTR was treated with salvage mastectomy in 30 patients and wide excision in 2 patients. 14 patients underwent systemic therapy after salvage mastectomy. Multiple times of recurrence was observed in 2 patients. Among the patients with IBTR, 4 cases of mortality were observed. Median survival of the patients with IBTR was 36 months.

Conclusions: Although IBTR rate was low in the patients treated with BCS, personalized treatment for recurred tumor is necessary according to the tumor status.

No conflict of interest.

110 Poster

Do patients with breast cancer receive the optimal personalized follow up?

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Background: The incidence of breast cancer has increased in the last 15 years. Due to improved survival, the 10-year prevalence has increased even more, resulting in more focus on the late effects of cancer treatment and survivorship. Good quality of follow up and aftercare means that late effects of treatment and disease can be prevented or signaled at an early stage and that patients receive tailored care. However, it is unclear how optimal and efficient follow up and aftercare should look like, from the patients perspective as well as the perspective of health care organizations.

Therefore, in the Netherlands, a national inventory was initiated to gain more insight in the organization of follow up and aftercare for patients with breast cancer. Best practices within health care organizations will be shared to benchmark follow up and aftercare.

Materials and Methods: Interviews will be performed in 20+ hospitals (of which 7 Santeon hospitals). The interviews focus on: tasks and responsibilities of health care professions in follow up and aftercare, coordination of care, guidelines, personalized care, shared decision making, referral to dedicated psychosocial care. The interviews are being held with the specialized breast cancer nurse or nurse practitioner together with a breast surgeon and/or a medical oncologist. Before the interviews take place the

transmural care pathway, and if available the follow up or aftercare pathway has been studied, as well as PREM and PROM outcomes. A patient advocate is actively involved to provide valuable input.

Results: Preliminary results after the first interviews indicate variation regarding the following topics: tasks and responsibilities of health care professionals in breast cancer follow up and aftercare, patient information and quality of shared decision making.

Conclusion: Preliminary results show that for several topics regarding follow up and aftercare for breast cancer patients variation is present. After presenting these variations and sharing best practices on national level, we hope to achieve (1) more uniformity as well as an improved follow up and aftercare for breast cancer patients in the Netherlands based on best practices, (2) the revision of the section "follow up and aftercare" in the national guideline for breast cancer, (3) the deployment of nursing disciplines, and (4) the application of PROM outcomes.

No conflict of interest.

111 Poster

Long-term prognosis is associated with residual disease after neoadjuvant systemic therapy but not with initial nodal status

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Background: This is a follow-up analysis of the Swedish prospective multicenter trial with the primary aim to determine invasive disease-free (IDFS), breast cancer-specific (BCSS) and overall survival (OS) rates and their association with axillary staging results before and after neoadjuvant systemic therapy (NAST).

Patients and Methods: In this follow-up analysis, 417 women treated with NAST for a clinically node-positive (cN+) or -negative (cN0) primary breast cancer between 2010 and 2015 were included. Patients had a sentinel lymph node biopsy (SLNB) before and/or after NAST and a completion axillary lymph node dissection (ALND) after NAST. Follow-up was until February 2019. The main outcome measures were IDFS, BCSS and OS. Uni- and multivariable Cox regression analyses were used to identify independent factors associated with survival.

Results: Median follow-up was 48 months (range 7-114). Nodal status after but not before NAST was significantly associated with crude survival: residual nodal disease (ypN+) resulted in a significantly shorter five-year OS when compared with complete nodal response (ypN0: OS 83.3 versus 91.0%, p=0.017). The agreement between breast (ypT) and nodal (ypN) status after NAST was high, and more so in cN0 (64/66, 97.0%) than in cN+ patients (49/60, 81.7%, p=0.005). On multivariable analysis, ypN0 (HR 0.41, 95% CI 0.22-0.74, p=0.003) and local radiotherapy (HR 0.23 (0.08-0.64, p=0.005) were associated with improved, while triple-negative tumors were associated with worse IDFS.

Conclusions: The present findings underline the prognostic significance of post-NAST but not pre-NAST nodal status and thus confirm the clinical value of surgical axillary staging after NAST.

No conflict of interest.

112 Poster

Development of an information standard for breast cancer in the Netherlands

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Background: In clinical practice the same data items needed for clinical decision making are often registered many times by different caregivers in different systems. This is time consuming, prone to mistakes. In the Netherlands an Information Standard for Oncology (ISO) for breast cancer has been developed. An ISO is a defined set of items, directly related to the course of the disease and care pathway[1]. Why is this important and what are the implications?.

Methods: The ISO breast cancer was developed along the revision of the evidence based guideline which was released in 2012. The size and complexity of this guideline, over 200 pages text, gave rise to develop a schematic representation of the recommendations in the form of decision trees. Each decision tree contains nodes (representing patient- or disease characteristics, e.g. tumor stage), branches (representing cut-off points, e.g. stage <II) and leaves (recommendations). An ISO is based on these nodes (data-items) and branches (values) and thus contains all information needed to support clinical decision-making about treatment.

Results: Implementation of ISOs in electronic health records (EHR) has a considerable impact on clinical practice. Standard terminology First, by using a standard terminology an ISO reduces the huge registration burden for caregivers. The ISO facilitates the reuse and electronical exchange of data. Secondly, the availability of standardized structured information in an EHR supports clinical decision making during multidisciplinary team meetings. This makes it possible to support application of clinical decision support tools like Oncoguide (www.oncoguide.ai), which become increasingly important with the growing complexity of guidelines. And finally, structured data can be reused for export to external registries for auditing or research.

Currently, the ISO breast cancer contains 114 data items, originating from pathology (49%) and radiology reports (27%), patient characteristics (12%) and items for multidisciplinary team discussion (12%). The items are coded by international systems such as SNOMED-CT. It is co-designed by members of the National Breast Cancer Network Netherlands (NABON) guideline working group. It is published online (in Dutch) on the ART-DECOR platform (http://tiny.cc/ISObreastcancer) and NABON website (www.nabon.nl). The implementation of the ISO breast cancer into the EHR has started in two Dutch hospitals.

Conclusion: ISOs are a prerequisite to maximize reusing patient information for improved continuity of care and research, with minimal registration burden for caregivers. The ISO breast cancer is developed and implementation in the first EHRs has started.

No conflict of interest.

113 Poster

PD-L1 and HSP-70 molecules are part of immunosupressive environment in the deep layer of the lymphocyte predominant breast cancer (LPBC)

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Background: Tumor infiltrating lymphocytes (TILs) are involved in host imunity against tumor cells. However, in later phases of the disease high TIL infiltration is related to disease progression. Tumor immunogenicity is strongly correlated with the higher tumor mutation burden. Triple negative (TN) and HER-2 enriched breast cancers have the highest immunogenic potential so the aim of our study was to investigate the TIL infiltration and expression of PD-L1, HSP-70 in such tumors.

Material and Methods: TIL infiltration was investigated in the 112 tissue samples of TN and HER-2 enriched breast cancers of women diagnosed and treated in the Clinical Hospital Centre Rijeka, Croatia, in the period between 2008 and 2016. The invasive front of the tumor (host-tumor interface), the surface layer, as well as the deep layer of the tumor were analysed. Immunohistochemistry staining of PDL-1 (SP142), HSP70 (ab2787), CD4 (SP35 Cell Marque) and CD8 (144B DakoCytomation) was performed. The results were analysed using Statistica 13 software.

Results: Overall, there is a statistically significant correlation of high (over 50%) TIL infiltration with longer 5-year survival ($p = 0.035$, Long rank test). In the surface layer of the tumor (invasive front) there is statistically significant correlation of the intermediate TIL infiltration with the higher survival ($p = 0.051$, Long rank test) whereas there is no significant difference in the deep layer of the tumor. There is significant association of TIL infiltration with CD8+ T lymphocyte expression in the surface and deep layers of the tumor (Mann Whitney U test, $p = 0.004$ and $p < 0.001$, respectively), CD4+ lymphocyte expression ($p < 0.001$, $p < 0.001$, respectively) and PDL-1 expression ($p < 0.001$, $p < 0.001$, respectively). Statistically significant correlation of TIL infiltration and HSP-70 protein was only detected in the deep tumor layer (Mann Whitney U test, $p < 0.001$). Furthermore, in the TIL infiltrated deep tumor layer there is statistically significant positive correlation of PD-L1 and HSP-70 expression (Mann Whitney U test, $p = 0.029$) as well as positive

correlation of the HSP-70 expression and the stage of the disease (Anova, p = 0.08).

Conclusion: Although TIL infiltration in the surface layer of the tumor is corellated with higher survival rate, there is no such correlation in the deep layer. We have shown that in both layers there is increased expression of CD4 and CD8 positive T lymphocytes. However, the increased expression of inhibitory molecules PD-L1, and in the deep layer HSP-70 protein is noted as well. It is possible that in this context HSP-70 is involved in activation of Tregs and thus inducing immunotolerance to oncoproteins and along with PD-L1 molecule stimulates the development of immunosuppressive environment in the deep tumor layer thus supporting tumor immune evasion.

No conflict of interest.

114 Poster

Prognostic role of breast pathologic complete response after neoadjuvant chemotherapy in node-positive breast cancer patients

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Background: It is uncertain whether all patients with initially node-positive breast cancer who undergo neoadjuvant chemotherapy (NAC) should be submitted to axillary dissection. We assessed the long-term outcome of node-positive breast cancer patients depending on the pathologic complete response in the breast.

Methods: We retrospectively reviewed cT1-3, cN0-3 breast cancer patients who were treated with NAC and followed by surgery in a tertiary institution from 2008 to December 2016. Women were divided into 2 groups based on pathologic response in the breast and stratified by initial clinical node stage. Clinical node-positive was defined as proven metastasis by axillary FNA or core needle biopsy. Kaplan-Meier curves and Cox proportional hazards models were used to estimate recurrence-free survival (RFS) and overall survival (OS).

Results: Out of 1169 women with advanced breast cancer were treated with NAC followed by surgery, 1017 patients were eligible and included in the study. A total of 287 patients (28.2%) achieved breast pathologic complete response (pCR), and patients who became ypN in each initial cN0, cN1/2, cN3 stage were 151(84.4%), 288(46.3%), and 90 (41.7%) After a median follow-up of 48 months, in patients who achieved breast pCR, 5-year RFS rates for initially cN0, cN1/2, cN3 patients were 90.5% (95% CI, 81.9%-100.0%), 92.7% (95% CI, 88.5%-97.1%), and 77.5% (95% CI, 66.9%-89.6%) respectively. For patients without breast pCR, 5-year RFS rates for initially cN0, cN1/2, cN3 patients were 79.7% (95% CI, 72.7%-87.4%), 63.9% (95% CI, 59.2%-69.0%), and 62.1% (95% CI, 54.6%-70.5%) respectively.

Conclusion: In clinically node-positive patients, breast pCR is associated with improved survival outcome and could be an indicator for de-escalation of axillary surgery.

No conflict of interest.

115 Poster

Prognosis according to the timing of recurrence in breast cancer

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Background: Breast cancer is a heterogeneous neoplasm. Clinically, there are four subtypes: luminalA, luminal B, basal (triple-negative breast cancer), and HER2, the classification of which is based onER, PR, HER2, and Ki67. Considering that recurrence patterns differ according to subtype, we soughtto determine whether prognosis among subtypes differs according to the timing of recurrence.

Methods: A total of 2,730 patients who underwent surgery for breast cancer were included. Earlyrecurrence was defined as recurrence within 5 years of diagnosis and late recurrence was defined asrecurrence after ≥5 years after diagnosis.

Results: The proportion of patients with hormone receptor-positive tumors was significantly higher inthe late recurrence group than in the early recurrence group (early vs. late: ER+, 47.8 vs. 78.7%; PR+: 72.1% vs 44.4%; P < 0.001). However, there was no difference in the rate of HER2 overexpression (HER2+: 38.1% vs. 39.0%, P = 0.904). Subgroup analysis by subtype showed thatearly recurrence was a significant prognostic factor for overall survival (OS) in all subtypes. However, late recurrence was a significant prognostic factor for OS with a hazard ratio of 4.30 (95% confidenceinterval 2.12–8.72) in the luminal B subtype only.

Conclusions: Breast cancer exhibits different recurrence patterns depending on subtype. In the luminalA, TNBC, and HER2 subtypes, early recurrence was associated with poor OS, while late recurrencewas not a prognostic factor for OS. However, the luminal B subtype exhibited a high rate of laterecurrence (>5 years after diagnosis), and late recurrence was a poor prognostic factor for OS.

No conflict of interest.

Local Regional Treatment – Surgery

116 Poster

Vacuum intraoperative specimen mammography: A novel technique

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Background: Intraoperative specimen mammography (ISM) is a diffuse technique that allows surgeons to check specimens immediately after lumpectomy. In spite of the specimen being compressed, the radiological image is sometimes distorted by tissue overlap. The tissue overlap during this intraoperative radiological procedure might alter the correct evaluation of tumour borders, resulting in extension of the lumpectomy. Since ISM might be less precise due to inadequate compression, we applied the vacuum effect on the specimen to increase the precision of the margin detection technique.

Material and Methods: The study was conducted at St. Anna Hospital Breast Unit (Turin, Italy). Both standard ISM (sISM) and vacuum ISM (vISM) were performed. We scanned 18 specimens obtained after lumpectomy from 1 April 2018 to 31 April 2018. The specimens were put in a vacuum, and vacuum ISM was obtained. A dedicated breast surgeon at our institution performed and interpreted both the surgery and radiological scans. A dedicated radiologist reviewed all the images. Standard ISM (two orthogonal projections) was obtained. Then, the specimen was put into a vacuum, and vacuum ISM (vISM) was obtained; the exam was completed with a second orthogonal projection after removing the vacuum, replacing the specimen and repositioning the vacuum. Additional tissue was taken if the surgeon indicated inadequate excision. Finally, the specimen was sent for definitive histopathological analysis, which is the gold standard for the assessment of surgical margins. Intraoperative histologic margin assessment was not performed. We compared sISM and vISM images and final histopathology reports.

Results: sISM specificity was 46% (CI 95% 24–70), and sensitivity was 66% (CI 95% 41–85), with PPV 20% (CI 95% 6–45) and NPV 87% (CI 95% 62–97). vISM specificity was 100% (CI 95% 69–99), and sensitivity was 66% (CI 95% 26–73), with PPV 100% (CI 95% 26–73) and NPV 93% (CI 69–99).

Conclusions: vISM images seem to be easier to interpret, because they are characterized by a vacuum created radiolucent rim that define the tumour margins better than standard ISM. In our study, the sensitivities for ISM and SSM were the same (66%), but the specificity of vISM was higher than that of sISM (100% versus 46%); these data reflect the ability of vISM to identify only the real involved margins that sometimes are wrongly identified by sISM. Consequently, the PPV and NPV of vISM were higher than the PPV and NPV of sISM (100% versus 20% and 93% versus 87%, respectively). Our data suggest that the vacuum technique is feasible, “cost-saving” and yields results similar to frozen section but without its limitations, such as prolonged operating time, high variability in sensitivity linked to the different abilities of pathologists, risk of compromising the histological lecture and unreliability for small lumps and DCSI.

No conflict of interest.

117 Poster

Angiosome theory findings using new protocol of CT-angiography improves outcomes in DIEP-flap reconstruction surgery in breast cancer patients

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Introduction: Autologous breast reconstruction with deep inferior epigastric artery perforator flap considered as a gold standard of final esthetic result. More and more centers are trying to perform DIEP flap reconstruction, but still there are some problems appears. What method to use? What perforants to choose? Is there a «Plan B»?. Nowadays, the best method of preoperative preparation is CT-angiography. Only this method, among others, improves of outcomes of DIEP-flap surgery: lower complication rate, lower donor side morbidity, reduce operation time, improves overall results.

Material and Methods: Breast cancer surgery group altogether with radiology department of our institute we've started a new protocol of planning DIEP flap operations. 41 patients were included in this study. We carry out CT (a) with extended fields. With that, we can track down where and how epigastric arteries move away from iliac artery. Also we can answer very important questions: What variant of DIEA according to Moon and Taylor? Caliber of perforants? With the extended fields we can also make sure that intramammary artery and vein are suitable for that kind of operation. Radiologist are tracing all the perforants and choose 2 or 3 of them on the assumption of caliber, Moon and Taylor theory, length in rectus abdominis, and Hartrampf zones of perfusion. After that we do our second trick, CT(A) with narrowing of the scan field and new settings of scanning (protocol of CT-angio scanning). Its some kind of target CT(A) on the area where previously radiologist and surgeons did choose the most valuable perforant. With that we can better understand motion of perforant, their twist, and give a 3D coordinates of entry into the subcutaneous adipose tissue. But the gold finding here is that we can see the angisome. An angiosome is an anatomic unit of tissue (consisting of skin, subcutaneous tissue, fascia, muscle, and bone) fed by a source artery and drained by specific veins. Presence of angiosome statictically improves the survivability of the flap. Technically it shows like connection between superficial and deep vessels, but there are more important things to know. Most of the complications of DIEP flap comes from venous system, maybe because of the anatomical structure of deep epigastric vein, its caliber, usually, smaller than superficial vein. With that knowledge we've started to do double vein anastomosis: superficial vein to internal mammary vein (proximal end), deep inferior vein to internal mammary vein (distal end).

Results: Complication rate of total flap loss, with a new protocol of preoperative planning, decreased from 21% to 4%. Partial flap loss from 18% to 6%.

Conclusion: CT(A) with 3d mapping must be done every time before DIEP flap surgery.

No conflict of interest.

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The value of removing more than one sentinel node in breast cancer

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Background: In breast cancer the standard of care for staging the axilla is the sentinel lymph node biopsy (SLNB). An extensive SLNB is associated with higher post-operative morbidity and does not comply with the goal of minimally invasive axillary surgery. The aim of our study was to analyse the additional value of removing more than one sentinel lymph node during the SLNB.

Methods: Data were retrospectively collected for 651 patients undergoing an SLNB for the treatment of invasive breast cancer between January 2014 and December 2017. An analysis was made of how often the first sentinel lymph node (SN1) was tumor negative while another lymph node contained a metastasis. False negative rates (FNR) were calculated for the removal of one or two sentinel lymph nodes, with the pathological outcome of all removed lymph nodes as a reference.

Results: 207 (31.8%) of 651 patients had metastatic nodal involvement. In 38 patients (5.8%), the metastases were found in another lymph node than SN1. In three patients (1.4%), the metastases were found in palpable extra lymph nodes with negative sentinel lymph nodes. In two patients (1%), internal mammary chain lymph nodes were positive with a negative axilla. If only one sentinel lymph node (SN1) would have been removed, the FNR would have been 18.4%. With the removal of two sentinel lymph nodes (SN1 and SN2), the FNR would have significantly reduced to 7.2%. Removing a palpable lymph node after removing two sentinel lymph nodes further reduced the FNR with 1.4%. There was no additional value of removing second echelon lymph nodes.

Conclusion: In case of multiple sentinel lymph nodes, the removal of two sentinel lymph nodes stages the axilla more accurately than the removal of one sentinel lymph node.

No conflict of interest.

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Predictors of surgical margin involvement in breast cancer surgery

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Background: The involvement of surgical margins remains one controversial aspect in the management of breast-conserving surgery (BCS). The objective was to evaluate our positive margin (PM) rate and to identify the risk factors related to involved margins.

Material and Methods: We conducted a retrospective study with breast cancer patients undergoing BCS between 2004 and 2015. Patients undergoing neoadjuvant treatment and ipsilateral recurrences of tumors prior to 2004 were excluded.

Data corresponding to clinical, pathological, therapeutic and follow-up variables were extracted. A univariable and multivariable analysis was performed using logistic regression, including variables of interest identified in the literature as predictors of involved margin. The margin was considered to be affected if invasive or in situ disease was found in contact with the stained margin.

Results: 1054 patients were included. The overall definitive positive margin rate was 10.7% (113 patients).

Our univariate analysis identified 10 factors significantly associated with the presence of PM: The median age of the group of involved margins was significantly lower than that of the free margin group (55.2 vs. 58.5; p = 0.008). In addition, patients with a personal history of benign breast disease had a higher risk of PM (22.1% vs. 9%; p = 0.000). Non palpable tumors were also associated with PM (12.8% vs. 8.2%; p = 0.019). The presence of microcalcifications in mammography and non-nodular ultrasound imaging were associated with a higher rate of PM compared to the absence of microcalcifications and nodular ultrasound imaging (16.5% vs. 8.3% and 19.9% vs. 7.9% respectively).

When no preoperative histological diagnosis was available, (2.7% of patients), the risk of PM was 16 times higher (62.1% vs. 9.3%; p = 0.000). When the specimen was not assessed intraoperatively (229 cases), a strong association was found with the presence of involved margins (OR = 6.198; p = 0.000). When intraoperative resected specimen mammography was performed, it had a significantly higher risk of PM than when it was not performed (12.3% vs. 8%, p = 0.039).

DCIS presented 2.3 times greater risk than infiltrating carcinomas (18.2% vs. 9.4%; p = 0.001). In addition, the larger total tumor size was identified as a risk factor (p = 0.002).

In the multivariable study, the variables younger age, personal history of benign breast disease, no intraoperative margin assessment, DCIS, total tumor size and the absence of preoperative diagnosis remained statistically significant.

Conclusion: Intraoperative margin assessment of the specimen by a pathologist is an important strategy to reduce the rate of PM. In addition, young age, personal history of benign breast disease, the absence of preoperative diagnosis, DCIS and larger tumor size were independent predictors of PM.

No conflict of interest.

121 Poster

Multicenter study to evaluate the efficacy and standardize radiofrequency ablation therapy for small breast carcinomas

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Background: Given the increasing number of early-stage breast cancers detected by screening mammography, we aim to establish RFA as a minimally invasive, cost-efficient, and cosmetically acceptable local treatment. In our Phase 1 study, localized tumors with a maximum diameter of 2 cm, preoperatively diagnosed by imaging and histopathology, were treated with RFA. A 90% complete ablation rate was confirmed histopathologically.

Subjects and Methods: From Nov. 2009 to Nov. 2012, 58 patients with early-stage breast cancer received non-surgical RFA therapy. Patients had localized solitary N0 tumors with a maximum diameter of 1 cm. They underwent RFA and SNB under general anesthesia and adjuvant therapy and breast radiation [A1]. Follow-up evaluation for residual tumor at 3, 6, and 12 months after RFA included clinical examination, diagnostic imagings and vacuum-assisted biopsy. Surgical resection was recommended for patients with suspected residual disease or incomplete ablation. The primary endpoint was the frequency of adverse events. Secondary endpoints included the complete ablation rate and ipsilateral breast relapse-free rate.

Results: The follow-up period ranged from 15 to 109 months (median, 85 months). The 57 patients completed the non-surgical RFA procedure and underwent diagnostic imaging and needle biopsy after 3 months. Seven patients with suspected incomplete ablation underwent surgical resection; incomplete ablation was confirmed in 5 (8.6%, 2 with invasive and 3 with non-invasive ductal carcinoma). During subsequent follow-up, 1 patient each was diagnosed with contralateral breast cancer and ipsilateral breast tumor relapse. No distant recurrence was documented. Cosmetic results were excellent in 94% of patients.

Conclusions: RFA is a promising alternative to surgery for treating localized, early-stage breast cancer.

No conflict of interest.

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Non-intervention vs. surgical interventions in (Low-Risk) Ductal Carcinoma In Situ: A DCIS multi-state model for decision analytics

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Background: An active surveillance strategy has been proposed for patients with low- and intermediate-grade ductal carcinoma in situ (DCIS). Prospective trials to measure clinical outcomes are on-going, and results will not be available for >10 years. In lieu of prospective data, there is value in creating a disease model for low-risk DCIS to understand the potential impact of an active surveillance strategy.

Methods: Multi-state models were developed using patient-level data from the SEER 18 Registries database, for 4 treatment strategies (no local treatment, breast conserving surgery [BCS], BCS + radiotherapy [RT], mastectomy), and for women with low-risk features. Eligible cases included women with grade 1, 2, and 3 histologically-confirmed DCIS as first primary, diagnosed between 1992–2016, aged ≥40 years at diagnosis, and known laterality, local treatment status, survival time, and cause of death. The multi-state model considers 5 mutually exclusive states: DCIS diagnosis, ipsilateral invasive breast cancer (iIBC) ≤5 years post-DCIS diagnosis, iIBC >5 years post-DCIS diagnosis, death preceded by iIBC, and death not preceded by iIBC. Transitions between each state were modelled with Cox proportional hazards models. The effects of treatment strategy, age, diagnosis year, grade, ER status, and race on each transition was assessed. Missing covariate values were imputed.

Results: Data on n = 86,803 DCIS patients, including n = 2,008 with no local treatment, were used for model development. Increased risk of iIBC ≤5 years after DCIS diagnosis was demonstrated for women aged 40–49 (Hazard ratio (HR) 1.45, 95% Confidence Interval (CI) 1.25–1.69 compared to women aged 50–69), grade 3 lesions (HR 1.35, 95% CI 1.16–1.56) compared to grade 2 lesions, lesion size >1 cm (HR 1.29, 95% CI 1.18–1.42), and Black race (HR 1.56, 95% CI 1.31–1.86 compared to White race). ER+ status was associated with lower iIBC risk (HR 0.57, 95% CI 0.48–0.66). Results from the multi-state models on the subset of 13,903 patients with low-risk features (age 50–69, White, grade 1 or 2, lesion size ≤1 cm, ER+) showed that the probability of surviving iIBC-free at 10 years was 89.8% for women with no local treatment, 89.0% for BCS only, 91.5% for BCS+RT, and 92.0% for mastectomy.

Conclusions: Baseline DCIS characteristics are predictive of iIBC events diagnosed within 5 years, and are therefore useful in selecting patients for treatment. Women with low-risk features represent 16% of the studied population, and demonstrate minimal differences by treatment strategy in the probability of surviving iIBC-free at 10 years. This suggests there is opportunity to de-escalate treatment for women aged 50–69 at diagnosis, with ER+, grade 1+2, ≤1 cm DCIS lesions. This work was supported by Cancer Research UK and by KWF Kankerbestrijding (ref. C38317/A24043).

No conflict of interest.

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Psycho-social assessment of post-surgery outcomes after breast reconstruction surgery

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Breast Cancer (BC) surgery leads to mutilation of breast shape with negative effects on body image and self-esteem. Reconstructive and oncoplastic breast surgery can satisfy patients and improve their quality of life (QoL). It is important to assess the patient experience post-surgery using patient-reported outcome measures (PROMs) based on patient's perception of surgical care, psychosocial well-being and physical functioning.

Our objective was to identify predictors of patient satisfaction in a selective sample of women (age 26–75 years) who underwent breast reconstruction surgery. 120 patients underwent unilateral breast reconstruction using implant. While 38 patients underwent reconstruction with opposite breast reduction symmetrization, 27 patients underwent therapeutic mammoplasty. All patients were asked to complete the standardized BREAST-Q questionnaire 1 year after surgery. The response rate for BREAST-Q questionnaire completion was 98% with 147 out of 150 study participants completed the questionnaire.

PROMs could be distributed into 4 distinct groups based on the reconstruction outcomes namely (a) very much satisfied (93%) (b) definitely and mostly satisfied (94%) (c) satisfied with the outcome (88%) (d) definitely agree on having reconstruction rather than the alternative of having no breast (91%). Significant improvement was observed in post-surgery satisfaction about breast appearance, psychosocial, sexual and physical well-being. Reconstruction surgery had an overall positive impact on quality of life. In patients that did not undergo breast reconstruction, psychological issues related to sexuality were observed.

We propose that BC Management protocols should also include additional counseling support to explore benefits of breast oncoplasty surgery.

No conflict of interest.

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Combined iodinated radiographic contrast and Tc99 radioisotope (i-ROLL) as technical improvement for the preoperative localization of non-palpable breast lesions: A comparative study with ROLL

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Background: Radioguided occult lesion localization (ROLL) is considered of reference for presurgical assessment of non-palpable breast lesions. A technical variation adding iodine contrast to the radioisotope tracer was previously described. The aim of our study was to compare our experience with ROLL and the iodine variant (i-ROLL) in a cohort of patients.

Material and Methods: A retrospective review of 100 patients who underwent surgery for non-palpable breast lesions (January 2013 to April 2019) was performed. For localization process ultrasound or stereotactic guide were used. For ROLL, 0.3 ml Tc-99 albumin macro-aggregate was injected into the lesion and for i-ROLL 0.2 ml iodine contrast (Omnipaque^{R}) was added to the radioisotope mixture. A localization scintigraphy in all patients and a post injection mammography specifically for i-ROLL were carried out as localization methods. All this information served radiologist and surgeons to optimize the resection strategy. Need of intraoperatory reexcision, rate of correct radiological and pathological extraction, technical complications and reinterventions were revised.

Results: ROLL was performed in 70 and i-ROLL in 30 patients. We could detect wrong post injection contrast positioning in 4 cases (13%) for i-ROLL while none in ROLL ($p = 0.007$). Correct radiological excision rate was higher with i-ROLL respect to ROLL (76% vs 57%, $p = 0.05$) and less cases presented radiological affected margins (23.3% vs 35.7%, respectively). Intraoperative immediate reexcision rate was lower with i-ROLL respect to ROLL (26.7% vs 47.1%, $p = 0.05$). Pathological examination of all specimens revealed no differences in tumor exeresis rate between i-ROLL and ROLL (100% vs 95.7%, $p = 0.50$). Reoperation rates were similar for i-ROLL and ROLL techniques (10% vs 18.6%, $p = 0.40$).

Conclusions: Preoperative localization of non-palpable breast lesions improved with i-ROLL respect to classical ROLL without adding morbidity and allowing a more accurate surgical planning that reduced the intraoperative immediate reexcisions of surgical margins.

No conflict of interest.

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Quality of life improvement and pain reduction in implant-based breast reconstruction by means of selective pectoralis major muscle denervation

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Background: Implant-based breast reconstruction (IBBR) is the preferred choice of breast reconstruction after mastectomy worldwide. Even in the era of pre-pectoral reconstructions, the retro-pectoral approach is still largely used for its reliability and surgical safety, especially in case of previous radiation therapy, in smokers, in diabetics or in case of skinny mastectomy flaps. However it often leads to unsatisfactory aesthetic and functional results. To avoid such limits and reduce post-mastectomy pain syndrome (PMPS) to the minimum, in 2016 we introduced a novel technical approach, namely, pectoralis major muscle selective denervation, either in tissue expander or DTI retro-pectoral dual plane procedures.

Material and Methods: From September 2016 until April 2019, 152 selective pectoralis major muscle denervations in 121 patients were performed at University of Florence, Italy, teaching hospital. A subjective evaluation was conducted using the postoperative reconstruction section of BREAST-Q (Memorial Sloan-Kettering Cancer Centre and The University of British Columbia 2006, all rights reserved) at 6, 12 and 24 months from definitive implant positioning (DTI or second stage after TE removal). An objective pain evaluation was conducted summing up pain medication doses per patient both during in-hospital stay and in the 6 months following surgery. The same evaluation was conducted in a control group of 121 women, from the same period, submitted to retro-pectoral breast reconstruction without selective pectoralis major muscle denervation. All patients were followed-up for pain meds use and completed at least once the BREAST-Q questionnaire.

Results: Among all the 121 patients analyzed, 49 had undergone a previous radiation therapy. Ninety-one cases were TE reconstruction in a complete sub-muscolar pocket, 44 cases were DTI retro-pectoral dual plane reconstructions, by means of a titanium-coated polypropylene mesh (Ti-LOOP Bra, pfm medical Cologne, Germany). Seventeen cases were re-do surgeries of previous sub-muscolar implant reconstructions in patients with Baker grade III-IV capsular contracture. Median follow-up was 21 months. The two scales of "satisfaction with outcome" and "physical well-being" reported a median of 99 and 97 scores in the denervated group, while the median scores of the not denervated group of patients were 83 and 91 respectively. In particular, the 11 items of the "physical well-being/chest" scale, showed a median score of 98 versus 82 in the two groups respectively. Pain control medications use was 60% lower in the denervated group.

Conclusions: Selective pectoralis major muscle denervation seems to be very promising as for aesthetics, functionality and PMPS in patients who need to undergo retro-pectoral breast reconstruction, especially when compared to the traditional technique.

No conflict of interest.

126 Poster

Good cosmetic outcome after vacuum assisted excision of benign breast lesions

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Background: Benign breast lesions can be excised through a vacuum assisted excision under local anesthetics. Vacuum assisted excision is assumed to have a better cosmetic outcome as compared to surgery, but no valid studies have been performed to prove this assumption.

Objective: To evaluate the patient reported cosmetic outcome after VAE and to identify the factors influencing cosmetic outcome.

Material and Methods: In this cross-sectional study, patients who underwent a vacuum assisted excision between July 2017-December 2018 were invited to complete the cosmetic subscale of the Dutch Breast Cancer Treatment Outcome Scale. For each patient, the mean cosmetic outcome was calculated and cosmetic outcome was classified as either good or suboptimal. All clinically relevant variables were independently tested for the influence on cosmetic outcome using Pearson or Spearman's correlation coefficients, one-way ANOVA or the Kruskal-Wallis H test and the unpaired Student's t-test or Mann Whitney U test or Chi-square as appropriate depending on the type and skewness of data. Variables that were possibly associated with cosmetic outcome (univariate $p < 0.2$) were included included in a weighted least squares multiple linear regression analysis (for mean cosmetic outcome) and a binary multivariable logistic regression analysis (for dichotomized cosmetic outcome).

Results: Of the 65 included patients, 47 responded (72.3%). Only minor complications were seen after vacuum assisted excision. Overall cosmetic outcome was good in 74% of patients (mean score 1.5). Cosmetic outcome was not different between tumors small and large (≥/<3 cm) (respectively mean 1.74 ± 0.66 vs. 1.53 ± 0.45, $p = 0.36$). The absence of follow-up complications was the only significant factor associated with a better mean cosmetic outcome score ($\beta = 0.359$, $SE = 0.150$, $p = 0.02$) and with the dichotomized cosmetic outcome ($OR = 12.5$, 95% CI 1.10–140.79, $p = 0.04$) in the multiple regression analyses.

Conclusions: Advantages of the vacuum assisted excision are: lower costs, less invasiveness and good cosmetic outcome. The cosmetic outcome after vacuum assisted excision seems to be better than after open surgical excision of benign breast lesions. The absence of complications was the only factor that contributed to a better cosmetic outcome. It was already known that VAE is safe and effective and this study confirms that the patient reported cosmetic outcome after vacuum assisted excision is good.

No conflict of interest.

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Breast Lesion Excision System as a treatment method for small invasive breast cancers

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Background: The Breast Lesion Excision System (BLES) has been developed as an automated, image-guided, single-pass biopsy system using radio-frequency (RF) energy. As opposed to most devices used for histological breast biopsy that sample only tissue fragments, the BLES aims to excise and retrieve an intact breast tissue specimen for diagnosis. The aim of this study was to assess whether it is feasible to remove small breast cancers completely by using the BLES as a therapeutic device under ultrasound (US) guidance.

Material and Methods: From February 2018 to July 2019, a total of 22 patients who had invasive carcinomas that were diagnosed with core needle biopsy (CNB) and a size ≤15 mm on US were enrolled in this prospective

study. Of these, 11 patients (50%), whose lesions also had a diameter ≤15 mm on MRI, underwent both BLES and subsequently surgery during one procedure. All lesions were removed using the BLES device with 20 mm probe size. Histopathology findings from BLES and the subsequent surgery were compared and total excision findings were assessed.

Results: The mean age of patients was 60 years. Median lesion diameter on MRI was 11.5 mm (range 8.0–13.9 mm). BLES revealed ten (91%) invasive carcinomas of no special type (NST) and one (9%) invasive lobular carcinoma. Identical histological results between needle biopsy, BLES, and surgery samples were seen in all lesions. Margin assessment was good in all cases and radiofrequency-related thermal damage to the specimen showed a mild (<0.5 mm) damage in 54.5% of the cases, moderate (0.6–1 mm) in 18.2%, and extensive (1.1–1.5 mm) in 9.1%. None of the resections was complete. Margins were usually compromised on both sides of the specimen, indicating that the targeting is accurate, but the excised volume too small. In one case a technical complication occurred: empty basket. It was possible to retrieve the BLES specimen during subsequent surgery.

Conclusion: BLES allows accurate diagnosis of small invasive breast carcinomas. However, the 20 mm BLES probe is a diagnostic tool and cannot be considered to be a therapeutic device in the case of small invasive breast carcinomas because no complete excision was observed.

No conflict of interest.

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SPIO-guided Sentinel Lymph Node Biopsy (SLNB) in early Breast Cancer – first monoinstitutional data and perspectives

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Background: Super-paramagnetic iron oxide particle (SPIO)-techniques are reasonable alternatives to Tc99m-localization of SLNB in early breast cancer with a similar detection rate but benefits regarding patient comfort and scheduling of OR time. In former reports SPIO guided SLNB with 5 ml Sienna+® solution concerns regarding staining and postoperative MRI were reported. The German AGO-guidelines recommend SPIO-techniques as ±. SLNB with 2 ml Magtrace® solution was implemented into clinical routine at our site.

Material and Method: A retrospective analysis was done from 5/19 to 10/19 in 50 patients with breast conserving surgery (BCS), mastectomy (M) or nipple-sparing mastectomy (NSM). 24% were treated pre-operatively with primary systemic chemotherapy. Data regarding patient demographics, treatment indication, feasibility, detection rate, staining and artefacts in postoperative imaging due to the use of Magtrace® were analyzed.

Magtrace® was injected peritumoral (BCS) or periareolar (M/NSM) in about 15 mm depth under the skin pre-operatively in the OR-setting followed by a 5 min massage from the injection site towards the axilla and an additional 20 min waiting time thereafter. A first measurement for confirmation of a sufficient transcutaneous signal was done immediately before incision.

Results: Age of the patients was between 33 and 83 years (mean: 58.3). SLN-detection rate was 94.0%; one detected SLN was infraclavicular -with no signal in the axilla and two SLNBs were counted as insufficient because of uncertainties to get a transcutaneous or transaxillary signal but a successful detection after a LN-sampling in level I. Operation time (only SLNB) ranges from 3 to 28 min (median: 8 min). Staining of the skin did not occur due to using the injection technique described above.

Conclusions: During our learning curve SPIO-guided SLNB was easy to handle and the results sufficiently independent in regards to primary systemic therapy and targeted axillary dissection.

Due to an increasing number of data from prospective clinical trials including the 1 ml-injection dosage SPIO-guided SLNB will become more prevalent in clinical routine especially as an alternative to ICG- and Technetium-based procedures and therefore implemented in the AXSANA-Registry of the EUBREAST. An ongoing trial (Karsten M, Blohmer JU; Charité; Berlin) will focus on efficacy data comparing SPIO to Tc99m-based procedures.

Detailed results especially in regard to post surgical imaging reports will be presented at the EBCC-meeting.

Conflict of interest:
Other Substantive Relationships:
Dr. Stefan Paepke: Advisory activities, support of advanced medical training events and travel expenses by: Grünenthal, Invitrocue Europe, HC 21, Medtronic, Neodynamics, Novusscientific, pfm medical, Sysmex, and Roche in financing advanced medical training events (Clinic).

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Association of axillary lymph node evaluation with survival in women aged 70 years or older with breast cancer

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Background: Survival in elderly patients undergoing sentinel lymph node biopsy (SLNB) and axillary lymph node dissection (ALND) have not been specifically analyzed. This study aimed to investigate the association of different types of axillary lymph nodes evaluations with survival in elderly breast cancer.

Material and Methods: A retrospective cohort study was conducted including primary invasive breast cancer patients aged 70 or older with accurate register information and no distant metastasis, diagnosed between 2004 and 2016, and documented by the Surveillance, Epidemiology, and End Results (SEER) database. Patients with 5 or less lymph nodes examined were categorized as receiving SLNB while 6 or more as undergoing ALND. Analyses were performed to compare the baseline characteristics and prognosis of patients who received surgical lymph nodes dissection and without. Breast cancer specific survival (BCSS) was compared by propensity score matching (PSM) analyses to account for selection bias from covariate imbalance.

Results: Of the 75,950 patients analyzed, patients without lymph nodes evaluation had a significantly worse prognosis, and there were no significant differences in BCSS between patients in SLNB and ALND groups [adjusted hazard ratio (HR) 0.991, 95% confidence interval (CI) 0.925–1.062; p = 0.800] after adjustment for known covariates. According to the subgroup analyses after PSM, ALND did not show the significant BCSS advantages compared with SLNB in different patient-, tumor- and treatment- level subgroups, except that the N stage was N2 or above. Furthermore, after PSM of patients with N1 stage, SLNB group was associated with a significant poor outcome in BCSS in hormone receptor negative (HR–) patients (HR 1.536; 95% CI 1.213–1.946; p < 0.001), whereas the hormone receptor positive (HR+) group was not (HR 1.150; 95% CI 0.986–1.340; p = 0.075).

Conclusions: Our study suggests that ALND doesn't yield superior prognosis compared with SLNB for elderly patients with N1 stage HR+ breast cancer. Although our findings are limited by the bias associated with retrospective study design, we believe that in the absence of randomized clinical trials, our findings should be considered when recommending the omission of ALND for elderly breast cancer.

No conflict of interest.

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Mesh-Pocket supported prepectoral implant-based breast reconstruction: Final results of a retrospective analysis

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Background: Implant based breast reconstruction gained a high and increasing level of importance during the past years, currently performed with placement of the implant in a pre-pectoral pocket. Although the safety and breast aesthetics of this approach are well recognized prepectoral techniques the development of the next generation of specifically for prepectoral implant placement created titanized implant pockets adds a whole new dimension to this approach especially in patients with smooth implants.

Material and Methods: A retrospective net-based documentation was done from the introduction of the Tiloop®Bra-Pocket in 10/2017 in 135 patients (42 patients with bilateral procedures). Data focused on patient demographics, indication, feasibility and short term cosmetic outcome were analysed.

Conclusion: From on 10/2017 until 09/2018 mesh-pocket supported breast reconstructions were analysed. Age of the patients was between 23 and 81 years. The mean of the BMI was 24.7 ± 4.6 kg/m^2. Cosmetic outcome, judged by breast surgeons, was rated in 85.9% as very satisfied (excellent), in 11.9% as somewhat satisfied (good) and in 0.7% as somewhat dissatisfied (moderate insufficient). Handling and feasibility of this new product and the prepectoral implant position was easy and sufficient in all cases.

Discussion: Use of TiLOOP®Bra-Pocket enables a new standard of prepectoral reconstructive techniques. It preserves the natural anatomy, thereby avoiding adverse effects associated with submuscular reconstruction, minimizing postoperative pain, risk of bleeding and hematoma, and the lack of animation deformity like "jumping breast phenomenon." Pocket-supported reconstructive techniques become more valuable in times of changing to implants with smooth surface due to the excellent stabilization of implant position. Since 7/2019 a prospective international multicenter trial is ongoing to demonstrate patient reported outcome parameters (PRO TiLOOP®-Pocket-Trial CLINICALTRIALS.GOV NCT03868514 and DRKS00016673).

Conflict of interest:
Other Substantive Relationships:
Dr. Stefan Paepke: Advisory activities, support of advanced medical training events and travel expenses by: Grünenthal, Invitrocue Europe, HC 21, Medtronic, Neodynamics, Novusscientific, pfm medical, sysmex, and Roche in financing advanced medical training events (Clinic).

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How I do it: Lymphatic mapping and sentinel lymph node biopsy with Indocianine Green in Breast Cancer patients, a prospective trial experience

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Background: Near infrared fluorescence imaging is an emerging modality that allows real time image guided procedures. It is inexpensive, and has become widely available on recent years. Due to current interest, we decided to validate the technique under the hypothesis that axillary lymphatic mapping with ICG can be equivalent to technetium 99 in breast cancer patients.

Methods: Between 2018–2019, patients with node negative breast cancer, including complete response after primary systemic treatment were consented and enrolled to receive ICG and technetium guided SLNB to be performed by a single breast surgeon. A total of forty patients were enrolled, 0.25 ml of 0.5% ICG solution was subdermally injected after anesthesia induction, in four periareolar injection sites (1 ml total) where technetium had been injected the previous day. Mapping and localization of ICG sentinel lymph nodes was achieved with our videolaparoscopic device (Stryker 1588). All ICG nodes where removed and subsequently tested for technetium radioactivity using a standard gamma probe. Axillary region was then inspected with this probe to asses any residual radioactive nodes, and findings compared with pre-operative gamma images. All SLNs were sent for intraoperative pathologic analysis. Patient and tumor data were collected and SLNs were compared to identify concordance among those that were fluorescent, radioactive or both, and these results were then analyzed.

Results: No adverse events were documented. One patient had a failed mapping with both techniques (2.5%). Patients median age was 61 years, median ICG migrating time from injection to axillae was 4,8 minutes. Primary systemic treatment had been administered in 25% of the patients. A total of 58 nodes positive to one or both tracers were obtained and analyzed. The median number of SLNs removed with ICG was 1.38 (range 1 to 4), and with Tc99, 1.44 (range 1–3). Dual tracer was found in 52 (90%) SLNs, ICG alone identified 2 SLNs, and technetium alone was found in 4 SLNs, 3 of them belonged to patients with primary systemic treatment, this was statistically significant (SLNs positive to only one tracer were all found within patients with more than one SLNs), the concordance for the first SLN was 100%. Eleven pathologically positive nodes were found in 10 patients, all positive to both tracers. Paired sample test and McNemar concluded no significant differences between both techniques in finding SLNs. Kappa analysis was also statistically significant finding high concordance between techniques with a 0.7 value.

Conclusions: ICG mapping and SLNB can be safely use in breast cancer patients, performing similarly to Tc99. The manageable size of this sample, and the fact that it was performed by a single surgeon, allows us to deeply analyze technical aspects, tips and videos in the learning process and validation of the technique.

No conflict of interest.

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Oncological safety of oncoplastic breast conserving surgery- compare with conventional surgery

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Background: In recent decades, the surgical management of breast cancer has steadily and considerably improved. Now oncoplastic technique applies to breast-conserving surgery (BCS) allows large-volume resection without compromising oncological safety. A satisfactory cosmetic result could be difficult to obtain due to high tumor to breast size ratio, unfavorable location, close to the nipple and contralateral ptosis. Oncoplastic techniques allows the performance of wide excision, conserving an excellent breast shape, may be helpful in many cases. This study was aimed to evaluate the oncological safety of oncoplastic surgery for primary breast cancer.

Methods: We compared 1320 consecutive patients who underwent surgery between August 2011 and December 2014 for breast cancer at Seoul National University Hospital by one experienced surgeon. Retrospectively medical chart review was done and patients divided into three groups. Among them 42.65% (n = 563) underwent oncoplastic surgery (OPS), 49.70% (n = 656) underwent conventional breast conserving surgery and 7.65% (n = 101) underwent total mastectomy. Among the OPS group, level I technique (round block, Batwing, Nipple reposition) was excluded. Finally 418 patents' data of OPS group was analysed. Each groups were compared using Fisher Exact or Chi squared tests.

Results: 1175 patients' data were analysed (OPS: n = 418, conventional BCS: n = 656, TM: n = 101). Tumor size (including DCIS, 3.12 cm vs 2.75 cm), resected area (37.1 cm^2 vs 28.6§^{2}) and volume (74.5.0 cm^3 vs 60.1 cm^3) in OPS group were significantly bigger than conventional BCS group ($p < 0.05$). Distance to nipple in OPS group was closer than conventional BCS group (2.42 cm vs 4.2 cm $P < 0.001$). Also margin safety (margin clear rate; 80.6% vs 76.1%) in OPS group was better than conventional BCS group ($P < 0.001$). But operation time was longer in OPS group (94.6 minutes vs 57.2 minutes) and re-excision rate was not significantly difference within two groups (6.4% vs 4.1%).

Conclusion: OPS technique allows large-volume resection in more diffuse cancer and closer lesion to nipple with maintenance of oncological safety. Outcomes of OPS are oncologically acceptable with low frequencies of positive margins, while cosmetic results are much improved by OPS. OPS is no longer an option, it is treatment of choice in many patients.

No conflict of interest.

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Oncoplastic breast-conserving surgery offers low local recurrence rates and excellent survival rates despite worse tumor characteristics

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Background: Oncoplastic techniques are used to an increasing extent in breast-conserving surgery (BCS) and offer improved patient satisfaction and quality of life. Tumors excised with oncoplastic BCS (OPBCS) are often larger than tumors included in the early randomized trials that showed the oncological equivalence of BCS followed by whole-breast irradiation, and mastectomy. Furthermore, tumors removed by OPBCS are more often node-positive and show a more aggressive tumor biology; on the other hand, margins may be larger when using oncoplastic resection techniques. This large retrospective cohort study aimed to assess local recurrence risk and overall survival after OPBCS in comparison to standard BCS techniques.

Material and Methods: Tumor and treatment data on women operated with BCS at all three Breast Centers in Stockholm in the years 2010–2016

were extracted from the Swedish National Breast Cancer Register. As OPBCS is rare in the smallest tumors, a random sample of approximately 25% of patients with tumors ≤10 mm was selected. For those and all other cases, including all patients receiving neoadjuvant treatment, medical charts were individually reviewed to extract information on surgical technique (classified according to Wallwiener 1–6), resection margins, postoperative radiotherapy, and local recurrence. Patients not given radiotherapy and those with positive margins (tumor on ink) were excluded. Date of death was received by cross-linking with the Central Bureau of Statistics Sweden. Five-year local recurrence-free, overall survival (OS) and breast cancer-specific survival (BCSS) were calculated using Kaplan-Meier survival analysis, and tumor and treatment characteristics compared by Chi-square and Kruskal Wallis tests, respectively.

Results: 4178 patients were analysed, of whom 3720 were operated with standard BCS, 243 with a simpler OPBCS technique (Wallwiener 3–4), and 214 with complex OPBCS (Wallwiener 5–6). Median follow up-time was 64 months (24–110). The percentage of T2-T3 and of node-positive tumors was significantly higher in OPBCS than in standard BCS (both $p < 0.001$). The use of OPBCS increased over time ($p < 0.001$). The median smallest resection margin was 9, 7, and 10 mm, respectively ($p = 0.002$). There was a total of 61 local recurrences, 57 (1.5%), 1 (0.4%) and 3 (1.4%), respectively, in the three groups ($p = 0.368$). Five-year local recurrence-free survival was 98.5, 99.6 and 98.5% for the three surgery groups, respectively ($p = 0.484$). 297 patients had died, resulting in five-year OS rates of 94.7, 93.1 and 92.6% ($p = 0.310$). Of all deaths, 102 were due to breast cancer, and five-year BCSS was 97.9%, 98.3% and 95.0%, respectively ($p = 0.052$).

Conclusions: Breast-conserving surgery with oncoplastic techniques is a safe surgical option even in larger node-positive tumors with extremely low recurrence rates and excellent survival rates.

No conflict of interest.

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Omission of axillary dissection after neoadjuvant chemotherapy for node-positive primary breast cancer

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Background: Anthracycline and taxane-based neoadjuvant chemotherapy (NAC) has been shown to downstage axillary lymph nodes in approximately 40% of node-positive patients. However, the feasibility of sentinel lymph node biopsy (SLNB) following NAC for initially node-positive patients is unclear because of high false-negative rates reported in previous trials. The aim of this study was to evaluate whether axillary lymph node dissection (ALND) could be safely omitted for patients with clinically node-positive breast cancer treated with NAC.

Material and Methods: We identified 128 patients with clinically node-positive breast cancer who received NAC from March 2006 to March 2017. A correlation between axillary pathologic response and clinicopathological factors was analyzed. Preoperative clinical assessment of lymph-node status was performed by palpation and diagnostic imaging such as ultrasound and MRI. Lymphatic mapping was performed using a combined method of blue dye and radioisotope.

Results: The median age was 56.5 (range: 29–79) years and the mean tumor size was 3.6 ± 2.37 cm. Of 128 patients, 72 (56.2%) patients had luminal, 32 (31.3%) had HER2-positive, and 24 (18.8%) had triple negative disease. Sequential anthracycline and taxane were administered for 115 (89.8%) patients, and 25 (78.1%) patients with HER2-positive-disease received concomitant trastuzumab preoperatively. Overall, 53 (41.4%) patients achieved axillary pathologic complete response (ypN0). The ypN0 status was significantly correlated with clinical complete response (cCR) in breast (67.9%, $p = 0.004$), ER negative disease (59.5%, $p = 0.004$) and HER2 positive disease (56.3%, $p = 0.049$). Multivariate analysis demonstrated that cCR in breast ($p = 0.015$) and ER negativity ($p = 0.006$) were significant predictive factors for ypN0. In 14 ER-negative patients achieving cCR in breast, ypN0 was found in 12 (85.7%) patients. Among 85 patients who converted to clinically node-negative, ALND was omitted in 16 patients (18.8%) after SLNB. Of these 16 patients, irradiation to whole-breast and axilla was performed in 14 (87.5%) and 5 (31.3%) patients, respectively. After a median follow-up of 53.2 months, no axillary recurrence was observed in entire patients and 5-year disease-free survival was not significantly different between patients with or without ALND (85.5% vs. 87.5%, $p = 0.965$).

Conclusions: As ER-negativity and cCR in breast were correlated with high eradication rate of initially positive lymph nodes, these patients might be good candidates of omission of ALND after NAC.

No conflict of interest.

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Variation in the rates of surgical treatment of older women with operable breast cancer between UK breast units: Analysis of the Bridging the Age Gap Study

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Background: Non-surgical management of older women with ER positive, operable breast cancer is common in the UK with up to 40% of over 70 s receiving primary endocrine therapy. Whilst this may be appropriate for frailer patients, for some it may result in treatment failure, contributing to the inferior outcomes seen in this age group. Wide variation in the rates of non-operative management of breast cancer in older women exists across the UK. Case mix may explain some of this variation in practice.

Materials and Methods: Women >70 with operable BC were prospectively recruited from 56 UK breast units between 2013 and 2018. Data were analysed to identify whether variation in treatment at hospital level persisted following adjustment for case mix. Expected case-mix adjusted surgery rates were derived by logistic regression using the variables age, Charlson Comorbidity Score, tumour size, stage, grade and nodal status. Funnel plots were used to plot unadjusted and adjusted surgery rates to identify outlying practice.

Results: A total of 3375 women with primary operable breast cancer were recruited to the study between February 2013 and June 2018. Patients with ER negative disease were excluded from analysis. The median age of the surgery group was 76 years (70–94) and the PET group was 84 years (70–102). Data on 2854 women over 70 with ER+ operable breast cancer were analysed, of these 2354 were treated with surgery and 500 were treated with PET.

The unadjusted rates of surgery varied substantially between hospitals, with 6 of 56 (10.7%) falling outside of the outer 99% limits and 23 of 56 (41.1%) falling outside of the inner 95% limits on the funnel plots, meaning that they statistically differ from the expected norms.

Taking account of patient level characteristics and adjusting for case mix reduced, but did not eliminate, the variation in surgery rates between hospitals, with 5 of 56 (8.9%) still falling outside of the outer 99% limits and 10 of 56 (17.9%) falling outside of the inner 95% limits on the funnel plot.

Conclusion: This study demonstrates variation in selection criteria for older women for operative treatment for early breast cancer, meaning that some older women may be under or over treated and may partly explain the inferior disease outcomes associated with this age group. It emphasises the urgent need for evidence based guidelines for treatment selection criteria in older women with breast cancer.

No conflict of interest.

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Quality of life outcomes following breast surgery in older women with operable breast cancer: Analysis of the Bridging the Age Gap study

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Background: In women over 70 breast cancer (BC) surgery is often non-standard or omitted due to concerns about morbidity. Older women have been shown to have different priorities in terms of treatment outcomes and some prioritise quality over quantity of life. The Age Gap prospective multicentre cohort study aimed to determine factors influencing selection for and outcomes from surgery for older BC patients.

Materials and Methods: Women >70 with operable BC were recruited from 56 UK breast units between 2013 and 2018. Data on type of surgery to the breast (breast conservation surgery [BCS], mastectomy) and axilla (axillary node clearance [ANC], sentinel node biopsy [SLNB] or no axillary surgery [NAS]) were recorded and Quality of life (QoL) data were compared

at baseline and then at intervals up to 2 years post-treatment using validated tools: EORTC QLQ C30 (generic), BR23 (BC related) and ELD14 (elderly specific) and the EQ5D. QoL was only assessed in patients consenting to full participation. Scores were converted to a 0–100 scale as described in the EORTC Scoring Manual and a comparison of means was performed using the independent t-test in the statistical package IBM SPSS Version 25.

Results: Of 3375 recruited women, surgery was performed in 2816. The median age was 76 (range 70–95). Breast surgery was by mastectomy in 1138, BCS in 1798. Axillary surgery comprised 575 ANC, 2203 SLNB and 76 NAS.

There were significant differences in QoL scores between mastectomy and BCS patients for the Global Health Status domains of the QLQ-C30 questionnaire at 6 weeks (68.9 vs 71.44; 95% CI for difference in scores 0.74–4.32; p = 0.006; higher score denotes better QoL), the functional domains of the QLQ-ELD15 questionnaire at 2 years (65.58 vs 71.13; 95% CI for difference in scores 2.34–8.75; p = 0.001; higher score denotes better function) and Body Image Scores (QLQ-BR23 BRBI) post-surgery (82.54 vs 92.15; 95% CI for difference in scores 7.90–11.32; p < 0.001; higher score denotes better body image).

There were also significant differences in QoL scores between ANC and SLNB patients for Global Health Status domains of the QLQ-C30 questionnaire (66.43 vs 70.80; 95% CI for difference in scores 1.38–7.36; p = 0.004), functional domains of the QLQ-ELD15 questionnaire (62.50 vs 71.10; 95% CI for difference in scores 4.72–12.48; p < 0.001) and Arm Symptoms domain of the QLQ-BR23 (mean score 22.22 vs 12.71; 95% CI for difference in scores 6.52–12.50; p < 0.001; higher score denotes worse symptoms).

There were no deaths reported within 30 days of surgery in this large prospective series.

Conclusions: Some of the differences in mean QoL scores are small when taken in context of the 0–100 scale so may be of little clinical or practical importance, however we have shown that surgery has a negative impact on QoL which must be considered when counselling patients about choices.

No conflict of interest.

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Patient Reported Outcome and cosmetic evaluation following implant-based breast-reconstruction with a titanized polypropylene mesh: A prospective clinical study in 269 patients

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Background: Immediate or delayed implant-based breast reconstruction is an established surgical method after mastectomies due to breast cancer or to prophylactic reasons. In a prospective, single-arm, multi-center study the patient reported outcome (PRO) after breast reconstruction with a synthetic surgical mesh was investigated. The focus of this study was the analysis of patient reported outcome (PRO) 12 months after breast reconstruction.

Material and Methods: In 269 patients primary or secondary implant-based breast reconstruction with support of a titanium-coated polypropylene mesh (TiLOOP® Bra) was performed in the course of the PRO-BRA study. Patient reported outcome 12 months after breast reconstruction was evaluated using the established Breast-Q questionnaire. 210 cleaned patient data sets were eligible for analysis. Cosmetic outcome was evaluated by two independent experts based on core questions of the Breast-Q questionnaire.

Results: The Breast-Q and 12 months FU were completed by 210 women. Patients without AE had a significantly higher Breast-Q score for "sexual well-being"; "psychosocial well-being" was negatively influenced by prior therapies, and older patients (>40 years) had significantly lower scores compared to pre OP for "satisfaction with breasts" while the opposite was true for patients ≤40 years. The BMI only influenced PRO preoperatively, no influence could be detected. Unilateral surgery resulted in reduced "satisfaction with breast" compared to pre OP; a higher UICC stadium (II-IV) resulted in worse "satisfaction with breast" compared to patients with lower UICC stadium. Radiotherapy before or after surgery negatively influenced "satisfaction with breast"; radiotherapy only after surgery also had a negative impact on "sexual well-being" and "physical well-being chest." The cosmetic evaluation showed a significant difference in the evaluation by the patients and experts with the patients' assessment being worse compared to experts' assessment for patients who did not receive radiotherapy and those who received radiotherapy only after surgery.

Conclusion: Our study showed that two years after implant-based breast reconstruction with support of TiLOOP® Bra PRO is influenced by different factors. This information can be used to improve the decision-making process for women who chose implant-based breast reconstruction.

Conflict of interest:
Other Substantive Relationships:
Prof. Dr. Marc Thill:
RTI Surgical und pfm Medical: Consulting and lecture honoraria and Travel reimbursement.

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Evaluation of the breast lesion excision system, a percutaneous, vacuum assisted, intact-specimen, breast biopsy device

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Background: Percutaneous, vacuum-assisted, large-gauge core needle biopsy (VACNB) provides an alternative to open surgical biopsy as an initial diagnostic tool for breast lesions, yet rates of underestimating malignant diagnoses remain sufficiently high to warrant surgical biopsy in some cases. The current study was performed to determine if the Breast Lesion Excision System (BLES) provides a feasible alternative to VACNB.

Methods: A retrospective review was conducted of 212 consecutive mammographic lesions with microcalcifications classified as Breast Imaging Reporting and Data System (BIRADS) IV or V that had stereotactic percutaneous biopsy using BLES. Initial diagnoses obtained from the histopathologic examination of tissues retrieved at biopsy were compared with the histopathologic examination of tissues received from surgical excision or lumpectomy. Underestimation rates for atypical ductal hyperplasia (ADH) and ductal carcinoma in situ (DCIS) were recorded if open surgical biopsy revealed DCIS or invasive cancer, and invasive cancer, respectively.

Results: Of the 742 breast lesions, 40 displayed ADH upon biopsy with the BLES device. Two patients did not receive open surgical biopsy. Of the 38 patients who had open surgical excision, 3 (7.9%) had DCIS or invasive cancer. There were 74 diagnoses of DCIS upon biopsy with the BLES device. Four patients did not receive open surgical biopsy. Of the 70 patients who had open surgical excision, 6 (8.5%) had invasive cancer.

Conclusions: Breast biopsy can be performed accurately using the BLES device. Compared with VACNB, it does not alter the need for surgical excision in women diagnosed with ADH or DCIS at core biopsy.

No conflict of interest.

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Hospital variation in the use of Sentinel Lymph Node Biopsy for patients with a biopsy diagnosis of ductal carcinoma in situ

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Background: For patients with the biopsy diagnosis Ductal Carcinoma In Situ (DCIS) a Sentinel Lymph Node Biopsy (SLNB) can be considered, since 20% of these patients have occult invasive cancer. The indications for SLNB vary between guidelines; some guidelines advise against SLNB if it is possible to keep the lymph vessels draining the tumour bed intact and other guidelines consider the risk factors for underestimation of invasive breast cancer and aim at maximizing the use of SLNB in patients who turn out to have invasive breast cancer. In the Dutch guideline several risk factors are identified, however without any indication on how to balance these factors. We therefore aimed to determine the variation in the SLNB rate among Dutch hospitals and to assess the accuracy of the decision whether or not to perform SLNB.

Material and Methods: Data concerned DCIS, diagnosed at biopsy. Data were nationwide and retrieved from the Dutch Pathology Registry and the Netherlands Cancer Registry. For each hospital the rate was calculated,

hospitals were grouped into eight regions and four volume groups. The decision whether or not to perform the SLNB was considered accurate if no SLNB was performed for pure DICS, and SLNB performed for invasive breast cancer, as diagnosed at excision.

Results: The study comprised of 2892 DCIS, from 89 hospitals diagnosed in 2011/2012. First excision was breast conserving surgery (BCS) in 1821 cases (63%) and mastectomy in 1071 cases (37%). The SLNB was performed in 66%. The SLNB rate ranged from 25% to 100% between hospitals; for mastectomy 88% (range 40–100%), for BCS 53% (range 0–100%). In the BCS group, the rate was above average in 18 hospitals (20%) and below average in 15 hospitals (17%). In the mastectomy subgroup, 3 hospitals (3.4%) had a rate below the average. The SLNB rate was associated with the region range where the hospital was located (55%–72%) but not with hospital volume (range 64% to 68%). The accuracy was 45% (range 0–80%); 33% for mastectomy, 52% for BCS.

Conclusions: This study shows a large variation both in the decision whether or not to perform SLNB after biopsy diagnosis of DCIS and in the accuracy of that decision. The variation between hospitals was largest in the DCIS group that underwent BCS. This large variation is undesirable and including an earlier developed prediction model (Meurs et al. Br J Cancer 2018;119:1155–1162) in guideline recommendations would improve clinical decision making in whether or not to use the SLNB.

No conflict of interest.

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Radioactive seed versus wire-guided localization for ductal carcinoma in situ of the breast: Comparable resection margins

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Background: There are currently two widely used methods for pre-operative localization of ductal carcinoma in situ (DCIS) of the breast: wire-guided localization (WGL) and radioactive seeds localization (RSL). WGL has historically been used as the gold standard for pre-operative localization of non-palpable lesions, but in recent years, RSL is regarded as an attractive alternative. Several studies compared these localization techniques in small cohorts. The aim of this study was to compare the surgical resection margin status between RSL and WGL in a large national cohort.

Patients and Methods: We included all patients in the Netherlands who underwent breast-conserving surgery for DCIS by either RSL (n = 1852) or WGL (n = 2190) between 2009 and 2019. Several clinicopathological characteristics were compared between these two groups, including the resection margin status and the number of re-excisions.

Results: RSL was associated with high grade DCIS (P < 0.001), presence of comedonecrosis (P < 0.001) and absence of microcalcification (P < 0.001) compared to WGL. There was no difference in resection margin status between both groups (P = 0.35) and the number of re-excisions (P = 0.435). With regard to RSL, single seed implantation was associated with older age (P = 0.013), smaller DCIS diameter (P < 0.001) and larger resection margin (P = 0.004).

Conclusion: In this large national cohort study, we demonstrated that a more aggressive DCIS phenotype is more often seen in patients localized with RSL compared to patients localized with WGL. However, there was no difference in the resection margin status between both procedures or in the number of re-excisions. The preferred localization method should therefore be based on other parameters than surgical outcome measures.

No conflict of interest.

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Predicting lymph node metastases for biopsy diagnosis ductal carcinoma in situ: The DCIS-met model

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Background: Axillary staging is not necessary for patients with a ductal carcinoma in situ (DCIS), but it is offered to patients with a biopsy diagnosis DCIS because 20% of these patients have occult invasive breast cancer at excision and therefore are at risk for metastasis. The aim of this study was to develop a prediction model for risk of lymph node metastasis in biopsy DCIS.

Material and Methods: The cohort was population based with patients that were diagnosed with DCIS based on a biopsy between 2011 and June 2012. Data were retrieved from the Dutch Pathology Registry and the Netherlands Cancer Registry. Multivariable logistic analysis resulted in a prediction model, which was internally validated using bootstrap replications. The area under the curve (AUC) of the receiver operating characteristic curve of the model was calculated and a calibration plot was drawn. The clinical benefit of using the model was analyzed with decision curve analysis.

Results: Of 2892 biopsy DCIS patients, 66% underwent Sentinel Lymph Node Biopsy (SLNB) before or at the first surgery, and eventually 71% underwent axillary staging by SLNB or axillary lymph node dissection. Metastases were found in 127 patients (4.4%). In multivariable analysis, risk factors were age, not detected by screening, a suspected invasive component at biopsy, a palpable tumor, a BI-RADS score 5, intermediate grade DCIS and high grade DCIS (see Table).

		OR	95% CI	p-value
Age	Linear	0.97	0.95 to 0.99	<0.001
Detection mode				
	Screen-detected	1		
	Otherwise	1.55	1.01 to 2.38	0.047
Palpable				
	No	1		
	Yes	2.06	1.34 to 3.18	0.001
BI-RADS score				<0.001
	3	0.72	0.36 to 1.43	0.346
	4	1		
	5	2.41	1.53 to 3.78	<0.001
DCIS histological grade at biopsy				0.028
	Low	1		
	Intermediate	3.01	1.27 to 7.15	0.012
	High	3.20	1.36 to 7.54	0.008
Suspected invasion biopsy				
	No	1		
	Yes	1.86	1.01 to 3.41	0.045
Intercept	0.0535			

The AUC was 0.75 in internal validation. The calibration plot had a slope of 1.03 and an intercept of 0.09. The predicted risk was up to 40%, with a median of 2.8%. For 24% of the patients the risk was above 5%. In the decision curve analysis the net benefit of the model showed that the model is clinically useful between a predicted risk of 0% and 25%. In this dataset 99% of patients have a risk of at most 25%.

Conclusions: With the DCIS-met prediction model clinicians can easily calculate individual risks of lymph node metastasis based on information routinely available in clinical practice of patients preoperatively diagnosed with DCIS. This risk can be used in shared decision making in whether to perform a Sentinel Lymph Node Biopsy (SLNB) or not.

No conflict of interest.

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Optimization of wire-guided technique with bracketing reduces resection volumes in breast-conserving surgery for early breast cancer

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Background: Wire-guided localization (WGL) of early breast cancer can be facilitated using multiple wires, which is called bracketing wire-guided localization (BWL). The primary aim of this study is to compare BWL and conventional WGL regarding minimization of resection volumes without compromising margin status. Secondly, BWL is evaluated as an alternative method for intra-operative ultrasound (US) guidance in poorly definable breast tumors on ultrasound.

Methods: In this retrospective cohort study, patients with preoperatively diagnosed breast cancer undergoing wide local excision between January 2016 and December 2018 were analyzed. Patients with multifocal disease or

neoadjuvant treatment were excluded from this study. Optimal resection with minimal healthy breast tissue removal was assessed using the calculated resection ratio (CRR).

Results: BWL was performed in 17 (9%) patients, WGL in 44 (22%) and US in 139 (70%). The rate of negative margins was comparable in all three groups. CRR was significantly smaller for BWL (0.6) than WGL (1.3) in tumors larger than 1.5 cm. Additionally, BWL (0.8) led to smaller CRRs than US (1.7). This could be explained by the high number of small tumors (≤1.5 cm) in the US group for which greater CRRs are obtained than for large tumors (>1.5 cm) (1.9 *versus* 1.4, $p = 0.005$).

Conclusion: For breast tumors larger than 1.5 cm, BWL achieves more optimal resection volumes without compromising margin status compared to WGL. Moreover, BWL seems a suitable alternative to US in patients with poorly ultrasound-visible breast tumors and patients with a small tumor in a (large) breast.

No conflict of interest.

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A Randomised Controlled Trial (RCT) of 3-dimensional simulation of the aesthetic outcome of Breast Conserving Treatment (BCT)

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Introduction: Almost two thirds of women with surgically-managed breast cancer in the UK undergo BCT. Standard practice is to describe likely aesthetic changes. Photographs are shown prior to reconstructive surgery or more complex oncoplastic procedures. Patients have expressed the desire for more information about likely appearance after surgery. Simulation of a patients' individual aesthetic outcome has been used in aesthetic breast and facial surgery. We hypothesise that viewing a personalised 3D simulation improves patients' preparedness for surgery.

Methods: A randomised controlled trial of 117 women planning unilateral BCT was undertaken at a single centre after Research Ethics Committee approval. The randomisation was three-way, into standard care (verbal description), viewing standard photographs (matched for body mass index, age, and tumour location), or 3D-simulation and was performed pre-operatively. Randomisation was stratified by BMI, intention to undergo axillary lymph node dissection, and operation type (standard wide local excision or mammoplasty). The primary end point was comparison of a 10 cm Visualise Analogue Scale (VAS) between groups for "How confident are you that you know how your breasts are likely to look after treatment?" administered pre-operatively. Sample size calculation was based on a 1.5 cm difference between groups (SD of 2.0, Bonferroni correction, 80% power).

Results: The median VAS in the control was group 5.4 cm; 2D photography, 8.0 cm; and 3D simulation, 8.9 cm. There was a significant difference between groups (Kruskal-Wallis test $p < 0.01$) with post-hoc pairwise comparisons demonstrating a statistically significant difference between both standard care vs 3D-simulation and viewing of photographs vs 3D-simulation ($p < 0.01$, $p = 0.012$ respectively), but not between standard care and viewing photographs ($p = 0.61$).

Conclusions: Viewing of an individualised 3D-simulation of an average aesthetic outcome for BCT improves confidence going into surgery compared to standard care and viewing photographs of other women. Longer-term follow-up is in progress and will provide further information as to whether simulated appearance meets reality between groups and the influence this may have on patient satisfaction.

No conflict of interest.

147 Poster

Predicting postoperative complications in older patients with breast cancer

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Background: In recent years, the number of older patients with breast cancer who are surgically treated has strongly declined in the Netherlands, possibly due to age, comorbidities, frailty and patients' preferences. In order to inform patients on risks and benefits of surgery and improve individualized treatment, the primary aim of this study was to develop a prediction model for postoperative complications. Secondly, we aimed to investigate if complications affect functional status and quality of life in the first year after surgery.

Methods: We selected patients from the prospective "Climb Every Mountain study," and included patients aged 70 years and older who were surgically treated for breast cancer stage 0-III, and diagnosed between 2013 and 2018. A geriatric assessment was conducted at baseline. Questionnaires including the QLQ-C30 and the GARS were sent at three, six and twelve months after surgery. The primary outcome was any postoperative complication within 30 days after surgery. Secondary outcomes included functional status and quality of life in the first year after surgery. A prediction model was built using multivariate logistic regression. Bootstrapping was performed in order to avoid overfitting of the model. The receiver operating characteristic curve was used to test internal validity. Linear mixed models were used to assess quality of life and functional status over time, according to postoperative complications.

Results: Overall, 535 older patients with breast cancer were included. Forty-three percent developed a postoperative complication within 30 days after surgery. An accurate prediction model for postoperative complications was made with an Area Under the Curve of 0.80 (95% CI 0.76–0.84). For the secondary outcomes, 346 women received follow-up questionnaires with a high response rate of 83–89%. There was no association between postoperative complications and functional status or quality of life within the first year after surgery, after adjusting for confounders ($p = 0.467$ and $p = 0.591$).

Conclusion: An accurate prediction model was designed to identify older patients with breast cancer at risk for postoperative complications. This model can be used to inform patients about the postoperative period, which is usually associated with more hospital visits and additional treatment measures in patients with complications. In the near future, external validation of the model will be conducted in a large UK multicenter prospective cohort. This study also showed that postoperative complications did not affect functional status and quality of life within one year after surgery. Thus, according to these data, omission of surgery based on complication risk may not be justified.

No conflict of interest.

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Breast cancer in elderly patients: are we choosing wisely? A critical review of the breast unit of Trieste

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Background: Increasing age is the most important risk factor in the development of breast cancer (BC) after female gender and about 30% of female BC are diagnosed in patients aged older than 70. Optimal treatment remains controversial because elderly patients are often excluded from clinical trials and the large variety in patient's characteristics makes treatment decision making process generally difficult. The aim of this study was to analyze treatment choices and outcomes in our series of elderly patients affected by BC.

Materials and Methods: A retrospective observational study was conducted. We included BC patients aged over 75 years and treated at Eusoma certified SSD Breast Unit of Trieste between 2006 and 2018. Data was collected from clinical records and extracted from data base Data Breast. Surgical treatment, survival outcomes and clinico-pathological characteristics were compared among patients aged 75–79 years, 80–84 years and aged over 80 years.

Results: A total of 993 BC patients aged over 75 years were included. Of them, 636 (67%) were surgically treated and 323 (33%) were not. Stage of BC at presentation was higher in the oldest group, consequently the mean size of the primary cancer and rates of nodal disease were higher: tumors in patients aged over 85 years were significantly larger than those in patients aged 75–79 and 80–84 ($P < 0.001$). No differences in molecular profiles among three groups ($p = 0.66$) were noticed. Among patient who were surgically treated the choice of mastectomy was higher in older women (30%, 41% and 44% respectively). Patients aged over 85 years were less likely to undergo axillary treatment (67%) than those aged 75–79 (96%) and 80–84 years (94%) ($P < 0.001$). Patients aged 75–84 years received

ormonotherapy and radiotherapy more often than patients aged over 85 years (P < 0.001). Overall survival analysis (OS) (median follow-up 3.5 years) demonstrated that tumor size >=50 mm, positive lymph nodes and Ki-67≥20 were negative prognostic factors, while surgical treatment contributed to increase OS: median OS for age 75–79, 80–84, ≥85 were respectively 12.13, 6.48 and 7.61 years (p < 0.001). Moreover, comparing OS after adjusting for age between elderly women who received surgery or not, it was confirmed that surgically treated women had better prognosis (HR = 0.45, 95% CI: 037;0.56, p < 0.001), even among the very old group.

Conclusions: Management of BC in elderly patients needs careful assessment and a multidisciplinary team approach. Surgical treatment seems to be, in our experience, feasible and safe and relies on a survival advantage. So, comorbidity and frailty should be identified in order to calculate risk and benefits of treatment. In all cases elderly patients should be offered the best treatment choice and the opportunity to engage with the decision-making process.

No conflict of interest.

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Cosmetic outcome and symmetry for patients who have undergone bilateral therapeutic mammoplasty for breast cancer

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Background: Breast-reduction techniques are commonly used in oncoplastic breast surgery. Bilateral therapeutic mammoplasty has the benefit of reducing the volume of the breasts as well as assuring good symmetry post-surgery. The evaluation of cosmetic results after oncoplastic surgery has previously often been assessed by the surgeon. The aim of this study was an objective assessment of cosmetic outcome of therapeutic mammoplasties using the software BCCT.core and to compare this score with the surgeon's score and patient's own assessment and to evaluate if other defined parameters including smoking, BMI and volume of the breasts have an impact on the cosmetic outcome. A second aim was to compare the asymmetry measurements pre- and postoperatively in BCCT.core.

Material and Methods: 146 consecutive patients with primary breast cancer operated with bilateral therapeutic mammoplasty between 2011 and August 2018 in Kristianstad hospital, Sweden, were included in this study. Retrospective data were collected from patient records. BCCT.core analysis of post-operative pictures was done to evaluate the cosmetic outcome and pre-operative photos were analysed to compare pre- and post-operative symmetry. Values on a 10-grade scale for cosmetic outcomes were registered for both patients and surgeon's evaluation at the time of 1-year follow-up and used for comparison.

Results: The median age in the cohort was 64 years, median mammographic size of the tumor was 20 mm and the median breast size was 1000 ml. The weight of the specimen had a median of 166 g (range 34–1142). In total there were 11 re-operations due to either bleeding (n = 7), second operation for axillary clearance (3) or lack of radicality (n = 1). The majority of women, 88.4%, received a score of good or excellent on BCCT.core. The scores on BCCT.core showed a correlation with the surgeon's score. The patient's scores showed that overall the patient is more satisfied with the cosmetic outcome then the surgeon. None of the defined clinicopathological variables showed a significant effect on the cosmetic outcome. In all patients with asymmetry before surgery the symmetry was improved after surgery, shown by a positive difference between preoperative and postoperative BCCT.core asymmetry measurements.

Conclusion: Therapeutic bilateral mammoplasty gives a very good cosmetic outcome, when evaluated by an objective software, as well as by the surgeon and the patient herself. Importantly, symmetry can be improved in patients with asymmetry. In our study we found no other factors that significantly affected the cosmetic outcome.

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No conflict of interest.

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A patient- and assessor-blinded randomized controlled trial of axillary reverse mapping (ARM) in patients with early breast cancer

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Background: Axillary lymph node dissection (ALND) in breast cancer patients is infamous for its accompanying morbidity. Selective preservation of upper extremity lymphatic drainage and accompanying lymph nodes crossing the axillary basin – currently resected during a standard ALND – has been proposed as a valuable surgical refinement.

Methods: Peroperative Axillary Reversed Mapping (ARM) was used for selective preservation of upper extremity lymphatic drainage. A multicentre patient- and assessor-blinded randomised study was performed in clinically node negative, sentinel node positive early breast cancer patients. Patients were randomized to undergo either standard-ALND or ARM-ALND. Primary outcome was the presence of surgery-related lymphedema at six, 12 and 24 months post-operatively, as measured with the water displacement method. Lymphedema was defined as a volume increase of the arm at the affected side exceeding 10%, as compared to baseline. Secondary outcomes included patient-reported symptoms of lymphedema, pain, paraesthesia, numbness, loss of shoulder mobility, quality of life and risk of axillary recurrence.

Results: It was decided to stop this study after inclusion of 107 patients instead of the planned 280 patients. These patients were included in four dedicated breast cancer centres in the Netherlands between June 2013 and August 2016. No significant differences were found between both groups using the water displacement method with respect to measured lymphedema (Table). ARM-ALND resulted in less patient-reported lymphedema and less pain and at six, 12 and 24 months postoperatively (Table). No axillary recurrences occurred.

Table Upper extremity lymphedema using the water displacement method* and patient reported outcomes

Characteristic	Standard-ALND (%) (n = 54)	ARM-ALND (%) (n = 53)	p[#]
10% volume increase*			
6 months	9/42 (21.4)	11/44 (25.0)	0.191
12 months	9/39 (23.4)	4/40 (9.1)	0.080
24 months	10/31 (32.3)	8/35 (23.5)	0.432
Do you have much/very much swelling or lymphedema?			
6 months	5/44 (5.7)	0/43 (0)	0.023
12 months	8/41 (19.5)	2/40 (5.0)	0.047
24 months	8/30 (26.7)	2/33 (6.1)	0.025
Do you have much/very much pain in your arm or shoulder?			
6 months	13/44 (29.5)	6/43 (11.6)	0.039
12 months	9/41 (22.0)	6/40 (15.0)	0.421
24 months	8/30 (25.8)	3/33 (9.1)	0.076

[#]Chi-Square Test.

Conclusions: In contrast to results of volumetric measurement, patient reported outcomes support selective sparing of the upper extremity lymphatic drainage using ARM in case of ALND in clinically node negative, sentinel node positive early breast cancer. If completion ALND is considered in these patients, selective sparing of upper extremity axillary lymphatics by ARM is recommended in order to reduce morbidity.

No conflict of interest.

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Which are the predictive factors for the status of resection margins in breast conserving surgery and how they influence the overall survival and local recurrence?

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Background: The gold standard treatment for early-stage breast cancer is represented by breast conserving therapy, which consists of lumpectomy and adjuvant radiotherapy. The most important predictive factor associated with local recurrence represents the status of resection margins.

Aim: The aim of this study is to analyze the local recurrence and overall survival in patients who have received conservative treatment for early-stage breast cancer and to identify the preoperative predictive factors for positive resection margins.

Material and Methods: We retrospectively reviewed the medical records and pathological reports of 143 patients that underwent BCS for BC between 2009 and 2017 in General Surgery Department from Mures Country Hospital. The postoperative evolution was evalueted by phone contact of the patients. The follow-up period was between 20 and 120 months. 46 patients could not be contacted, therefore, 97 patients were completely included in the study, and 46 were included only in determining the preoperative parameters associated with the positive resection margins. Statistical analysis were done using GraphPad Prism, Fisher exact's test, Chi square test and Kaplan Meier survival curves.

Results: Of the 143 patients included in this study, positive resection margins were identified in 11, representing 7.69%. The overall mortality is 16.66% for patients with positive resection margins (one patient out of 6) and 6.59% for patients with negative resection margins (6 patients out of 91). For the overall survival $p = 0.50$, and for the specific survival $p = 0.53$, statistically insignificant. No patient had local recurrence during the follow-up period. Positive margins were significantly associated with neoadjuvant chemotherapy ($p < 0.0001$) and the presence of DCIS ($p = 0.01$). Patient's age ($p = 0.2$), patient's BMI ($p = 0.54$), tumor diameter ($p = 0.75$), histological type ($p = 0.39$), grade ($p = 0.96$) and IHC profile of the primary tumor ($p = 0.31$), multifocale tumors ($p = 0.09$), the presence of microcalcifications ($p = 0.18$), lymphovascular embolous ($p = 0.29$), necrosis ($p = 0.14$) and inflammatory infiltrate ($p = 0.43$), axillary limph nodes status ($p = 1$), axilary surgery ($p = 1$) and oncoplastic surgery ($p = 1$) do not statistically influence the positivity of resection margins in our study.

Conclusions: In our series, 2 out 16 factors analysed are significantly asociated with positive resection margins in BCS. They should be considered when planning surgical management of early-stahe breast cancer.

No conflict of interest.

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Knowledge attitude and practice of surgeons for breast conserving surgery: Results from an Indian cohort

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Background: Breast conservation surgery (BCS) is now standard practice across the western world. However, in India numerous groups have attributed the low uptake of BCS to patient related factors. In India, breast cancer is treated by general surgeons and trained breast surgical oncologists. Making the choice between Mastectomy (MRM) and BCS is a complex process and surgeons play a vital role in that choice. We conducted a survey among treating surgeons to evaluate the knowledge, attitude and practice for BCS in India.

Methods: A structured questionnaire with 20 questions regarding various aspects of physician details and their impact on breast surgery was distributed to 100 surgeons who manage patients with breast cancer, including general surgeons, trained breast surgeons across India. The questionnaire was developed by a group of breast surgeons at a large tertiary cancer center in India and the results were analyzed using SPSS version21.

Results: Of the 100 surgeons invited to participated in the survey, 72 responded at the close of the survey in October 2019. Twenty-one (29.2%) respondents were from cancer centers, 25(34.7%) from medical colleges and 26(36.1%) in private practice, with 43(59.7%) having been in practice for more than 10 years and 33 (45.8%) from tier 1 cities. Of these 64 (88.9%) offer BCS to eligible patients with early breast cancer (EBC). Those that do not offer BCS in EBC cited reasons of patient compliance, fear of recurrence and inadequate training in breast surgery. Physician related factors that appeared to negatively impact the choice of BCS in EBC were, inadequate breast surgery training ($n = 17$, 17.2% opt for BCS vs 75% opt for mastectomy, $p = 0.002$), volume of cases (less than 5 cases a month, $n = 21$, 21.9% BCS vs 87.5% mastectomy = 0.001). There was no impact of gender, years in practice, type of practice, tier of city, multidisciplinary or individual decisions. When asked about BCS post neo-adjuvant chemotherapy (NACT), only 36/72 (50%) routinely performed BCS and 24(33.3%) performed in select cases. Of these 60, 33(55%) performed in all T size if feasible for BCS post-NACT, while 19 (31.6%) offered BCS post-NACT in women with pre-NACT T1-T3 lesions. The factors impacting choice of BCS post-NACT included training, volume of cases and access to mammography. However, there was a large variability in the understanding evidence for post-NACT BCS among surgeons, suggesting a need for clarity of the same, for the locally advanced cancers with heavy tumor burden seen in India.

Conclusion: The surgeons' training, availability of resources, volume of cases, affected the decision making between MRM and BCS. Fear of recurrence was responsible for making BCS less popular, and there was a large variability in the understanding of safety to post-NACT BCS.

No conflict of interest.

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Current clinical practice and determinants of the use of delayed breast reconstruction in the Netherlands

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Background: Delayed breast reconstruction (DBR) is a valid option for post-mastectomy breast cancer patients who did not receive immediate breast reconstruction (IBR) due to (oncological) contra-indications or personal preferences. The objective of this study was to investigate the clinical practice and determinants of the use of delayed breast reconstruction (DBR) in the Netherlands.

Materials and Methods: Early-stage breast cancer patients treated with mastectomy between January and March 2012 in the Netherlands were selected from the Netherlands Cancer Registry (NCR). Routinely collected patient, tumor, treatment and hospital characteristics were completed with data on DBR up to five years after diagnosis. Treatment groups (DBR, immediate breast reconstruction (IBR), and mastectomy only (MAST)) were compared using Pearson Chi-square tests. A multivariable logistic regression analysis was performed to determine which factors were independently associated with post-mastectomy DBR. To determine factors influencing the time between mastectomy and DBR, a Cox regression analysis was performed.

Results: In total, 1,415 patients underwent mastectomy of whom 10.2% underwent DBR, 13.7% IBR and 76.1% MAST. Treatment groups differed based on patient, tumor, treatment and hospital characteristics. The mean time between mastectomy and DBR was 2.4 years [range 1–6 years]. DBR patients more often received autologous reconstruction compared to IBR patients (37.5% versus 6.2%, $p < 0.001$). Age below 50 years (35–49 versus 50–75 years OR 4.3, 95%CI 2.9–6.3) and chemotherapy treatment (adjuvant or neoadjuvant versus no chemotherapy OR 2.99, 95%CI 1.84–4.85; OR 2.85, 95%CI 1.52–5.35, respectively) were predictive factors for use of DBR, but did not exclusively explain the use of DBR. Time between mastectomy and DBR was significantly shorter in when radiation therapy (HR 0.61, 95%CI 0.42–0.89, $p = 0.011$) or adjuvant chemotherapy (HR 0.53, 95%CI 0.30–0.93, $p = 0.028$) was not given.

Conclusions: Although treatment with radiation therapy and adjuvant chemotherapy could explain time between mastectomy and DBR, the use of DBR over mastectomy alone could not be fully explained by age below 50 years and chemotherapy treatment. More information on for instance patient preferences is needed to understand the use and timing of DBR.

No conflict of interest.

155 Poster

Clinical, imaging and pathology factors related to residual axillary disease after neoadjuvant treatment

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Background: Performing a sentinel node (SN) after neoadjuvant treatment (NAT) is still controversial. The SN false-negative rate may be acceptable for cN0 tumours but too high for cN1 tumours. Defining which clinical, imaging and pathology factors modulate the risk of residual axillary disease after neoadjuvant treatment could be helpful to determine the patient's eligibility for post-chemotherapy SN.

Material and Methods: A retrospective review of prospectively entered data contained in our institutional Tumour Registry. Data on patients submitted to NAT between 2009 and 2018 were retrieved. Several clinical (age at diagnosis, diagnosis made by screening mammography or symptoms, chemotherapy scheme used), imaging (ultrasound axillary features previous to neoadjuvant treatment, axillary FNAC positivity previous to treatment, MRI axillary description after neoadjuvant treatment) and pathology factors (pathology type, breast pathology response to treatment, grade, oestrogen receptor status, progesterone receptor status, Her2Neu status, p53 status) were evaluated as possible predictors of post-treatment

residual axillary disease, both in a univariate (Xi2) and a multivariate (logistic regression) analysis.

Results: 153 patients were included in the study. In the univariate analysis, factors related to axillary residual disease after NAT were a diagnosis made by symptoms (p = 0.034), Her2Neu negativity (p = 0.000), p53 negativity (p = 0.05) and pathology grade I and II (p = 0.013). In the multivariate analysis, the factors associated with an increased risk for residual axillary disease after NAC were diagnosis made by symptoms (OR 0.66, p = 0.001), suspected residual disease after NAC by MRI (OR 3.58, p = 0.029) and progesterone receptor positivity (OR 4.084, p = 0.043); factors found as protective for residual axillary disease were Her2Neu positivity (OR 0.171, p = 0.003) and grade III (OR 0.188, p = 0.043).

Conclusions: Several clinical, imaging and pathology factors determine the risk of residual axillary disease after NAC. These factors could be of use to decide in which patients an intensive re-evaluation of the axillary disease should be recommended before surgery.

No conflict of interest.

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The impact of radiotherapy on patient-reported outcomes of immediate implant-based breast reconstruction: Results of a prospective multicentre cohort study

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Introduction: Post-mastectomy radiotherapy (PMRT) is increasingly given to improve breast cancer outcomes but can adversely impact complication rates following implant-based breast reconstruction (IBBR). Little, however, is known about the impact of PMRT on health-related quality of life (HRQL) following IBBR, especially in the context of newer mesh-assisted techniques. This study explores the impact of PMRT on patient-reported outcomes (PROs) following IBBR in the iBRA cohort.

Materials and Methods: The iBRA study prospectively recruited 2108 consecutive women undergoing IBBR with and without mesh at 81 UK centres. Demographic, operative, oncological and 3-month complication data were collected, and consent was sought from recruited patients to receive post-operative questionnaires at 3- and 18-months. The 18-month questionnaire assessed patient satisfaction and HRQL using the validated BREAST-Q.

The association between PMRT and BREAST-Q domain scores and overall satisfaction was investigated using mixed-effects regression models adjusted for clinically relevant confounders and including a random effect to account for potential clustering by centre. Modification of the effect of PMRT by biological mesh was evaluated using an interaction term.

Results: 1693 iBRA participants underwent mastectomy for malignancy, of whom 1187 (70%) consented to receive the 18-month questionnaire and 732 (62%) completed it. Of these, 214 patients (29%) received PMRT.

Results of the mixed-effects regression models are shown in Table 1. Patients undergoing PMRT reported worse HRQL across 3 BREAST-Q domains: "Satisfaction with Breasts," "Satisfaction with Outcome" and "Physical Well-being." Overall satisfaction was worse in the PMRT group (odds ratio 0.497, p = 0.002, 95% confidence interval [0.32–0.77]). Use of biological mesh did not ameliorate the impact of PMRT on BREAST-Q scores or patient satisfaction (p = 0.173–0.826).

Table 1 Impact of PMRT on BREAST-Q domains 18-months after IBBR

Outcome	N	Adjusted mean difference in score*	p value	95% confidence interval
Satisfaction with breasts	647	–6.27	0.008	[–10.91, –1.63]
Satisfaction with outcome	642	–7.53	0.002	[–12.20, –2.85]
PsychoSocial Well-being	643	–3.44	0.118	[–7.76, 0.87]
Sexual Well-being	465	–4.00	0.200	[–10.12, 2.11]
Physical Well-being	643	–6.55	<0.001	[–9.43, –3.67]

*Mean differences in scores adjusted for age, BMI, smoking status, ASA grade, type of IBBR, unilateral vs bilateral surgery, 3-month complications, adjuvant systemic therapies and axillary surgery.

Conclusions: PMRT adversely affects HRQL, in particular patient satisfaction, following IBBR. These findings should be discussed with patients considering IBBR, especially if PMRT is anticipated and/or PMRT indications are considered to be borderline, to allow them to make informed decisions about their oncological and reconstructive options.

No conflict of interest.

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P53 and axillary tumor burden in breast cancer

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Background: p53 mutations exist in many types of cancer and they are especially known in breast cancers. High expression of this protein has been associated with an adverse prognosis. Furthermore, previous studies have shown that p53 positive (p53+) tumors show a lower axillary tumor burden (ATB) compared with those p53 negative (p53-) tumors, because of a higher tendency for hematological dissemination. Here, we hypothesize that taking p53 expression levels into account together with other routine anatomic, pathologic and molecular factors, could improve the prediction of ATB in breast cancer patients, ultimately helping to personalize surgical treatments.

Material and Methods: We planned a retrospective cohort study including all women with a diagnosis of invasive breast carcinoma, and with surgery as primary treatment in Hospital del Mar from January 2000 to September 2014. We analyzed the association between p53 status in the primary tumor and ATB both in a univariate analysis, and including other clinical and pathologic factors in a multivariate model. ATB was analyzed as a dichotomic variable, so that patients with 0–2 positive axillary nodes were considered to have low ATB, while patients with ≥3 positive axillary nodes were classified as having high ATB.

Results: Our study comprised 1762 cases, of which 329 (18.7%) were p53+. In the univariate analysis, p53 positivity was associated with low ATB only in the Luminal B-HER2 neg (95.5% of p53+ in low ATB vs 4.5% of p53+ in high ATB, p = 0.025) subtype. In contrast, other factors such as lobular histology, increased size, lympho-vascular infiltration, high histological grade, multicentricity, and high proliferation (ki67) index were associated with high ATB in the univariate analysis in overall population. Only p53+ (p = 0.029), lympho-vascular infiltration (p = 0.001) and Ki67 > 14% (p = 0.040) remained significantly associated with high ATB in the multivariate analysis. Overall survival was better in p53- patients than in p53+ patients (p = 0.0018).

Conclusions: p53+ primary breast cancers are associated with low ATB, especially in some immunophenotypes as Luminal B-HER2 negative. Further studies are needed to clarify the potential role of p53 expression and other factors for personalizing surgical treatment in the different breast cancer subtypes.

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No conflict of interest.

159 Poster

Do clinical trials truly mirror their target population? An external validity analysis of national register versus trial data from the Swedish prospective SENOMIC trial on sentinel node micrometastases in breast cancer

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Background: Increasing evidence suggests that completion axillary lymph node dissection (ALND) may be omitted in breast cancer patients with limited axillary nodal metastases. However, the representativeness of trial participants for the original clinical practice population, and thus, the generalizability of published trials has been questioned. We propose the use of background data from national registers to assess whether trial participants mirror their target population and to strengthen the generalizability and implementation of trial outcomes.

Material and Methods: The Swedish prospective SENOMIC trial, omitting a completion ALND in breast cancer patients with sentinel lymph node micrometastases, reached full target accrual in 2017. To assess the generalizability of trial results for the target population, a comparative analysis of trial participants versus cases reported to the Swedish National Breast Cancer Register (NKBC) was performed.

Results: Comparing 548 trial participants and 1070 NKBC cases, there were no significant differences in age, tumour characteristics, breast surgery, or adjuvant treatment. Only the mean number of sentinel lymph nodes with micrometastasis per individual was lower in trial participants than in register cases (1.06 versus 1.09, p = 0.037).

Conclusions: Patients included in the SENOMIC trial are acceptably representative of the Swedish breast cancer target population. There were some minor divergences between trial participants and the NKBC population, but taking these into consideration, upcoming trial outcomes should be generalizable to breast cancer patients with micrometastases in their sentinel lymph node biopsy.

No conflict of interest.

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Women diagnosed with Ductal Carcinoma In Situ (DCIS) and healthcare providers' views on active surveillance for DCIS. Results from focus groups and in-depth interviews

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Background: Low-risk ductal carcinoma in situ (DCIS) lesions carry a risk of progressing to invasive breast cancer (iBC). Therefore, women with DCIS undergo surgery±radiotherapy which will yield many of them no/limited survival benefit whilst the associated side-effects can significantly impact their quality of life (QoL). The safety of active surveillance (AS) via yearly mammographic screening for low-risk DCIS is now being investigated. AS minimizes the physical burden associated with the standard treatments, but foregoing treatment could cause increased worry about progression of the DCIS lesion to iBC. If AS is proven safe, it could become a standard treatment option for DCIS endorsed by clinical guidelines. Patients' and healthcare professionals' (HCP) attitude towards AS will be a key factor for successful clinical implementation. We, therefore, examined patients' and HCP' attitudes towards AS for low-risk DCIS.

Methods: (1) HCP were interviewed, (2) focus group sessions were held with women treated for DCIS, and (3) as it was logistically unfeasible for women under AS to join a focus group, they completed a questionnaire based on the focus group topics. We explored patients' experiences and which factors influence patients' and HCP preferences for DCIS management strategy. We performed a thematic analysis on the transcripts of the interviews and focus group sessions using a self-developed coding scheme and analyzed the survey data.

Results: We interviewed 7 surgeons, 6 radiation oncologists, and 4 nurse specialists (mean age = 48 years, range: 34–63). Patients underwent surgery (n = 17; mean age = 58, range = 49–68) or were under AS (n = 16; mean age = 57, range = 45–73) and 53% were highly educated. Patients' preference for AS was associated with the wish to conserve their breast and avoid surgical side-effects, whilst a preference for surgery was associated with misperceptions about DCIS (is it iBC or not?) and fear of developing interval iBC (developing untreatable distant metastases within 1 year). HCP treatment preferences were driven by their estimation of the risk of progression to iBC and expected treatment benefit. HCP preferred AS for grade I DCIS and surgery for grade III DCIS. There was no consensus regarding treatment for grade II DCIS. Some HCP were concerned about AS for grade II DCIS given the potential for misclassification of grade III lesions as grade II. If facing a DCIS treatment decision for themselves, 41% of patients who underwent surgery, 85% of those under AS, and 88% of HCP would choose AS for grade I DCIS.

Conclusions: Treatment preferences of HCP were driven by clinical prognostic factors, whereas patients' preferences were driven by DCIS knowledge and worry about rapid progression. Patients and HCP are open to AS for grade I DCIS, but need reliable evidence on the safety of AS to help them make informed treatment decisions.

No conflict of interest.

162 Poster

Breast conserving surgery in breast cancer after neoadjuvant chemotherapy – opportunity of radioopaque tumor marking clips

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Background: Neoadjuvant chemotherapy (NACT) is increasingly used in locally advanced breast cancer (BC) because it improves resectability and increases the rate of conservative surgery and aesthetic outcomes. Tumor bed marking is important to accurately identify the tumor bed in patients with good response to NACT and to enable conservative surgery in patients with complete clinical and/or pathological response after NACT.

Material and Methods: Our study prospectively evaluates 34 patients, with confirmed breast cancer on ultrasound guided core biopsy, diagnosed and treated between 01.2017 and 08.2019, in Filantropia Clinical Hospital, Bucharest, Romania; they underwent radiopaque clips placement (Ultraclip®, Bard) under ultrasound guidance before starting NACT and/or Trastuzumab.

For tissue marker insertion patients with locally advanced BC were selected, with stage T2-3 N0-2 M0 and increased probability of significant response to NACT. The majority of patients selected had triple negative or HER2 positive breast cancer.

After finishing NACT, mammography and localizing breast ultrasound were performed. Cutaneous marking at ultrasound evaluation was used with patient in surgical position. Radiograph of specimen was performed to objectivate removal of the tumor bed and clip.

Results: The average age was 52 years old, with 51% of patients premenopausal. All patients had biopsy proven invasive mammary carcinoma NST, 44.1% were HER2 positive, 14.7% were triple negative and the rest of them were Luminal B. Most patients had T2 stage, with 14.7% having T3 stage, while nodal status was N0 in 35.3%, N1 in 50%, N2 in 14.7%. Pathological complete response (pCR) was found in 58.8% patients. Breast conserving surgery was successfully undertaken in 85.3% patients. Sentinel lymph node biopsy was performed in 29.4% patients. Local recurrence rate for a mean follow up of 21 months (range 11–29 months) was very low 2.9% and distance recurrence rate, 5.9%. There were no positive margins at final pathology in our cohort. Postoperative complications rate was low, with one patient developing postoperative surgical site infection and three patients developing postoperative axillary lymphocysts.

Conclusion: Conservative surgery in locally advanced BC patients with neoadjuvant treatment and tumor bed marking appears to be safe, increases the rate of conservative surgery and is followed by low local recurrence rates. The insertion of tumor markers before NACT should be part of standard multidisciplinary approach for locally advanced BC patients.

No conflict of interest.

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Usefulness of locoregional nerve blocks in breast surgery. A comparative study

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Background: Ultrasound-guided locoregional nerve blocks have been recently used in patients undergoing surgery for breast cancer. In particular, Paravetrebral block (PVB) and newer Pectoralis nerve (PECS) blocks can be used with the main aims of improving postoperative pain control and reducing use of opioids during general anesthesia. In this comparative study we investigated the effects of PVB and PECS in intraoperative opioid consumption, postoperative opioid consumption, postoperative nausea and vomiting (PONV), operative time, and post-operative hospital stay.

Material and Methods: Between January and August 2019, 198 patients underwent surgery for breast cancer. Among them, 91 patients received ultrasound-guided locoregional blocks (Block group) and 107 patients did not (Control group). Demographic characteristics, type of surgery and outcomes of interest were compared between the two groups by using the Sudent t-test, the Chi-square test or the Fisher exact test when indicated.

Results: Mean age was similar in the Block group and the Control group (62.5 vs 61.8 years, $p = 0.48$). Type of performed operation (breast conserving surgery, mastectomy, mastectomy plus immediate reconstruction) did not differ between the two groups ($p = 0.35$). In the Block group, 65 (71.4%) patients received PECS block, 3(3.3%) PVB block, and 23(25.3%) PECS + PVB block. Intraoperative opioid consumption (Fentanyl) was significantly lower in the Block group (mean 182.75 vs 245.65 μg, $p < 0.001$), as well as the use of perioeraptive antimetics (15 patients vs 42 patients, $p < 0.01$). Operative time was slightly longer in the blocks group (102.8 vs 89.7 minutes, $p = 0.16$). We did not observe difference in postoperative opioid consumption (5.6% vs 14.05% patients in the Block and Control group, respectively, $p = 0.38$), postoperative PONV (6.5% vs 12.1% patients in the Block and Control group, respectively, $p = 0.14$), and postoperative hospitals stay (2.5 vs 3.0 days in the Block and Control group, respectively, $p = 0.21$). Interestingly, in the Block group, 16 (17.6%) patients received surgery with sedation without general anesthesia. None of them complained of PONV or required opiods after surgery.

Conclusions: Locoregional blocks in breast surgery can reduce the use of intra-operative opioids and antiemetics. Further studies are needed to ameliorate patient selection, in order to identify those suitable of locoregional blocks and sedation, avoiding the use of general anesthesia.

No conflict of interest.

164 Poster

Multidisciplinary breast cancer guideline in the Netherlands: Modular revisions aiming for improved personalized breast cancer care

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Background: In 2000 the first national evidence based guideline on screening and diagnostics for breast cancer was released. Two years later, in 2002, the first national multidisciplinary guideline for treatment followed. In 2008 these two guidelines were merged and revised in 2012, resulting in one national guideline for breast cancer which is widely accessible in the online guideline database Oncoline (www.oncoline.nl).

Materials and Methods: Due to new developments and insights, we executed a modular revision process in four parts. The revision was carried out by a working group consisting of mandated representatives from several scientific and professional associations, the Dutch Breast Cancer Organization (NABON) and the Breast Cancer Patient Association.

Results: In contrary to previous revisions performed each five years, the new modular revisions are characterized by a solid interaction with clinical practitioners supplemented with insight in new developments and up to date evidence leading to a more up to date guideline. The following topics were revised in the breast cancer guideline using the modular revision process:

Individualized diagnostics, treatment, follow up and aftercare.

Screening advices for new mutations of breast tumors (such as CHEK2 and PALB2).

Imaging for screening, diagnostics, staging and response monitoring, also for pregnant women.

Treatment options for DCIS and low risk invasive carcinoma, including no treatment or less treatment.

Locoregional treatment in multiple phases of the treatment.

Gene expression testing.

Indication for systemic treatment (specific for N0-tumours).

Available drugs for systemic treatment (neo adjuvant and adjuvant treatment, metastatic settings).

Inclusion of prediction models in the guideline.

Preventive removal of ovaries as a part of endocrine treatment.

Systemic treatment after recurrence.

Sexual problems and fatigue.

Impact of cancer on family life.

Breast cancer in men, pregnancy and fertility.

Further, throughout the whole guideline more focus on shared decision making was realized.

Conclusion: The new developments in breast cancer treatment are going fast. Therefore, the working group will continue making modular revisions of the multidisciplinary guideline for breast cancer patients as an ongoing process involving mandated representatives from several scientific and professional associations, NABON and patient representatives. Parallel and based on guidelines, we developed digital decision trees (www.oncoguide.nl), leading to recommendations for diagnosis and treatment based on individual patient and disease characteristics. We hope that the guideline improves the care for over 17000 newly diagnosed breast cancer patients.

No conflict of interest.

165 Poster

Versatility, clinical outcomes and mammographic follow-up of Chest Wall Perforator Flaps (CWPF): A single-centre experience

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Background: Partial breast reconstruction (PBR) using chest wall perforator flaps (CWPF) is offered as a means of volume replacement, to facilitate better cosmetic outcomes in breast conservation surgery. We hereby present a 4-year prospective database of all CWPF performed in University Hospitals of Leicester, to evaluate the clinical outcomes and any impact on mammographic follow-up.

Material and Methods: We undertook a retrospective analysis of a prospectively maintained database of 40 patients who underwent a CWPF between September 2015 and August 2019. Analysis of clinical outcomes included demographics, indications, complications, re-operation rates, recurrence rates, and the proportion of patients who were seen in a symptomatic clinic post-operatively. All mammograms at one-year after surgery and annually thereafter were double reported and reviewed to evaluate whether the flap could be seen, the proportion with new calcifications and flap necrosis, and the recall and subsequent biopsy rates.

Results: 33 Lateral (LICAP) and 7 Anterior (AICAP) Intercostal Artery Perforator flaps were analysed. The median age was 54.6 (range 32–75) and median follow-up was 17.6 months (range 3–46 months). 5% were performed for the correction of deformity after previous Wide Local Excision and radiotherapy, and 12.5% had mastectomy and immediate reconstruction with autologous flap. The remaining 82.5% were indicated to prevent deformity in BCS. 95% were immediate and 97.5% were single stage

reconstructions. There was one wound infection (2.5% complication rate) and 12.5% had re-excision of margins, including one patient who required a mastectomy due to extensive Ductal Carcinoma in Situ (DCIS). 15% attended the symptomatic clinic and had additional imaging, but with no findings and no requirement for biopsy. There were no cases of interval cancer or recurrence.

The flap was visible in 40% of the mammograms. 12.5% of mammograms showed calcifications, while fat necrosis was seen in 5%. Post-radiation changes were seen in 17.5% of cases. No patients were recalled from mammographic surveillance for further imaging or biopsy.

Conclusions: PBR with CWPF is safe, with good clinical outcomes, and surveillance mammograms are accurate, with low recall and biopsy rates.

No conflict of interest.

166 Poster

Comparative accuracy of preoperative tumour size of invasive ductal carcinoma on Magnetic Resonance Imaging, Digital Breast Tomosynthesis, Ultrasound and Computed Tomography: Radiologic-pathologic incongruence and clinical implications

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Background: Magnetic resonance imaging (MRI) is used selectively in addition to digital breast tomosynthesis (DBT), ultrasound (US) and computed tomography (CT) in the preoperative assessment of breast cancer patients. The aim of this study was to evaluate the preoperative size assessment of invasive ductal carcinoma (IDC) on DBT, MRI, US, and CT compared with final histology, and evaluate the impact of MRI on the type of surgery and extent of treatment.

Material and Methods: Records, imaging and final pathology of all women with IDC, diagnosed in between 2015 and 2018 were reviewed retrospectively. Tumour measurements from all imaging modalities were recorded and compared with the final pathology as the gold standard. A correlation was assessed using concordance within a ±5 mm range. Final cohort size was 15 IDC patients. 1 patient excluded as no definitive surgery was performed.

Results: The tumour size measured on MRI was overestimated in 33% and was greater than that measured on both DBT and US. The MRI concordance with histology was 53.85% and discordance of 46.15%.

Conclusions: Preoperative MRI significantly overestimated tumour size. DBT mammography has been shown to improve the assessment of dense breast tissue by reducing overlapping of tissue. Our study; however, demonstrates that DBT significantly underestimated the size of the final pathology.

No conflict of interest.

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Retrospective analysis of survival of breast cancer patients with ipsilateral supraclavicular lymph node metastasis

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Background: At present, there is no specific guidance for the treatment of ipsilateral supraclavicular lymph node metastasis patients. Regional surgeryis not a part of conventional radical mastectomy for breast cancer, and the value of regional surgery is controversial. This study retrospectively analyzed the clinical data of newly diagnosed breast cancer patients with ipsilateral supraclavicular lymph node metastasis, and evaluated the efficacy of supraclavicular lymph node dissection plus radiotherapy and radiotherapy alone in the treatment of breast cancer with ipsilateral supraclavicular lymph node metastasis.

Methods: 91 cases of breast cancer without distant metastasis were analyzed. According to whether the patients underwent supraclavicular lymph node dissection or not, they were divided into two groups: dissection plus radiotherapy group (Surgery group) (75 cases) and simple radiotherapy group(Radiotherapy group) (16 cases).

Results: The follow-up time was 1–86 months, and the median follow-up time was 34 months. 18 (19.8%) died, 15 (19.7%) in surgery group and 3 (18.7%) in radiotherapy group. Distant metastasis occurred in 56 patients (60.2%), including 41 cases (53.9%) in surgery group and 11 cases (64.7%) in radiotherapy group. Kaplan-Meier survival analysis showed that the 5-year disease-free survival rate (DFS) was 27.9%, and the overall survival rate (OS) was 66.8%. The 5-year DFS was 35.1% in the surgery group and 12.6% in the radiotherapy group, and the difference was not statistically significant ($\chi^2 = 0.442$, P = 0.506). The 5-year OS was 69.5% and 60.0%, and the difference was not statistically significant ($\chi^2 = 0.400$, P = 0.527). Univariate analysis showed that, ER (P = 0.018) was the prognostic factor of OS.

Conclusion: Breast cancer combined with ISLM is considered to be a potential cure for a localized disease. Local treatment may help to enhance local control and correspondingly reduce distant metastasis, but systematic treatment is still needed, and whether regional surgery can improve the prognosis remains to be further studied.

No conflict of interest.

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Internal audit of an Indian breast oncosurgery unit using EUSOMA guidelines

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Background: Breast cancer care varies substantially from one breast unit to another. To provide optimum treatment to women with breast cancer, structured algorithms and guidelines should be adhered to. This review is an endeavor to audit breast oncology services at our institute as per EUSOMA guidelines.

Materials and Methods: The study was of retrospective and observational design. All patients who underwent surgery for breast cancer in our unit from 1st January 2018 to 31st December 2018 were included and evaluated. Data of these patients was retrieved from patient e-prescriptions and medical record files. Data analysis was performed by using Microsoft Office 2010. Compliance with mandatory and recommended quality indicators (QIs) of EUSOMA, was noted.

Results: Results of compliance with mandatory QIs of EUSOMA guidelines are presented here. Clinical and imaging work up, and preoperative diagnosis of breast cancer patients, met EUSOMA standards. Prognostic and predictive characterization of breast tumor was performed in all cases. Surgical approach in treatment of invasive cancer and ductal carcinoma in situ (DCIS) was in accordance with guidelines. Adherence to post-operative radiation (Post op RT) in breast conservation surgery (BCS) and pN2a post mastectomy groups was below standards. While adherence to minimum standards of post op RT was seen in pN1 post mastectomy group. More mastectomies than recommended were performed in patients with invasive cancer <3 cm in size. Over treatment was avoided in every other subgroup. Minimum standards of adherence to endocrine therapy were not met. Adjuvant and neoadjuvant chemotherapy, and adjuvant targeted therapy were utilized adequately. Neoadjuvant targeted therapy was underutilized. Attrition of patients was seen in follow up, minimum standards were not achieved.

Conclusion: This study has helped in conducting an extensive audit of our breast services. It has set benchmarks for future annual audits and helped highlight areas where, improvement of service delivery is needed. Boosting adherence to post op RT in BCS and pN2a post mastectomy groups, neoadjuvant targeted therapy, endocrine therapy, and patient follow up will be targeted. Various reasons for non-adherence like logistics, financial issues, family influence and fear of follow up will be assessed.

No conflict of interest.

169 Poster

Selective axillary dissection after axillary reverse mapping in node positive breast cancer patients to prevent breast cancer related lymphedema. The issue of safety

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Objective: Despite the need for Axillary Lymph Node Dissection (ALND) is decreasing, in selected patients with breast cancer it is still necessary. Breast Cancer Related Lymphedema (BCRL), which may occur in up to 65% of patients undergoing ALND, is the most dreaded complication of this operation and may be a lifelong problem. BCRL consequences include poor quality of life and body image, interference with social life and work, and increased health costs; hence the interest in BCRL prevention. Axillary Reverse Mapping (ARM) allows the detection of upper extremity lymphatic

drainage that may be variably spared during a Selective Axillary Dissection (SAD) in order to reduce the risk of (BCRL). In this study we deal with the issue on oncological safety of SAD after ARM.

Background: Crossover between the drainage of the breast and of the upper limb at axillary level is well known and ARM nodes have been found involved in a not negligible number of patients. Therefore SAD, as a nodal sparing surgery, has been seen with suspicion despite the awaited efficacy of SAD in reducing BCRL; nowadays controversies on its safety exist.

Methods: We reported the outcome of the firsts consecutive 100 patients treated with SAD after ARM as a part of two distinct prospective clinical trials. Axillary nodal relapse (ANR) was considered the overt reappraisal disease at ipsilateral axillary region. The rate of ANR occurrence, referred to a 5-year time horizon, was calculated in two ways: as a crude rate, assuming an exponential distribution of occurrence time; as the cumulative risk, taking into account other breast recurrences and deaths as competing events.

Results: All patients were node positive and the median number of lymph nodes excised was 18. During a median follow-up of 51 months (IQ range 34–91) 7 patients developed distant metastases, one had an ipsilateral breast tumour recurrence, 2 had a contralateral Breast cancer (CBC) and one patient developed an ANR as isolated event. The crude rate of ANR occurrence was 1.36 (95% CI: 0.19–9.63) for 6000 women-month at risk (100 women exposed for 5 years), and the estimated 5-year crude cumulative incidence was 1.85% (0–5.47%).

Conclusions: Our findings support the oncological safety of this procedure when ALND is still indicated, since the occurrence for ANR does not exceed the expected rate of regional failure observed after a standard treatment of axilla. This novel surgical procedure should therefore be considered when ALND is still indicated: after a SLNB when patient does not meet the Z0011 criteria, when there is still evidence of residual nodal involvement after neo-adjuvant chemotherapy or when there is evidence of axillary involvement ascertained with a fine needle biopsy. SAD after ARM is a promising surgical approach and its investigation with randomised clinical trials should be encouraged.

No conflict of interest.

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Predictors of seroma formation after breast cancer surgery

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Background: Seroma formation after breast cancer surgery is a common problem. At het University Hospitals Leuven, a suction drain is placed after mastectomy and/or axillary lymph node dissection (ALND). The drain is removed at discharge, usually three to five days after surgery and weekly wound care consultations for seroma aspiration are planned. The aim of this study was to define predictors of prolonged seroma formation after breast cancer surgery.

Patients and Methods: A retrospective analysis was performed on 104 patient files that underwent breast cancer surgery with placement of suction drain between 2018 and 2019. Clinical characteristics and information about seroma formation were prospectively collected in electronic patient files.

Results: Clinical characteristics are summarized in the table. The median duration of seroma formation was 22 days (range 3–166). So, patients needed a median of 4 wound care consultations (range 1–17) with a median of 3 seroma aspirations (range 0–17). In 20 patients (19%), no seroma aspiration was needed. The total volume of seroma ranged from 0 to 5360 ml with a median of 270 ml. In an univariable analysis, a significant association between the duration of seroma formation and the following variables was found: age, body mass index, breast weight, drain volume (see Table). Patients who underwent a mastectomy with ALND had a significant longer duration of seroma (Est. = 9.557 days, p = 0.0161), a higher total fluid volume (Est. = 1108.1 ml, p < 0.0001) and also needed more wound care consultations (Est 1.497, p = 0.0002) in comparison with patients who underwent a mastectomy without ALND.

Table Overview of the patient characteristics and the univariate analysis for predictors of the duration of seroma formation

Patient characteristics		
	Median	Range
Age (n = 104)	55.0	(26.0; 93.0)
BMI (n = 104)	25.0	(13.7; 46.9)
Breast weight (g) (n = 103)	650.0	(83; 2020)
Type of surgery (n = 111)	**n**	%.
BCS (+SLNB) + ALND	7	6.30
ME (+SLNB)	57	51.35
ME (+SLNB) + ALND	47	42.34
Univariate analysis for predictors of the duration of seroma formation		
	Estimate	P-value
Age (1 year)	0.339	0.0127
BMI (per unit)	1.213	<0.001
Breast weight (g)	21.058	<0.0001
Total drain volume (ml)	2.813	0.0008
24 h flow at removal of drain (ml)	1.396	<0.0001

BCS = Breast-conserving surgery, SLNB = sentinel lymph node biopsy and ALND = axillary lymph node dissection.

Conclusions: Several predictors of prolonged seroma formation after breast cancer surgery were identified and can be used to optimise individualized patient care.

No conflict of interest.

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Nationwide population-based study: Patterns of care in young breast cancer patients in the Netherlands

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Background: Breast cancer (BC) is one of the most common cancers in young women (<40 years). Since 2011 all patients who are surgically treated for BC in the Netherlands are registered in the NABON Breast Cancer Audit (NBCA). Around 600 new young BC patients are registered per year. Breast cancer care is becoming more complex requiring a multidisciplinary approach especially in this young patient population. This nationwide population-based study evaluates the patterns of care in the young breast cancer patient in the Netherlands.

Material and Methods: All surgically treated breast cancer patients registered in the NBCA for invasive breast cancer from January 2012 to December 2017 were included. The Chi-square test was used to compare factors of patient, tumour and clinical management. Multivariable logistic regression was used to assess the effect of age on clinical management, focusing on preserving the breast contour during treatment.

Results: In total 83,234 patients were registered; 3,677 (4.4%) young patients <40 years, 12,175 (14.6%) patients between 40 and 50 years and 67,380 (81%) patients >50 years of age. 44.1% of the young women had a stage II breast cancer (43.2% in the patients 40–50 years and 30.6% in patients >50 years) and 14.4% stage III disease (13% in patients 40–50 years and 6.7% in patients >50 years). In young women the majority of the patients presented with a no special type (ductal) histologic subtype (90%) and a tumour grade III (44.1%). Triple-negative breast cancer was seen more often in the young patient group <40 years (29.1% vs 16.8% in patient 40–50 years and 13.3% in patients >50 years). Also more neoadjuvant systemic therapy was given to young patients (48% vs 36% vs 13%).

Over years, less “primary” breast conserving surgery (BCS) was performed in young patients (29.2% in 2012 vs 17.2% in 2017) and more young patients underwent neoadjuvant systemic treatment (NST) followed by BCS (7.2% in 2012 vs 23.4% in 2017). Furthermore, percentage of young patients receiving immediate breast reconstruction (IBR) after mastectomy increased from 29.3% in 2012 to 47% in 2017.

We will present further details on the use of radiotherapy and in a sub-analysis we compared the patients that received IBR with the patients that underwent BCS.

Conclusion: This study shows that young patients with breast cancer more often present with a higher stage of disease and triple-negative breast cancer. Over years we observed an increase in the use of multidisciplinary treatment approaches such as NST and IBR.

No conflict of interest.

172 Poster

Defining a "dedicated" breast cancer team

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Background: The quality of breast cancer (BC) care in the Netherlands is high. All patients are discussed in pre- and post-operative multidisciplinary meetings and treated by certified medical specialists. Some characteristics of the medical team and the organization involved in BC care are monitored in the national multidisciplinary NABON breast Cancer Audit (NBCA) by quality indicators measuring the structure of the teams. The scientific committee of the NBCA is responsible for the multidisciplinary set of quality indicators. For some quality indicators variation is seen. The aim of this study was to explore if the presence of a defined "dedicated" BC team influences this variation.

Material and Methods: We chose the following characteristics at hospital level to define a "dedicated" BC team: minimum of 50 new BC patients per year, two certified surgical oncologists who treat BC patients, two certified internist oncologists who treat BC patients, one plastic surgeon who treats BC patients, plastic surgeon participating standard in multidisciplinary meeting, radiotherapist participating standard in multidisciplinary meeting, PALGA protocol (synoptic pathology reporting) being used, the median time between diagnosis and surgery (excluding direct reconstruction) being ≤30 days. The composite measure "dedicated" BC team was used to assess if a "dedicated" BC team influences the outcomes of quality indicators.

Table 1

	6 criteria	7 criteria	8 criteria
Preserving breast contour	56.5%	71.5%	72.7%
Consultation radiotherapist in 28 days	13.3%	57.5%	72.9%
MRI by patients receiving neo adjuvant chemotherapy	76%	86%	91%

Results: In 2017 83 hospitals registered their BC patients in the NBCA. 75.9% (n = 63) from all the hospitals meet all criteria of a "dedicated" BC team. 19 (22.9%) hospitals meet seven and one hospital meets six (1.2%) criteria.

The results show that hospitals that meet all the criteria of a "dedicated" breast cancer team scored on average higher on the quality indicators preserving breast contour, breast MRI performed in patients treated with neo-adjuvant chemotherapy (NAC), and consultation with the radiotherapist within 28 days after start NAC, compared with hospitals that meet seven or six criteria (Table 1).

Conclusion: The results suggest that defining a "dedicated" BC team and motiving hospitals to develop these treatment teams can lead to better outcomes of BC care.

No conflict of interest.

173 Poster

Predictive factors involved in determining response to neoadjuvant chemotherapy in breast cancer and impact of response on 5 years disease free survival and overall survival

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Background: The advantages of Neo-Adjuvant chemotherapy (NAC) are more breast conservation surgeries and ability to monitor treatment response in vivo. Not all patients respond well to NAC in term of tumor size reduction and lymph nodal response. The goal of the study is to identify all the known factors that may play a role in predicting response to chemotherapy, thus identifying a group of patients which would be resistant to NAT and thus potential harmful effects are avoided in that subset of patients.

Material and Methods: We retrospectively reviewed data from Jan 2012 to Dec 2012 in a single center in Shaukat Khanum hospital Lahore, Pakistan. All those who received NAC (as they were not candidates for upfront surgery) and having no distant metastasis were included. 156 patients were studied. Tumor grade, receptor status, menopausal status, family h/o ca breast, parity, initial T and N stage were studied as predictive factors for response to chemotherapy. HER-2 Neu positivity was not considered as only 2 patients received Transtuzumab. The response was measured in term of percentage reduction from 1st radiological size on presentation to final size on histopathology (on resected specimen). Four groups were identified, complete responder group with 100% reduction, Non responder group, Partial responder PR (<50% reduction), Responders R (>50% reduction). 5 year disease free survival, overall survival and recurrence were noted for each group.

Results: Mean Age was 47 years. 96% of patients were invasive ductal carcinoma, rest were lobular. 57% of patients were grade III, 90% of patients were T2 and 66% were LN positive (both at presentation). 67% of patients underwent BCS (Breast conserving surgery) rest underwent Mastectomy. Mortality for whole group was 19%, and recurrence was shown in 30% (Majority was distant 26%, while contralateral were 3%). Out of 156 patients, 25% of patients were complete responders, 13% were non responders, 23% were partial responder (<50% reduction) and 37% were responders (>50% response). ER and PR negative Tumors and Grade III tumors showed more complete responses. Rest of factors, including triple negative, Initial T and N stage and other factors showed no impact on chemo-response. Survival was significantly poor in non responder group (45% OS, 40% DFS), while rest of 3 groups had comparable survival outcome, with complete responder group having best survival outcome (86% OS, 80% DFS).

Conclusion: Only ER and PR negative tumors and grade 3 tumors showed more complete response. Survival outcomes were significantly poor in Non-responders while it was better in complete responders.

No conflict of interest.

174 Poster

Male breast cancer: A high volume centre experience

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Background: Male breast cancer (MBC) accounts for less than 1% of all cancers in men. Several genetic disorders, such as Lynch, Cowden, Klinefelter and Li-Fraumeni syndrome contribute to increase the lifetime risk to develop breast cancer in males.

In general population, the lifetime risk for MBC is 0.1%, but it rises to 7–8% with a BRCA2 mutation and 1% with a BRCA1 mutation.

Material and Methods: We describe the surgical experience of a single high volume center (Breast Surgical Oncology Unit of Modena University Hospital) from 2006 to 2019.

Results: We treated 29 patient with MBC.

Median age at diagnosis was 64 years (minimum 45 to maximum 84).

A minority of patients presented with bilateral disease at the onset (10.3%). Most patients (75.1%) had retroareolar tumor.

41.4% had significant familiar history for breast cancer. Genetic testing was performed in all patients, but only 26.1% was positive for BRCA2 mutation. No BRCA1 mutation was found.

All the patients underwent simple mastectomy. The 3.4% had distant metastasis, but surgery was performed for local control of the disease.

We performed immediate axillary dissection in 21.8% of patient for nodal positivity at the time of diagnosis; the remaining were treated with sentinel node biopsy and only three of them underwent following axillary dissection for sentinel node positivity.

No significant post-operative complications were observed and medial hospital stay was two days.

At the final histology ductal carcinoma was found in all breasts, in only one specimen lobular carcinoma coexisted with the ductal one.

Almost all cases showed intermediate or high grade disease (G2-G3).

None of patients had triple negative cancer; c-erbB2 positivity was found in only 8%, the rest of tumors were luminal-like.

In addition to surgery 10.9% of patients received neoadjuvant chemotherapy, 24.1% adjuvant chemotherapy and 82.8% endocrine therapy, mostly tamoxifen.

Radiotherapy was applied in locally advanced disease, in one case for the treatment of nodal recurrence and in another case on bone metastasis.

Conclusions: Our experience does not differ from other case series described in literature in terms of epidemiological, histopathological and genetic findings.

From a surgical point of view we confirmed radical mastectomies as the preferred choice of resection. Sentinel node biopsy is safe and feasible in men as in women. Post-operative course in men is similar to women's one and also oncological adjuvant strategy is chosen following the same guidelines.

To achieve optimal management of male breast cancer, patients must be centralized to a hospital with a breast unit, to give the possibility of genetic counseling and to share with the multidisciplinary team every step of both diagnostic and therapeutic phases.

No conflict of interest.

175 Poster

Surgical margin involvement increases distant recurrence, not just local recurrence

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Background: Involved margins following surgery in early breast cancer is associated with an increased risk of local recurrence but the effect on distant recurrence is unknown. ASCO and ASTRO endorsed a policy that negative margins of no ink on tumour represented sufficient margin for local control and that the routine practice of obtaining a more widely negative margin was not indicated.

The aim of this audit was to assess local and distant control in four breast units in Greater Manchester and determine if involved margins predict distant recurrence.

Material and Methods: In total 3409 patients who underwent surgery for early breast cancer (T1-3) in four breast units were included in the study. All patients had margin status prospectively recorded (reported by micrometer according to NHSBSP pathology guidelines), local and distant recurrence recorded. All patients received adjuvant therapy according to local guidelines. Statistical analysis using Cox proportional hazard regression was used to identify clinicopathological factors predicting recurrence in the multivariate analysis.

Results: Overall 2897 (70.1%) had clear margins, 712 (20.9%) involved margins (<1 mm) and 308 (9.0%) close margins (<2 mm). Median follow up was 63.8 months. Overall the local recurrence rate was 3.9% (range 3–8.6%) and distant recurrence rate was 4.5% (range 4.1–11.8%) at five years. Distant recurrence was higher in symptomatic compared to screen detected cancers.

In multivariate analysis for patients treated by both Breast Conservation (HR 1.98 (95% CI 1.14–3.43)) or Mastectomy (HR 1.51 (95% CI 1.1–2.2) involved margins (<1 mm) predicted increased Distant Recurrence. Triple negative cancers had higher local and distant recurrence (see Table).

A margin less than 2 mm was associated with both local (HR 1.61 (1.03–2.51)) and distant 1.67 (1.2–2.5)) recurrence compared to a clear margin (Table 1). T stage, N stage, molecular phenotype and mastectomy (compared to breast conservation) also predicted distant recurrence, while molecular phenotype and mastectomy predicted local recurrence.

Table 1 Multivariate analysis of factors predicting cancer recurrence

	Local HR(95%CI)	p-value	Distant HR (95%CI)	p-value
Margins less than 2 mm vs clear	1.61 (1.03–2.51)	0.038	1.67 (1.15–2.49)	0.013
T1a vs T3	0.77 (0.22–2.75)	0.693	3.55 (0.45–27.79)	0.013
N0 vs N3	1.76 (0.73–4.28)	0.211	4.66 (2.42–8.98)	<0.001
Molecular Phenotype Luminal A vs Basal-like	5.66 (3.12–10.01)	<0.001	5.13 (2.86–9.20)	<0.001
Mastectomy (compared to WLE)	2.74 (1.77–4.24)	0.001	2.39 (1.46–3.90)	0.001

Conclusions: Clearing surgical margins increases both local and distant recurrence free survival and should be essential surgical management particularly in triple negative cancers. Current ASCO guidelines on surgical margins need to be based on preventing distant not local recurrence to prevent deaths from breast cancer.

No conflict of interest.

176 Poster

Size discrepancy of residual tumor between post chemotherapy sonography and on post excision histopathology after Neo adjuvant chemotherapy and its impact on 5 years disease free survival

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Background: With advent of neoadjuvant chemotherapy (NAC), more patients can be offered breast conserving surgery. At near completion of NAC all patients are subjected to ultrasound examination to measure remaining size of tumor. The accuracy of ultrasound is important because it may alter the decision of breast conserving surgery and size of lumpectomy specimen. The objective of surgery is to find out the discrepancy in mm showed by ultrasound examination compared with the final histopathological (H/P) measurements.

Material and Methods: The date was retrospectively reviewed between Jan 2012 to Dec 2012 in a single center in Shaukat Khanum Hospital Lahore, Pakistan. Total 145 patients were included. All patients received chemotherapy before surgery. Both mastectomy and BCS were included. Ultrasound examination was done before surgery and final H/P sizes were noted. Discrepancies lesser than 10 mm were ignored (considered as no discrepancy)b/c of operator dependency and b/c both were different mode of examinations.

Results: Out of 145 patients 113 (79%) showed no discrepancy (Group A),32(21%) patients showed more than 10 mm discrepancy (Group B), out of these 21 patients. Largest discrepancy was shown to be 100 mm in which ultrasound showed no lesion (occult) however on final H/P it was 100 m, this patients underwent re-surgery and had local recurrence. 2nd largest discrepancy was 48 mm in which ultrasound showed 48 mm tumor size however final H/P showed no tumor (occult). Total 4 (2.7%), had to undergo re-excision due to positive margin, 2 from group A and 2 from group B. In Group A (n = 113) 33 (29.2%) patients, whereas in group B (n = 32) 8 (25%) patients had some sort of recurrence. The difference in 5-year disease free survival and overall survival between the two groups was statistically insignificant (p Value >0.05).

Conclusion: The ultrasound examination by large is a sensitive mode for determining size of tumor after NAC as shown in our study, 79% showed insignificant discrepancy. However in some cases due to tumor lysis it may not appear discrete measurable entity and may show significant discrepancy (both over and under stating). Surgeon need to be aware of these limitations for his/her surgery planning. However size discrepancy didn't show any impact on re-excision rate and survival outcomes.

No conflict of interest.

178 Poster

Outcomes of Magseed localisation of non-palpable breast lesions in a large university hospital

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Background: Magseed is a new alternative method of localising non-palpable breast lesions that has addressed many of the limitations of wire guided localisation. It is a nonradioactive inducible magnetic seed that can be visualised on mammography and ultrasound. The Sentimag® probe is used for Intraoperative localisation of the seed. The aim of this study is to evaluate this new technique introduced to our department over the last two years.

Methods: This is a prospective audit of all patients who underwent Magseed localisation surgery in our centre for non-palpable breast lesions between January 2018 and September 2019.

Results: Total number of 114 cases underwent Magseed localisation for breast lesions. We performed 49 cases in 2018 which increased to 65 cases in 2019. Mean age of the patients was 61 years (range, 28–85 years). Mean BMI in these patients was 30.79 (range, 18.1–48.3). Most of these cases (n = 108,94.7%) had only one seed for localisation while the rest of cases (n = 6, 5.3%) had two seeds (4 for bracketing, and 2 for 2 separate lesions). Altogether, there were 120 Magseed localisations, out of which 94 were localised under ultrasound guidance while the remaining 26 were localised via stereotactic guidance. Acceptable margins have been achieved by initial dissection in 86 cases (75.4%). There were 12 patients (10.5%) who needed re-excision of the margins. Our success rate is 97.6% with only 3 cases (2.6%) who needed additional wire for localisation. This was due to probe failure in 2 cases and magseed displacement in 1 case. Mean duration of Magseed insertion was 6 days (range, 0–27). Mean size of the index lesion removed was 9.88 mm (range, 0–85 mm) and mean weight of the excised specimen was 61.56 gms (range, 2–1900 gms).

Conclusions: We found that this new technique of localising breast lesions is simple and logistically less demanding. There were few complications in our series and there was a quick learning curve. We also

found that lesions in periphery of large ptotic breasts did not pose any challenge. Moreover, patients do not have to undergo another procedure for localisation on the day of surgery and hence are less anxious.

No conflict of interest.

179 Poster

A human-derived acellular dermal matrix for breast reconstruction: The first European experience

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Background: The growing diffusion of direct-to-implant breast reconstruction (DTI-BR) following mastectomy for breast cancer (BC) is largely related to the introduction and increasing use in clinical practice of acellular dermal matrices (ADMs). Human-derived ADMs (H-ADMs) showed optimal outcomes in breast reconstruction and a better integration in the host tissues when compared with animal-derived products; according to the European legislation, H-ADMs are considered "human products," subjected to the European laws on transplantation, and not "medical devices." The Skin Bank of the Bufalini Hospital (Cesena, Italy) in 2009 obtained from the Italian National Transplant Center and National Health Institute the approval for the production and distribution of a new human cadaver-donor-derived ADM (named with the Italian acronym, MODA – Matrice Omologa Dermica Acellulata – Homologous Decellularized Dermal Matrix); in 2015 we started to use MODA in breast reconstructions following mastectomies for BC. To our knowledge, this is the first European experience about the routine use of H-ADMs in breast reconstruction surgery reported.

Materials and Methods: From June 2015 to August 2019 we prospectively enrolled women undergoing "conservative mastectomies" (NAC-sparing, Skin Reducing and Skin Sparing) for BC in our Breast Surgical Unit, excluding patients with a history of previous chest wall irradiation, heavy tobacco smokers or diabetic, patients with a BMI > 30 kg/m^2 and those requiring more than 550 cc silicone implants. We assessed short-term outcomes, postoperative complications presenting in the first 30 post-operative days and long-term outcomes at 6 and 12 months.

Results: 67 of 85 enrolled patients underwent DTI-BR (18 bilateral, 49 unilateral procedures), 18 received the first stage of a two-step surgical reconstruction with tissue-expanders; 108 breasts were treated. At a mean follow-up of 24.4 months, 8 minor complications (limited wound dehiscences, conservatively managed with complete resolution) and 5 major complications requiring re-intervention (3 post-operative hematomas, 1 implant dislocation, 2 wound dehiscences) were observed. No implant exposure, seroma, cancer relapses, infections were recorded.

Conclusions: Our preliminary results show the safety of MODA in breast reconstruction surgery for BC, with satisfactory clinical and cosmetic outcomes and a low complications rate: this is particularly relevant for the European market, where no other human-derived devices are available for breast reconstruction, due to regulatory restrictions. However, a longer follow up to assess long-term complications such as capsular contracture is required.

No conflict of interest.

180 Poster

Young age as an independent prognostic factor in breast cancer

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Background: The aim of this study is to evaluate the young age in association with survival and negative prognostic factors in primary breast cancer patients.

Material and Methods: 212 consecutive breast cancer patients treated in our clinic between 2014 and 2017 were included in the study, in which malignancy was confirmed by ultrasound guided core biopsy. We considered young age </= 40 years at the moment of diagnose. The patients were contacted telephonically, and survival was evaluated. For clinical and morphological data, we used the patient's files and the pathological reports. Variables studied were histological type of the primary tumor, tumor dimensions, immunohistochemical profile, hormone receptor expression, Ki67 expression, type of surgery in relation with age groups.

Statistical analysis was performed using GraphPad Prism 8, Fisher exact test and Log-Rank test. We considered statistically significant the value of $p < 0.05$.

Results: In our series we did not find a statistical significant difference in age groups regarding the histological type of the tumor ($p = 0.72$), tumor dimensions ($p = 0.6$), molecular profile ($p = 0.14$), hormone receptor status ($p = 1$), Ki67 expression ($p = 0.42$), and the type of surgery ($p = 1$). There was no significant difference of survival between young and elderly patients. ($p = 0.3$).

Conclusions: In our cases young age is not associated with negative prognostic factors for breast cancer. We suggest that young age should not be considered alone as a criteria for a particular treatment, but in association with tumor biology.

No conflict of interest.

181 Poster

Do surgical margins matter after mastectomy? A systematic review and meta-analysis

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Background: There is no consensus regarding adequacy of margins after mastectomy. After breast conserving surgery and radiotherapy, ASCO Guidelines advise "no tumour at margin edge" is adequate clearance of invasive cancer but DCIS requires a 2 mm clearance.

To determine if margins involved with Invasive cancer or DCIS after mastectomy were associated with subsequent local or distant recurrence.

Materials and Methods: A systematic review of literature published between 1980 and 2019 and meta-analysis was conducted. Where possible unpublished data was sought from authors. This study was registered with PROSPERO (CRD42019127541).

From 34 studies, 34,833 breast cancer patients were included in the quantitative synthesis. Studies eligible for inclusion reported on a population of patients undergoing curative mastectomy for invasive or in-situ breast cancer (stages I-III) allowing an estimation of outcomes in relation to margin status/width, and microscopic margins had to be reported quantitatively with defined threshold distances/widths.

The PRISMA guidelines were followed. Study data were pooled using random effects inverse variance modelling.

Study level meta-analysis was used to compare margin status (positive: negative) and width on local and distant recurrence. Local and distant recurrence proportion was modelled using random effects modelling.

Results: Positive margins were associated with increased local recurrence on multivariable analyses (HR, 2·64, (95% CI 2·01–3·46). Involved margins had a higher local recurrence regardless of the distance of tumour from the margin defined as positive (HR, 95%CI; tumour at margin edge: 2·29, 1·35–3·89; margin <1 mm: 3·08, 1·60–5·93; margin <2 mm: 2.96, 2·20–3.98; margin <5 mm: 7·09, 1·32–37.9).

The odds ratio of local recurrence with positive margins increased with follow-up time of >5 years compared to <5 years (OR <5 years: OR 2.15, 1.14–3.27 to OR >5 years OR 3.50, 2.13–5.75). Data were available from five studies for patients not receiving radiotherapy and positive margins were associated with a three-fold risk of local recurrence (OR: 3.01, 1.96–4.61).

In patients (all stages) after Skinsparing mastectomy, positive margins increased local recurrence (HR 3·52, 2·56–4·84 and HR 3·40, 1·9–6·2 respectively).

Four studies reporting distant recurrence, found patients with involved margins had a worse survival (HR 1·53, 1·03–2·25).

Conclusions: The risk of local and distant recurrence after mastectomy is associated with margin proximity. Adequate margin clearance greater than 1 mm is required to prevent recurrence after mastectomy and this should be clearly stated in international guidelines.

No conflict of interest.

182 Poster

Axillary management in patients with breast cancer and positive axilla at diagnosis

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Background: In breast cancer with axillary involvement, lymphadenectomy has been the standard procedure until recently. Axillary involvement and the number of metastatic nodes was one of the main prognostic factors. There is an evidence that the administration of radiotherapy on ganglion areas in patients with positive axilla decreases the risk of recurrence. Nowadays a more conservative management is valued and this avoid comorbidities. The objective was to evaluate the axillary treatment, the evolution over time and to assess patients follow-up.

Material and Methods: A retrospective observational study of patients diagnosed with breast cancer with positive axilla between 2010 and 2017 was done. The objective was to evaluate the axillary treatment, the evolution over time and to assess patients follow-up.

Results: In a total of 1100 patients diagnosed of breast cancer, 168 of them were women with clinically and histologically positive axilla at diagnosis. 76% received primary chemotherapy (127/168) and they were subsequently treated with sentinel node biopsy, axillary lymphadenectomy or both tecniques. Those with positive sentinel node biopsy were studied differentiating the treatment on those who received radiotherapy or were into lymphadenectomy. 60 patients (46% of total) resulted in complete pathological axillary response after neoadjuvant chemotherapy. 5 axillary recurrences appeared (2.9%) of which none of them were registered in the sentinel node biopsy group associated with radiotherapy, avoiding axillary lymphadenectomy. These results compared to randomized studies as EBCTCG 2005 or AMAROS would support the benefit of lymph node radiotherapy treatment, bypassing the axillary lymphadenectomy, in situations with positive sentinel node biopsy in those patients who received primary chemotherapy. Likewise, according to the consensus of San Gallen 2015 sentinel node detection is considered appropriate after axillary negativization after chemotherapy. The asociation of Trastuzumab to chemotherapy has demonstrated a higher response rate in both axilla and breast as studies like Neosphere shows, wich significantly improves its results with the adition of Pertuzumab in neoadjuvant.

Conclusions: With a 40% of complete axillary response rate to chemotherapy, sentinel node biopsy provides valid and reliable information about cancer stadification and could prevent lymphadenectomy, replacing it with radiotherapy and thus decreasing morbidity. The pathological response to systemic treatment has emerged as the most important predictive factor of disease-free survival on breast cancer.

No conflict of interest.

183 Poster

Accuracy of Magnetic Localisation device placement and retrieval in breast cancer patients from a single internationally Accredited Breast Centre in Johannesburg South Africa

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Background: A variety of techniques are used to localise breast cancers prior to breast surgery. One such technique involves the placement of a magnetic seed (Magseed®). Studies to date have assessed the safety, usefulness; and retrieval ease of these devices.

The aim of the study was to conduct a review of Magseed® placement and ease and efficacy of retrieval across varying depths within the breast. Of interest when assessing the demographics of the average South African woman's breast size it is larger in comparison to European breast sizes (~1500 mm in Africa and ~327 mm in Europe).

This study looks at the Magseed® placement data from one radiology unit in a multi-disciplinary centre consisting of 4 radiology units over a 6 month period which sees an average of 450 newly diagnosed breast cancer patients per year and places an average of 340 Magseeds® per 6 month period.

Material and Methods: The seed used and analysed in this study is constructed of medical grade stainless steel, is transiently magnetisable, 1 × 5 mm in size and can be implanted long-term in any soft tissue.

The seeds were placed both under ultrasound guidance and stereotactically without complications. Measurements of distances from the nearest perpendicular skin surface were provided by the radiologist.

Post placement ease of localisation and retrieval of the magnetic markers in the specimen was confirmed with a magnetometer (Sentimag® probe). Further verification was achieved by intraoperative radiology (Biovision®) and intraoperative pathology.

Results: The summative results of our investigation are presented in the table below.

Table 1 Summative presentation

N patients	N seeds	Min depth/mm	Max depth/mm	Median depth/mm	Average depth/mm
45	50	8.33	87.00	37.00	37.80

Conclusion: Data collection confirmed that magnetic marker placement and retrieval is possible across a wide range of depths in South African women without complications. Ease of transcutaneous localisation with a 100% retrieval rate was confirmed. In all cases clear margins were achieved with aid from audio and count from Sentimag® probe; intraoperative radiology and intraoperative pathology.

No conflict of interest.

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Population trends in lobular carcinoma of the breast: The Ontario experience

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Introduction: Lobular breast cancer is less common that ductal carcinoma, and can be more difficult to diagnose by both physical examination and mammography. Previous studies have shown a general increase in lobular breast cancer rates over the 1980s-1990s, however this was during a time when the use of combined hormone replacement therapy (CHRT) – a known risk factor for breast cancer – was increased. As CHRT use has declined since the mid 2000s, this study endeavoured to evaluate current trends in the incidence of invasive lobular carcinoma (ILC) in women diagnosed with breast cancer, and to describe the 5-, 10-, and 15-year survival probabilities for women diagnosed with ILC in Ontario.

Methods: This retrospective cohort analysis included all women aged 18 and older diagnosed with breast cancer between January 1991 and December 2015. Health administrative data from the Institute for Clinical Evaluative Sciences (ICES) and the Ontario Cancer Registry was used to identify all breast cancer cases. Age adjusted incidence rates were plotted by year of diagnosis, and adjusted to the 2011 female Ontario population. Crude proportions were plotted by year of diagnosis for stage and hormone receptor status. Kaplan-Meier Survival curves were generated to determine the 5-, 10-, 15-year survival probabilities for ILC and invasive ductal carcinoma (IDC).

Results: From 1991 to 2015 there were 194,065 cases of breast cancer in Ontario, Canada, including 28,561 cases (14.7%) of ILC. In 1991, ILC comprised 10.7% of breast cancer cases, compared to 15.9% in 2015. The age-adjusted incidence rate of breast cancer increased 1.04-fold from 1991 to 2015 (168/100,000 to 175/100,000). In comparison, ILC incidence rates increased 1.53-fold (86/1000 to 132/1000), and rates increased across all age groups. All cases of bilateral breast cancer diagnosed from 2010 to 2015 in Ontario were of lobular origin. The proportion of Stage 1 ILC decreased

(39% to 34%) from 2007 to 2015, while the proportion of Stage 2–4 ILC increased (34.8 to 38.9%; 14.6 to 16.3%; 3.9 to 5.7%). The 5-, 10-, and 15-year survival probabilities for women diagnosed with ILC from 1991 to 2010 were 82.7% (95% CI 82.2–83.2), 65.3% (95% CI 64.6–66.0), and 50.2% (95% CI 49.4–51.1) respectively.

Conclusions: This study contains the largest population dataset of lobular breast cancer evaluated to date. While total breast cancer incidence rates in Ontario have remained largely unchanged between 1991 and 2015, invasive lobular carcinoma incidence rates continue to increase steadily. When stratifying by stage at diagnosis, there appears to be a general trend towards the diagnosis of ILC at later stages of disease. These trends highlight the ongoing diagnostic and treatment challenge ILC presents for clinicians today.

No conflict of interest.

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Short-term outcome and complications rate after immediate breast reconstruction with implants and acellular dermis

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Background: Skin-sparing mastectomy (SSM) and nipple-sparing mastectomy (NSM) followed by immediate reconstruction with implants have become populated methods in the field of surgery for breast cancer (BC). In postmastectomy breast reconstruction acellular dermal matrices are used for tissue support, implant positioning, rapid revascularization and aesthetic results. The aim of this study was to analyze short term outcome and complication rates in patients undergoing mastectomy followed by immediate implant reconstruction surgery for BC or prophylactic surgery in case of family predisposition with implants and acellular dermal Matrices.

Material and Methods: We assessed indication, peri- and postoperative results in 104 patients undergoing immediate postmastectomy breast reconstruction with implants and acellular dermal matrices between 2012 and 2016 for for DICS, BC or prophylactic surgery in case of family predisposition.

Results: 104 patients with a total number of 135 breast reconstructions were included in this study. In 71.9% (n = 97) of cases the operation was performed for breast cancer, in 28.1% (n = 38) prophylactic breast reconstruction was performed for positive family breast cancer history. In 65% (n = 80) of cases NSM was performed, in 35% (n = 53) SSM, respectively. The NAC could be preserved in 80.0% (n = 108) of cases while it had to be removed in 20.0% (n = 27) of cases. The most common complications were haematoma (12%), necrosis (7%), and wound infection (13%). Reoperations occurred for various reasons; 16% (n = 22) of cases reoperation had to be performed for wound healing issues (necrectomy), 12% were reoperated for haematoma. In 1.7% (n = 2) of cases reoperation had to be performed for residual cancer, in 5.8% (n = 7) of cases nipples were tattooed after NAC removal. Out of the total study population only 5% (n = 7) had a complete loss of implant.

Conclusions: Our results are consistent with previously published data. The most common complications are haematoma, necrosis, and wound infection. Patients considering NSM/SSM and immediate reconstruction should be informed about the moderate risks for complications.

No conflict of interest.

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The enduring rise of the contralateral prophylactic mastectomy: Population trends in Ontario, Canada

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Introduction: The use of contralateral prophylactic mastectomy (CPM) continues to grow despite the absence of evidence supporting a survival benefit. The objectives of this study were to, 1) describe the trends in the rates of unilateral and bilateral mastectomy in women diagnosed with unilateral breast cancer (UBC) in Ontario, Canada from 1991 to 2013, and 2) describe the factors associated with undergoing unilateral versus bilateral mastectomy to treat UBC.

Methods: This retrospective cohort analysis included all women aged 18 and older diagnosed with UBC between January 1991 and December 2013. Health administrative data from the Institute for Clinical Evaluative Sciences (ICES), the Ontario Cancer Registry, and the Discharge Abstract Database (DAD) was used to identify all breast cancer and mastectomy cases. Clinically significant covariates considered to be potentially associated with undergoing bilateral over unilateral mastectomy were age, income quintile, Charlson Comorbidity Index (CCI), community size, receptor status, tumour histology, location of hospital, teaching vs non-teaching hospital, availability of reconstruction, hospital local health integration network (LHIN), and year of diagnosis. The age adjusted rates of mastectomies were plotted over time, and all years were standardized to the 2011 female Ontario population. Univariable and multivariable analyses were completed with SAS 9.4.

Results: From 1991 to 2013 there were 172,165 cases of breast cancer diagnosed and 64,886 mastectomies (37.7%) performed in Ontario. 13.6% of the mastectomies were bilateral (8832 cases). Overall the rate of mastectomies is decreasing (43.9% to 33.7%), but the rate of bilateral mastectomies is increasing (4% to 25%). The rate of bilateral mastectomies is increasing across all age groups except for those aged 70 and older (OR 0.16, 95% CI 0.13–0.19). Those who received a bilateral mastectomy were younger (52.03 ± 12.36 years of age), had a higher income quintile (Q5 26.4%), had less comorbidities (94.4% CCI = 0), and had early stage disease (18.8% stage 1, 22.6% Stage 2) compared to those who received a unilateral mastectomy. On multivariable analysis, age, income quintile, CCI, community size, stage, cancer histology, availability of reconstruction and hospital type were associated with increased odds of a bilateral mastectomy.

Conclusions: During our study period, the rate of bilateral mastectomies increased more than 6-fold among those undergoing mastectomies for unilateral breast cancer. This is despite overwhelming evidence suggesting limited or no survival benefit. This is the largest population study of breast cancer patients in Canada, a country that appears to follow the global trend for rising CPM.

No conflict of interest.

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Psychosocial outcomes following contralateral prophylactic mastectomy in women with unilateral, nonhereditary breast cancer

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Background: Rates of contralateral prophylactic mastectomy (CPM) continue to rise in average-risk women with unilateral breast cancer. We previously reported that women who opt for CPM have decreased preoperative levels of breast satisfaction and dispositional optimism. Here, we aim to characterize how psychosocial functioning changes after surgery in average-risk women with unilateral breast cancer.

Methods: Women with a first diagnosis of unilateral, nonhereditary breast cancer were recruited at University Health Network in Toronto, Canada between 2014 and 2017. Patients completed demographic and validated psychosocial questionnaires that assessed breast satisfaction and quality of life (Breast-Q), cancer-related distress (Impact of Event Scale), and anxiety and depression (Hospital Anxiety & Depression Scale) at 6 and 12 months after surgery. Outcomes were assessed between CPM and non-CPM groups with the x^2 test or student t-test. P values < 0.05 were considered statistically significant.

Results: 506 patients were enrolled in the study, with 109 opting for CPM (21.5%).

At 6- and 12-months after surgery, there were no differences in scores across all psychosocial measures evaluated between CPM and non-CPM patients (Table 1). In particular, the significant differences in breast satisfaction and chest physical well-being seen pre-operatively (previously published) were no longer seen following surgery, due to a decrease in psychosocial scores in the non-CPM group.

Table 1

Psychosocial Measure	Time Point	CPM (n = 109)	Non-CPM (n = 397)	*P* values
Mean (SD)				
Breast Satisfaction	6 months	57.5 (19.6)	62.3 (22.9)	0.15
	12 months	60.9 (19.4)	63.7 (21.7)	0.29
Psychosocial well-being	6 months	67.8 (22.6)	69.2 (21.2)	0.67
	12 months	70.9 (22.8)	73.6 (21.4)	0.31
Chest physical well-being	6 months	66.7 (16.9)	68.7 (16.5)	0.42
	12 months	73.6 (16.4)	71.1 (17.0)	0.23
Sexual well-being	6 months	48.4 (26.8)	47.5 (22.1)	0.80
	12 months	49.6 (23.5)	48.1 (25.5)	0.64
Cancer-related distress – total distress	6 months	20.8 (17.3)	20.4 (16.6)	0.82
	12 months	17.9 (17.1)	19.2 (17.5)	0.55
Cancer-related distress – intrusive symptoms	6 months	9.8 (8.5)	9.3 (8.4)	0.60
	12 months	8.5 (8.4)	8.6 (8.4)	0.89
Cancer-related distress – avoidance symptoms	6 months	11.0 (10.0)	11.1 (9.56)	0.94
	12 months	9.5 (10.0)	10.6 (10.2)	0.36
Anxiety	6 months	6.7 (4.7)	6.2 (4.3)	0.35
	12 months	6.3 (5.1)	5.7 (4.1)	0.54
Depression	6 months	4.1 (4.1)	3.9 (3.7)	0.63
	12 months	3.4 (3.2)	3.4 (3.6)	0.89

Conclusion: In average-risk women with unilateral breast cancer who opt for CPM, there is no difference in psychosocial scores at 6- and 12-months after surgery compared to women who do not undergo CPM. While CPM did not improve body image and psychosocial functioning following surgery per se, we observed a decrease in breast satisfaction amongst women who did not choose CPM. This emerging data may be used to further facilitate decision-making regarding CPM.

No conflict of interest.

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Outcomes of breast cancer patients with nodal micrometastasis treated with sentinel lymph node biopsy versus axillary lymph node dissection

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Background: Sentinel lymph node biopsy (SLNB) has become standard of care as a staging procedure in patients with early stage breast cancer. Patients with nodal micrometastasis (N1mi) on SLNB are likely to have low nodal disease burden. Therefore, in this retrospective study we aim to review the outcome of our patients with pN1mi treated with SLNB versus axillary lymph node dissection (ALND).

Material and Methods: We identified patients with newly-diagnosed, non-metastatic pN1mi breast cancer patients, treated with either lumpectomy or mastectomy in our institutions from 1998–2018. Clinicopathologic factors were evaluated. Axillary recurrence rate (ARR), disease-free survival (DFS) and overall survival (OS) were determined.

Results: 413 patients with pN1mi disease were analysed. Median age at diagnosis is 53 (range 27–92) years, 398 (96.4%) patients had primary tumor size up to 5 cm (median 2.2 cm, range 0.06–8.5), with majority of patients (69.7%) underwent mastectomy, expressed estrogen receptor (83.5%) and had negative HER2 status (75.1%). 161 (39%) patients underwent SLNB only, while 252 (61%) had ALND. Adjuvant radiation (RT) was given to 203 (49.2%) patients, and 389 (94.2%) received adjuvant systemic treatment. At a median follow-up of 62 months, the overall ARR was 1.8% (n = 3) in the SLNB only group, vs 1% (n = 4) in ALND group (p = 0.30). There was no significant association between ARR and receipt of RT (p = 0.12) and type of breast surgery (p = 1). DFS and OS were not significantly different among patients who had SLNB alone versus ALND (p = 0.35 and p = 0.45, respectively). Among 106 patients who had mastectomy and SLNB alone, DFS and OS were not significantly different between those who had RT versus no RT (p = 0.15 and p = 0.12, respectively).

Conclusions: Our results suggest that patients with tumor up to 5 cm, luminal A feature, and pN1mi disease detected on SLNB can be safely spared from ALND and its associated morbidities without significant effect on survival, even following mastectomy. In addition, RT is not routinely indicated in patients with mastectomy and SLNB only.

No conflict of interest.

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SentiDose Trial: Optimizing dose and injection timing in magnetic sentinel node detection for early breast cancer

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Background: Superparamagnetic iron oxide nanoparticles (SPIO) is a sentinel node tracer with comparable performance to isotope and blue dye. Most studies have evaluated a 2 ml dose, with or without dilution, injected periareolarly on the day of the operation. This has been associated with the brown skin staining in 40%. Aim of the SentiDose trial was to investigate the performance of smaller doses in a different timeframe (1.5 ml periareolarly on the operation day vs 1 ml periareolarly or peritumorally 1–7 days preoperatively). A background mapping with Tc and blue dye was performed for assessment of concordance.

Method: In all, 330 patients were recruited from 6 sites in Sweden, divided in two cohorts, as described above. Patients that were injected on operation day received a 5-minute massage to allow for tracer migration, and were injected at least 20 minutes before the operation. Results are compared on a patient-level to the SentiMag Nordic trial.

Results: Demographics and outcomes are illustrated in Table 1. Detection for the 1.0 ml cohort was 100%, comparable to the 1.5 ml cohort (97.5%) and to the Nordic trial data (97.6%). Preoperative injection identified more magnetic SLNs (2.15 vs 1.85 vs. 1.83, p = 0.001) with much higher counts that were always brown, thus facilitating dissection. Comparing SPIO to the isotope, the results were as follows: Nordic 97.6 vs 97.1%, SentiDose 1.5 ml 97.5 vs 98.2% and SentiDose 1.0 ml 100 vs 94.9%. Discoloration rates respectively were 38.2, 14.3 and 8.8% (p = 0.002) with breast conservation and peritumoral injection being the strongest predictors for no skin staining on regression analysis.

	Nordic SentiMag Trial (n = 206)	SentiDose 1 (n = 163)	SentiDose 2 (n = 159)	p-value
Age (yrs)	61.7	64.3	62.5	0.096
BMI (kg/m^2)	27.9	27.2	26.5	0.570
Size (mm)	19.1	20.0	19.7	0.826
Type of Surgery BCS	154 (74.8%)	130 (79.8%)	134 (84.3%)	0.266
Mx 52 (25.2%)	33 (20.2%)	25 (15.7%)		
SPIO Detection Rate	97.6%	97.5%	100%	0.139
SPIO-Tc Concordance	98%	98.8%	100%	0.424
Mean SPIO detected SN	1.83	1.85	2.16	0.005
Nodal detection rate	93.5%	85.8%	97.2%	0.001
Metastasis Rate	24.8%	17.2%	17.6%	0.121
SPIO nodal rate in malignancy	91.2%	81.6%		0.216
Brown skin staining	38.2%	14.3%	8.8%	0.001

Conclusion: The peritumoral injection of 1.0 ml SPIO 1 to 7 days preoperatively results in successful SLN detection, harvests adequate sentinel nodes and has a low skin staining rate, providing effectivity and flexibility. On the other hand, the perioperative periareolar injection of 1.5 ml SPIO provides adequate rates for SLN detection, combined with removal of less SLNs. The refinement of the magnetic technique provides the niche for isotope free SLN detection in patients with breast cancer.

No conflict of interest.

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Symptomatic presentation and involved margins lead to Ductal Cancer In Situ recurrence

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Background: Around 20% of UK DCIS presents symptomatically but management does not vary from screen detected DCIS. Involved margins following wide local excision (WLE) and mastectomy for DCIS are associated with an increased risk of local recurrence.

This study aimed to assess the factors causing local recurrence rates after surgery for DCIS in a large UK population.

Material and Methods: Overall, 430 patients who were diagnosed with DCIS, and underwent wide local excision or mastectomy in four breast units across Greater Manchester between 2011–13, were included in the study. Clinical and pathological factors including the grade, margin status, mode of presentation, tumour size and local recurrence events were recorded. Cox-proportional hazard regression was used to identify factors predicting recurrence in a multivariate analysis.

Results: The mean age of DCIS patients was 59 years and 91 (21.2%) presented symptomatically whilst the remaining 339 (78.8%) DCIS were screen detected. Overall local recurrence rate was 4.7% (0–28.6%). In 269 patients undergoing wide local excision, local recurrence was 5.6% (n = 15) compared to 3.1% (5) in the 161 mastectomy patients. Clear margins were obtained in 277 patients (68.1%) and involved (<1 mm) in 121 (28.1%). Age (symptomatic 57 years), grade and tumour size (28 mm symptomatic; 26 mm screening) did not differ with mode of presentation.

A symptomatic presentation of DCIS (HR 3.74 (1.37–10.24) and involved margins (<1 mm) following surgery (HR 2.57 (1.09–6.05)) predicted local recurrence. Other factors were not predictive (Table 1).

Table 1 Multivariate analysis of factors predicting DCIS local recurrence

	Local Recurrence	p-value
Clear margins vs margins less than 1 mm	2.74 (1.16–6.45)	0.022
Screening vs Symptomatic	4.22 (1.58–11.25)	0.004
WLE vs Mastectomy	0.95 (0.34–2.68)	0.922
Grade 1 vs Grade 3	1.35 (0.29–6.37)	0.704
Size	0.99 (0.97–1.01)	0.517

Conclusion: In DCIS, symptomatic presentation and margin involvement in DCIS predict local recurrence. With margin involvement being a modifiable factor, it is imperative that all margins are cleared as essential surgical management to prevent local recurrence.

No conflict of interest.

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Magseed localisation for loco-regional breast and lymph node recurrences. Placement prior to chemotherapy allows focused removal of the initially diseased tissue

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Background: Loco-regional recurrences: defined as a breast cancer diagnosis on core biopsy in patients having previous same-side breast cancer either in the breast or regional lymph nodes. The setting of no systemic metastases provides oncology dilemmas as to the order and type of treatment. Multi-disciplinary meeting decisions may suggest chemotherapy prior to surgery (subtypes: HER 2; triple neg; high Ki 67% luminal B). Prior to chemotherapy, localisation of the diseased tissue is important to ensure retrieval.

Magseed® is an inducible magnetic seed that received clearance for breast lesion localisation by the U.S. Food and Drug Administration in 2016. Magseed® is induced to become a magnet (and is localisable) when used in conjunction with a detector. It is composed of stainless steel and is used for preoperative localisation of non-palpable breast lesions and can be placed weeks or months before surgery.

The aim of this study was to assess accurate placement, localisation and retrieval of a Magseed® from a radiologically suspicious loco-regional recurrence in patients requiring chemotherapy prior to surgery.

Methods: Patients with loco-regional recurrence (axillary; infraclavicular; supraclavicular; breast) that had been assessed in the multidisciplinary meeting as requiring chemotherapy, as well as being potential candidates for surgery post chemotherapy, were referred for placement of a Magseed® prior to commencing or during the course of treatment.

The seed was placed by a senior radiologist in the unit. Ten patients have currently completed chemotherapy and surgery. Two patients had more than one Magseed® placed. In one patient, 2 axillary seeds were placed. One patient had axillary and infraclavicular seeds placed.

Results: Seed localisation with the Sentimag® probe was successful in all cases. Retrieval was confirmed with these readings, as well as radiological confirmation of the seed within the node post excision.

Across these patients we found a 100% placement, all seeds were found and localised with the aid of the sensor. The retrieval rate however was recorded at 93%. In one case the lymph node had undergone fibrosis, the seed was found next to the lymph node, hence resulting in the retrieval rate of 13/14 seeds in tissue.

Table 1 Seed localisation, placement to surgery time and retrieval rate

N seeds placed	1	1	1	1	1	1	2	2	2	2
Time from seed placement to surgery in days	249	90	121	240	215	116	155	148	145	106
Localisation Y/N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y

Conclusion: Magseed® is successful in localising and retrieving loco-regional recurrences in patients requiring surgery post chemotherapy. Localisation prior to or during chemotherapy is accurate. Retrieval is possible due to high recordings on the sensor in all cases. Magseed® thus provides the treating clinician with an alternative to conventional radiological markers with the benefit of single placement to retrieval methodology.

No conflict of interest.

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Innovative magnetic tracers for sentinel node detection in primary breast cancer surgery and after neoadjuvant therapy

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Background: A novel method of marking and detecting sentinel nodes has been tested. 2 ml suspension of superparamagnetic iron oxide particles (SPIONs) Magtrace® (formerly Sienna+® 5 ml suspension) was used to mark the sentinel nodes (SLNs), and a Sentimag® probe was used to detect the SLNs during surgery. The aim of our retrospective analysis was to assess the feasibility and SLNs detection rate using SPIONs.

Methods: From April to August 2019 we recruited a total of 137 patients with biopsy verified invasive breast cancer or high-grade DCIS. Lumpectomy or mastectomy with SLN biopsy were performed in all patients. The Magtrace® 2 ml suspension was applied within 24 hours before surgery. Sentimag® probe was used to detect the SLNs during surgery. Before starting to use Magtrace®, we applied Sienna+® to approximately 600 breast cancer patients in the period from September 2017 until April 2019.

Results: These are the results from our unicentric Magtrace® retrospective analysis. Average age was 60.1 years. 3 patients (2.1%) tested positive for pathogenic genetic mutations at the time of surgery (1 patient BRCA 2 positive, 2 patients CHEK-2 mutations). Lumpectomy was performed in 97 patients (71%), and mastectomy was performed in 40 patients (29%). Final pathology reports confirmed invasive carcinoma in 89.8% of patients, 63.5% with luminal A, 12.4% with luminal B, 6% with TNBC, 4% were HER 2 positive. 10.2% patients had high-grade DCIS. 29 patients (21%) received neoadjuvant therapy. 18 patients (13%) with biopsy proven metastases to the axillary nodes before the start of treatment were indicated for primary axillary lymph nodes dissection. SLN dissection with clinically negative axillary status (with or without neoadjuvant therapy) was performed in 119 patients (87%). 16 patients (11.6%) underwent secondary axillary lymph node dissection after SLNs showed macrometastases. Using the Sentimag® probe, the SLN detection rate of 99.3% has been achieved for the Magtrace®. The average number of SLNs retrieved per patient was 3.52 in the group of patients after neoadjuvant therapy. The average number of SLNs retrieved in the group of patients with primary surgery was 2.33. The average number of sentinel nodes retrieved with Sienna+® was 1.9 per patient.

Conclusion: Current research shows non-inferiority of SPIONs tracer compared to conventional techniques used for SLN detection. Magtrace® is preferred to Sienna+® due to smaller volume applied. A similar SLN detection rate of over 99% was achieved with both Magtrace® and Sienna+®. A higher number of SLN identified was observed in patients after neoadjuvant therapy. Magtrace® showed non-inferiority in terms of SLN detection rate and average number of SLN retrieved when compared to the previously used tracer (Sienna+®). More prospective trials are required to confirm our findings.

No conflict of interest.

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Did the BOOG 2013–08, which examines the value of omission of the sentinel lymph node in cT1-2 breast cancer treated with BCT, induce a change in axillary staging and treatment?

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Background: The BOOG 2013-08 is a Dutch multicenter randomized controlled trial, which investigates whether the sentinel lymph node biopsy (SLNB) can be safely omitted in clinically node negative T1-2 breast cancer patients undergoing breast conserving therapy (lumpectomy followed by radiotherapy). Not all eligible patients visiting BOOG 2013-08 active hospitals participate. Patients informed on the study, decline for various reasons. Sometimes because they want to know the SLNB outcome or they prefer one of both study arms and therefore are not willing to be randomized. Sometimes the doctor is in favor of one of both study arms. This study investigates the influence of the BOOG 13-08 study on axillary staging and treatment, in patients eligible for the BOOG 2013-08 study in the Netherlands in general as well as in hospitals participating in the BOOG 2013-08 study.

Methods: A database was assembled by the Netherlands Cancer Registry (NCR) of all cT1-2N0M0 unilateral breast cancer treated with breast conserving therapy in the Netherlands from 2015–2017. Thereafter the in- and exclusion criteria of the BOOG 2013-08 study were applied. First, we aim to evaluate the percentage of patients eligible for inclusion in the BOOG 2013-08 study in the Netherlands in general, as well as in hospitals participating in the BOOG 13-08 study. Thereafter we examined the percentage of BOOG 2013-08 patients in whom the SLNB was omitted in the Netherlands in general, as well as in hospitals participating in the BOOG 2013-08 study.

Results: The database from the NCR included all newly diagnosed cT1-2N0M0 breast cancer patients from 2015–2017 in the Netherlands treated with breast-conserving therapy and resulted in 19525 patients. Of these 19525, 2047 were diagnosed in BOOG 2013-08 active hospitals and 17478 in non BOOG 2013-08 active hospitals. In both the active and non-active hospitals all patients met the BOOG 13-08 inclusion criteria of whom 434(%) patients were included in the BOOG 2013-08 study. Of the 2047 newly diagnosed patients in the active hospitals, the SLNB was omitted in 257 (13.6% of 2047) patients of whom 217 participated in the BOOG 2013-08 study and 43 (2.3% of 1867) outside the study. In the non-active hospitals the SLNB was omitted in 98 (0.6% of 17478) patients. Altogether, the SLNB was omitted in 355 (1.8%) patients. Of these patients in whom the SLNB was omitted, 115 patients (30.7%) represented non BOOG 2013-08 active hospitals versus the remaining 260 patients (69.3%) represented the BOOG 13-08 active hospitals.

Conclusion: There is a rising number of patients in whom the SLNB is omitted mostly due to the inclusions of the BOOG 2013-08 study in participating hospitals. This suggests that if doctors and patients are informed about the study, they can consider it as a valid alternative and chances for omission of the SLNB continue to increase.

No conflict of interest.

194 Poster

Endofascial axillary dissection – a novel method to reduce seroma formation

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Background: The pathogenesis of seroma formation following axillary dissection is poorly understood. The greater the surgical disruption of the axilla, the higher the incidence of seroma and lymphedema. In view of the disease burden of breast cancer and also to refine the fast track approach to treatment; we looked at a method of dissection of the axilla which might reduce the seroma incidence and quantity thereby allowing early drain removal and reduced morbidity.

Materials and Methods: Endofascial axillary dissection is a novel technique of axillary lymphadenectomy initially described by King and Meredith from The Breast Centre Bowen Hospital, Wellington, New Zealand. In this method the anterior laminae of the clavipectoral fascia (CPF) are preserved and reconstituted. It reduces the dead space, restores pressure gradients and facilitates collateralisation to improve lymphatic flow. Between July 2018 and June 2019, 36 patients with histologically proven carcinoma breastundergoing breast conservation surgery underwent axillary dissection by the endofascial technique. These patients were operated by a single surgeon and compared with an equal number ofpatients who underwent breast conservation with routine axillary dissection before the study period (historical controls). Patients were discharged on first post operative day and the axillary drain output was monitored on outpatient basis. Drains were removed when the output was less than 40 ml for 2 consecutive days.

Results: The mean number of days for which the axillary drain was kept in situ was significantly higher for conventional axillary dissection as compared to endofascial dissection (14 v 8 days p 0.003). The mean total amount of axillary drain output for the period for which the drain was in place was also significantly different between the two groups (1230 ml v 690 ml p 0.04). There was no significant difference between the mean number of nodes harvested (17.2 v 16.4 p = 1). There was no significant differences between wound complications and the requirement of seroma aspiration after drain removal between the two groups.

Conclusion: Endofascial method of axillary dissection is a very effective method in reducing the axillary seroma, leading to early drain removal; thereby reducing the operative morbidity, without compromising the oncologic safety in breast cancer patients.

No conflict of interest.

195 Poster

How many sentinel lymph nodes in addition to the clipped node are needed to accurately stage the axilla after neoadjuvant treatment in breast cancer?

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Background: Identifying residual disease in the axilla after neoadjuvant treatment (NAT) is important to select patient for sparing an axillary node dissection (ALND). Controversy exists on the optimal number of sentinel nodes (SLNs) needed to excise along with the axillary clipped node. The aim of the study is to assess the false negative rates (FNR) in the SLN after NAT and to refine the axillary surgery using intraoperative ultrasound (IOUS) for excising axillary clipped nodes as a part of axillary staging after NAT.

Methods: Patients with clinically biopsy proven positive axillary node and a clip placed in the positive node who underwent NAT were eligible in this prospective study. After NAT, IOUS-guided excision of the US visible clipped node along with SLNB (dual tracer) was performed. ALND was completed in the majority of patients as part of the initial study.

Results: One hundred and fifty-four patients were included. Of this, 36 (23%) patients achieved a pathologic complete response (pCR), with Her2 and TN tumors having the highest pCR ($p < 0.001$). Axillary pCR was found in 56 patients (36%), with higher rates in Her2 positive and TN patients (88% and 76% respectively) ($p = 0.001$).

After NAT, 12 patients (7.8%) had a direct ALND performed for suspicious or biopsy proven axillary nodes before surgery. The clipped node was successfully removed by IOUS-guided excision in 135 patients (95%). Of 51 (37.8%) patients with axillary pCR, 12(21%) did not undergo an ALND. The SLN was the clipped node in 98 (73%) patients. False negative rate (FNR) with one SLN excised and the clip node, with 2 SLNs and the clip node excised and with 3 SLNs and the clip node excised were 8.3%, 4.3% and 2.3% respectively. In patients with axillary residual disease, mean number of positive nodes was 2.6 in luminal B HER2– tumors, 3.2 nodes in luminal A, 2.9 in luminal HER2+, 1 in HER2 no luminal, and 1.5 in triple negative ($p = 0.022$).

Higher rates of pCR were achieved in those patients who received carboplatin-taxol + Adrymicin/Cyclofosfamide (60%), and double agent antiHER2 therapy associated or not to chemotherapy (68%).

After a median follow-up of 19 months (range 10–31 months), 6 patients (3.8%) developed metastasis. Of this, 2 (33%) had also a regional recurrence.

Both patients had residual disease in the axilla and have had an ALND. Five year disease free and overall survival was 82% and 96% respectively.

Conclusions: Excising at least 2 SLNs along with the clip node results in <5% of FNR after NAT. Residual disease after NAT remains a prognostic factor so refining technical issues are important to improve outcomes. The use of IOUS-guided excision of the axillary clipped node in combination with SLN after NAT is a feasible, safe and accurate technique.

No conflict of interest.

196 Poster

Risk of contralateral breast cancer and ovarian cancer in BRCA1 founder mutation (5382insC or 4154delA) carriers with primary breast cancer

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Background: Current scientific evidence suggests that BRCA1/2 mutant phenotypic characteristics depend on specific site of mutation in gene. The objective of this study is to estimate the risk of new cancer events, (metachronous contralateral breast cancer (CBC) and ovarian cancer (OC)) in BRCA1 mutation carriers with primary breast cancer in population of Latvia, dominated by two founder mutation types. Secondary goal is to verify the risk reduction associated with contralateral prophylactic mastectomy (CPM) and bilateral prophylactic salpingo-ophorectomy (BPSO) procedures.

Patients and Methods: In this retrospective observational cohort study we selected women with BRCA1 gene mutation (5382insC or 4154delA) who had treatment for primary unilateral breast cancer in stage 1 to 3. Information regarding BRCA1 mutation was obtained from RSU Oncology Institute database (Latvia). Primary study endpoints were CBC and OC. Data about new cancer events was obtained from national oncology register (*eveseliba.gov.lv*). Information about CPM procedures was obtained from *Pauls Stradins Hospital* database. Risk of cancer events was calculated using Kaplan-Meier and Log-rank type analysis.

Results: Between February 1980 and September 2019, 178 patients were enrolled in study. Mean age at primary breast cancer diagnosis was 46.5 (±1.7, 95% CI) years. Total of 128 (71.9%) subjects had mutation "5382insC" and 50 (28.1%) subjects had mutation "4157delA" At median follow up of 11.9 (IQR 10.1–13.6) years, 27 (15.2%) subjects developed CBC. Mean time to CBC was 10.7(±3.2, 95% CI) years. Cumulative risk of CBC at 10 years was 21.5%. Total of 25 (14.0%) subjects developed ovarian cancer at mean age of 55.2 (±3.9, 95% CI) years. 10 years cumulative risk for developing ovarian cancer was 15.6%. CPM procedure was performed in 31 cases, mostly synchronous with primary cancer operation. Mean follow-up of this subgroup was 3.8 (±1.0, 95% CI) years. None of patients who had CPM developed CBC. BPSO was performed in 40 subjects, with mean follow-up time of 8.2 (±2.7, 95%CI) years, there were no cases of ovarian cancer in this subgroup. In subgroup without CPM (N = 147), 10 years cumulative risk of CBC was 25.6% and in subgroup without BPSO (N = 138), 10 year cumulative risk of OC was 19.7% In multivariate analysis of CBC/OC risk, there was no significant statistical difference between two types of mutations.

Conclusion: Carriers of BRCA1 mutations 5382insC or 4157delA and primary breast cancer have high risk of CBC and OC. Prophylactic procedures should be strongly encouraged in this group. The risk of CBC and OC in this BRCA1 founder population is relatively comparable to other non-founder/mixed BRCA1 populations.

No conflict of interest.

198 Poster

The role of cryoablation in patients with metastatic breast cancer at the time of presentation

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Background: At the moment of their initial diagnosis, 5–15% of women with breast cancer have distant metastatic disease, with important differences in incidence among low- and high-income countries. Removal of the primary tumor in those situations has been usually used to treat local complications such as bleeding, ulceration, infection or pain, while it has been historically avoided in patients with asymptomatic breast cancer. The aim of this study is to evaluate the role of CT-guided cryoablation in patients with metastatic breast cancer.

Patients and Methods: We evaluated data of patients with metastatic breast cancer at the time of the presentation treated with CT-guided cryoablation of the primary tumor between 2010 and 2019. All patient were preoperatively and postoperatively evaluated with breast MRI to assess the extent of tumor necrosis. Redo cryoablation was performed in case of incomplete ablation.

Results: Fifty-one patients, with a mean age of 61 ± 13 years, receiving CT-guided cryoablation were evaluated. The most frequent site of distant metastases was bone, followed by lung and liver. All procedures were carried out under conscious sedation and local anesthesia. Mean tumor size was 3.32 ± 1.5 cm. Forty-six patients (90.2%) had an invasive ductal carcinoma, while 5 (9.8%) had an invasive lobular carcinoma. Seven patients had multicentric disease. Complete tumor necrosis was 88.9% and 100% at 2-month and 6-month follow-up respectively, due to the fact that 6 (11.7%) patients with tumor size larger than 3 cm required a redo cryoablation for incomplete necrosis. No patient developed major complications. Minor transient side effects, such as ecchymosis, oedema, and skin pigmentation occurred in 35 patients (68.6%). All patient were discharged the same day of the procedure. During a mean follow-up of 60 months (range 6–102), 9 patients (17.6%) experienced local recurrences that were treated with redo cryoablation.

Conclusions: Our results suggest that cryoablation of the primary tumor is safe and effective in the treatment of patients presenting with metastatic breast cancer. Further studies are needed to evaluate the possible effects of cryoablation on survival outcomes in this subgroup of patients.

No conflict of interest.

199 Poster

Direct or delayed oncoplastic reconstruction after wide local excision for breast cancer in breast conserving therapy: A single centre cohort study of 252 cases

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Background: Breast conserving surgery (BCS) is performed in >65% of Dutch breast cancer patients. Breast remodeling by reduction or level II tissue replacement after a wide local excision (WLE) results in better aesthetic outcomes and enables resection of larger tumor volumes. However, in case of tumor-positive resection margins requiring re-excision, the cosmetically successful reconstruction has to be dismantled. Compared to immediate reconstruction (IMR), delayed reconstruction (DR) allows for simultaneous re-excision. To date, no consensus exists on indications for this two-step approach. We performed an exploratory analysis of the patients in our institute.

Methods: Patients with invasive or in situ (DCIS) breast cancer who were treated with BCS and oncoplastic reconstruction from Jan. 2016 to Dec. 2018 were selected. Oncoplastic treatment was determined after multidisciplinary meetings and patient consultation. Pre-operatively known risk factors for tumor-positive resection margins (eg. DCIS, ILC, multifocality) were used to estimate the risk of positive margins, in which case DR was planned. Patients with IMR or DR were compared on patient-, tumor-, and treatment characteristics. Primary outcome was the rate of positive margins and secondary outcome was complication rate.

Results: Among 247 women, 252 oncoplastic reconstructions were performed. BCS indications were invasive ductal carcinoma (65%, IDC), DCIS (17%), lobular carcinoma (15%, ILC) and other type carcinomas (3%). Most tumors were hormone receptor+/HER2-negative (75%). Patients received neoadjuvant systemic treatment (NST) in 130/252 of cases (52%). After WLE, IMR was performed in 176/252 cases (70%) and DR in 76/252 cases (30%). Patients with DR were more likely to have larger tumors on MRI (OR 1.01, 95%CI: 1.01–1.03) and ILC or DCIS compared to IDC (OR 3.03, 95%CI: 1.37–6.72 and OR 7.94, 95%CI: 1.12–56.18) in multivariate analysis. There was no difference between the groups in tumor subtype, multifocality or NST. IMRs compared to DRs differed in mean weight of specimen (101 vs. 74 grams, p = 0.019) and reconstruction methods (tissue

reduction: 75% vs.46%, level II replacement: 26% vs. 51%, p < 0.000). Tumor margins were positive in 32/176 IMRs (18%) compared to 50/76 of DRs (66%), respectively (p < 0.000). There were 56/252 (22%) postoperative complications, consisting mostly of infections requiring antibiotic treatment (64%). The complication rate was higher in patients with DR compared to IMR (36% vs. 16%, p = 0.001). There was no difference, however, in the need for unplanned re-operation (8% vs. 4%).

Conclusion: Despite the higher risk of minor complications, DR allows re-excision in case of tumor-positive margins without dismantling the reconstruction. Multidisciplinary pre-operative risk assessment successfully selected cases with an increased risk of positive margins.

No conflict of interest.

200 Poster

Importance of intraoperatory surgical margin assessment for positive margin diagnosis in breast cancer-conserving surgery

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Background: Surgical margin status is an important prognostic factor. We studied the accuracy of our intraoperative specimen evaluation protocol as a positive margins diagnostic probe.

Methods: This retrospective study included breast invasive cancer diagnosed patients who underwent breast conserving surgery between 2004 and 2015. Patients who received neoadjuvant therapy and ipsilateral recurrences of tumors prior to 2004 were excluded.

Our margin management protocol began with the specimen palpation by the surgeon. Previously it had been oriented with clips. In non-palpable lesions, specimen radiography was performed to check the inclusion of the lesion. The specimen was inked, and just in infiltrating lesions, a macroscopic pathological assessment of surgical margins was carried out in the operative time. If in any of the post-extraction procedures the margin was considered to be close or affected by the tumor, the corresponding margin was intraoperatively re-excised. The margin was considered affected if disease (invasive or in situ) was found in contact with the inked margin.

Results: The study included 799 patients. In 312 patients the margin was considered affected or threatened, and underwent intraoperative re-excision. 123 of them (39.4% of re-excised samples) were confirmed to have initial positive margins on microscopic evaluation. Residual tumor was present in 81 of the 312 re-excised samples. In 18 cases a second surgical procedure was required to achieve a free margin. On the other hand, 487 samples were deemed to have clear initial margins and did not undergo intraoperative re-excision. A clear final margin status was subsequently confirmed in 459 of these patients (94.2%), avoiding a second procedure. 28 patients deemed to have clear margins intraoperatively, but needed a second operation due to final affected margin.

If the intraoperative assessment of the margin had not been carried out, the definitive affected margin rate would have been 18.9% (151 patients out of 799). Thanks to intraoperative re-excisions, definitive affected margin rate in infiltrating tumors was reduced from 18.9% to 5.7% (46 patients had a final affected margin: 28 from intraoperative free-margin group, and 18 from intraoperative compromised-margins group).

The sensitivity of the procedure was 0.81; the specificity 0.71; Positive predictive value 0.39; and negative predictive value (NPV) 0.94.

Conclusion: Our intraoperative margin assessment protocol reduces positive margin rate in infiltrating tumors from 18.9 to 5.7%. It offers a high NPV, allowing to select patients who will avoid a second surgery. Although it requires important economic and technical resources, the intraoperative macroscopic margin assessment reduces significantly second interventions, achieving more conservative, efficient and beneficial surgery for patients.

No conflict of interest.

201 Poster

Axillary staging with supine 18F-FDG PET/CT is useful in breast cancer patients undergoing tailored axillary treatment after neoadjuvant systemic therapy according to the MARI protocol

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Background: Staging in breast cancer patients can be performed with FDG-PET/CT in supine position. At the NKI, a prone position scan is added to the supine scan protocol to improve visualization of FDG-uptake in the breast. In clinically node-positive (cN+) patients with neoadjuvant systemic therapy (NST), the number of FDG-positive axillary lymph nodes (ALNs) on PET/CT pre-NST (cN < 4 or cN ≥ 4) in combination with the MARI procedure (Marking Axillary lymph nodes with Radioactive Iodine seeds) is used to tailor axillary treatment post-NST. It is unclear however whether the use of prone scanning compared to supine scanning affects the adjuvant axillary treatment strategy.

Methods: Patients with PET/CT in both supine and prone position from the 2014–2017 MARI cohort were selected. cN < 4 patients who have a tumor-negative MARI node post-NST receive no further axillary treatment and cN < 4 patients with a tumor-positive MARI receive axillary radiotherapy (ART), as well as cN4+ patients with a tumor-negative MARI. Axillary lymph node dissection (ALND) is performed in cN4+ patients with a tumor-positive MARI. Prone images were acquired one hour after administration of 180–240 MBq 18F-FDG using a mock-up coil. Subsequent supine PET/CT scan was performed with a low-dose CT scan. Prone and supine images were separately assessed (>7 day interval) by two experienced nuclear medicine physicians. Primary outcome was up- and downstaging (i.e., <4 or ≥4 FDG-ALNs), secondary outcomes were interobserver agreement and number of ALNs.

Results: 153/159 patients had both prone and supine FDG-PET/CT images. The interobserver agreement of the two reviewers on prone and supine scans was 86% (k = 0.67) and 92% (k = 0.80), respectively. The agreement between the reviewers and the initial assessor, who staged the patients based on both scans, was 87% for the prone scans (Fleiss k = 0.73, 95%CI: 0.64–0.82) and 83% for the supine scans (Fleiss K = 0.78, 95%CI: 0.69–0.86). Overall, assessment of prone scans compared to supine scans upstaged 18/153 (12%) patients to cN4+ and downstaged 8/153 (5%) patients to cN < 4. The mean number of ALNs assessed differed only for reviewer 2 (supine: 3.1 vs. prone: 3.6, P < 0.000), as did staging category (downstaged 3 patients, upstaged 14, p = 0.015). Of the downstaged patients, 4/8 (2.6% of 153) had a positive MARI node. Of the patients that were upstaged, 10/18 (6.5% of 153) had a positive MARI node. Thus, 2.6% of patients may be overtreated without a prone scan (ALND instead of ART) and 6.5% may be undertreated without a prone scan (ART only), according to the MARI protocol.

Conclusions: Axillary staging can be performed with FGD-PET/CT in both supine and prone position in cN+ breast cancer patients receiving tailored axillary treatment after NST according to the MARI protocol. However, undertreatment must be considered when only supine scan images are used.

No conflict of interest.

202 Poster

Blood group and save samples for elective breast surgery: An unnecessary cost?

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Introduction: Local and national guidelines on peri-operative blood test requesting requires all patients undergoing elective breast cancer surgery to have blood grouped, screened and saved as an part of a pre-operative assessment. Elective breast cancer surgery is usually a safe procedure with a low risk of major bleeding complications and a low blood transfusion. At our trust, most patients are routinely subject to two pre-operative group and save (G&S) samples at a cost of £10.69 per sample plus an estimated additional labour and disposables cost per sample of £17.296. This study aimed to provide an interim analyses of the first quarter of a planned 2 year analysis into our local peri-operative transfusion need and whether it warranted our current G&S policy.

Materials and Methods: We performed a retrospective review of all patients who underwent elective breast and axillary cancer surgery in our institution between 1st January 2019 and 1st April 2019. As a result, 107 consecutive elective breast cancer operations including mastectomies, wide local excisions, breast reconstruction and axillary procedures were identified for analysis. Patients were identified using HES Operative Procedure Codes. Transfusion department records were reviewed to see which patients had undergone pre-operative G&S or cross-match, and peri-operative transfusion.

Results: There were 107 procedures performed in 3 months. The majority of patients were female (84/107; 78%). The mean age was 57 (Median 57.5, Range 23–90). 12 patients were on anticoagulation. Of the 107 patients, 95 (88.7%) had blood sent for group-and-save. Of the total 107 patients identified, only 2 (1.8%) patients received a blood transfusion. An estimated total cost of G&S samples over the study period was £5,989.

Conclusions: Risk of requiring peri-operative transfusion at our institution is 1.8% for the study period. Estimated G&S sample cost is £23,956 extrapolated over 12 months. Although the applicability of this study is limited by sample size, this interim analysis suggests that modification of the preoperative assessment protocol and an "opt in" policy may reduce superfluous G&S samples and would lead to a substantial financial saving per annum. A further larger study is warranted to identify predictable risk factors for transfusion so as to introduce judicious use of pre-operative G&S.

No conflict of interest.

203 Poster

Realising true day-case breast surgery: A review of factors influencing same-day discharge (SDD)

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Introduction: Over the last decade elective breast cancer surgery has become less invasive and more amenable to day surgery with SDD. The British Association of Day Surgery recommends that 95% of Wide Local Excisions (WLE) and 50% of mastectomies are performed as zero-night-stay cases. The aim of this study was to establish our unit's performance for Same Day Discharge (SDD) and assessing factors affecting this.

Method: A retrospective analysis of 107 patients following elective breast cancer surgery (including axillary and reconstructive procedures) in a day-surgery unit was performed. Perioperative variables of 107 patients were analysed. Primary endpoints were: postoperative length of stay, rate of patients discharged after 24 h, and rate of those discharged on the same day. Secondary endpoints were rate of 30-day readmission. Planned overnight cases and emergency cases were excluded.

Results: Of the 107 cases included in this study, 85/107 (79%) had SDD with 22/107 (21%) failing SDD. Readmission within 30 days occurred in 2 cases. Analysing risk factors across SDD group and failed SDD group revealed that the following variables were significant in preventing SDD; prolonged operative time (76 minutes vs 43 minutes, $p < 0.01$), drain insertion ($p < 0.05$), Post operative Nausea & Vomiting ($p < 0.05$), BMI > 35 ($p < 0.05$) and positive smoking status ($p < 0.01$). Age greater than 65 although resulted in a number of patients failing SDD, did not reach significance ($p = 0.08$). There was insufficient data with regards to intra-operative anaesthetic regimen and analgesia used.

Conclusion: Day-case breast cancer surgery is with an acceptable rate of early patient discharge in our unit but there is considerable room for improvement. Potentially modifiable factors adversely affecting SDD include smoking, PONV, BMI and drain insertion. Therefore patient selection, stringent preoperative assessment with smoking cessation clinics, reduction in unnecessary drain insertion, pre-emptively allocating greater estimated operative time or scheduling complex cases earlier in the day in addition to a detailed assessment of intraoperative anaesthesia and analgesia may identify modifiable factors to aid SDD.

No conflict of interest.

204 Poster

Nipple sparing mastectomy (NSM) after surgical delay (SD) and prepectoral direct to implant (DTI) reconstruction with polyurethane prostheses: Preliminary results

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Background: Reconstructive techniques after mastectomy evolve, with the goal of optimizing aesthetics while minimizing morbidity. Nipple Sparing Mastectomy (NSM) is an oncological safe procedure for treatment of breast cancer with aesthetically pleasing results. Ischemic necrosis of the nipple areola complex is the main concern of NSM. It can be minimized by a surgical delay procedure undermining the nipple and the skin flap around 2–3 week before performing the mastectomy. We found this technique useful in selected patients with large and ptotic, radiotreated breast or with previous breast surgery. Prepectoral breast reconstruction is experiencing a revival. Despite the growing of early reports about subcutaneous breast reconstruction, literature lacks in long-term results.

Materials and Methods: Between January 2016 and December 2018 we examined a total of 44 patients (11 bilateral and 33 unilateral) who underwent a surgical delay procedure before NSM with prepectoral DTI immediate reconstruction with polyurethane implant placement. The surgeons performing the mastectomies were experienced board-certified with decade of experienced. Each patient was evaluated for post op complication such us infection, poor perfusion and debridement procedure. The data were assessed for potential quality improvement in outcomes in breast reconstruction by performing the BREAST-Q questionnaire.

Results: The average follow-up period was 11.7 months. Postoperative complications that require a second operation occurred in 5 cases (9%). Patients scored high level of satisfaction with outcome. Overall satisfaction with breasts, psychosocial well-being, and sexual well-being was all increased after the surgery.

Discussion: In a systemic review of literature NSM, the rate of skin or total nipple necrosis was reported from 11% to 5%. Furthermore, many patients are not candidates for NMS. A 2-step surgical delay approach increase perfusion to the nipple areola complex decreasing ischemia at the time of mastectomy and extending the indications of NSM to large and ptotic breasts or in presence of radiotherapy or previous breast surgery. Moreover DTI prepectoral implant placement showed several advantage: eliminate the animation deformity, loss of muscle function and chronic pain, usually observed in submuscular implant placement. Using polyurethane covered implant can simulate the effect of ADM or synthetic mesh commonly used, stabilizing the prosthesis and improving skin flap integration after nac sparing mastectomy.

Conclusion: Coupling delay technique with prepectoral DTI polyurethane covered implant breast immediate reconstruction after NSM represents a safe, cost effectiveness and feasible alternative with acceptable complications in presence of radiotreated, large and ptotic breast or in presence of previous breast surgery.

No conflict of interest.

205 Poster

Epidemiological characteristics of invasive lobular carcinoma of the breast in North Africa: Example of a Tunisian population

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Background: Invasive lobular carcinoma (ILC) is the second histological type, after invasive carcinoma of no special type, accounting for 5 to 15% of invasive breast cancers. It is characterized by a different genetic profile resulting in significant racial diversity. The aim of this study was to report the epidemiological and clinical characteristics of ILC in Tunisia as an example of a North African country.

Materials and Methods: We performed a retrospective analyses of all female patients treated in Salah Azaiez Cancer Institute for invasive lobular carcinoma histologically proven over a period of 12 years between January 2000 and December 2012.

Results: A total of 156 patients were eligible for inclusion in our study. During the study period, the frequency of lobular carcinoma was 2.2% of invasive breast cancers. The average age at diagnosis was 51 years with extremes ranging from 27 to 76 years. Patients were menopausal in 48.7% of cases. Among risk factors of ILC, hormone replacement therapy and history of benign mastopathy were noted in 10.9% and 11.5% of cases, respectively. A family history of breast cancer was found in 15.4% and gastric cancer in 1.3%. Mammographic screening was inaugural of the disease in 5.1% of cases. The perception of a breast nodule was noted in 79.5%. Average consultation time was 4 months [0 day–36 months]. On clinical examination, the tumor was localized in the right breast in 53.2% of cases, it was bilateral in 6% of patients and mulicentric in 8.3% of cases. The tumor was located in the

supero-outer quadrant in 42.3%, it was retro-areolar in 10.9% of cases. The breast was fully invaded in 9% of cases. Mean clinical tumor size was 54 mm [10–180]. Clinical lynph node invasion was found in 70.5%. According to the TNM classification 7th edition, our patients were classified as cT2 and cN1 in respectively 36.6% and 51.3% of cases. The tumor was classified as stage UICC II in 36.5% of cases. Twenty eight patients (17.9%) were metastatic at initial diagnosis. Metastases were localized in bone in 75% of cases. Ovarian and digestive metastases were found in 10.7% and 7.1% of cases.

Conclusion: Our study shows comparable characteristics with other African countries but some epidemiological differences of ILC features in our country compared to Europe, with a lower frequency, and a younger age of onset.

No conflict of interest.

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Definitive treatment of premalignant lesions of the breast with "double crown": An innovative percutaneous technique

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Background: Nowadays, after a diagnosis of a proliferative lesion with atypia in a breast biopsy (flat epithelial atypia -FEA-, atypical ductal hyperplasia -ADH-, atypical papilloma…) it is recommended the excision due its premalignant character and the possible underdiagnosis in the initial biopsy (around 20% in published series).

We describe an innovative technique of percutaneous excision for therapeutic purposes using a vacuum-assisted biopsy (VAB) system, which we are called "double crown," and we analyze the results of this technique in the first cases performed.

Material and Methods: The "double crown VAB" technique includes a first VAB biopsy to remove the target lesion (first crown) and in the same act a second outer concentric biopsy to remove the margins of that lesion (second crown). We conducted a prospective observational analytical study of our initial experience.

Results: From January 2017 to October 2019 we have performed 43 "double crown VAB" procedures for therapeutic purpose of B3 NHSBSP lesions (lesions of uncertain malignant potential). The median age of the patients was 50 years. The detection of the biopsied radiological lesion was performed through screening mammography in 74%, with microcalcifications being the most frequent finding (86%). The initial biopsy showed in the majority of cases the presence of flat epithelial atypia (42%) or atypical ductal hyperplasia (38%), with an average mammographic size of 8 mm and no pathological uptake in magnetic resonance in the majority of cases (77%). The definitive anatomopathological study of the "double crown VAB" showed postbiopsy changes without residual lesion in 60% of cases and 2 cases (5%) initially an underdiagnosed carcinoma in situ that was surgically rescued; the cases with residual lesion in the first crown presented free margins in 72% and the rest lobular neoplasia (12%) or flat epithelial atypia (16%) although they did not require surgery, after assessment in interdisciplinary committee.

Conclusions: In our initial experience in the treatment of premalignant lesions using this innovative "double crown VAB" technique, we have been able to avoid the need for surgical intervention in 95% of the cases and it has also allowed us to demonstrate the presence of an underdiagnosed lesion in the initial biopsy in 5%.

No conflict of interest.

208 Poster

Automatic detection of perforators for microsurgical reconstruction and correlation with patient's body-mass index

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Background: The deep inferior epigastric perforator (DIEP) is the most commonly used free flap in mastectomy reconstruction. Preoperative imaging techniques are routinely used to map deep inferior epigastric perforator branches that will supply the DIEP flap.

Most commonly, a computed tomography or magnetic resonance angiography is used to detect the diameter and course of perforators with direct intervention from the imaging team, who subsequently draw a chart that will help surgeons in choosing the best vascular support for the reconstruction. This process is both subjective and time consuming. Aiming at solutions to overcome this problem, we developed an automatic detection algorithm and we tried to analyse if body-mass index could influence the automatic detection.

Material and Methods: In this work, the feasibility of using a computer vision software to support the preoperative planning of 35 patients proposed for breast reconstruction with a DIEP flap was evaluated. Blood vessel centreline extraction and local characterization algorithms are applied to identify the perforators and compared with the manual mapping with the aim of reducing the time spent by the imaging team, as well as the subjectivity inherent to the task.

Results: In vessel calibre, results showed no significant difference between both methods. Regarding vessel location in the abdomen the differences, although statistically significative, were not clinically relevant.

There was an important reduction on the time spent using automatic identification (2 hours/case).

Using body-mass index we detected no statistically significant influence on the automatic detection of perforators.

Conclusions: The introduction of artificial intelligence in clinical practice aims to simplify the work of health professionals and to provide better outcomes to patients.

The automatic detection is not influenced by patient's body-mass index. This pilot study paves the way for a success story.

No conflict of interest.

Nursing

209 Poster

Clinical decision trees provide a means for systematic registration and evaluation of multidisciplinary team recommendations

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Background: The Dutch breast cancer guideline has been modelled into clinical decision trees (CDTs, www.oncoguide.nl) in order to support guideline-based decision making. A path through a CDT follows "nodes" that represent patient- and/or disease characteristics (i.e. data-items) and results in a "leaf" representing a guideline- recommendation. We evaluated whether all required data-items were available during multidisciplinary team meetings necessary to result in a recommendation.

Materials and Methods: This retrospective single center study evaluated 394 randomly selected female patients diagnosed with non-metastatic breast cancer between 2012 and 2015. Two researchers (MH and SH) analyzed independently from each other to which degree the patient electronic health records (at the time of decision making) contained data-items which are required per CDT to result in a recommendation. This was done for four different pivotal CDTs: indication for performing a magnetic resonance imaging (MRI) scan, neo-adjuvant (NST) and adjuvant systemic therapy (AST) and immediate breast reconstruction (IBR).

Results: In 70%, 13%, 97% and 13% of patients (see table), all data-items were available as required in de CDT to come to a guideline-based recommendation: for MRI scan (six data-items), NST (five data-items), AST (six data-items) and IBR (four data-items) respectively. The most frequent missing data-items were "clinical M-stage" and "mammography well assessable."

Availability of data during MDT meetings			
Indication	Data-item	Availability Number	Percentage
MRI (n = 394)			
	Pregnant	394	100
	Age	394	100
	Morphology	394	100
	Mammography well assessable	282	72
	Tumor distribution	383	97
	Discrepancy tumor size	394	100
	All data-items available	276	70
Neoadjuvant systemic therapy (n = 394)			
	Clinical M stage	52	13
	Clinical N stage	394	100
	Clinical T stage	394	100
	Gender	394	100
	ER status	390	99
	All data-items available	52	13
Adjuvant systemic therapy (367 patients underwent surgery)			
	Pathologic N stage	367	100
	N0 risk status.		
	Age	367	100
	pathologic T stage	367	100
	tumor grade	359	98
	HER2 status	367	100
	ER status	364	99
	Age	367	100
	All data-items available	356	97
Immediate breast reconstruction (n = 367)			
	Clinical M stage	50	14
	Clinical N stage	367	100
	Clinical T stage	367	100
	Tumor distribution	356	97
	All data-items available	46	13

Conclusions: This study identified data-items that were not explicitly documented during the multidisciplinary team meeting. CDTs provide a means for systematic and explicit registration of necessary data-items to come to a guideline-based recommendation. CDTs can help to improve guideline-based decision making by making this process verifiable.

No conflict of interest.

210 Poster

Cryotherapy to prevent doxorubicin-associated oral mucositis

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Background: In oncology, oral mucositis (OM) is a common adverse event caused by chemotherapy as well as targeted agents. The overall incidence of OM in patients receiving chemotherapy is approximately 40%. Cryotherapy is used occasionally to prevent OM during treatment with melphalan and 5-fluorouracil. Oral cryotherapy might also limit OM in patients receiving doxorubicin, but evidence to support this is currently lacking. Therefore, the objective of the current study is to investigate if oral cryotherapy is effective for reducing the incidence of OM in patients treated with doxorubicin chemotherapy.

Material & Methods: Risk of contamination in a randomized trial was deemed high, because most patients likely prefer cryotherapy when made aware of this possibility. Therefore, we conducted a single institute (Netherlands Cancer Institute), open label-controlled study employing a two-group serial cohort design. Data from the first cohort (n = 100) under usual care were used to estimate the incidence and severity of OM in patients treated with doxorubicin and cyclophosphamide (AC) chemotherapy. After implementing oral cryotherapy at the daycare center, we collected data in the second cohort (n = 106) to estimate the effect of oral cryotherapy on OM. Oral cryotherapy consisted of administering oral ice chips for approximately 15 minutes during the infusion of doxorubicin. Eligible patients were over 18 years of age, diagnosed with breast cancer, and scheduled for four cycles of doxorubicin (60 mg/m^2) in combination with cyclophosphamide (600 mg/m^2) every two or three weeks. Exclusion criteria included prior radiotherapy in the head and neck region, pre-existing mouth problems (OM, ulcers), diabetes mellitus and psychiatric or cognitive disorders. Data on OM was collected with the CTCAE version 4.03 as administrated by the oncology nurse.

All patients gave written informed consent.

Results: A total of 90 out of 111 patients (81%) completed oral cryotherapy as intended. The cumulative incidence of any grade of OM was 28 (28%) unique events in the intervention group versus 46 (43.4%) events in usual care group (RR = 0.65; 95%CI 0.44–0.95; p = 0.03).

Grade of OM	After cycle 1 Control N (%)	Intervention N (%)	After cycle 2 Control N (%)	Intervention	After cycle 3 Control N (%)	Intervention N (%)
0	90 (83.3%)	99 (89.1%)	82 (75.9%)	91 (81.9%)	82 (75.9%)	92 (82.8%)
1	13 (12%)	6 (5.4%)	16 (14.8%)	12 (10.8%)	16 (14.8%)	8 (7.2%)
2	4 (3.7%)	3 (2.7%)	8 (7.4%)	5 (4.5%)	7 (6.5%)	2 (1.8%)
3	–	–	1 (0.9%)	–	–	–
Any	17 (15.7%)	9 (8.1%)	25 (23%)	17 (15.3%)	23 (21%)	10 (9%)
Missings	1	3	1	3	3	9

Conclusion: Application of cryotherapy with oral ice chips during doxorubicin chemotherapy is well tolerated and reduces the incidence and severity of OM in patients treated with doxorubicin-based chemotherapy.

No conflict of interest.

211 Poster

Implementation of a nurse-led wound care consultation after breast cancer surgery

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Background: In Belgium, wound care consultations after breast cancer surgery are generally performed by surgeons, since legislation on nurse-led care is lacking. We hypothesised that a high-quality nurse-led wound care consultation is feasible. Therefore, a training program for nurses was started. This abstract reports the content of the training program and the feasibility of making a structured consultation report.

Material and Methods: The development and content of the training is described. To check the feasibility of making a structured report we analysed 150 consultation files.

Results: The training program was designed by breast cancer nurse specialists. To assure a well-structured and uniform consultation format structured electronic reporting was developed. Important topics for anamnesis and clinical examination are included in this form as well as advice for further follow-up. Hereafter, a structured report within the patient file, can be generated with one click. This structured reporting form was extensively tested and fine-tuned by the surgeons in routine daily care. In addition, a theoretical session was organised for the nurses working at the consultation. The training included theory and exercises on anamnesis, clinical assessment (e.g. infection, seroma and shoulder mobility), evidence based wound care (protocol, seroma aspiration) and self-management support. Films and practical guidelines were linked to the electronic file to support the nurses. Afterwards, a hands-on training by surgeons was performed. A large variation in the learning curve to perform seroma aspirations was observed.

Analyses of 150 patient files resulted in 625 unique consultations. Clinical wound assessment and type of performed wound care were registered in 92% of consultations. Information about pain, shoulder mobility and quality of sleep were present in respectively 77%, 60% and 70% of the files. However, details about the type of pain were only present in 34% of reports. The need for further psychosocial support was reported in 65% of cases. Analysis shows that compliance decreases over an increasing number of consults within a patient (type of wound-care). A learning curve was observed since over time compliance for pain, sleep, and support increased. In 82% of the cases the collected information was converted in a letter for the general practitioner. However, the date and type of surgery were mentioned correctly in only 39% of reports.

Conclusion: High-quality nurse led wound care consultation after breast cancer surgery seems feasible. We developed a training program and a structured electronic reporting form that might serve as a template for other breast cancer centres.

No conflict of interest.

213 Poster

Improving pain outcomes after breast cancer surgery using a novel psychoeducational intervention

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Background: Breast cancer patients have high levels of psychological distress and unmet informational needs that impact their Health Related Quality of Life (HRQoL). There is vast evidence showing that providing written pain information improves patient wellbeing in a range of HRQoL outcome measures. This has yet to be demonstrated in breast cancer patients. Though verbal information is readily provided, very little written information is provided on post-operative pain control at the local breast cancer department.

Materials and Methods: A novel psychoeducational intervention in the form of a patient information leaflet (PIL) was approved for implementation. It included information on pain management and empowered patients to make decisions about their analgesia usage at home. Using a mixed methods approach, data was collected on a range of HRQoL outcomes before and after the implementation of the PIL. The outcome measures in the group of patients who received the PIL were compared with those who did not receive the PIL.

Results: The groups were closely matched for age, type of breast cancer surgery and pre-study analgesia usage. Improvements in 7-and 10-day pain scores and in patient satisfaction were observed after the implementation of the PIL. This group also showed an improved adequacy of analgesia usage and a reduction in analgesia associated side-effects. High rates of patient satisfaction in both groups indicated that the department were achieving above the national average.

Conclusions: A simple intervention was shown to improve HRQoL outcomes in several domains. The PIL can be tailored to meet the needs cancer patients undergoing surgery across multiple disciplines and at further locations. With further patient input, the content of the PIL can be examined to ensure it is providing the most beneficial information that can help reduce pain levels after cancer surgery.

No conflict of interest.

Supportive and Palliative Care Including End of Life Treatment

215 Poster

The effect of Scalp-Cooling System on the prevention of alopecia after chemotherapy

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Background: Breast cancer is the most common cancer among women worldwide. Post-operative chemotherapy plays an essential role in preventing recurrence and metastasis in patients with breast cancer. Since breast cancer chemotherapy has markedly improved in efficacy and has become more widely used, it is being administered to increasing numbers of patients. However, many patients may decline treatment because they are anxious about adverse effects, in particular hair loss. Cyclophosphamide, anthracycline, and taxane agents commonly cause hair loss, nausea, vomiting, and fever. Nausea, vomiting, and fever can be treated pharmacologically, but since there have been no medically preventive measures for hair loss, patients have had no choice but to use wigs or hats. The Paxman Scalp Cooling System, used to prevent hair loss, was approved as a medical device in Japan in March 2019, but we had already started using it in our hospital just before its approval. The goal of this study is to clarify its effect.

Material and Methods: We used the Paxman Scalp Cooling System (Paxman Coolers Limited, West Yorkshire, United Kingdom) to retrospectively analyze female patients with breast cancer who completed 4 cycles of postoperative adjuvant TC (docetaxel 75 mg/m^2 + cyclophosphamide 600 mg/m^2) or AC (doxorubicin 60 mg/m^2 + cyclophosphamide 600 mg/m^2) chemotherapy between October 2018 and August 2019. We have also been gathering data from an additional 8 patients since August 2019; this data collection will be completed in December 2019. All patients are scored from grade 0 to grade 4 following the WHO classification criteria when the last cycle is complete.

Results: At the time of this writing, we have evaluated 28 patients: 16 who received TC therapy and 12 who received AC therapy. The numbers of patients with grades 0–4, respectively, were 0, 5, 5, 1, and 0. The grades of the 8 patients whose data are still being analyzed (6 receiving TC and 2 receiving AC) will be presented when the analysis is complete. The current results show that hair loss in most patients was below grade 2; this degree of hair loss prevention is generally sufficient to avoid the need for a wig.

Conclusions: Scalp-cooling equipment can benefit patients with breast cancer by effectively preventing hair loss caused by chemotherapy. The Paxman cooling system will likely encourage increasing numbers of patients to undergo chemotherapy without too much hesitation. We will continue this study in order to increase the quality of life of patients who receive chemotherapy.

No conflict of interest.

219 Poster

Use of an alfa-lipoic, Methylsulfonylmethane, Boswellia serrata and Bromelain dietary supplement for Aromatase Inhibitors-related Arthralgia Management (AIA): A prospective phase II trial (NCT04161833)

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Background: Aromatase Inhibitors (AIs) are recommended for the adjuvant treatment of hormone receptor positive breast cancers in the postmenopausal population. Approximately 25% of postmenopausal women on AI report arthralgia, skeletal, and muscle pain as main cause of discontinuation of therapy. OPERA® (GAMFARMA srl, Milan, Italy) is a new dietary supplement where α-Lipoic acid (240 mg), Boswellia serrata (40 mg), Methylsulfonylmethane (200 mg) and Bromelain (20 mg) are combined together in a single hard-gelatin capsule to be taken once a day. The aim of this prospective study (ClinicalTrials.gov Identifier: NCT04161833) is to determine the efficacy and safety of OPERA® in a series of patients affected by arthralgia during AIs treatment.

Material and Methods: 53 patients with arthralgia (NCI-CTCAE v4.0 grade of ≥1), evolving during AIs therapy were enrolled. All patients received OPERA®, 1cp/die from enrollment (T0) up to sixth months (T3). Patients' AI-related arthralgia was evaluated every two months with VAS Scale, PRAI questionnaire and CTCAE scale. Quality of life was assessed with FACT-ES questionnaire. The primary study end point was the change from start to end of the initial treatment period in arthralgia severity, defined as a 10% decrease in any grade arthralgia between late and baseline assessment. Secondary end points were patient's QoL and compliance to AIs therapy.

Results: Treatment with OPERA® supplement was overall well tolerated; no relevant toxicities related to OPERA® intake were reported. 7 subjects (13, 2%) stopped prematurely the dietary supplement due to poor treatment benefit. 46 participants were eligible for final analysis. A significant reduction of VAS score between T3 time and T0 was observed (p 0.02). Analysis of PRAI score and CTCAE scale, showed a significant reduction in arthralgia-related pain perceived (p = 0.0001 and p = 0.0009, respectively). Treatment adherence to AIs in overall population (n = 53) was high (85%).

Conclusion: OPERA® was able to reduce the intensity of arthralgia related to AIs therapy. Randomized, double-blind studues are warranted to confirm the effectiveness of this dietary supplement in the management of this common AIs-related toxicity.

No conflict of interest.

220 Poster

Distress and effectiveness of Brief Cognitive Behaviour Intervention for patients with family history of cancer

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Background: However, cancers resulting from genetic predispositions are thought to account for only 15% to 20% of all diagnosed cases, cancer sufferings of immediate family members becomes stressor to newly diagnosed cancer patients, triggering different psychological reactions. The study aimed at investigating relationship between family history of cancer and distress, and effectiveness of Brief Cognitive Behaviour Intervention (CBI) among breast cancer patients.

Material and Methods: 18 breast cancer patients, categorized into three groups: patients having family history of breast cancer (Group A, n = 5), patients with family history of any other cancer (Group B, n = 7) and patients with no family history of any cancer (Group C, n = 6). All participants answered on Depression Anxiety and Stress Scale (DASS-21, Hindi version). The Cognitive Behaviour Intervention (8 sessions) extended for 45 to 60 minutes each was held once weekly.

Results: During pre-intervention assessment although all patients showing mild-moderate level distress, mean scores of Group C patients was higher than Group A and Group B patients on Depression ($F = 3.77$, $p < 0.05$), Anxiety ($F = 5.33$, $p < 0.05$) and Stress ($F = 4.21$, $p < 0.05$). Although the intervention was effective in all groups of participants, Group A patients reported significantly lesser distress symptoms as compared to Group B and Group C patients during post intervention assessment.

Conclusions: Brief Cognitive Behaviour Intervention is effective to reduce distress symptoms associated with family history of cancer. As it is found that family history affects the outcome of psychological interventions, it is recommended that health professionals and intervention providers should become more aware about this factor while planning for intervention for patients at the time of their cancer diagnosis and prognosis.

No conflict of interest.

222 Poster

The effect of a chamomile compound on pain and heaviness in breast cancer patients with lymphedema: A double-blind and randomized controlled trial

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Background and Purpose: Alleviating pain and heaviness is the primary goal when lymphedema occurs in breast cancer patients. As the anti-inflammatory feature of chamomile on skin, we aimed to explore the effect of a chamomile compound with combined decongestive therapy (CDT) on primary outcomes including pain, volume as well as heaviness.

Methods: We used simple randomization method to allocate patients into three parallel groups including CDT (routine care), CDT with placebo and CDT plus chamomile compound. 67 patients underwent randomization, and ultimately 20 patients assigned each group. Pain quantified using VAS checklist. All outcomes were measured three times including before treatment, in middle of treatment and after treatment.

Results: Between May 2018 and July 2019, 64 breast cancer patients with lymphedema received CDT (n = 21), CDT with placebo (n = 20) and CDT with chamomile compound (n = 23). Mean age of patients was 55.4(±10.1). Allergic reaction occurred in three patients (4.7%) in chamomile with CDT group and one withdraw was reported during study. The results of Repeated Measure ANOVA indicated that there was no statistically difference between groups in terms of mitigating in pain, volume and heaviness, while there was a noticeable decrease in pain, volume and consequently in the range of motion in patients who received chamomile compound. All interventions in three groups had a significant impact on outcomes.

Conclusion: Although there was not seen a statistically significant difference between groups, it seems that the anti-inflammatory effect of chamomile compound can cause a reduction in pain, volume and heaviness in breast cancer patients with upper extremity lymphedema.

No conflict of interest.

223 Poster

Symptom talk during clinic visits for treatment of breast cancer: Do we get an accurate picture?

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Background: Optimal symptom management requires ongoing symptom assessment and communication between women with breast cancer and their oncologists. The purpose of this study was to determine the extent to which women receiving chemotherapy for breast cancer discussed at their clinic visit the symptoms that bothered them during the week prior to the visit and whether symptom discussions changed in content or length over subsequent visits and cycles of treatment.

Material and Methods: Utilizing an observational design, women reported the severity of 11 common symptoms (0–10 scale) on a daily basis during the interim between clinic visits using an automated patient-reported outcomes (PROs) platform. Participants understood that these reports would not be shared with their oncologist and they should report symptoms of concern directly to their oncologist. The conversations of clinic visits were audio recorded then transcribed and symptom discussions were timed and coded using a pre-defined codebook. Utilizing descriptive statistics, symptoms reported at moderate to severe levels ($\geq$4 on 10-point scale) in the week prior to the visit were compared to the symptoms actually discussed and the length and focus of symptom discussions were compared across serial visits.

Results: Twenty-six clinic visits of 10 women receiving chemotherapy for breast cancer were recorded. Participants mean age was 51.6 years; half had stage II disease and half had stage III or IV disease. In the week prior to their visits, participants provided 183 reports of moderate-to-severe level symptoms. Most common were fatigue, disturbed sleep, and pain. Reported symptoms were only discussed at 49.5% of visits and the patient initiated only 36% of these discussions. Symptom discussions were more likely to occur with younger women (60% of visits for women 40–49, 52.3% of visits for women 50–59, and 18.8% of visits for women 60 or older). The discussions averaged 27.8% of visit time across all visits but, despite continued moderate-to-severe symptom reports, symptom talk decreased over subsequent visits (37.8% baseline visit, 29.5% visit 2 and 3, 19.5% visit 4).

Conclusion: Troublesome symptoms are often not fully discussed at clinic visits. Only half of moderate to severe symptoms experienced by women are discussed and even with similar symptom severity, older women are less likely to have their symptoms discussed. Women tend to wait for their oncologist to ask about symptoms and are less likely to self-advocate for further symptom care. While symptoms at moderate to severe levels continue over chemotherapy cycles, their discussion decreases, affecting quality of life and functioning. Strategies such as routine standardized assessment of symptom PROs at clinic visits and persistence in treating symptoms over cycles of treatment should be considered for optimal symptom care.

No conflict of interest.

224 Poster

Variation and efficacy of scalp cooling in Dutch hospitals among >5000 breast cancer patients

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Background: The population-based Dutch Cancer Registry shows that 60% of patients with breast cancer received chemotherapy and 99% of these treatments are known to introduce severe alopecia. Worldwide scalp cooling is being implemented to prevent chemotherapy-induced alopecia (CIA). FDA clearance has been approved for scalp cooling among breast cancer patients in 2015. It is heading towards standard care as it is added to the NCCN guideline for breast cancer in 2019.

Material and Methods: From 2006–2017 data were collected in a prospective, longitudinal scalp cooling registry. 75% of these patients had

stage I-IV breast cancer. The hospitals practiced scalp cooling according to their local protocols on e.g. cooling time, drug infusion time and wetting of the hair before the start of treatment. Patients were eligible for evaluation of hair loss after they received at least 2 cycles of chemotherapy or if they ceased scalp cooling because of severe hair loss after the first cycle. Failure was defined as feeling the need to use a wig or head cover. Logistic regression analyses were applied to evaluate the influence of infusion times and wetting the hair on scalp cooling efficacy.

Results: Preliminary results show data of >5000 breast cancer patients from 68 hospital locations. Variation was observed between hospitals in scalp cooling procedures: e.g. wetting the hair (0–100% of patients) and in satisfaction with information about scalp cooling (80–100%) and nursing expertise (55–100%). Also efficacy varied between hospitals per type and dose of chemotherapy. Largest groups were patients receiving adriamycine/cyclophosphamide (AC), 5FU/epirubicine/cyclophosphamide (FEC), docetaxel/adriamycine/cyclophosphamide (TAC), docetaxel, paclitaxel or eribuline. Of the >1400 patients receiving 4 times AC (A60 mg/m^2 C600 mg/m^2), 45% used no head cover. Efficacy for AC was not influenced by infusion times, but wetting the hair increased the results (OR 2.3, $p < 0.0001$).

Conclusions: Scalp cooling procedures and efficacy varied enormously between hospitals. A registry is a useful tool to identify best practices and to further improve results. Therefore an international registry has been set up to also collect data on CIA among scalp cooled patients in the USA, Australia and the UK.

Conflict of interest:

Other Substantive Relationships:

CH received funding from Dignitana and Paxman to set up an international scalp cooling registry and received reimbursement for travel costs for conferences from Paxman.

Systemic Treatment

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Administration of LHRH agonist as an adjuvant endocrine therapy for breast cancer is a risk factor of ovarian function recovery after switching from tamoxifen to aromatase inhibitor

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Background: Aromatase inhibitor (AI) is thought to be used with caution, when amenorrhea is induced in chemotherapy. But ovarian function recovery (OFR) is also observed in switching from tamoxifen to AI without chemotherapy. Considering the effect of AI, the identical caution is required. This retrospective study assesses the patients-related and therapy-related factors associated with OFR.

Material and Methods: Patients who were menopausal at the diagnosis of breast cancer and switched to AI from TAM treatment were included. Menopausal status and OFR were determined by the occurrence of menstrual bleeding and serum estradiol/FSH levels. We examined age at the start of AI, the duration of TAM therapy, the administration of LHRH agonist (LHRHa) and chemotherapy. Logistic regression was used to evaluate predictors of the resumption of menstruation.

Results: A total of 35 such patients were identified, with the median age of 50 years (Range, 42–58 years) at an AI initiation. The median duration of TAM therapy was 44 months. LHRHa administration, chemotherapy and radiotherapy were performed for 16, 22 and 19 patients (43%, 63% and 54%), respectively. In no cases was LHRHa used for the fertility preservation. The resumption of menstruation was observed among ten patients (29%). LHRHa as adjuvant hormonal therapy and younger age at AI initiation were significantly associated with OFR (OR 2.6 $p = 0.01$ and OR 1.5 $p = 0.04$, respectively). Chemotherapy was not a predictive factor ($p = 0.079$).

Conclusion: OFR during AI therapy was associated with LHRHa administration and youger age at the start of AI. Chemotherapy was not a predictive factor of OFR.

No conflict of interest.

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Finding existing drugs potentially active against BRCA-mutated breast cancers: A literature-based approach

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Background: Mutations in the *BRCA* genes predispose to developing breast, ovarian and other cancers. Poly (ADP-ribose) polymerase (PARP) inhibitors (PARPi) are one treatment option in *BRCA*-mutated cancers, as are platinum salts since they induce DNA breaks that then require proficient *BRCA* for repair. Next to this "soft" repurposing – using an anticancer drug to treat another cancer – we sought to identify "hard" repurposing opportunities – using non-cancer drugs, here in *BRCA*-mutated tumors.

Materials and Methods: A PubMed search was performed to identify which of the 293 ReDO (Repurposing Drugs in Oncology) drugs had evidence of interaction with *BRCA* or PARP. Each abstract was assessed for relevance, evidence (preclinical, clinical) and biological effect (single agent activity or in association with PARPi). For relevant drugs, we assessed whether trials in *BRCA*-mutated cancers or with PARPi were ongoing.

Results: From the 293 ReDO drugs, 147 (50%) had at least one article reporting an effect related to *BRCA* or PARP, for a total of 1,364 abstracts. 73 drugs (25%) were considered to have a possibly beneficial interaction with *BRCA* or PARP. We selected 15 drugs (5%) to be explored further in relationship to *BRCA* status or PARPi, with a focus on breast cancer (Table 1).

Five of these 15 drugs (aspirin, metformin, mifepristone, sirolimus and vitamin D3) are trialed in the preoperative, adjuvant, neoadjuvant and advanced breast cancer settings. Whereas 3 trials investigate the role of vitamin D3, metformin or mifepristone as chemo-preventive agents in high-risk patients (incl. *BRCA* patients), none of the 15 drugs is investigated therapeutically in *BRCA*-mutated cancers or with PARPi.

Table 1 Selection of non-anticancer drugs that could interact with *BRCA* or with PARPi

Drug	Main indication	Drug	Main indication
Aspirin	*Analgesia*	Mifepristone	*Abortion*
Ademetionine	*Depression*	Minocycline	*Bacterial infections*
Amiloride	*Hypertension*	Nicotinamide	*Vitamin B3 deficiency*
Artesunate	*Malaria*	Pyrvinium Pamoate	*Pinworm infections*
Chloroquine	*Malaria*	Sirolimus	*Post-transplant*
Ganciclovir	*CMV infection*	Spironolactone	*Hypertension*
L-arginine	*Diagnosis of growth hormone deficiency*	Vitamin D3	*Vitamin D deficiency*
Metformin	*Type 2 diabetes*		

Conclusions: We identified 15 non-anticancer drugs that deserve further research in *BRCA*-mutated cancers or with PARPi. Further studies are necessary to select which drugs could be repurposed as single agent, in combination with PARPi, or with other treatments in *BRCA*-mutated cancers. Since those drugs have well-known clinical features, window of opportunity trials represent an interesting option to study their role with PARPi or as single agent. The role of drugs widely used such as aspirin or metformin could also be investigated in retrospective datasets of patients with *BRCA*-mutated cancers or treated with PARPi.

No conflict of interest.

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Dynamic monitoring of CD45-/CD31+/DAPI+ circulating endothelial cells aneuploid for chromosome 8 during neoadjuvant chemotherapy in locally advanced breast cancer

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Background: Neoadjuvant chemotherapy (NCT) is the standard treatment for patients with locally advanced breast cancer (LABC). Circulating endothelial cells (CECs) are cancer biomarkers and crucial for angiogenesis. The relationship between NCT treatment and the number of aneuploid CECs in LABC has not been previously investigated. The aim of this study was to verify this relationship, and to estimate the clinic value of aneuploid CECs in LABC patients with different NCT responses.

Methods: Breast cancer patients received an EC4-T4 NCT regimen. Peripheral blood mononuclear cells were obtained before NCT, and after the 1st and last NCT courses. A novel SE-iFISH strategy was applied to circulating rare cells detection. CECs (CD45-/CD31+/DAPI+) and circulating tumor cells (CTCs) with different cytogenetic abnormality related to chromosome 8 aneuploidy were analyzed in LABC patients subjected to NCT.

Results: A total of 41 patients were enrolled. CD31+/Vimentin+ and CD31+/Vimentin– aneuploid CECs were counted during NCT. CD31+/EpCAM+ aneuploid endothelial-epithelial fusion cells were first reported in LABC patients. Aneuploid CECs increased after the 1st NCT course and then decreased. A strong positive correlation was found between aneuploid CEC and CTC numbers at three different time points ($p = 0.015$, <0.001, <0.001, respectively). The number of aneuploid CECs was positively correlated with that of platelets ($r = 0.387$, $p = 0.014$) and leukocytes ($r = 0.2667$, $p = 0.096$), and negatively correlated with the level of plasma VEGF ($r = –0.324$, $p = 0.042$) after the 1st course of NCT. According to postoperative pathology reports, 6 patients exhibited a >90% loss of tumor cells (Miller-Payne grade 4 and 5). The remaining 35 patients were grouped in Miller-Payne grades 1–3. Twenty patients exhibited a decline in the Ki-67 index of up to 33.33% (Low-R group), while the other 21 exhibited a decrease of more than 33.33%, compared to surgical bioptic samples (High-R group). Aneuploid, but not diploid, CECs increased significantly after the 1st NCT course ($p < 0.001$) but their number was lower after the 8th course than after the 1st course of therapy ($p = 0.028$). The number of aneuploid CECs remained stable in grade 4 and grade 5 patients, but increased continuously during NCT in grade 1–3 patients. When grouped by the Ki-67 index, all patients exposed to NCT exhibited an initial increase in aneuploid CECs, but only High-R patients had a lower number of CECs after NCT completion than after the 1st course of therapy.

Conclusion: Thus, aneuploid CECs in the peripheral blood showed a biphasic response during NCT, as they initially increased and then decreased, and were closely related to the NCT responses. Elucidating the potential cross-talk between CTCs and aneuploid CECs may help characterize the process of chemotherapy resistance and metastasis.

No conflict of interest.

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Real-life use of 21-gene signature: A retrospective analysis of 46 cases from private practice

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Background: The use of adjuvant chemotherapy in the treatment of early-stage breast cancer (BC) is usually based on clinicopathologic features. However, in grade 2 estrogen-receptor (ER)-positive HER2-negative tumors, this assessment could be of limited value for decision-making and may lead to under- or more frequently to over-treatment. Molecular genomic methods have been recommended by different international guidelines. The multigene assay Oncotype DX is available in France since 2016, thanks to the French public funding (RiHN) or enrollment into "RxPonder" clinical trial (NCT01272037).

The purpose of this study was to retrospectively determine whether the Oncotype DX Recurrence Score was adequately prescribed and whether the results influenced the decision to administer chemotherapy in the real life.

Material and Methods: A retrospective study was performed on 46 consecutive patients with estrogen-receptor–positive HER2-receptor-negative breast cancer for whom the tumor board recommended an adjuvant chemotherapy but requested an Oncotype DX Recurrence Score before final therapeutic decision. Both tumor and patient characteristics have been reported: histology, tumor grade and size, lymph node status, ER, PR, HER2 and Ki67, Oncotype DX Recurrence Score results, patient age at diagnosis, menopausal status, and post-test treatment decision.

Results: During 23 months (between February 2016 and December 2018), tumor boards of 5 private centers in Toulouse assessed 1053 cases of ER-positive, HER2-negative tumors out of 2270 early BC new diagnosis and recommended 46 times the Oncotype DX Recurrence Score to confirm the need for a chemotherapy for ER-positive BC (4%).

Patient's median age was 53 years (37–75). Mean tumor size was 23 mm (10–60). The median Oncotype DX Recurrence Score was 16 (7–47, 1 missing).

Mainly the Oncotype DX Recurrence Score has been prescribed for patient with age 45 to 65 (65%), post-menopausal (65%), treated for a ductal carcinoma (only 2 cases of lobular carcinoma), pT1c (52%), pN0 & Nmic (72%), grade 2 (93%).

For the 7 cases of pN1 BC cases, Oncotype DX Recurrence Score was mainly realized within the clinical trial Rx Ponder (64%).

Oncotype DX Recurrence Score is used in clinical intermediate risk context, not among patients with clinical high-risk factors (2 grade 3 patients were tested when no medical oncologist was attending tumor board) or low risk patient (0% grade 1).

Result of Oncotype DX Recurrence Score led to a change in management for 80% of patients, highlighting that the test reduces the use of CT.

Conclusions: In our real-life practice, the Oncotype DX Recurrence Score test is used based on international guidelines and impacts significantly treatment decision. Results will be updated with our 2019 data.

No conflict of interest.

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Should chemotherapy in neoadjuvant setting in node positive breast cancers be guided by biology over magnitude of tumour burden?

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Background: Neo-adjuvant chemotherapy (NACT) may downsize tumour enabling breast-conserving surgery (BCS), with success rates dependent on tumour biology. We ascertain whether in-breast response correlated with nodal response in pre-NACT node positive disease.

Material and Methods: NACT-treated patients over 5-years (August 2013–2018) were identified from a prospective database, and information extracted from electronic medical records. Response was assessed as residual pathological tumour size as a proportion of the largest recorded pre-treatment imaging size. Nodal positivity was confirmed pre-operatively with ultrasound-guided biopsy and post-operatively with the presence of any tumour cells as per current Royal College of Pathologists guidance. Statistical analysis involved comparison of proportions (two-tailed exact test) and multivariate analysis (logistic regression).

Biology (n = 39)	Tumour response in breast	Node positivity by breast response	Total Node positive post NACT
ER+ HER2– (18)	3pCR (16.5%) 14pPR (78%) 1poor (5.5%)	1/3 pCR (33%) 11/14 pPR (78.5%) 1/1 poor (100%)	13/18 (72%)
ER+ HER2+ (8)	4pCR (50%) 3pPR (37.5%) 1poor (12.5%)	2/4 pCR (50%) 2/3 pPR (66.5%) 1/1 poor (100%)	5/8 (62.5%)
ER– HER2– (9)	5pCR (55.5%) 4pPR (44.5%)	1/5 pCR (20%) 2/4 pPR (50%)	3/9 (33%)
ER– HER2+ (4)	1pCR (25%) 3pPR (75%)	0/1 pCR (0%) 0/3 pPR (0%)	0/4 (0%)

pCR = pathological complete response; pPR = pathological partial response.

Results and Conclusions: ER+ HER2– tumours had the lowest breast pCR rate (16.5%) associated with 72% residual nodal disease including one patient that had pCR in the breast primary. More chemo-sensitive tumour subtypes (ER–) had higher breast pCR rates associated with lower post-NACT nodal positivity ($P = 0.015$). Albeit limited by numbers, response in nodal metastasis may be worse than primary breast tumour response. At logistic regression analysis, ER+ and HER-2+ status were respectively associated with a lower (OR 0.12, 95% C.I. 0.02–0.59, $P = 0.0095$) and an higher (OR 2.40, C.I. 0.51–11.27, $P = 0.264$) probability of achieving a nodal pCR. Hence, selection for NACT in node positive disease (in trial or outwith) should be based on primary tumour biology (triple-negative and HER-2 positive) rather than disease burden/axillary spread.

No conflict of interest.

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Assessing the benefits and toxicities of platinum containing neoadjuvant chemotherapy in triple negative breast cancer

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Background: Neo-adjuvant chemotherapy (NACT) is an established treatment in triple negative breast cancer. Recently evidence has emerged of benefit of addition of platinum to the standard anthracycline and taxane based neoadjuvant chemotherapy, with improved pathological complete response rates (pCR). This led to change in clinical practice at University Hospital Leicester Oncology Centre (UHL) where patients with triple negative disease are offered neoadjuvant chemotherapy with 4 cycles epirubicin and cyclophosphamide followed by 4 cycles of carboplatin and a Paclitaxel.

Our aim is to assess if the addition of carboplatin to neoadjuvant chemotherapy for triple negative breast cancer at UHL improved pathological response rates. We carried out a retrospective analysis comparing outcomes of patients who were treated from 2014–2018 during which time the change of practice was implemented.

Methods: UHL cancer centre electronic records were used to identify all patients receiving neoadjuvant chemotherapy for triple negative breast cancer from 2014–2018. These were separated into standard arm (epirubicin and cyclophosphamide 3 cycles followed by docetaxel 3 cycles) and after Carboplatin was added in light of clinical evidence into intervention arm from 2017 (epirubicin and cyclophosphamide 4 cycles, followed by carboplatin and docetaxel/paclitaxel 4 cycles).

Results: Total of 45 patients identified over the 6 years, 23 Control arm (2014–2016) and 22 Intervention (2017–2018). Similar demographics and tumour stages were seen in each arm. Total pCR 35% (control) vs 23% (intervention), no response/progression was seen in 9% (control) vs 5% (intervention). G1 toxicities 27 (control) vs 37 (intervention) with similar total numbers of G2 and G3 toxicities. All the patients completed the full course of NACT in the standard arm but 3 patients stopped after 6th cycle in the intervention arm. In 2 patients carboplatin was omitted after one course due to toxicities.

Conclusions: Both arms had comparable demographics and presenting features, our primary objective showed lower complete pathological response rates in the intervention group. The dose reductions and dose delays may have contributed to the lower complete pathological response in the intervention group. Although G2/G3 toxicity rates were similar, there was increase in peripheral neuropathy which is likely to be related to the addition of carboplatin, and in keeping with trial data. Our study is limited by small patient numbers and by its retrospective nature. Our study suggests that patients receiving additional platinum containing neoadjuvant chemotherapy have increased toxicities but no increase in complete pathological response to chemotherapy. Further trials are needed to be carried out in the context of neoadjuvant chemotherapy in triple negative breast cancer to establish optimised treatment regimens.

No conflict of interest.

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Effects of chemotherapy on serum lipids in Chinese postoperative breast cancer patients

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Background: Chemotherapy is one of the comprehensive treatment methods for breast cancer, nevertheless its associated adverse effects are drawing consequential attention along its substantially improving efficacy. The changes of serum lipids of breast cancer patients induced by chemotherapy have been reported by previous studies, whereby the former increases the incidence rate of cardiovascular disorders. However, the variations in the changes of serum lipids with different chemotherapy regimens have seldom been reported.

Methods: From January 2011 to December 2017, 1740 breast cancer patients treated with chemotherapy were recruited at the First Affiliated Hospital of Nanjing Medical University. The chemotherapy regimens included anthracycline-based, taxane-based, and anthracycline-plus-taxane-based regimens, and dose-dense and standard-interval regimens. Lipid profiles which included TG (triglyceride), TC (total cholesterol), HDL-C (high density lipoprotein cholesterol), LDL-C (low density lipoprotein cholesterol) and Lpa (lipoprotein a) levels were collected prior to the first, second and last cycles of chemotherapy. The changes of serum lipids with the same and different chemotherapy regimens were analyzed and compared.

Results: It was observed that the levels of TG, TC, LDL-C and Lpa significantly increased and that of HDL-C decreased after adjuvant chemotherapy in breast cancer patients ($P < 0.05$). Besides, dose- dense regimens had more influence in TG and HDL-C than in TC and LDL-C and compared to standard-interval regimens as well. HDL-C was more sensitive to anthracycline-based regimens than taxane-based regimens. The level of TG with anthracycline-plus-taxane-based regimens was higher than those with only anthracycline-based or taxane-based regimens, and the level of HDL-C with anthracycline-plus-taxane based regimen was lower than that with taxane-based regimen.

Conclusions: Taken together, this study had suggested that dyslipidemia was significantly associated with chemotherapy in Chinese breast cancer patients after operative treatment. Furthermore, the changes in levels of serum lipids varied among patients with different chemotherapy regimens and taxane had less influence in dyslipidemia than anthracycline.

No conflict of interest.

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Management of early breast cancer by trastuzumab biosimilar: Insights from observational drug utilization registry

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Background: Most of the data available for approved trastuzumab biosimilar are in form of RCT's, this is the first observational clinical registry being conducted for trastuzumab biosimilar in India.

Material and Methods: This is an observational, real world drug utilization registry where data was collected for the patients eligible to receive trastuzumab biosimilar (Vivitra®, Cadila Healthcare). The study is registered in Clinical Trial Registry of India (CTRI/2018/05/013754) and conducted as per Good Clinical Practice.

Results: We collected data for 90 patients (89 female, 1 male) with Early Breast Cancer (EBC) data treated with trastuzumab biosimilar, age range: 29–69 years from 17 sites spreading pan India using electronic data capturing system (21 CFR part 11 compliant). 88/90 patients had reported dose for EBC (87% three-weekly, 8% weekly and 5% both three and weekly cycles). 84/90 patients had reported number of cycles with average of 11 treatment cycles (maximum of 24 cycles). 25 patients completed the 17 treatment cycle protocol. There was varied usage of chemotherapeutic agents as per Table 1. 81/90 patients had Left Ventricular Ejection Fraction (LVEF) measured at before initiation of trastuzumab biosimilar, out of which 74/81 had LVEF range between 55–70% and 7 had LVEF more than 70%. 57/81 had post dose LVEF evaluation with none reporting LVEF < 55% post dose. There was no discontinuation of the drug, all values for LVEF in post-dose phase for 57 subjects were reported in range of 55–74%. There were 4 SAE, 2 cases of death which were not unlikely due to the drug and 2 cases of LVEF reduction which reversed on supportive care.

Table 1 Frequency of other chemotherapeutic agents used

Chemotherapeutic Agent	Percentage Distribution (%)
Paclitaxel	40.6
Docetaxel	31.3
Docetaxel + Cyclophosphamide	15.6
Docetaxel + Carboplatin	7.8
Cyclophosphamide + Doxorubicin + Paclitaxel	1.6
Cyclophosphamide + Epirubicin	1.6
Letrozole	1.6

Conclusion: Safety of trastuzumab biosimilar was found to be acceptable. Approximately 28% patient completing the recommended treatment cycles in early breast cancer with trastuzumab biosimilar points toward accessible option in out of pocket healthcare scenario such as in India. There were marked differences in incidence of observed and expected adverse events, probably because of under reporting in real world clinical practice. Although a black box FDA warning, LVEF monitoring is still not very common in clinical practice.

No conflict of interest.

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Pyrotinib in HER2-Positive local advanced or metastatic breast cancer patients: Results from a retrospective study in real-world setting

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Purpose: Pyrotinib, an irreversible pan-ErbB inhibitor, showed promising antitumor activity and acceptable tolerability in breast cancer patients in some trials. The study is to investigate the efficacy and toxicity of Pyrotinib in patients with HER2-positive local advanced or metastatic breast cancer in the real-world setting.

Methods: In all, 108 patients were included in this study between September 8, 2018 and Octorber 1, 2019 from three cancer centers in Wuhan, China. Patients with HER2-positive local advanced or metastatic breast cancer previously failed treated Herceptin received Pyrotinib treatment. 18 patients received Pyrotinib as neoadjuvant therapy combined with chemotherapy and trastuzumab. Within the 90 patients with metastatic breast cancer, 33 patients received Pyrotinib as first line treatment and 57 patients as second or more lin treatment. Pyrotinib alone or combined with chemotherapy was continuously administered once per day in 21-day cycles. The pathological complete response(pCR), objective response rate (ORR), progression-free survival (PFS) and the toxicity were all indicators of observation.

Results: pCR was 12 of 18 (66.7%) in Pyrotinib neoadjuvant therapy. Of the 90 patients with metastatic breast cancer, complete response (CR) rate was 7 of 90 (7.8%), partial response (PR) rate was 44 of 90 (48.9%), stable disease (SD) was 3 of 90 (3.3%) and ORR was 51 of 90 (56.7%). The median PFS was 6.3 months (1.5–12.8 m) in the 90 patients after 1.5–13 months of follow up. The most frequent grade 3 to 4 adverse events were diarrhea in 8 of 108 patients (7.4%).

Conclusion: Pyrotinib exhibited good efficacy in HER2-positive local advanced and metastatic breast cancer with manageable toxicity.

No conflict of interest.

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Optimal duration and effectiveness of neoadjuvant endocrine therapy in breast cancer – Retrospective series

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Background: Neoadjuvant endocrine therapy (NAET) is increasingly used in ER+/Her2– breast cancer (BC). Its optimal duration as per current guidelines is 4–8 months or until maximal response. We studied efficacy outcomes and relationship between US assessed response and proliferative response/Ki67 dynamics. We analysed 2 cohorts of pts according to NAET goal: A) for tumor downsizing and B) frail or refusing other therapies.

Patients and Methods: This is a single center retrospective cohort study, including menopausal women with stage I–III ER+/Her2– BC, diagnosed 2012–2018 and treated with NAET. Pts were assessed with breast US every 90± 15 days. We examined the impact of NAET duration on 1) clinical response; 2) surgical treatment [BCS vs mastectomy]; and 2) Ki67 dynamics.

Results: 53 BC cases were included with a median follow-up 38.5 months. Median age at diagnosis was 69 years (47–85). Most pts had stage II (65%), invasive NST (81%), grade 2 (72%) BC. Reasons for NAET were tumor downsizing (n = 37; 70%) or pts refusal for surgery/comorbidities (n = 16; 30%). For *cohort A* (n = 37) median NAET duration was 240 days/8.5 months. Median Ki67 was 18% at diagnosis and 7.7% at surgery (n = 32). 1 patient achieved pCR (NAET for 8.3 months). Overall response rate (RR), assessed by US, was 89% (54% partial response (PR), 32% stable disease (SD), 3% complete response (CR)). Median time to US assessed max response was 183 days/6.5 months. Progressive disease (PD), based on US, was seen in 4 pts (11%) with median Ki67 at surgery 7.75 with all having Ki67≤10 and a median drop of –6%. In cohort A, the proliferative RR was 87.5% (n = 28). 4 pts (12.5%) didn't achieve proliferative response and were classified by US as responders (3 SD and 1 PR). BCS was done in 92% of pts. Adjuvant chemotherapy was given in 2 (5%) pts with risk factors. At time of the analysis there were no recurrences and all pts are alive. For *cohort B*, median NAET duration was 314 days/11.2 months. Median Ki67 was 20% at diagnosis (n = 16) and 14% at surgery (n = 12). pCR was achieved in 2 pts (median duration NAET 233 days). US assessed response (n = 13) yield an overall RR of 69% (69% SD). PD based on US was seen in 31% (n = 4) pts. In cohort B the proliferative RR was 67% (n = 8). 4 pts (33%) didn't achieve proliferative response and were classified by US as PD (n = 2) or SD (n = 2). 5 deaths occurred (2 due to systemic recurrence). Median PFS is 34.8 months and median OS is 5.8 years.

Conclusions: NAET is effective for tumor downsize, allowing BCS and regarding long-term outcomes. Optimal duration of NAET and defining maximal response remain unknown. Our results support current recommendation for 4 to 8 months NAET. US dynamics fail to identify pts with response, defined by Ki67 suppression and do not support the use of US to guide duration of therapy. Other techniques as MRI should be tested.

No conflict of interest.

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Quality of life (QL) in elderly breast cancer survivors. Effects of surgery. Global QL determinants

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Background: Quality of Life (QL) is a key target of the attention that is offered to elderly breast cancer patients survivors.

The aims of the present study are to assess QL in a sample of elderly early-stage breast cancer survivors; to study QL differences based on clinical variables; and to identify Global QL determinants.

Material and Methods: A consecutive sample of stages I-III elderly breast cancer patients who had received treatment at the Oncology Departments of the Complejo Hospitalario de Navarra was invited to participate in the study. Patients were >65 years old at the study entry and have had a follow up period of at least 5 years after surgery. They might have received adjuvant radio, chemo and/or hormotherapy. They had no relapse. Patients filed in once the EORTC QLQ-C30 (general QL), QLQBR45 (breast specific QL) and QLQ-ELD14 (elderly specific QL) questionnaires. Demographic and clinical data were recorded.

QL differences between groups based on breast surgery (conservative – mastectomy) and presence of limiting comorbidity were studied (Wilcoxon tests). Univariate and multivariate logistic regression analyses were performed to identify demographic, clinical and QL areas related to low global QL (≤50 points considered low global-QL score).

Results: 277 patients filled in the questionnaires. 132 patients (48%) had limiting comorbidity. Karnofsky mean (sd) score was 81(9.2). 228 patients (83%) received endocrine treatment.

QL scores were high in most areas (>80/100 points functioning, <20 in symptoms areas) with moderate limitations (>30 points) in worries about others, maintaining purpose, joint stiffness (elderly specific); sexual functioning and enjoyment (breast specific); and light limitations (20–30 points) in emotional functioning, sleep disturbance, fatigue, pain, global QL (general QL); future worries and breast satisfaction (breast specific); and future perspective and family support (elderly specific) areas.

Patients with limiting comorbidity showed lower QL in eight general areas, seven breast specific and four elderly specific QL areas. There was no difference in any area between breast surgery groups.

Performance status, age, comorbidity, eleven general, ten breast and seven elderly areas had a statistically significant relationship with low global QL. Fatigue and Endocrine Therapy Symptoms showed the highest R2 (0.38).

The best model to explain low global QL included, as explanatory variables, high fatigue, worries about others and endocrine therapy symptoms as risk factors (R2 = 0.60).

Conclusion: Elderly early-stage breast cancer patients adapted well both to their disease and treatments over the follow-up period. Comorbidity has a key role in their QL, whereas QL did not differ between surgery-treated groups. Fatigue, endocrine secondary effects, and worries about others have a key role in QL in elderly breast cancer patients.

No conflict of interest.

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Compliance to adjuvant endocrine treatment – real world data from 1019 consecutive luminal breast cancer patients with long follow-up

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Background: Data on compliance to adjuvant endocrine treatment (ET) is mainly reported from prospective clinical trials or from smaller retrospective cohorts.

Aims: To investigate compliance and reasons for termination of adjuvant ET and the impact on survival in a population based larger series of patients with Luminal primary breast cancer (BC) advised ET. Patients and methods: 1092 consecutive patients with hormone receptor positive (HR+)/HER2 negative primary BC diagnosed from 1 January 1997 through 31 December 2003 were included. Data on primary tumour stage and biology, as well as, type of endocrine treatment, side-effects, compliance, reason for termination, date and type of metastases, cause of and date of death were extracted from patients' records. Statistical analysis of compliance and survival were calculated with patients split into four groups: Group A: the patient has taken the treatment as prescribed. Group B: the patient has taken the treatment for a period longer than 2 years. Group C: The patient has taken the treatment for a period longer than 6 months but shorter than 2 years. Group D: The patient has not taken the treatment longer than 6 months.

Results: Seventy-three patients were excluded for the following reasons: de novo stage IV BC, not possible to judge compliance, or lost from follow-up leaving 1019 evaluable patients. Patients had a Luminal stage I to III BC out of which 690 patients were diagnosed with an invasive ductal cancer, 220 with a lobular BC and 109 with other morphological subtypes. Treatment were as follows; tamoxifen (n = 779); AI (n = 54); planned switch n = 53; switch due to toxicity (n = 65); ovarian suppression + endocrine treatment (n = 33) combined with tamoxifen in all but two patients; other ET n = 23. A total of 752 (73.8%) patients were fully compliant to therapy; 158 (15.5%) patients continued for more than 2 years; 77 patients (7.6%) patients less than 2 years and 31 (3.0%) patients received treatment less than 6 months.) With a median follow-up of 18 years (range 16–22), a total of 297 patients (29.1%) were diagnosed with a recurrence; 118 loco-regional and 179 distant (41 bone only and 138 visceral out of which eight patients were diagnosed with brain metastasis). Patients that were compliant to therapy had statistically significantly fewer recurrences; 149 out of 752 (19.8%) in patients that completed the treatment; 67 out of 158 (39.6%) for patients that were adherent for 2 but less than 5 years; 30 out of 77 (39.0%) for patients adherent less than 2 years and 13 out of 31 (41.9%) for patient compliant for a maximum of 6 months.

Conclusions: Our preliminary data shows that compliance to adjuvant endocrine therapy was high and confirms previous published data showing that fully compliant patients had an improved survival. Additional statistical analyses including multivariate analyses will be presented.

No conflict of interest.

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Efficacy and safety of eribulin in combination with trastuzumab in HER2-positive metastatic breast cancer patients: Real life experience

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Background: We sought to describe treatment patterns of eribulin and clinical outcomes of metastatic HER2-positive breast cancer treated with eribulin plus trastuzumab combination in community oncology practices across the Russian Federation.

Methods: Patients treated with eribulin anytime between Jan 1, 2014 and Sep 1, 2019 with a diagnosis of MBC was identified by 32 providers from Russia. Providers retrospectively reviewed the health records and abstracted selected data points into an electronic case report form for each eligible patient.

Results: 100 HER2-positive pts received eribulin in combination with trastuzumab. Median age was 55 (31–80) yrs and ECOG status 0–3. 67% pts had visceral metastases. Eribulin was administered as 1st and 2nd line to 23 (23%) pts, 3rd line to 31 (31%) pts, 4th line and later to 46 (46%). ORR was 12%, SD was 72%. Median PFS was 5.07 months (95% CI 4.021–6.119). According the ER-status of MBC patients the response to eribulin was different. ORR was 9% in pts with ER-positive MBC (n = 42) and 3% in ER-negative MBC (n = 58). Median PFS was 6.97 months (95% CI 3.924–10.016) in pts with ER-positive MBC and 4.67 months (95% CI 3.841–5.499) in ER-negative MBC. The combination was well tolerated: dose reduction required in 12% pts, withdrawal due to toxicity in 4% pts. The most common type of toxicity was hematological with neutropenia Gr III-IV in 14 (14%) pts. Peripheral neuropathy Gr III was observed in 5 (5%) pts. No cardiotoxicity was detected.

Conclusions: This is the real-life data of clinical outcomes for patients receiving eribulin plus trastuzumab therapy for HER2-positive MBC throughout the Russian Federation. Our experience with eribulin plus trastuzumab demonstrates that this combination may be a potential treatment option for HER-2 positive MBC patients, and further research is warranted including ER status.

Conflict of interest:
Corporate-sponsored Research:
Eisai LLC.

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Pathological complete response to neoadjuvant trastuzumab and pertuzumab therapy is dependent on HER2/CEP17 ratio in HER2-positive breast cancer

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Background: HER2 is amplified approximately 20% of breast cancers and HER2 receptor targeting therapy is associated with a significant improvements in disease-free and overall survival. In NeoSphere and TRYPHAENA clinical trials, the pathologic complete remission (pCR) rate was significantly increased when combined with pertuzumab and trastuzumab treatment. Although the efficacy and safety of anti-HER2 dual blockade therapy has been reported, the markers that predict the response are still unclear. This study aimed to investigate the relationship between the HER2 and centromere 17 (CEP17) ratio and the pCR to neoadjuvant therapy based on trastuzumab and pertuzumab.

Material and Methods: Twenty HER2-expressing breast cancer patients who had received neoadjuvant docetaxel, carboplatin, trastuzumab, and pertuzumab (TCHP) therapy were included in this study. HER2/CEP17 ratio was measured by fluorescence in situ hybridization analysis. The relationship between HER2/CEP17 ratio and tumor pCR status (ypT0 ypN0) was investigated.

Results: The Median age was 47.5 years (range: 36–62). 30.0% of the patients were hormone receptor (HR) positive and 70.0% of the patients were HR negative. The pCR rate in the breast and axilla was 70.0%. The patients who experienced a pCR had a median HER2/CEP17 ratio of 7.07 (range: 3.16–10.40) in comparison with median ratio of 4.89 (range: 1.06–6.15) if they did not ($p = 0.019$).

Conclusions: pCR was highly correlated with HER2/CEP17 ratio in the neoadjuvant setting with anti-HER2 dual blockade. This suggests that the HER2/CEP17 ratio can be used as a predictive marker to predict pCR in neoadjuvant trastuzumab and pertuzumab therapy.

No conflict of interest.

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Mantle cell lymphoma in the context of breast cancer

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Background: Concomitant breast carcinoma (BC) and non-Hodgkin lymphoma (NHL), especially mantle cell lymphoma (MCL), is rarely reported. No biological correlation has been established yet between the two pathologies. The optimal treatment strategy is not defined, especially when the diagnosis is simultaneous. We report two cases of BC and MCL, where the diagnosis of lymphoma was delayed due to misinterpretation of axillary lymph nodes (LNs).

Materials and Methods: We collected the medical history of the two patients followed in our center from their medical files. The medical history was analyzed since the diagnosis of first cancer, which was BC in both cases. After the formal diagnosis of the associated MCL, we collected older tissue samples from axillary LNs for retrospective detailed pathological review by specialized hemato-pathologists.

Results: A 78-year-old woman was diagnosed in January 2018 with a stage IA breast cancer and no lymph node (LN) involvement. She was referred to our center in March 2018. At that time, because she had enlarged bilateral axillary lymph nodes, we requested a review of the LN biopsy performed in January 2018. This analysis revealed an infiltration by the MCL (stage II). She was treated with tamoxifen and ibrutinib for the MCL. Unfortunately, the patient died a few months after the lymphoma diagnosis due to a rapid progression of her disease.

The second 63-year-old patient had in May 2005 a bilateral BC (stage IA) treated with double mastectomy and adjuvant endocrine therapy for 5 years. In August 2017, the biopsy of a cervical LN revealed a MCL (stage IVA). In 2015 she had an axillary LN sampling for slightly enlarged LNs, which was considered as free of cancer. However, after collecting and reviewing this sample, we could show that the MCL was already present. The patient was treated with 6 cycles of rituximab/bendamustin and she is now in complete clinical remission with rituximab maintenance.

Conclusions: The diagnosis of lymphoma can be missed in the context of a breast cancer staging. Despite LN sampling a long delay of diagnosis can be observed with potential prognostic impact. The professionals should be aware of this rare association in order to avoid misinterpretation as reactive LNs, especially in the presence of small LNs. Thirty-eight cases of NHL coexisting with BC, including 3 MCL, were described in the literature to our best knowledge. The majority of the reported cases demonstrates a wide disparity between stages of the two diseases and confirmes the risk of delayed diagnosis.

No conflict of interest.

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A high rate of pathological complete response is possible by incorporating cisplatin in neoadjuvant therapy of locally advanced triple-negative breast cancer: A single-institution experience

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Background: Breast cancer is the commonest cancer among women in India with 162468 new cases diagnosed in 2018. Triple-negative breast cancer accounts for 20–30% of these cases. It is a heterogeneous and poorly understood disease that has worse outcomes as compared to the other subtypes of breast cancer. Carboplatin has been shown to improve outcomes in the neoadjuvant setting in early triple-negative breast cancer. Studies on cisplatin in the neoadjuvant setting, especially in combination with anthracyclines and taxanes are very few. This study analysed the safety and efficacy of neoadjuvant cisplatin-based combination chemotherapy.

Material and Methods: This retrospective study analysed 62 women treated for locally advanced triple-negative breast cancer. Patients received 3-weekly cisplatin with weekly paclitaxel for 12 weeks either preceded or followed by 2-weekly anthracycline with cyclophosphamide for 8 weeks as neoadjuvant therapy. Standard hydration was given with cisplatin. The cumulative dose of cisplatin aimed at was 240 mg/m^2 for all patients. Following surgery, the pathological response to chemotherapy was graded according to the Miller Payne system.

Results: The mean age of the patients was 42.5 years. Fifty-nine per cent of women were premenopausal, 11.5% were perimenopausal and 29.5% had attained menopause. The tumour histopathology was ductal carcinoma in 97% patients with 1.6%, 25.8% and 72.6% of grades 1, 2, and 3 tumours respectively. Fifty-two per cent of patients completed all planned cycles of chemotherapy and overall, patients completed 88% of the total chemotherapy cycles planned. Only 2% of patients underwent breast conservation surgery while the rest underwent mastectomy. Pathological complete response (Miller Payne grade 5) was seen in 60.3% of patients. Good partial response (Miller Payne grades 3 and 4) was seen in 34.5% of patients. The median duration of follow up was 28.5 months (IQR 18.5–38.0). The recurrence-free survival at 1 year was 91% and at 3 years was 75%. The percentage of patients surviving at 1 year was 93% and at three years was 85%. The most common grade 3 and 4 adverse events were anemia (grade 3–35.5%; grade 4–1.6%) and neutropenia(grade 3–6.5%; grade 4–27.4%). Febrile neutropenia occurred in 6.4% of patients. Peripheral neuropathy occurred in 11.4% of patients. There were no treatment-related deaths.

Conclusions: Combination neoadjuvant chemotherapy with cisplatin is effective in locally advanced triple-negative breast cancer yielding higher pathological complete response rates as compared to published literature from India as well as historic cohorts from our institution. Cisplatin may be more effective than carboplatin in the treatment of triple-negative breast cancer. The haematological toxicity profile of the regimen was significant but manageable. Non-haematological toxicity was low.

No conflict of interest.

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Tumor-Infiltrating Lymphocytes: Predictive changes in tumor size after neoadjuvant treatment

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Background: Primary administration of antineoplastic treatment may allow to decrease tumor size. This situation favors the "rescue" of surgical patients with clinically large or unfavorable lesions to perform conservative surgery safely. There are immunological parameters, including Tumour-infiltrating lymphocytes (TILs), which have been identified as predictors of the radiological and pathological response to neoadjuvant chemotherapy in the breast cancer patients.

We are interested in assess the relationship between Tumour-infiltrating lymphocytes (TILs) and residual tumor volume in the lumpectomy or mastectomy specimens in breast cancer patients with neoadyuvant treatment.

Material and Methods: We performed an observational study of breast cancer patients operated after neoadyuvant treatment (NT) in a University Breast Unit from January to December 2018. TILs were estimated in corebiopsy specimen before NT and after the treatment in breast surgical specimens. The tumor response to the NT was also assessed by Miller and Payne (M&P) system and the residual cancer burden (RCB). MRI was performed before and after NT to assess the radiological response to the treatment.

Results: In this period 48 pacients were included. The average age was 52 (32–77) years old. The most frequent histological type was invasive ductal carcinoma (85.1%) and the distribution of intrinsic phenotypes was luminal 44.7%, erb2 38.3% and triple negative 17%. The average ki 67 was 33.7 ± 19. TILs were observed in 69.8% of the biopsies with an average infiltrative lymphocytes percentage of 37.4 ± 24%. After NT was observed a complete radiological response (CRR) in 62.8% of the patients and a complete pathological response (CPR) in 40.4%. The concordance between radiological and pathological response was 59.3%.

Patients who presented CPR had a greater inflammatory component (TILs (%) 38.1 ± 26 vs. 18.9 ± 23; p = 0.019). We observed a significant association of the TILs with: the decrease in the size of the lesion after NT (R = –0.48, p = 0.002), the RCB (R = –0.49, p = 0.001), the My P scores (R = 0.51, p = 0.001) and Ki 67 (R = 0.36, p = 0.017).

Conclusions: TILs is a predictive factor of pathological response after neoadjuvant chemotherapy. The quantification of the TILs could assist to plan the surgery given its relationship with the real decrease of the tumour size after treatment.

No conflict of interest.

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Diagnostic performance of noninvasive imaging for assessment of axillary pathologic complete response after neoadjuvant systemic therapy in clinically node-positive breast cancer: A systematic review and meta-analysis

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Background: Neoadjuvant systemic therapy (NST) is increasingly used and can lead to downstaging of the axilla. Imaging modalities can provide information about the axillary response to NST and, therefore, tailor surgical management. The purpose was to perform a systematic review and meta-analysis to determine the diagnostic performance of noninvasive imaging modalities for assessment of axillary pathologic complete response (pCR) after NST in clinically node-positive breast cancer patients.

Material and Methods: PubMed and Embase were searched to identify studies that compare noninvasive imaging after NST with axillary surgery outcomes in patients with initial pathologically proven axillary lymph node metastasis. Two reviewers independently screened the studies and extracted the data. A meta-analysis was performed for axillary ultrasound and breast MRI to compute sensitivity and specificity for the identification of axillary pCR and residual axillary lymph node disease, respectively. For whole-body ^{18}F-FDG PET-CT, a meta-analysis was not possible due to the limited number of studies.

Results: Thirteen studies involving 2380 patients were included for final analysis. Of these patients, 1322 had undergone an axillary ultrasound, 849 a breast MRI, and 209 a whole-body ^{18}F-FDG PET-CT. Overall axillary pCR was 41.4% (986 of 2380). For axillary ultrasound, the pooled sensitivity and specificity were 65.3% (95% CI 55.4–74.0%) and 63.3% (95% CI 47.8–76.5%), respectively. For breast MRI, the pooled sensitivity and specificity were 77.2% (95% CI 63.5–86.7%) and 59.6% (95% CI 49.5–68.8%), respectively. For whole-body ^{18}F-FDG PET-CT, the sensitivity and specificity ranged from 84.6–86.0% and 21.9–63.2%, respectively.

Conclusions: The diagnostic performance of current noninvasive imaging modalities is limited to assess axillary pCR after NST in clinically node-positive breast cancer patients.

No conflict of interest.

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Quality of life in postmenopausal breast cancer patients with localized disease after 5 years of endocrine treatment: A prospective study

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Background: Quality of Life (QL) is a key target of the attention that is offered to breast cancer patients survivors. More research on the effect of endocrine treatment (ET) on QL is needed.

The aims of the present study are to assess QL in a sample of early-stage breast cancer survivors who had received 5 years of ET; to compare QL of ET groups, and study the changes in QL after ET cessation.

Material and Methods: A consecutive sample of stages I-III breast cancer patients treated at the Oncology Departments of the Complejo Hospitalario de Navarra was invited to participate in the study. Patients were postmenopausal at diagnoses and had just stopped ET after receiving either tamoxifen or aromatase inhibitor (AI) for five years. Patients had no relapse.

134 patients filed in the EORTC QLQ-C30 (general QL) and QLQBR45 (breast specific QL) questionnaires, 70 of these patients (>65 years old) filled in also QLQ-ELD14 (elderly specific QL) questionnaire. 74 consecutive patients have filled in the same QL instruments (48 also the QLQ-ELD14) six months after ET cessation.

Differences in ET modality (tamoxifen-AI) in QL (QLQ-C30, QLQ-BR45 and QLQ-ELD14) were studied through U *Mann-Whitney* test. These comparisons were confirmed through univariate logistic regression analyses using the categorized version of QL questionnaires areas as response variables and ET modality as explanatory variable. QL changes between the two assessments in the three QL questionnaires were assessed (Wilcoxon test).

Results: Mean age was 69 (range 50–93); 29 patients (21.6%) had tamoxifen, 54(49%) chemotherapy, 120(90%) radiotherapy; 94(70%) conservative surgery; 46(34%) limiting co morbidity.

QL scores were high in most areas (>80/100 points functioning, <20 points in symptoms areas) with moderate limitations (>30 points) in sexual functioning and enjoyment (breast specific), joint stiffness (elderly specific); and light limitations (20–30 points) in emotional functioning, sleep disturbance, pain, global QL (general QL); ET Symptoms, future worries (breast specific); and future perspective, worries about others, maintaining purpose and family support (elderly specific) areas.

Tamoxifen patients had less pain (7/100) and more constipation (7/100 small differences) (general QL); better sexual functioning (11/100 medium difference) and worse body image (6/100 small) (breast specific). These differences were confirmed in the univariate logistic regression analyses.

Changes between the two assessments appeared in pain (4/100 trivial change) (general QL), endocrine treatment (8/100 small) and sexual enjoyment (12/100 medium) (breast specific), with better QL in the second assessment.

Conclusions: Postmenopausal early-stage breast cancer patients adapted well to five years of ET and to their disease.

Few QL differences were observed between ET groups. There was some QL recovery after ET cessation.

No conflict of interest.

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The gene expression profile in clinically node negative T1–2 breast cancer patients: Its additional value in case of sentinel lymph node biopsy is not performed

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Introduction: Several trials are currently investigating whether the sentinel lymph node biopsy (SLNB) can be safely omitted in cT1-2N0 breast cancer patients treated with breast conserving therapy (BCT). A consequence of omitting the SLNB is the absence of pathological lymph node status information, as one of the indicators for the recommendation of adjuvant chemotherapy. Gene expression profiles (GEP) have been developed to select patients who most likely benefit from adjuvant chemotherapy. The aim of this study was to determine the value of GEP in cT1-2N0 breast cancer patients treated with BCT in whom the SLNB potentially could be omitted.

Methods: Data were retrieved from the Netherlands Comprehensive Cancer Organisation (IKNL). Patients were included in case of cT1-2N0 breast cancer treated with BCT, SLNB and in whom GEP (Mammaprint® or 21-gene Oncotype DX Breast Recurrence Score®) is performed. Patients were excluded in case of neoadjuvant treatment and age >70 years. Adjuvant chemotherapy recommendation was determined based on the breast cancer guideline and theonline prediction tool PREDICT, both forpatient's true pathological lymph node status and for unknown (e.g. negative) pathological lymph node status, as if SLNB is not performed. For each patient, recommendations based on the clinicopathological factors (breast cancer guideline and theonline prediction tool PREDICT) were compared with the outcome of GEP.

Results: GEPwas performed in 3,803 (18.4%) of the cT1-2N0 breast cancer patients treated with BCT. Based on breast cancer guideline, 93.5% had an indication for adjuvant chemotherapy compared to 42.9% using the online prediction tool PREDICT. Assumed that SLNB was not performed, the lymph node status changed in 736 of the 3,803 patients (36.6%). There was a change from recommendation to no recommendation for adjuvant chemotherapy in 239 of the patients. Of these, 201 (84.1%) had a genomic low risk and 38 (15.9%) a genomic high risk. The recommendation for adjuvant chemotherapy changed in 6.3% based on the breast cancer guideline and in 1.2% based on the online prediction tool PREDICT.

Conclusion: If SLNB is omitted, the recommendation for adjuvant chemotherapy will change due to unknown pathological lymph node status in only small percentage of the patients. If controversy based on the clinicopathological factors will remain, the 70-gene signature test Mammaprint® could be implemented for the recommendation of adjuvant chemotherapy.

No conflict of interest.

Advanced Disease

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The survival outcomes for the subsequent therapy after treatment with trastuzumab emtansine in human epidermal growth factor receptor 2-positive metastatic breast cancer patients

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Background: Trastuzumab emtansine (T-DM1) has been widely used for human epidermal growth factor receptor 2 (HER2)-positive metastatic breast cancer (MBC) patients who previously received trastuzumab (Tmab) and a taxane since 2013 in Japan. However, there is a lack of evidence for treatment outcomes after exposure to T-DM1 in Japanese HER2-positive MBC patients. This study aimed to describe the survival outcomes of patients with HER2-positive MBC who received subsequent treatment after T-DM1 and clarify the predictive factors of their prognosis.

Patients and Methods: We retrospectively identified patients with HER2-positive MBC who received T-DM1 between April 1, 2014 and December 31, 2018 in the National Cancer Center Hospital, and focused on the population who received another line of therapy after T-DM1 discontinuation. Survival analyses were performed using Kaplan-Meier Method.

Results: Thirty patients were available for outcome analysis. The median follow-up period was 21.8 months. The median number of prior chemotherapy regimens for metastatic disease before the subsequent therapy was 2 (range 1–7) and 13 (43.3%) of patients received pertuzumab (Pmab). Thirteen (43.3%) patients were administered a regimen containing Tmab and/or lapatinib for the first subsequent line after T-DM1. The median progression free survival (PFS) and the median overall survival (OS) of T-DM1 were 3.7 months (95% confidence interval [CI] 2.7–5.5) and 28.9 months (95%CI 18.3-not reached), respectively. The median PFS of the first subsequent therapy was 6.0 months (95%CI 4.1–6.4). The median OS from the first administration of the first subsequent therapy was 20.6 months (95% CI 13.5-not reached). The median PFS of the first subsequent line was shorter for the patients who received Pmab before T-DM1 (n = 13) than the patients who received a regimen without Pmab (n = 17) [5.1(95%CI 3.72–6.18) versus 6.2(95%CI 2.53–11.4) months, $P = 0.03$]. In addition, we divided the patients into two groups according to the PFS of T-DM1 treatment and compared the PFS of the following treatment. There was a significant difference in the median PFS of the first subsequent treatment between patients with the PFS of less than 3 months and more than 3 months [5.1 (95%CI 1.7–6.2) versus 6.2 (95%CI 4.0–11.3) months, $P = 0.03$]. Univariate analysis showed that brain metastases ($P < 0.004$), prior use of Pmab ($P = 0.03$) and the PFS of T-DM1 ($P = 0.03$) were significant predictive factors for the PFS of the first subsequent therapy in HER2 positive MBC patients.

Conclusions: This is the first report to evaluate the survival outcomes for the post-T-DM1 therapy in Japanese HER2-positive MBC patients. Our study showed brain metastases, prior use of Pmab, and PFS of T-DM1 treatment were significantly associated with the PFS of the subsequent treatment after T-DM1 for patients with HER2-positive MBC.

No conflict of interest.

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An exploratory phase II study of Eribulin re-challenge after short term therapy of 5-fuluorouracil for HER2-negative, advanced or recurrent breast cancer

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Background: Eribulin (ERI) demonstrated improvement of survival when used in late-line therapy for metastatic breast cancer(MBC). We previously conducted a phase II study to investigate the efficacy of ERI as the first-line chemotherapy for human epidermal growth factor receptor 2 (HER2)-negative MBC. It showed 54.3% of objective response rate (ORR) and 5.8 months (25 weeks) of progression free survival (PFS) with mild toxic profiles. From this result, it was thought that resistance for the first-line ERI might develop in around 4 months. If the resistance could be blocked by switching to a drug of different mode of action for a certain period in the timing when resistance arises, the tumor may retrieve sensitivity for ERI and it might contribute to improve quality of life by prolonging the duration of ERI with mild toxic profile. Actually, docetaxel that is one of the tubulin inhibitors demonstrated efficacy of re-challenging.

This study was conducted to investigate efficacy of re-challenge of ERI for advanced or recurrent breast cancer patients who received prior ERI and to evaluate extension of disease control period exploratorily.

Material and Methods: We enrolled individuals who had HER2-negative MBC with measurable lesion and received no chemotherapy for advanced disease. Eligible patients started to receive first-line chemotherapy with ERI (1.4 mg/m^2 on day1 and 8 of 21 days cycle) and continued for 18 weeks if they did not have disease progression, then they received one cycle of S-1 (80 mg/m^2/day, 4 weeks on and 2 weeks off) that may inhibit ERI resistance by its different mode of action against cancer cells. After completion of S-1 phase, ERI was re-introduced.

The primary endpoint was PFS of re-introduced ERI (PFS2). A threshold of 2.5 months for PFS2 would be promising based on the results of our previous clinical trial for the first-line ERI.

Results: Fifteen patients were recruited. ORR of initial ERI was 60%. Three patients were discontinued and 12 patients (57% of targeted number) received ERI re-introduction. The PFS of re-introduced ERI therapy was 13 weeks. Time to failure of strategy defined as the period between initial ERI administration and disease progression was 39.9 weeks and median overall survival was 115 weeks. Total duration of ERI use was 30 weeks. The incidence and severity of adverse events were consistent with previous reports and no new safety concerns were identified.

Conclusions: We obtained 13 weeks additional PFS by re-introduction of ERI and the total duration of ERI was numerically prolonged (30 weeks) in comparison with our previous result of the first-line therapy (25 weeks). It is difficult to give definite conclusion about this strategy due to the small number study. Further evaluation would be warranted.

Conflict of interest:
Corporate-sponsored Research:
Eisai Co., LTD.
Other Substantive Relationships:
Personal fees from Taiho Pharmaceutical Co., Ltd., personal fees from Chugai Pharmaceutical Co., Ltd., personal fees from Kyowa Hakko Kirin Co., Ltd., personal fees from Eisai Co., Ltd., personal fees from Pfizer Japan Inc., personal fees from Novartis Pharma K.K., personal fees from AstraZeneca K.K., personal fees from Takeda Pharmaceutical Co., Ltd. Eli Lilly Japan K.K.

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Characteristics of metastatic breast cancer patients obtaining a clinical complete response with systemic therapies

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Background: Metastatic breast cancer (MBC) is basically regarded as being incurable. However, there are reports describing cases with a clinical complete response (cCR) to multidisciplinary therapies. Because these cases are rare, their characteristics have not been well investigated. Herein, we investigated MBC cases obtaining cCR with systemic treatments.

Methods: There were 247 cases who developed MBC after curative surgery or had stage IV disease and were treated during the 2006 to 2018 period at our department. Fourteen patients (6%) obtained cCR only in response to systemic therapies and the details of these cases were retrospectively investigated. Patients who received surgery or radiation therapies for metastatic sites were excluded. The remaining 233 cases with

MBC, treated at our hospital during the same period, were compared as controls.

Results: Mean age at relapse of the 14 patients was 58 (31–72) years. The primary tumor subtype was luminal-HER2-negative in 8 (57%), luminal-HER2 (+) in 3 (21%), HER2 type in 2 (14%), and triple negative (TN) in 1 (7%) case. The median recurrence-free interval was 30 (0–96) months. Organs with metastases were: bone in 4 (29%), the lungs in 5 (36%), liver in 3 (21%), soft tissue in 2 (14%) and others in 1 (7%) case. Median cCR duration was 73 (39–180) months. The mean number of treatments after relapse was 2.0 (1–4). The last/ongoing treatments were endocrine therapies (7 patients), chemotherapies (2) and anti-HER2 treatments (5). Among the 14 patients, 7 have maintained cCR, to date, since terminating their therapies. Compared to control cases, luminal-HER2 type was frequently observed in cCR cases while TN was rare. There was no difference in the distribution of metastatic sites but brain metastases were observed only in the control group.

Conclusions: Our data confirmed that MBC is potentially curable, although at a very low frequency, with systemic treatments. We need to accumulate more cases to reveal the biological features of such MBC, in order to establish curative treatments for MBC.

No conflict of interest.

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Lactate dehydrogenase as a prognostic biomarker in patients with hormone receptor-positive metastatic breast cancer treated with palbociclib: An exploratory cohort study

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Background: Cyclin-dependent kinases (CDK) 4/6 inhibitors have recently reshaped the therapeutic scenario for hormone receptor (HR)-positive/HER2-negative metastatic breast cancer (MBC). Elevated serum lactate dehydrogenase (LDH) levels correlate with poor prognosis in various malignancies, including MBC. However, no data are available on LDH prognostic value in patients treated with CDK4/6 inhibitors. Henceforth, we explored whether plasmatic LDH could represent a prognostic biomarker in patients treated with endocrine therapy (ET) and the CDK4/6 inhibitor palbociclib.

Material and Methods: We review data of patients with HR-positive/HER2-negative MBC consecutively treated with palbociclib plus ET at two Italian cancer centers from 2017 to 2019. A multivariate Cox regression model evaluated the independent prognostic impact of baseline plasmatic LDH levels on both progression-free survival (PFS) and overall survival (OS). Relevant clinicopathological factors were included as covariates in the regression model (e.g., age, progesterone receptor (PgR) status, tumor grade, performance status, treatment line, bone-only or visceral disease, tumor burden, companion ET). Survival differences were compared through the log-rank test.

Results: Overall, 202 patients were deemed eligible. Of these patients, 133 (65.8%) received palbociclib plus fulvestrant, 69 (34.2%) palbociclib with an aromatase Inhibitor, and 111 (55.0%) were treated first-line. The 37.2% of cases were PgR-negative, and 33.2% were grade 3 tumors. Visceral involvement was detected in almost half of patients (46.5%), whereas 34.1% presented with bone-only disease. Of note, 60.9% of patients received a prior CT, 25.2% in the metastatic setting. After a median follow-up of 15.2 months, the median PFS was 14.1 months (95% CI: 10.97–18.17), and the median OS was not reached. At baseline, 20% of evaluable patients (24/120) had elevated pre-treatment LDH levels according to the local laboratory cut-off. Through multivariate analyses, baseline elevated plasmatic LDH emerged as an unfavorable and independent prognostic factor in terms of both PFS (HR: 2.18, 95% CI: 1.12–4.25, p = 0.02) and OS (HR: 4.65, 95% CI: 1.59–13.55, p = 0.004). Consistently, high LDH levels were associated with shorter median PFS (9.5 vs. 17.4 months, p = 0.01) and median OS (15.3 months vs. not reached, p = 0.0004) compared to normal LDH values.

Conclusions: Serum LDH levels independently predict PFS and OS in MBC patients treated with palbociclib in association to ET. Although the small sample size and the limited follow-up, this is the first study to confirm a prognostic role for LDH while commencing on a treatment with CDK4/6 inhibitors. Further studies are warranted to clarify the biological relevance of serum LDH elevation in patients with luminal MBC and explore possible correlations with mechanisms of endocrine resistance.

Conflict of interest:
Advisory Board:
FP: Astrazeneca, Eli Lilly, Novartis, Pfizer LG: Eli Lilly.
Corporate-sponsored Research:
FP: Astrazeneca, Novartis, Roche.

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Does Neo-adjuvant chemotherapy response in the primary breast tumour correlate with axillary response in proven node positive ER positive HER2 negative disease?

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Background: The indication for Neo-adjuvant chemotherapy (NACT) has expanded from down-staging of locally advanced tumours to routine management of T2 node positive tumours. We ascertain whether in-breast response correlated with nodal response at axillary node clearance (ANC) in ER+ve HER2-ve proven node positive disease.

Materials and Methods: Patients treated with NACT over a 4-year period (March 2013–May 2017) were identified from a prospective database. Response was assessed as residual pathological tumour size as a proportion of the largest pre-treatment imaging size. Nodal positivity confirmed pre-operatively with ultrasound-guided biopsy was defined post-operatively as the presence of any residual tumour cells (Royal College of Pathologists guidance). Multivariate analysis (logistic regression) was performed of standard prognostic factors.

Results: Of 56 ER+ve HER2-ve tumours; 46 were NST and 10 special type cancers (5 lobular and 5 micropapillary). Overall 5 tumours had pCR in breast. Axillary response post-NACT: 8 (6 G2, 2 G3) had axillary pCR with no positive nodes (14%), 2 (G3)had axillary response with residual ITC's only, and 46 had residual micro- or macro-metastatic disease [6 (5 G2, 1 G3) with one node, 10 (1 G1, 6 G2, 3 G3) with 2 nodes, 6(4 G2, 2G3) with 3 nodes and 24(16 G2, 8 G3) with 4 or more nodes].

Conclusions: Albeit with limited numbers, the pCR rate in nodal metastasis is low (14%) and independent from tumour histology, grade, pre-NACT size and breast pCR (P values: 0.85, 0.71, 0.30 and 0.06 respectively). 24 (42%) patients with persistent disease in 4 or more nodes would have met staging CT criteria (if fully confirmed pre-operatively). Hence, proven nodal disease should not be an indication for administration of NACT in patients with ER+ve HER2-ve disease as tumour biology is a more important indicator of chemo-sensitivity than overall disease burden/axillary spread. Trials like Optima may provide more insights.

No conflict of interest.

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Compared expression of Tumour Infiltrating Lymphocytes and FOXA1 in matched pairs of brain metastasis and primary breast cancer and prognostic implications – a pilot study

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Background: Forkhead box A1 (FOXA1) a transcription factor for ER and the androgen receptor and Tumour infiltrating lymphocytes (TILs) are studied for their impact on prognosis for breast cancer (BC) subtypes. More patients appear to be affected by brain metastases (BM). However, data on biology of BM is limited and there is need for increased knowledge on how BM compare to primary BC. We aimed to compare levels of TILs and FOXA1 in matched pairs of BC and BM, and to determine the effect on prognosis.

Methods: Matched pairs of tumours from fifty-five patients who had undergone surgery for BM from BC (17 Luminal, 24 TNBC and 11 HER2+) 1994–2014 were re-evaluated for ER, PgR, HER2, FOXA1, and TILs.

Results: Levels of TILs were grouped as 1–9% = low, 10–49% = intermediate, 50–74% = high, 75–100% very high. Most of the BM had low levels of TIL (n = 44, 84%), and 8 intermediate (14.5%). The corresponding figures for primary tumours were 32 low (58%), 17 intermediate (31%), 3 high

(5.5%), 2 very high (3.5%). TILs were highest in TNBC in the primary tumour with 14.3% high and very high compared with 6.3% and 0 in luminal and HER2+BC. A significant difference was found between TILs between the primary BC and BM with in the vast majority a lower level in the BM ($p = 0.0042$) driven mainly by the TNBC results. None of the survival parameters studied varied with TILs. There was a statistically significant difference between BC subgroups regarding FOXA1 positivity in the BM; Luminal (93.3%); TNBC (13.0%) and HER2+ (100%) ($p < 0.001$). A similar difference was found in the primary tumours; Luminal (68.8%); TNBC (22.7%) and HER2+ (81.8%) ($p = 0.011$). No difference was found in FOXA1 when BM was compared with the primary BC; 84.4% had equal expression ($p = 0.1$). TNBC was the only subgroup with reduction in FOXA1 in the BM. Luminal BC with FOXA1 had a non-significant prolongation of BM free interval (BMFI) of 1850 vs 1134 days, and survival following BM (1005 vs 435 days). Expressed FOXA1 in BM or primary BC of TNBC did not affect BMFI or survival after BM. Overall survival (OS) was doubled in TNBC according to FOXA1 (negative vs positive; 1255 vs 3277 days) $p = 0.024$. A gain of FOXA1 in TNBC was associated with a prolonged OS ($p = 0.052$).

Conclusions: TILs were highest in TNBC but lower levels were found in the BM compared with the primary BC in all BC subgroups. As one of few studies, we show a significant change in TILs between primary BC and BM above all in TNBC. FOXA1 was expressed in the majority of Luminal BC both in the primary BC and the BM but did not have significant prognostic impact in patients with BM. Interestingly, FOXA1 was expressed in a proportion of primary TNBC and correlated to survival and a gain of FOXA1 in BM was related to improved OS. Our material is too small to draw definite conclusions but we hope this can act as hypothesis generating for other studies.

Conflict of interest:
Corporate-sponsored Research:
Antibodies for FOXA1 excluding reagents and lab equipments were provided free of charge by AH diagnostics (Stockholm, Sweden)for the study. No instructions on study design were stipulated.

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Evolving psychosocial, emotional, functional, and support needs of women with advanced breast cancer (ABC) in Asia and Middle East (ME): Results from the Count Us, Know Us, Join Us (CUKUJU) survey

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Background: Breast cancer is the most common cancer in women and has varying rates of incidence, mortality, and survival across different geographical regions.[1] Even though the survival in women with ABC has improved with new treatment (tx) strategies, their psychosocial, emotional, and functional needs remain unmet.[1,2] In the year 2018, Novartis in association with the Harris Poll conducted the CUKUJU survey to understand these unmet challenges faced by patients (pts) in Asia and ME. Here, we report the key results from the CUKUJU survey.

Material and Method: The first global CUKUJU survey, conducted in 2013, was extended in Asia and ME regions in 2018 (15 January – 10 July). Total sample data are not weighed, and therefore, representative only of the individuals interviewed online.

Results: A total of 381 women (>21 y; median age at diagnosis 40–44 y) with ABC completed the survey in 7 countries: Egypt (n = 58), Hong Kong (n equals; 51), India (n = 78), Lebanon (n = 15), Saudi Arabia (n = 56), Singapore (n = 50), and Taiwan (n = 73), and 93% of them reported of being treated for their ABC. Majority of pts (81%) felt that the communication with HCPs improved their outlook. The most common topics, which the pts discussed with their HCPs, included tx-related adverse events (AEs; 57%) and strategies to manage AEs (55%). Most pts (77%) proactively sought information on their own to learn about ABC. Majority of pts (82%) were satisfied with the support received from family and friends. However, 43% of them felt the support had waned, as they had continued to manage ABC. Majority of pts (71%) said that ABC had a lot/moderate negative impact on their lives and 60% of pts no longer felt like an active member of the community, since diagnosis. Table 1 depicts the key challenges as reported by the pts.

Table 1 Key Challenges

Challenges	Pts (n%) reporting challenges
Tx in ABC	
Limited tx options for ABC	68%
Need for new tx for ABC	90%
Pt-HCP communication	
Expects HCPs to spend more time to discuss their needs during their visits	83%
Expects HCPs address their emotional needs during their visits	69%
Support	41%
Not enough support from advocacy, voluntary, or charitable organizations	26%
Information	
Difficulties to find information specific to ABC	50%
Impact on self and society	
Worry about ability to help their family/society	70%

Conclusion: Overall, the results from the 2018 CUKUJU survey from Asian and ME countries highlighted that in these regions of the world, a substantial proportion of women with ABC still face several important psychosocial/emotional challenges, which negatively impacts their quality of life. These results should be interpreted with caution, keeping in mind the caveats of a survey-based analysis.

Conflict of interest:
Other Substantive Relationships:
Aimee Vella Ripley, Jamie Lehr, Mohamed Shaalan, Smruti Koppikar, Vandana Gupta, Melisa Gao and Noha Abdelbaky have nothing to disclose. Fatima Cardoso reports personal fees from Amgen, personal fees from Astellas/Medivation, personal fees from AstraZeneca, personal fees from Celgene, personal fees from Daiichi-Sankyo, personal fees from Eisai, personal fees from GE Oncology, personal fees from Genentech, personal fees from GlaxoSmithKline, personal fees from Macrogenics, personal fees from Medscape, personal fees from Merck-Sharp, personal fees from Merus BV, personal fees from Mylan, personal fees from Mundipharma, personal fees from Novartis, personal fees from Pfizer, personal fees from Pierre-Fabre, personal fees from prIME Oncology, personal fees from Roche, personal fees from Samsung Bioepis, personal fees from Sanofi, personal fees from Seattle Genetics, personal fees from Teva, outside the submitted work.

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Neutrophil to lymphocyte ratio (NLR) may predict survival and efficacy of eribulin in advanced breast cancer patients

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Background: Several studies have shown that Neutrophil to lymphocyte ratio (NLR) is an unfavorable prognostic factor for many cancers including early breast cancer. Some studies also suggest that NLR may predict the efficacy of chemotherapy. The aim of this study is to examine the relationship between NLR and efficacy of Eribulin treatment.

Method & Aim: 88 patients with advanced unresectable breast cancer including both hormone receptor positive or negative and human epidermal growth factor receptor positive or negative who received Eriblin at our institution from September 2009 to December 2018 were registered. We omitted 6 patients because laboratory test results were missing at the time of eribulin treatment. 2 other patients were also excluded because one patient had a recurrence of ovarian cancer during the treatment of breast cancer, and the other patient received eribulin off-lbel. We retrospectively analyzed patients' background, tumor subtypes and overall survival (OS) and divided

in two groups according to NLR at the timing of terminating Eriblin's administration with cut-off 2.76(Low-NLR and High-NLR).

Result: 50 patients were in Low-NLR and the rest were in High-NLR. There were significantly more patients with visceral metastasis and patients who developed a new metastatic lesion at the time of termination of eribulin in High-NLR in univariate analysis. However, there were no significant differences in other background factors in multivariate analysis. The median OS in Low-NLR was 815 days, which was significantly longer than that of High-NLR, 287 days. There was also a significant difference in the distribution of NLR which is comparing with that of starting and terminating Eriblin. We also analyzed the distributions of NLR when starting the preceding treatment before Eriblin and NLR when started Eriblin, however there was no significant difference. Propensity score-matched analyses were also performed. 48 patients were matched and OS was analyzed. The median of OS were 503 days in Low-NLR and 299 days in High-NLR, but the difference was not significant (p = 0.0567).

Conclusion: Patients with Low-NLR had significantly better overall survival rate. Some studies have shown that NLR could be a prognostic factor in breast cancer patients. However, there were only limited reports on the relationship between NLR and OS. There was no significant difference in propensity score-matched analyses, although the p-value was close to 0.05. We also found out administering Eriblin may possibly improve the distribution of NLR. Some studies suggest that NLR are a reflection of tumor microenvironment and Eriblin is said to be acting as a unique effect of it. We require further investigates to verify our findings.

No conflict of interest.

258 Poster

Use of indocyanine green (ICG) alone as a tracer for sentinel lymph node detection after neoadjuvant chemotherapy in breast cancer patients

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Background: In breast surgery, the rate of patients receiving an indication to neoadjuvant chemotherapy is increasing, thanks to a progressive improvement in terms of survival rates and tolerability of therapies. Consequently, an increasing number of patients is cN0 at the end of the oncologic therapies. These patients might be eligible to a conservative axillary surgery through a sentinel lymph node detection. In previously treated patients, a single sentinel lymph node is not enough to grant a safe procedure: the bigger number of lymph nodes is collected, the higher predictability increases. The procedure has been considered predictive with a number of collected lymph nodes equal to five (Galimberti, St. Gallen 2016), and then, after an indication amendment, three (Gentilini, AIS 2017).

The standard method based on the Tc99 injection alone is not able to reach the required number of lymph nodes. Therefore studies are being conducted considering two different tracers used together: Tc99 and blue dye.

ICG, which normally detects a higher number of lymph nodes in comparison with the other tracers, might be enough to reach a predictive number of specimens even used alone.

Materials and Methods: Since 2016 we have performed 51 sentinel lymph node detections using ICG alone in patients treated with neoadjuvant chemotherapy. We used an infrared camera able to detect the 780 nm length wave emitted by ICG, injected subcutaneously. The mean time to surgical cut has been 6.2 minutes, longer than usual in order to let ICG flow into the axilla and detect a higher number of nodes.

Results: ICG has detected a mean of 4.21 lymph nodes for each patient (3–7). In 25 cases nodes were positive. 45 patients are alive, with a mean follow up of 16 months. All the 6 deceased patients had a positive lymph node. After a mean follow up of 18 months, no ypN0 patient has shown an axillary cancer relapse.

Conclusion: Considering our data, ICG appears as a safe and predictive tracer, even used alone, able to comply the specific requirements of patients previously treated with chemotherapy and eligible to an axillary conservative surgery.

No conflict of interest.

259 Poster

Breast cancer patients with leptomeningeal carcinomatosis: Treatment results and validation of prognostic indexes

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Introduction: Specific prognostic scores for patients with breast cancer (BC) brain metastases and/or leptomeningeal carcinomatosis (LMC) can help predict expected survival in order to choose the most appropriate treatment. The aim of this study was to perform a validation of recently published prognostic survival indexes, namely Breast Graded Prognostic Assessment (Breast-GPA), Simple Survival Score for Brain Metastases (SS-BM) and Index score.

Material and Methods: We reviewed medical records of 70 patients with BC LMC, who received radiotherapy (RT) of the whole brain between the years 2005 and 2015. The statistical analyses included the Kaplan–Meier method, the log-rank test, the Cox proportional hazards model to calculate the effect sizes (given as hazard ratios, HR with confidence intervals, CI) and the Concordance index (Harrell's C-index) to quantify the quality of the predicting abilities of the prognostic indexes.

Results: Median OS for patients with LMC was 2.3 months (95%CI; 1.5–3.2) and 1-year survival rate was 16%. Up-scaling of the performance status within the first month after RT (n = 33, 47.1%) was associated with better OS (3.6 vs. 0.3 months, p = 0.0005). Significant differences in median OS were demonstrated for primary BC biologic sub-types as follows: 0.7 months for primary HER2-positive (N = 2), 0.8 months for triple-negative (N = 9), 2.2 months for Luminal B HER2-negative (N = 30), 3.2 months for Luminal A (N = 20) and 12.3 months for Luminal B HER2-positive (N = 7) (p = 0.017). In the Cox proportional hazards model, poor Karnofsky performance status (PS) at the time of RT (KPS < 70) (HR 12.9, 95%CI 01.2–134.4, p = 0.020), non-improvement of neurological symptoms within the first month after RT (HR 2.4, 95%CI 1.36–4.39, p = 0.003) and non-hormonal receptor positive BC (HR 2.13, 95%CI 1.10–4.13, p = 0.038); resulted in an increased risk of dying. However, lower RT total dose, 20 Gy (HR 1.22, 95%CI 0.62–2.0), age <53 years (HR 0.69, 95%CI 0.39–1.23), uncontrolled extra-cranial disease (HR 0.80, 95%CI 0.37–1.72), treatment before year 2010 (HR 1.23, 95%CI 0.71–2.12), not-receiving intrathecal chemotherapy (HR 1.55, 95%CI 0.67–3.61) or systemic treatment (HR 1.15, 95%CI 0.35–3.73) did not predict for worse OS. Breast-GPA (class 1 vs. 4: 1.3 vs. 14.2 months; p < 0.005), SS-BM (group A vs. C: 1.7 vs. 5.9 months; p = 0.044) and Index score (group D vs. A: 0.3 vs. 6.0 months; p < 0.0005) all predicted OS with statistical significance. Breast-GPA showed the best predictive ability for survival in patients with LMC, with C-index of 0.886 compared to SS-BM (C-index, 0.674) or Index score (C-index, 0.768).

Conclusions: BC subtype, PS at the time of RT and its improvement within the first month after RT all influenced median OS in our series of investigated LMC patients. Breast-GPA showed the best discriminating ability for predicting survival in patients with LMC.

No conflict of interest.

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Treatment efficacy and predictors of durable response to capecitabine monotherapy in advanced breast cancer: Real-world evidence from a large single-centre cohort

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Background: Capecitabine, an oral chemotherapeutic agent (fluoropyrimidines), is approved in monotherapy in metastatic breast cancer (MBC) after failure of taxanes and anthracycline. We investigated clinical and pathologic characteristics as possible predictors of durable response, time to progression (TTP) and overall survival (OS) in MBC patients treated with capecitabine monotherapy.

Methods: This retrospective study included patients with MBC treated at University Hospitals Leuven who started capecitabine monotherapy between March 1999 and November 2017. Treatment was ended in case of disease progression or for other reasons like toxicity. Durable response was defined as response duration >52 weeks and clinical benefit rate (CBR) as the percentage of patients who achieved complete response, partial response or stable disease based on Revised Evaluation Criteria In Solid Tumours v1.1. Comparison between patients with and without durable response was performed using Fisher exact test and Mann-Whitney U test. Cox regression models were used for analysis of time-to-event outcomes. A forward stepwise selection procedure was used for multivariable model.

Results: 506 patients were included with a mean age of 51 years (range 22–85 years), of whom 500 (98.8%) were pre-treated with taxanes and/or anthracycline. 392 patients (77.4%) stopped due to progression, 111 (21.9%) because of another reason and 3 (0.6%) where on treatment at moment of analysis. Median duration of treatment, median TTP and OS were 18, 28 and 58 weeks, respectively. CBR was 59.5%. 59 patients (11.6%) achieved durable response. Patients with durable response were, compared to patients without durable response, more likely oestrogen receptor (ER) positive (91.5% vs. 76.8%, p = 0.010) at diagnosis and had a higher incidence of lymph node (LN) negativity (64.4% vs. 50.1%, p = 0.039), as well as more frequent metastases limited to ≤2 involved sites (54.2% vs. 38.5%, p = 0.020) before start of capecitabine. Furthermore, time from first metastasis to start of capecitabine was longer (mean 3.5 years vs. 2.7 years, p = 0.020). In a final multivariable model, ER positivity and LN negativity remained statistically significant predictors of longer TTP (p < 0.0001 and p = 0.008, respectively).

Conclusion: Our data show that ER positivity at diagnosis and LN negativity before start capecitabine monotherapy are independent predictive factors of longer TTP.

No conflict of interest.

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Cyclin-dependent kinase 4/6 inhibitors palbociclib or ribociclib combined with endocrine therapy and radiation therapy for patients with metastatic breast cancer

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Background: The cyclin-dependent kinase 4 and 6 inhibitors (CDK4/6i) represented the standard I-II lines of hormone receptor positive (HR+), human epidermal growth factor receptor 2 negative (HER2–) metastatic breast cancer (MBC). Data regarding toxicity safety profiles when combining CDK4/6i with palliative radiotherapy (RT) are still lacking. RT use with palliative and ablative intents is currently increasing due to promising results in the oligometastatic setting. We aim to investigate acute adverse events (AEs) before, at the start, two, and six weeks after RT completion.

Material and Methods: Medical records of MBC patients on systemic treatment with CDK4/6i who underwent metastases directed RT were reviewed. Clinical, laboratory, and RT treatment planning data were collected. The statistical analyses included the chi-squared test and a logistic regression model.

Results: Of the 42 patients included in the study, 29 (69%) received palbociclib and 13 (31%) ribociclib. Median number of CDK4/6i cycles at the start of RT was 3 (range 1–28). Patients underwent 55 palliative RT treatments, with a median total dose (TD) 20 Gy (range 8–63) as follows: bone (n = 43; 75.2%), visceral metastases (n = 7; 12.7%), primary tumor of the breast (n = 2; 3.6%), and brain metastases (n = 3; 5.5%). Most patients were treated using 3DCRT technique (n = 34; 61.8%), followed by 2DRT (n = 11; 20%), SBRT (n = 7; 12.7%), and IMRT/VMAT/Helical Therapy (n = 3; 3.6%). CDK4/6i treatment was suspended in 66.1% of RT treatments (median 9 days; range 0–34). Total number of AEs (any grades, G) is presented in Table 1. All except one ≥G3 AEs were hematological. At logistic regression analysis accounting for age, type of CDK4/6i, CDK4/6i suspension during RT, planning target volume (PTV), TD, and RT technique, only smaller PTV was associated with a lower ≥G1 abnormalities in laboratory tests (cutoff 250 cm^3, HR 3.82; 95%CI 1.05–13.91; p = 0.042), but not for any other AEs. Nevertheless, in adjusted analysis accounting for the same confounding factors, none had the negative effect on abnormal laboratory tests, gastro-intestinal or cumulative toxicity. We found no correlation between dose distribution to organs-at-risk and AEs.

Table 1 Total number of AEs

	Before RT.	During or after RT.	
G0	26 (47.3%)	15 (27.3%)	p = 0.016
G1	18 (32.7%)	14 (25.5%)	
G2	9 (16.4%)	16 (29.1%)	
G3	2 (3.6%)	9 (16.4%)	
G4	0	1 (1.8%)	

Conclusions: Palliative RT seemed to moderately increase the rate AEs (any grade), regardless of CDK4/6i systemic therapy continuation or interruption. However, serious AEs incidence rates were in agreement with main pivotal trials on CDK4/6i. We found a correlation between PTV size and increased rates of AEs, which were mainly hematological. The fast-adopting use of CDK 4/6i in the MBC setting combined with ablative/palliative RT urgently calls for high-quality data from prospective studies and large cohorts registry.

No conflict of interest.

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Real-World data of triplet combination of trastuzumab, lapatinib and chemotherapy in HER2-positive metastatic breast cancer: A multi-center retrospective study

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Background: Trastuzumab(T) plus lapatinib(L) has been demonstrated to significantly improve the outcome of HER2 positive heavily pretreated metastatic breast cancer (MBC) patients. Whether TL combined chemotherapy (TLC) can further improve the efficacy in HER2+ MBC remains to be further studied. The aim of this study was to assess real-world treatment patterns and clinical outcomes of patients treated with TLC.

Material and Methods: Patients with HER2+ MBC treated with TLC in 5 institutions of China from September 2013 to July 2019 were included. Progression free survival (PFS), objective response rate (ORR), overall survival (OS), toxicity profile and treatment pattern were reported.

Results: Total of 285 patients were included. 88.8% were exposed to trastuzumab and 49.2% received 2 or more lines of systematic therapy previously. The most common chemotherapy combined with TL were capecitabine and vinorelbine. Almost 1/3 received maintenance treatment after TLC. Median PFS was 10.9 months while patients received TLC as first line showed longest median PFS of 20.7 months. In patients who had progressed on trastuzumab, the continuation trastuzumab on the basis of lapatinib and capecitabine showed a median PFS of 11.3 months. Patients with brain metastasis also showed a median PFS (intracranial and extracranial lesions considered) of 10.6 months. The median OS was not reached. 277 patients were included in ORR analysis. ORR was 42.6%. Toxicities were tolerable and the most common grade 3 to 4 adverse events were neutropenia (16.8%).

Conclusions: TLC demonstrated promising effects and tolerable safety in HER2+MBC, even in patients with brain metastasis.

No conflict of interest.

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Impact of Ki67 and progesterone receptor on PFS with cyclin-dependent kinase 4/6 inhibitors in HER2-negative advanced breast cancer: A real world mono-institutional experience

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Introduction: Current guidelines recommend the use of hormone therapy plus CDK 4/6 inhibitors (CDK4/6i) as initial treatments in patients (pts) with estrogen receptor (ER)-positive, HER2-negative advanced breast cancer

(ABC). The subgroup analyses of phase III studies of CDK4/6i did not identify any predictive marker that could help the clinicians to address the therapeutic choice.

We retrospectively analyzed the impact of progesterone receptor (PR) expression and Ki67 proliferative index, assessed by immunohistochemistry, on progression-free survival (PFS) in pts receiving CDK4/6i as first or second line therapy for ABC.

Material and Methods: We retrospectively collected the clinico-pathological and treatment response data from pts clinical charts. ER, PR, and Ki67 were assessed by immunohistochemistry (IHC), and HER2 by IHC or fluorescence in situ hybridization, on primary tumor samples. PR and Ki67 were analyzed both as continuous and as dichotomized variables: low (<20%) versus high (≥20%). Univariate analyses of the impact of PR, Ki67 and subtype (luminal A: PR high and Ki67 low; luminal B: PR low and/or Ki67 high) on PFS were done with Cox proportional hazard models, reporting hazard ratios (HR) and 95% confidence intervals.

Results: Of 97 pts treated from May 2017 to July 2019 with CDK4/6i for ABC, 48 were treated in 1st line (31 with letrozole and 17 with fulvestrant), 23 in 2nd line (with fulvestrant), and 26 in further lines.

Among 71 pts treated in 1st or 2nd line, PR and Ki67 were available in 67 and 66 cases, respectively. Most pts (63) received palbociclib, 4 ribociclib and 4 abemaciclib. Histotypes were ductal in 53, lobular in 11, other in 7 cases. PR was low in 26 pts and high in 41. Ki67 was low in 37 pts and high in 29. Luminal A tumors were 24, and the remaining 42 cases were luminal B.

PR and Ki67, when considered as dichotomized variables (high/low), as well as subtype (luminal A or B), were not significant predictors of PFS. On the contrary, when considered as continuous variables, Ki67 was significantly associated with PFS, whereas PR was not (Table 1).

Table 1

Characteristics	n	events	HR (95%CI)	*p-value*
PgR				
Low (<20%)	26	14	1.00	*0.468*
High (≥20%)	41	15	0.76 (0.36, 1.59)	
Ki67				
Low (<20%)	37	13	1.00	*0.383*
High (≥20%)	29	16	1.39 (0.66, 2.89)	
Luminal				
A	24	6	0.49 (0.20, 1.20)	*0.117*
B	42	23	1.00	
*PgR (*continuous)	67		1.00 (0.99, 1.00)	*0.588*
*Ki67 (*continuous)	66		1.03 (1.00, 1.07)	*0.035*

Conclusion: Our results are only hypothesis-generating, due to the limited sample size, the retrospective nature and the lack of a control group.

PFS with endocrine therapy plus CDK4/6i seems inversely correlated with Ki67 expression but not related to PR, suggesting that the effect of these cell cycle inhibitors could be related to tumor proliferation rate more than to PR expression.

Conflict of interest:
Advisory Board:

Andrea Rocca received travel grant and invitation for advisory from Novartis, Roche and Lilly. Other authors have not conflict of interest to declare.

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Improved QTcF diagnostic using tele-cardiology

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Background: Numerous anti-cancer drugs can lead to long QT syndrome as a cardiotoxic side effect, which can end in sudden death. Measurement of the QTcF (corrected QT using Fridericia) needs timely support of a cardiologist. The idea of the presented solution was to replace the current way of interaction by a single-lead ECG recorded at the cancer center and send it to a tele-cardiologist for immediate diagnosis (named QTc Tracker).

Material and Methods: While equipping 280 German breast centers with the QTc Tracker solution within the trials AdaptCycle and Ribanna, the centers were asked in a structured interview about their current ECG workflow, turnaround time, and satisfaction. After the implementation of the QTc Tracker, the centers were contacted again to evaluate the turnaround time and satisfaction with the new solution.

Results: The ongoing evaluation project discovered especially long turnaround times for oncologists without collaboration with a cardiologist. For these oncologists patients, the mean time from referral to the cardiologist until the QTc diagnosis was 3 weeks. Using the QTc Tracker, the mean timespan between ECG recording and QTc diagnosis by the centralized tele-cardiologist was 47 minutes. The final results will be presented at the conference.

Conclusion: The new tele-cardiologic system to monitor the QTcF interval delivered much faster diagnosis as the regular cardiologic evaluation and thereby enabled the ECG measurement on-site and the QTcF diagnosis to take place during a routine check-up.

Conflict of interest:
Ownership:

Timo Schinköthe: Managing Director and owner of CANKADO Service GmbH.

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Impact of BMI on the outcome of metastatic breast cancer patients treated with everolimus: A retrospective exploratory analysis of the BALLET study

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Background: Notwithstanding the encouraging results seen with everolimus in advanced breast cancer, reliable biomarkers of response to mTOR inhibitors are yet to be identified. As mTOR is heavily implicated in cell-metabolism, we investigated the relation between BMI variation and outcomes in metastatic breast cancer (mBC) patients treated with everolimus.

Material and Methods: The BALLET study evaluated the safety of everolimus plus exemestane in 2131 post-menopausal women with advanced hormone positive breast cancer which recurred or progressed on NS-AIs. In our analysis, we included only patients who further progressed during treatment. A total of 687 patients were evaluated, with weight measured at baseline and recorded in successive clinical assessments till the end or discontinuation of the study. The BMI was calculated as weight in kilograms divided by the square of height in meters (Kg/m^2). According to the world health organization (WHO) a BMI between 18.5 and 24.9 was considered normal and a BMI ≥24.99 defined "overweight." As the height remains constant over time, we used weight or BMI interchangeably for our analyses. The relationship between everolimus exposure time and Delta Weight Loss (expressed as absolute or as percentage) was evaluated using the Spearman *rho* coefficient. The Wilcoxon matched-pairs test was used for the statistical analysis and the Kaplan-Meier to analyse the correlation between BMI/weight and progression free survival (PFS), defined as the time between the start of everolimus and progression or death.

Results: we found a linear correlation between everolimus exposure duration and BMI/weight decrease. Whilst baseline BMI measurements did not have an impact on the outcomes, BMI variation during treatment exhibited prognostic value. Patients recording >2 kg weight loss or >3% BMI decrease from baseline at the end of treatment (EOT) had a statistically significant improvement in PFS. Interestingly, a similar BMI/weight decrease within the first 8 weeks of therapy identified patients at higher risk of progression.

Conclusions: even with the limitations of an exploratory retrospective study, our analysis suggests that a >3% BMI decrease/weight loss at EOT is associated with better outcome in mBC patients treated with everolimus and might be used as a tool to monitor response to therapy. On the contrary, a significant early weight loss represents a predictor of poor survival. As PI3K-inhibition also converges onto mTOR, these findings might extend to patients treated with selective PI3K inhibitors and warrant further investigation. Where specific biomarkers are not yet available, integration of surrogate biological markers of response into daily clinical practice has great potential and can ultimately facilitate the oncologist's decision-making process in the complex setting of metastatic disease.

No conflict of interest.

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HLX02, a China-manufactured trastuzumab biosimilar versus EU-sourced trastuzumab: Results of a global phase 3, randomized, double-blind efficacy and safety comparative study in metastatic breast cancer

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Background: Trastuzumab (TZB) is a fully-humanised monoclonal antibody biologic and antagonist of the human epidermal growth factor receptor-type 2 (HER2) receptor. It has significantly prolonged time to progression and survival of patients with HER2 positive metastatic breast cancer, as both a monotherapy or in combination with other agents. HLX02, the first China (CN)-manufactured TRZ biosimilar being investigated in a global setting, was developed to provide more cost-effective and readily available alternatives to TRZ. The clinical program followed the biosimilar guideline of China National Medical Products Administration (NMPA) and European Medicines Agency (EMA), which aims to increase global patient accessibility. We have reported the establishment of clinical PK bioequivalence between HLX02 and reference TZBs, later released Week 24 efficacy data. Here, we announce 1-year efficacy result and updated safety profile of the Phase 3 trial comparing HLX02 and European Union (EU)-sourced TRZ in metastatic breast cancer patients.

Methods: This Phase 3, randomized, double-blind, parallel-controlled study recruited adult women with HER2+ relapsed or metastatic breast cancer from 89 centres in CN, Philippines, Poland and Ukraine. Eligible subjects were randomized in a 1:1 ratio to receive either HLX02 or EU-TZB with docetaxel in 3-weekly cycles for up to 1 year. Primary endpoint was best overall response rate at Week 24 (ORR_{24}) after 8 treatment cycles. HLX02 and EU-TRZ were considered to be equivalent in terms of efficacy if 95% confidential interval (CI) of difference in ORR_{24} fell within the pre-defined equivalence margin (±13.5%). Secondary endpoints included disease control rate (DCR), duration of response (DoR), progression-free survival (PFS), safety and immunogenicity profiles up to 1 year.

Results: Of the 649 patients being randomised (HLX02 = 324; EU-TZB = 325), 292 has completed 1-year treatment. Difference in ORR_{24} (−0.1%; 95% CI: −7.0, 6.9) between the two groups were within the pre-defined margin. Both groups in all populations (overall, Asian vs. non-Asian, and Chinese vs. non-Chinese) had similar ORR_{24} ($p > 0.05$). All secondary efficacy analyses up to 1 year concluded the therapeutic equivalence ($p > 0.05$). The most common TEAEs in two groups were decreased leukocyte count, decreased neutrophil count, anemia and alopecia. Drug-related adverse cardiac events were similar between groups. Between groups, non-Chinese and non-Asian patients had fewer drug related SAE and TEAE events, but the incidence rate of each AE was similar.

Conclusions: HLX02 and EU-TZB has demonstrated efficacy equivalence by showing difference of ORRs at Week 24 fell entirely into the pre-specified margin. All secondary efficacy and safety analysis of HLX02 up to 1 year supported the conclusion of bio-similarity between the investigation drug and reference medicine.

Conflict of interest:
Corporate-sponsored Research:
Y. Li (Yue Li), B. Shan (Boyao Shan), J. Cheng (Jiancheng Cheng), X. Wang (Xian Wang), Y. Chen (Yiyuan Chen), W. Jiang (Weidong Jiang), S. Liu (Shigao Liu), X. Zhang (Xin Zhang), E. Liu (Eugene Liu), A. Luk (Alvin Luk) and Q. Wang (Qingyu Wang) are employees of Shanghai Henlius Biotech, Inc. The study is sponsorded by Shanghai Henlius Biotech, Inc.
Other Substantive Relationships:
B. Xu (Binghe Xu), Q. Zhang (Qingyuan Zhang), T. Sun (Tao Sun), W. Li (Wei Li), Y. Teng (Yuee Teng), X. Hu (Xichun Hu), I. Bondarenko (Igor Bondarenko) and H. Adamchukare (Hryhoriy Adamchuk) are the investigators of the Phase 3 study (ClinicalTrials.gov Identifier: NCT03084237 EudraCT: 2016-000206-10 Chinese Clinical Trial Register: 2015L01326).

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Reduction of Serious Adverse Events (SAE) under palbociclib treatment in patients using an interactive eHealth system

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Background: PreCycle (NCT03220178) is a multicenter, randomized phase IV Intergroup trial to evaluate the impact of eHealth-based Patient-Reported Outcome (PRO) assessment on quality of life (QoL) in patients with HR +/HER2− locally advanced or metastatic breast cancer treated with palbociclib and an aromatase inhibitor or palbociclib and fulvestrant. Patients willing to use the web/APP-eHealth solution CANKADO were eligible. Patients were randomized (2:1) to the active or inform arm (and stratified by line of treatment). In the inform arm, patients can document only their drug intake. Patients in the active arm are supported by CANKADO PRO–React, which additionally provides symptom-triggered questionnaires and corresponding recommendations to contact their physician. Primary endpoint is superiority for time to deterioration (TTD) of QoL in patients using ePRO.

Material and Methods: The trial is ongoing in 81 German breast centers and outpatient practices. Regular safety reports are routinely provided to the study sponsor. Analysis of the distribution of serious adverse events (SAE) was initiated by the trial leadership and performed using the safety report of Oct 15, 2019. Data that could bias primary or secondary endpoints were not analyzed. Bayesian inference (non-informative prior) was used to estimate probabilities; no corrections for potential multiplicities were made.

Results: At data cut-off, 261/281 randomized patients had received study medication and were documented. SAEs occurred in 26/175 (14.9%) of all active-arm patients vs. 18/86 (20.9%) of inform-arm patients (90% probability of reduction in inform patients). Total SAEs were 36 (active) vs. 27 (inform); corresponding SAE incidence per hundred patients was 20.6 vs. 31.4, a relative reduction of about one-third.

In the first-line stratum, SAEs occurred in 16/121 (13.2%) of active-arm patients vs. 14/50 (28.0%) of inform-arm patients. This data implies a 93% estimated probability of a 5% (or greater) absolute reduction among first-line inform patients. The SAE count in first-line patients was 22 (active) vs. 22 (inform); corresponding SAE incidence per hundred patients was 18.2 vs. 44.0, a relative reduction of about three-fifths.

Conclusion: The present (unplanned) analysis suggests a potentially substantial, clinically relevant reduction in relative SAE incidence among first-line patients using PRO-React, with a more modest decrease overall. The present analysis is preliminary, representing only a snapshot, and cannot provide a definitive explanation for reduction of SAEs under interactive eHealth support. Earlier contact with the treatment team could be associated with more timely or appropriate medical interventions. The PreCycle trial will continue to enroll patients in order to further evaluate the potential benefits of eHealth support.

Conflict of interest:
Corporate-sponsored Research:
Pfizer.

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Time to first health care contact, referral pathways and stage at presentation – the experience from four South African breast units

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Background: Breast cancer incidence is increasing in low-to-middle income countries yet patient outcomes remain poor. South Africa has no screening program, 80% of the population rely on public health care and there are only eight specialized public breast units to date. The public health system prescribes a tiered approach with primary health facilities as the first contact point and onward referrals to secondary and lastly tertiary hospitals. The purpose of this study is to examine factors associated with advanced stage at presentation in a limited resource environment.

Material and Methods: We analysed data from a cohort of women enrolled in the ongoing South African Breast Cancer and HIV Outcomes study from April 2015 to December 2018. Study sites included two units in the Gauteng province and two units in the KwaZulu-Natal province. The participants were grouped into early (I and II) and advanced (III and IV) stage breast cancer. Demographic data (age, residential distance, referral pattern), histological characteristics (intrinsic subtypes and grade) and social factors (level of education, employment status, household socio-economic status) were compared. We identified determinants of advanced-stage breast cancer using bivariate and multivariate logistic regression models.

Results: Of the 2930 participants enrolled in the cohort, 1682 (57.0%) presented with advanced-stage disease. On multivariate analysis, adjusting for age, level of education, knowledge of breast cancer and receptor subtype, the factors associated with advanced stage were time to presentation to the health system and mode of referral. Those taking 1–3 months (OR = 1.32, 95%CI: 1.04–1.69) and >3 months (OR = 1.98, 95%CI: 1.62–2.43) after noting a breast symptom to visit a healthcare facility were more likely to present with late-stage disease at diagnosis than patients who had taken less than one month. Indirect referral patterns such as referral via secondary hospitals were more likely to present with advanced-stage breast cancer (OR = 1.40, 95% CI 1.15–1.71) than direct referrals (self-referral, primary care clinic or general practitioner).

Conclusions: Our findings point to two distinct hurdles, which lead to advanced stage at presentation. Firstly, patients delay the first health care contact. Awareness needs to be improved and fear of treatment and anticipation of poor health service delivery alleviated. Secondly, referral pathways are an important barrier to care in the South African public sector. Breast care at regional hospitals cause major delays and direct referral routes are needed with facilitated access to specialised breast units.

No conflict of interest.

Advocacy

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Breast cancer community screening in low resource settings: Lessons from Pune, India

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Breast cancer (BC) incidence is on the rise in India. Early detection is limited due to lack of awareness in women about disease symptoms, screening modalities, breast self-examination and/or routine mammographic screening leading to negligence and costly delay in diagnosis and treatment.

Our team has established a 3-tiered community BC screening project in Pune, India. Paramedical professionals conduct awareness talks in local languages for sensitization of women about BC related facts and myths. Thereafter, BC screening is performed using a mobile mammography van fully equipped with an analog mammogram. Women under 40 are screened by clinical breast examination (CBE), while women above 40 years undergo mammographic screening. CBE or Mammography screen positive cases are referred to our tertiary care center for appropriate diagnosis, work-up and clinical management.

In the period between February 01, 2016 – July 31, 2017, we were able to sensitize approximately 58,000 women in 250 awareness talks. 217 screening camps were conducted in which 6477 women participated. 4070 women underwent CBE-based and 2257 women underwent mammography screening, respectively. 759 women (12%) were found to be CBE-positive while 416 women (18.5%) were mammography positive. Of the screen-positive cases, 11 suspicious cases underwent biopsy. 6 cases of BCs and 5 cases of benign breast diseases were identified and underwent complete treatment.

Our 3-tier model for community BC screening was found to be effective in early detection of BCs in Pune city. Further evaluations based on cost-effectiveness and scale-up feasibility are required for implementation in other low resource settings.

No conflict of interest.

272 Poster

Patient-informed learning to assist development of personalised treatment care plans for breast cancer patients and survivors

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Background: Breast cancer is the most common invasive cancer in women. In Ireland there are over 3,000 women diagnosed with the invasive form of the disease annually. Numbers of individuals surviving breast cancer has increased due to advancement in detection, diagnostics and treatments. Breast cancer survivorship is in its infancy and presents a paradigm shift from a life-threatening condition to a chronic illness requiring extension of care. Survivorship begins at diagnosis and continues until end of life. Survivors of breast cancer can face complex medical and psychosocial needs resulting from their disease and treatment that affects their quality of life going forward. The optimal structure for a breast cancer survivorship care plan has not yet been defined in Ireland.

This study outlines preliminary findings of a patient-centred approach taken to ascertain Irish Breast Cancer Survivors (BCS) understanding of their disease and treatment and what key attributes they would like to see addressed in a BCS treatment plan. Our study aims to inform the planning stage of an Irish treatment care plan framework.

Method: A qualitative mixed methods study was undertaken. A critical review of the literature and a focus group with Breast Cancer survivors (n = 6) all members of a breast cancer advocacy group were undertaken to identify how well BCS understand their disease and treatment and to ascertain existing models of BCS treatment plans. The findings resulted in us convening a publicly advertised workshop of BCS (n = 20) to explore key attributes for inclusion in a plan and what stage (s) of the cancer journey would be the optimal time for its delivery to the patient.

Results: The findings indicated disparity in understanding of; disease, diagnostic results, treatment side-effects, awareness of available services, and receipt of written information for individual treatment plans. Participants unanimously raised the need to have a BCS treatment plan. The workshop identified several key attributes that BCS would like Included in a plan but also disparity on quantity of information and timing of receipt.

Conclusion: We aim to develop a sample prototype based on the findings to date for consideration for implementation. We intend convening further consultations with multiple stakeholders from across the Irish breast cancer health service spectrum alongside patients to discuss and review this prototype and existing models of BCS plans utilised in Europe, the US and UK to determine the best approach.

No conflict of interest.

274 Poster

Unintended bias in clinical trials: The prevalence of entry criteria that exclude patients with invasive lobular carcinoma from metastatic breast cancer trials

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Background: Accurately measuring tumor size is challenging in invasive lobular carcinoma (ILC), which shows non-cohesive growth due to its lack of the adhesion protein E-cadherin. In the metastatic setting, ILC has a unique pattern of spread with a tendency to involve organs like the gastrointestinal

tract, peritoneal lining, leptomeninges, or pleura. This results in sheet-like disease or effusions that cannot be measured on routine imaging tests, with measurable disease developing later in the disease course. We hypothesize that clinical trials for stage IV breast cancer commonly require measurable disease for study entry and limit the number of prior lines of therapy allowed, thereby disproportionately excluding ILC patients. To evaluate this problem, we define the proportion of clinical trials for stage IV breast cancer that use response evaluation criteria in solid tumors (RECIST) or measurable disease as entry criteria, and determine the maximum lines of prior therapy allowed.

Materials and Methods: We queried the clinicaltrials.gov database to identify all actively recruiting, interventional clinical trials for stage IV breast cancer. Measurable disease criteria was defined as either (1) the explicit use of RECIST criteria, (2) the definition of measurable disease by RECIST criteria (imaging or physical exam that shows at least one measurable lesion with a minimum size in at least one diameter of $\geq$10 mm for lesions and $\geq$15 mm for lymph nodes), or (3) the explicit requirement for measurable or evaluable disease.

Results: We identified 146 actively recruiting, interventional clinical trials for stage IV breast cancer. 119 (82%) studies were drug trials. Overall, 108 (74%) required measurable disease for study participation. Of the 108 studies, 29 (27%) utilized RECIST in inclusion criteria; 22 (20%) utilized RECIST as an outcome measure; and 48 (44%) utilized RECIST in both inclusion criteria and outcome measures. Nine (8%) studies used measurable/evaluable disease or alternative minimum size criteria that did not qualify as RECIST. Of the 146 trials, 52 (36%) mandated a maximum line of cancer therapy prior to trial entry, with a mean maximum of 1.73 prior lines (standard deviation 1.4, range 0–6).

Conclusions: The majority (74%) of clinical trials for stage IV breast cancer require measurable disease, and over a third mandate no more than 2 lines of therapy prior to trial entry. Because ILC shows non-cohesive growth and is more likely to become measurable late in the disease course, patients with ILC may have limited access to life-extending therapies and study participation. Our next step is to evaluate a retrospective cohort of patients with stage IV ILC and determine the impact of such trial design on their eligibility. This study will hopefully aid in the development of novel clinical trial endpoints that include patients with ILC.

No conflict of interest.

Basic Science and Translational Research

275 Poster

Interplay between the Pan-Tumor Suppressor miR-939-5p and the oncogenic lncRNA-HEIH dually curbs Hydrogen Sulphide and Nitric Oxide production in breast cancer cells

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Background: Recent light has been cast on the detrimental oncogenic effect of the gasotransmitters, Hydrogen sulfide (H_2S) and Nitric Oxide (NO), in Breast Cancer (BC) progression. We and others have recently showed that H_2S and NO synthesizing machinery (Cystathione β Synthase (CBS) and Cystathione γ Lyase (CSE), Nitric Oxide Synthase 2/3 (NOS2/3), respectively), were found to be prominently elevated in BC patients. Numerous non-coding RNAs (ncRNAs) especially miRNAs have been acknowledged as upstream regulators for each of those individual enzymes. However, the regulation of H_2S and NO synthesizing machinery by lncRNAs has never been investigated. Nonetheless, the hijacking ability of their dual targeting has never been probed in terms of BC. Therefore, the main aim of this study is to pinpoint a novel upstream regulators for NO and H_2S synthesizing machinery, to investigate the interplay between ncRNAs and to finally evaluate its effects on BC hallmarks.

Methods: Breast tissue samples were collected from 40 Egyptian BC patients. Bioinformatics analysis was performed. MDA-MB-231 and MCF7 cells were cultured and transfected with different oligonucleotides. Total RNA was extracted and quantified by qRT-PCR. Cellular viability, colony forming ability and migration were measured using MTT, colony forming and scratch assays, respectively.

Results: Extensive *in-silico* analysis revealed that CBS, CSE, NOS2 and NOS3, could be conceivably targeted by only 1 ncRNA which is miR-939-5p. Screening for miR-939-5p in BC patients revealed that its expression level was significantly down-regulated in BC tissues compared to normal tissues, as opposed to the marked up-regulation of its targets (CBS, CSE, NOS2 and NOS3). Moreover, a novel interplay between miR-939-5p and lncRNA-HEIH has been investigated where lncRNA-HEIH expression level was found to be evidently elevated in BC patients. Mechanistically, forcing the expression of miR-939-5p in BC cells resulted in pan-repressing effects on the oncogenic lncRNA-HEIH, CBS, CSE, NOS2 and NOS3 transcripts. Functionally, this was translated into a drastic reduction in cellular viability, colony forming ability and migration capacity of BC cells.

Conclusion: This study highlights the potent tumor suppressor activity of miR-939-5p through its novel cross-talk with lncRNA-HEIH which results in a quadruple targeting of H_2S and NO producing enzymes, thus proposing miR-939-5p as a novel therapeutic agent for BC patients.

No conflict of interest.

277 Poster

miR-486-5p and miR-17-5p: Novel Immunomodulatory Non-coding RNAs Drawn Downstream 3′-O-Acetylvitexin in Triple Negative Breast Cancer

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Background: Recently, our research group has highlighted the potential ability of the natural compound, 3′-O-acetylvitexin, to modulate the oncogenic and the immunogenic profiles of TNBC cells. Yet, the exact molecular mechanism of such potential therapeutic agent has to be more extensively explored. Natural Killer cells (NKs) are the first invaders in the immune surveillance attack against TNBC. The major histocompatibility complex class I chain-related proteins A and B (MICA/B) are considered as ligands for the activating receptor NKG2D. We have recently showed the potent activity of 3′-O-acetylvitexin to induce the expression of MICA/B on TNBC cells. However, the detailed effect underlying such induced MICA/B expression has not been probed yet. So, the main aim of this study is to investigate possible regulators for MICA/B that could be drawn downstream 3′-O-acetylvitexin in TNBC cells.

Methods: Twenty-five TNBC patients were recruited. Computational target prediction analysis was performed. MDA-MB-231 and MCF-7 cells. MDA-MB-231 cells were cultured and transfected with miR-486-5p and miR-17-5p oligonucleotides and/or treated with 3′-O-acetylvitexin. Total RNA was extracted and quantified by qRT-PCR.

Results: *In silico* analysis has showed that miR-486-5p and miR-17-5p were among the top ranked microRNAs that could potentially dual target MICA/B simultaneously. Screening for miR-486-5p and miR-17-5p was performed where they showed a marked repressed expression in BC patients. Nonetheless, MICA/B were also found to be downregulated in MDA-MB-231 cells compared to MCF-7 cells. Ectopic expression of miR-17-5p and miR-486-5p resulted in a marked increase in MICA/B transcript levels. In the same manner, 3′-O-acetylvitexin showed that same potentiating effect on MICA/B levels. Finally, to draw the full picture, MDA-MB-231 treatment with 3′-O-acetylvitexin resulted in a marked elevation in miR-17-5p and miR-486-5p levels.

Conclusions: This study nominated miR-486-5p and miR-17-5p as novel immunomodulatory non-coding RNAs regulating MICA/B expression on TNBC cells and that could be drawn downstream 3′-O-acetylvitexin.

No conflict of interest.

279 Poster

Impact of CDK4 knock out using CRISPR/Cas9 gene editing technology on breast cancer progression

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Background: In recent years, there has been a focus on finding alternative treatment options for breast cancer. More than one subtype is resistant from the beginning to chemotherapy and others tend to develop a resistance

during treatment. Thus, providing doctors and patients with limited options since the prescribed regiment could become obsolete later on. The Clustered Regularly Interspaced Short Palindromic Repeats/Cas9 system (CRISPR/Cas9 system), is the defense mechanism in Streptococcus pyogenes against viruses, it is widely used by researchers as a precise gene editing tool that allows a targeted genomic editing. Although there has been research conducted on targeting genes related to the cell cycle, such as cyclin dependent kinases (CDKs); however only few studies have created a knockout model in order to observe this effect on cellular function and carcinogenesis. Therefore, we aimed to investigate the impact of CDK4 gene knockout on breast cancer progression and to determine how the cells behave without this crucial protein in several aspects.

Materials and Methods: Screening for CDK4 levels in 21 breast tissues (10 normal and 11 cancerous tissues) was performed. In silico sgRNA CRISPR designing tools were used to design a sgRNA targeting CDK4 gene. The insert was ligated into a Cas9 expressing plasmid and transformed into *E. coli*. The Plasmid was then extracted and sequenced. MDA-MB 231 cells was transfected with the cloned plasmid. Functional assays were performed.

Results: Screening results showed that CDK4 is overexpressed in breast cancer tissues compared to normal healthy breast tissues. Afterwards, sequencing results confirmed a successful sgRNA insertion into the Cas9 plasmid. Knocking out CDK4 in MDA-MB 231 cells led to a significant decrease in cellular viability compared to the cells that were transfected with empty plasmid. In addition, the ability of cells to proliferate and to form colonies was dramatically decreased in response to CDK4 knockout compared to that transfected with empty plasmid. In regards to cell migration assay, MDA-MB 231 cells showed a marked reduction in migration ability after transfection with the CDK4 cloned vector compared to the cells transfected with the empty vector.

Conclusion: CDK4 has an oncogenic effect on breast cancer, where its knockout showed a considerable impact on several hallmarks of cancer affecting tumor cell viability, clonogenicity and migration. These results indicate that CDK4 may act as a promising target for further studies to reveal its downstream impact on breast cancer progression. In addition, this may contribute in understanding the pathogenesis of breast cancer and thus creating new approaches for breast cancer treatment and for better treatment response.

No conflict of interest.

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Multi-targeting antibody to control proliferation, metastasis and angiogenesis in mammary gland tumor

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Background: Hepatocyte growth factor receptor (HGFR) or c-Met and vascular endothelial growth factor receptor (VEGFR) are protein kinase receptors that once binds to their ligands, hepatocyte growth factor (HGF) and vascular endothelial growth factor (VEGF), respectively, augment cell proliferation, invasiveness and scattering, resulting in tumor progression and angiogenesis in a broad spectrum of cancers. Intensified HGF/c-met signaling is also a well-known mechanism of resistance to VEGFR-TKIs and EGFR-TKIs. Thus HGFR-VEGF blocking dual antibody is being heralded as a key solution to reduce the signal transduction of HGFR and VEGF concurrently to overcome this resistance.

Material and Methods: We developed an anti HGFR-VEGF bi-specific antibody fragment by cloning and expression of its gene in the bacterial host, BL21. Expression was induced by IPTG, purified by passing through the nickel column, and finally concentrated using Amicon® Ultra Centrifugal Filters. SDS-page/western-blotting was done to detect and confirm the expression of the protein fragment. The binding potency of the fragment to the antigens was then measured using flow cytometry. Next, MDA-MB-231 cells were cultured and treated by the antibody to investigate cell proliferation, migration, invasion and apoptosis. Anti-angiogenesis function was evaluated using tube formation assay. Tumor growth rate and probability of metastasis in tumor-bearing BALB/c mice was assessed using an ultrasound monitoring and PET-scanning. Tumor proliferation, invasion and angiogenesis biomarkers were assayed by IHC and finally, survival rate was analyzed.

Results: We found that the anti HGFR-VEGF fragment could be successfully produced in BL21. Using the flow cytometry, we identified significant binding capacity of the antibody. Treatment of MDA-MB-231 cells by the antibody, significantly decreased cell proliferation, migration, invasion and tube formation, while promoted cell apoptosis. Ultrasound measurements showed decreased rate of tumor growth over time. IHC assays revealed meaningful decreased for proliferation, invasion and angiogenesis biomarkers. Also, survival rate increased significantly.

Conclusion: Taken together, our data indicated that the blockage of HGFR and VEGF concurrently could block both signaling pathways of angiogenesis therefore could overcome tumor resistance to anti-angiogenesis agents such as bevacizumab. Contrary to convenient antibodies, dual targeting antibody can be produced in bacterial hosts, which is not only more cost-effective, yet more applicable as a potential targeted therapy tool.

No conflict of interest.

282 Poster

Computerized scoring tool for identification and quantification of different immune cell populations in breast tumor regions

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Background: Important prognostic and predictive information can be obtained from the composition, functionality and spatial arrangement of different immune cell subtypes in breast tumors.

Materials and Methods: The tumor infiltrating lymphocytes (TILs) in 62 patients with luminal B-like like breast cancer (grade II-III, ER+, HER2–) were identified by immunohistochemical staining with classical markers and were subsequently classified and quantified using an analysis tool based on QuPath software. In different delineated tumor regions (invasive front, tumor center and whole tumor), the proportion and density of total T-cells ($CD3^+$ and $CD5^+$), T-helper cells ($CD4^+$), cytotoxic T-cells ($CD8^+$), B-cells ($CD20^+$) and regulatory T-cells ($FOXP3^+$) were assessed. Results of the software analysis were compared to manual counting.

Results: For CD8 and CD20 stainings, the QuPath scoring method scored very similar (no significant differences found) compared to manual counting for number of positive, negative cell counts, density and proportion of immune cells. For all markers the density of positively stained immune cells was higher in the invasive front than in the tumor center, pointing to an accumulation of immune cells near the tumor boundaries. The immune infiltrate in the invasive front proportionally contained more CD5 ($p = 0.025$) and CD20 ($p < 0.001$) positive cells, while FOXP3 expressing cells were slightly enriched in the tumor center ($p < 0.001$).

Conclusions: The QuPath pipeline was able to adequately identify different subsets of immune cells in breast tumors and allows to evaluate differences in immune cell proportion and density within different tumor regions. The whole tumor section can be quantitatively assessed quite rapidly and all measurements are obtained in a semi-automatic way.

No conflict of interest.

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Evaluation of circulating cell-free DNA and its integrity as a potential predictive biomarker of breast cancer onset: A pilot study

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Background: Although mammographic screening for breast cancer (BC) has substantially increased the rates of detection of early-stage BC, a significant proportion of patients continues to be diagnosed in locally advanced or metastatic settings. The early BC diagnosis is of utmost importance for long-term survival, improving the quality of life and reducing costs for public healthcare. New BC screening approaches integrated with the radiological ones, could improve the early identification of BC, offering more personalized monitoring and treatments. Cell-free DNA (cfDNA) is considered a new potential biomarker for cancer, whose importance has been gradually deepened thanks to the rapid improvement of molecular technologies. As reported in the literature, cfDNA can play an important role in the diagnosis, treatment, and prognosis of many tumors, and it could replace tissue biopsy with a simple blood test. To further understand the value of cfDNA in BC, we used the digital droplet PCR (ddPCR) to investigate ALU and LINE sequences in cfDNA as potential biomarkers for BC diagnosis.

Methods: Peripheral blood specimens (12 ml) were collected from 99 patients with primary BC before surgical treatment and from 103 healthy women selected as control group. The study was approved by Ethical Committee and an informed consent was obtained from all participants. DdPCR was developed to detect cfDNA abundance of long and short fragments, targeting two repetitive DNA elements: ALU (ALU-260 bp, ALU-111 bp) and LINE1 (LINE1-266 bp, LINE1-97 bp). The cfDNA integrity (cfDI) was obtained from the ratio of longer/shorter fragments. Receiver operating characteristic (ROC) analysis was carried out to assess the discriminatory power of cfDI between cases and controls and the area under the curve (AUC) was calculated with 95% confidence interval (95%CI).

Results: Patients with BC had a significantly lower cfDI (median ALU = 0.08, median LINE1 = 0.19) compared to the control group (median ALU = 0.10, median LINE1 = 0.27) (P < 0.001 for each). ROC analysis revealed that cfDI allow to distinguish patients with BC from healthy women with an AUC of 0.66, 95%CI: 0.59–0.73 for ALU and 0.78, 95%CI: 0.71–0.84 for LINE1. Comparing AUC curves, we found that the LINE1 marker has a more significant diagnostic performance than ALU (p = 0.005, De-Long Test).

Conclusions: The LINE1- cfDI seems to be a stable predictive marker of early BC detection. Although our results need to be further confirmed in a larger and independent cohort, the measurement of LINE1-cfDI with ddPCR may become a suitable predictive strategy. It could be integrated into a screening program to detect early BC and maybe to monitor women with a higher risk for BC. Furthermore, LINE1-cfDI detection by ddPCR could be very useful to monitor BC relapse due to the high sensibility, specificity and reproducibility of the technique.

No conflict of interest.

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PIK3CA mutations and predicting the therapeutic effects of neoadjuvant chemotherapy in primary breast cancer

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Background: *PIK3CA* mutations are known to be associated with a reduced pathological complete response (pCR) rate in HER2+ breast cancer, but the relationship between *PIK3CA* mutations and the therapeutic effects of neoadjuvant chemotherapy in hormone receptor (HR) -positive or HR –/HER2– breast cancer is not clear. We herein analyzed *PIK3CA* mutations in primary breast cancers of patients who had undergone neoadjuvant chemotherapy. We also investigated the associations of these mutations with the therapeutic effects of neoadjuvant chemotherapy.

Material and Methods: From May 2016 to September 2017, from among cStage I to III primary breast cancer patients scheduled to receive neoadjuvant chemotherapy at the Cancer Institute Hospital of JFCR, 122 were included in this study. Genomic DNA of the primary tumors was extracted from formalin-fixed and paraffin-embedded needle biopsy specimens collected before the treatment. The *PIK3CA* mutations at E542K, E545K, and H1047R were analyzed using droplet digital PCR. Anthracyclines and taxanes were used for neoadjuvant chemotherapy, and trastuzumab was added for HER2+ breast cancer. Pathological therapeutic effects were determined from surgical specimens after neo-adjuvant chemotherapy. The associations between *PIK3CA* mutations and therapeutic effects were then analyzed statistically.

Results: Genomic DNA was collected from 122 primary tumors of 113 cases. *PIK3CA* mutations were detected in 31% of these primary tumors. According to HR and HER2 status, 36% of HR+ tumors, 21% of HR–/HER2+ tumors, and 18% of HR–/HER2– tumors harbored *PIK3CA* mutations. Twenty patients received anthracyclines, 66 anthracyclines and taxanes, and 27 anthracyclines followed by taxanes and trastuzumab as neoadjuvant chemotherapy. Of the 122 tumors, 115 were evaluated for postoperative histopathological treatment effects. Overall, the pCR rate for *PIK3CA* mutant tumors and wild-type tumors were 29% and 21% ($P = 0.344$), respectively. Although there was no significant difference in the pCR rate between *PIK3CA* mutant and wild-type tumors in HR+ tumors (22% for *PIK3CA* mutant tumors vs. 17% for wild-type tumors; $P = 0.557$) and HR–/HER2+ tumors (33% vs. 36%; $P = 1.0$), the pCR rate for *PIK3CA* mutant tumors was significantly higher than that for wild-type tumors with HR–/HER2– status (100% vs. 15%; $P < 0.05$).

Conclusions: *PIK3CA* mutations were not associated with the pCR rate in HR–/HER2+ breast cancer in this study. Although the case number was small, we found HR–/HER2– breast cancer harboring *PIK3CA* mutations to be more likely to achieve pCR after neoadjuvant chemotherapy. *PIK3CA* mutations might predict pCR in HR–/HER2– primary breast cancer.

No conflict of interest.

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Project PRIMO – Combining Patient Derived Breast Cancer Microtumors and DigiWest protein signaling pathway profiling for therapeutic response prediction

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Background: Cancer patient outcome depends on a variety of different factors including tumor histology, genetic factors, and response to first-line treatment. In the era of **personalized medicine**, the ability of pre-selecting individualized treatment options and pre-defining their suitability in advance of clinical treatment, might facilitate therapeutic decision making and finally improve patient outcome. However, for preclinical validation of anti-cancer drug efficacy, it is crucial to design a **preclinical model** that reveals the influence of cellular interactions of the tumor microenvironment and cell heterogeneity on drug response. Within the PRIMO (Personalized Medicine for tailored cancer therapies) project, such a 3D preclinical model system comprised of **patient-derived** microtumors (PDM) and autologous tumor-infiltrating lymphocytes (TILs) that is derived from primary human breast tumor tissue specimen has been developed.

Material and Methods: PDM and TILs are isolated from fresh primary breast cancer tissue material using limited digestion and subsequently cultured in defined media in the absence of serum. The heterogeneous cellular composition of isolated PDM as well as autologous TILs is analyzed by FFPE immunohistochemistry and multi-color flow cytometry, respectively. For in-depth protein profiling of PDM we utilize the DigiWest technology, a proprietary high throughput immune assay screening tool, facilitating signaling pathway analyses with up to 200 analytes from low amounts of PDM sample material. Treatment efficacy in response to small molecules, chemotherapeutics as well as immunotherapeutic agents is assessed in PDM and PDM-TIL co-cultures using a functional viability assay in microplate format.

Results: The co-cultivation of patient derived PDMs with autologous TILs presents an effective experimental system that facilitates the parallel testing of therapeutically active compounds. We show that it is possible to combine chemotherapeutics with immunotherapeutic compounds and directly monitor the results of mono- and combination treatment. By adding the DigiWest protein profiling, wide-ranging expression data were obtained. They allow determining and confirming the pathological receptor grading in PDMs from individual patients as well as detecting activation differences in several key signal transduction pathways. Immunohistochemical analyses combined with protein profiling of breast cancer PDM enables drug mode-of-action analyses, biomarker identification together with personalized therapeutic sensitivity prediction.

Conclusion: The platform presented here expands the preclinical repertoire of in vivo relevant test systems for efficacy testing of drugs and investigational compounds, pre-identified by protein pathway as well as genetic profiling in personalized medicine of breast cancer.

No conflict of interest.

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Clinical correlation between Programmed Cell Death Ligand One (PD L-1) Expression, Tumor Infiltrating Lymphocytes (TILs) and pathological response of locally advanced Human Epidermal Receptor (HER 2) & Triple Negative (TN) Breast Cancer (BC) Egyptian patients undergoing neoadjuvant Therapy

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Background: There is a strong association between activation of the PD-1/PD-L1 pathway in breast cancer and poor prognosis. Patients undergoing primary neoadjuvant systemic therapy and achieving pathological response is reflected on their long-term survival outcomes (Cortazar et al. 2014), thus assessing the impact of baseline PD-L1 & TILs on achieving pathological response, could be an additive prognostic and predictive biological marker.

Patients and methods: From December 2015 till November 2016, we conducted a prospective observational cohort study on 114 locally advanced TNBC & Her 2 neu over expressed breast cancer patients, who were presented to the Breast Cancer Comprehensive center of the National Cancer Institute, Cairo University. The National Cancer Institute Independent institutional review board approved the study protocol (Approval number: 201516012.3) and subsequent amendment. Written informed consent was obtained from each participant, prior to study entry. Baseline PD-L1, PD-1, CD8 & FOXP3 by Immunostaining was done using Automated BenchMark ULTRA IHC/ISH system. All patients received standard neoadjuvant systemic therapy. Assessment of pathological response according to Residual Cancer Burden (RCB) (Symmans et al., 2017) and correlation of baseline PD-L1, PD-1, CD8 & FOXP3 with pathological response (RCB 0 & 1 were considered responders; while RCB 2 & 3 were considered non-responders), and Event Free Survival (EFS) were done.

Results: 106 patients (35 TNBC and 71 patients were Her 2 positive) were evaluable for response. 44 (41.5%) patients were PD-L 1 positive and 30 (68.2%) patients of them showed no response to neoadjuvant systemic therapy ($p = <0.001$). 55 (51.9%) patients were PD-1 positive and 35 (63.6%) patients of them showed no response to neoadjuvant systemic therapy ($p = <0.001$). 39 (36.8%) patients were FOXP3 positive and 22 (56.4%) patients of them showed no response to neoadjuvant systemic therapy ($p = 0.109$). 63 (59.4%) patients were CD 8 positive and 40 (63.5%) patients showed response to the neoadjuvant therapy ($p = 0.025$). Event free survival at 3 years for patients with baseline PD-L 1 positive, PD-1 positive, FOXP3 positive and CD8 positive were (84.1, 80.9, 77.0 & 95.1%) respectively.

Conclusion: In Locally advanced TNBC & Her 2 overexpression Breast cancer, undergoing neoadjuvant systemic therapy, baseline PD-L1 expression & PD-1 (sTILs) are associated with poor pathological response. While, Baseline CD 8 (sTILs) is associated with good pathological response. There is an initial correlation between baseline PD-L1, PD-1, FOXP3 & CD8 and (EFS), however data is not mature enough to draw any relations with long term outcome effects.

No conflict of interest.

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Plasma markers showing differential baseline expression in relapsing versus non-relapsing patients with hormone sensitive breast tumors

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Background: New biomarkers are awaited to more accurately predict recurrence of luminal breast tumors and to decide whether or not adjuvant chemotherapy is indicated for these patients. Both the chemokine and microRNA networks have been implicated in the metastatic process. As chemokines and microRNAs are also present in the plasma, these could potentially hold interesting prognostic biomarker candidates.

Material and Methods: In this retrospective study we used plasma samples from the blood bank of the Multidisciplinary Breast Center (UZ Leuven), collected at baseline from patients with newly diagnosed early breast cancer (grade II-III hormone sensitive, HER2-negative tumors on diagnostic core needle biopsy). We compared baseline plasma profiles of circulating chemokines and microRNAs in patients developing distant metastasis within 5 years after initial therapy (group 1, n = 48) and patients who remained disease-free for at least 7 years (group 2, n = 48). Both groups were matched for age, tumor size and lymph node status. A panel of 16 chemokines (fractalkine/CX3CL1; GROα/CXCL1; IP-10/CXCL10; SDF-1/CXCL12; TECK/CCL25; TARC/CCL17; IL-8/CXCL8; MCP-1/CCL2; ITAC/CXCL11; BCA-1/CXCL13; RANTES/CCL5; MIP-3b/CCL19; CTACK/CCL27; MIP-3α/CCL20; 6-Ckine/CCL21 and MIG/CXCL9) was assessed by multiplex cytometric bead array. After plasma RNA extraction and subsequent cDNA synthesis, 175 microRNAs commonly found in plasma were measured using the miRCURY LNA miRNA PCR system with the 96-well Serum/Plasma Focus microRNA PCR Panel (Qiagen).

Results: Baseline plasma samples from relapsing patients (group 1) on average showed slightly but significantly decreased levels of fractalkine ($p = 0.004$), GROα ($p = 0.023$), RANTES ($p = 0.004$), CTACK ($p = 0.001$) and MIP-3α ($p = 0.020$), compared to samples from non-relapsing patients. Also, the plasma microRNA profile significantly differed between patients who did or did not develop metastasis. Most notably, miR-21-3p ($p < 0.001$), miR-126-5p ($p < 0.001$) and members of the miR-320 family ($p < 0.001$ for miR-320a and miR-320b; $p = 0.009$ for miR-320d) showed significantly lower plasma levels, whereas concentrations of circulating miR-143-3p ($p = 0.001$) and miR-223-5p ($p < 0.001$) were increased in relapsing *versus* non-relapsing patients.

Conclusions: Our results suggest that the plasma chemokine and microRNA profiles in patients with grade II-III hormone sensitive breast tumors who develop metastatic disease within 5 years already exhibit small but significant differences at the time of primary diagnosis, as compared to patients with similar tumors who remain disease-free after primary surgery and adjuvant treatment. A validation study on an independent cohort is currently being set up.

No conflict of interest.

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The value of uPA and PAI-1 levels in triple negative breast cancer

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Background: Urokinase plasminogen activator (uPA) and plasminogen activator inhibitor-1 (PAI-1) are important prognostic biomarkers for poor response, especially in patients with node-negative breast cancer. There is currently little specific data showing prognostic value of increased uPA and PAI-1 levels in triple negative breast cancer (TNBC).

Methods: We identified patients with TNBC treated at the University Medical Centre Maribor between the years 2004 and 2017. Patients had had prospectively determined levels of uPA and PAI-1 as well as other traditional clinical and pathological prognostic factors. We compared the levels of uPA and PAI-1 against disease recurrence and disease specific survival using non-parametric statistical analysis (SPSS version 23 for Mac, IBM).

Results: We identified 67 women with triple negative breast cancer. The mean age at the time of diagnosis was 56.7 years (standard deviation (SD) 13.2). In 22.4% of women (n = 15) a recurrence or metastasis occurred during the time of follow-up. 20. 9% of women (n = 14) died due to disease specific causes. Our evaluation showed that neither elevated levels of uPA ($p > 0.699$), high PAI-1 ($p > 0.941$) nor a high uPA/PAI-1 ratio ($p > 0.720$) was statistically significantly correlated with recurrence or disease specific survival. uPA and PAI-1 levels did not correlate with lymph node status ($p > 0.532$), age at the time of diagnosis ($p > 0.340$) or size of the tumor ($p > 0.653$). Tumor size was significantly correlated with disease specific survival ($p > 0.027$), but not with disease recurrence ($p > 0.167$).

Conclusions: Our data show no correlation between recurrence and disease specific survival and levels of uPA and PAI-1 in women with triple negative breast cancer. This is in contrast with the current level of evidence in hormone positive or HER2 positive breast cancer. The insignificance of uPA and PAI-1 levels in TNBC might be due to the heterogeneity of molecular subtypes and their involvement in different carcinogenic signalling pathways.

A refined analysis of the correlation of specific molecular subtypes and their impact on uPA and PAI-1 levels is warranted.

No conflict of interest.

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Integration of genomic profiling and functional screening identifies potential driver somatic copy number alterations in triple-negative breast cancer

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Background: Triple-negative breast cancer (TNBC) is a kind of breast cancer with early recurrence and high heterogeneity, lacking targeted therapies. TNBC possessed few mutations but many somatic copy number alterations (SCNAs).

Material and Methods: Here, based on a cohort of 401 primary TNBC patients with clinical and genomic data, we found certain SCNAs were more frequent in tumors relative to paired normal tissues, including amplifications in drivers *MYC, NFIB, E2F*3.

Results: Further, we identified 10 candidate genes that were not investigated fully in previous studies: SDCCAG8, CNST, ANKH, AKR1E2, DIP2A, ZNF695, NUP210, B4GALNT3, METRN, TFB2M. These SCNAs were either enriched in tumor compared to normal tissue or associated with a worse prognosis. Using shRNA-based approach, we explore functional dependence on these genes in TNBC and non-malignant cell lines. Our data demonstrated that TFB2M and CNST, locating next to each other in chromosome 1q43, could promote tumor proliferation and invasion *in vitro* and *in vivo*. Mechanistical studies showed that TFB2M is a mitochondrial transcription factor and CNST is required for targeting of connexins to the plasma membrane.

Conclusions: We comprehensively characterized the SCNAs events in TNBC and tested the biological functions of candidate genes. Two adjacent genes were proved to enhance progression, motility and invasiveness of tumor cells by providing energy and decreasing the cell-cell adhesion between tumor cells, which could serve as drug targets in the treatment of TNBC.

No conflict of interest.

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Patient-assisted vs standard compression mode in mammography screening: A randomized clinical trial

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Background: An adequate breast compression is necessary to obtain uniform thickness, for optimal images quality. However, discomfort during screening mammography may negatively affect images quality and women attendance. We compare breast thickness, compression force and glandular dose, as well as women's experience between Patient-Assisted Compression (PAC) and Standard Compression (SC) modes.

Methods and materials: We included 274 women aged 52 to 69 years old, attending subsequent screening from December 2017 to December 2018. Mammograms included bilateral two-views (CC and MLO) images. Two of the four images were obtained using PAC and the other two using SC mode. To avoid woman's bias, the mode used in each image, was selected following a random list. Breast thickness (mm), compression force (N), and average glandular dose (mGy) were obtained for each of the 1096 images. We also collected woman experience immediately after the acquisitions of the mammogram, using a predefine survey with four questions.

Results: Breast thickness was not significantly different with PAC vs SC (mean [M] 56.40 mm vs 56.47 mm; p = 0.924). Compression force (M 91.30 N vs 90.76 N; p = 0.740) and average glandular dose were also similar between PAC and SC (M 1.34 mGy vs 1.35 mGy; p = 0.745). Nevertheless, most patients had a better experience with PAC.

Conclusion: The PAC maintains the technical quality of images while improves women's experience in screening mammography. Next step will be assessing the impact of PAC over the diagnostic image quality.

No conflict of interest.

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Prognostic utility of androgen receptor signaling pathway in invasive breast cancer

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Background: Androgen receptor (AR) and AR signaling pathway are thought to play a role in tumour progression and be potentially related to treatment responses and outcomes in invasive breast cancer. In present study, we investigated the clinicopathological significance of AR associated signaling pathway using the large transcriptomic database of early-stage invasive breast cancer.

Methods: Gene expression data from the Molecular Taxonomy of Breast Cancer International Consortium (METABRIC) cohort (n = 1980) was used as a discovery data-set and The Cancer Genome Atlas (TCGA; n = 1039) cohort was used as a validation data-set. In Gene Ontology terms of the biological process, genes related to "Regulation Of Androgen Receptor Signaling Pathway (GO: 0060765)" were selected and the relationships among AR-related genomic subtype based on the expression of these genes, clinicopathological features and patient outcomes were explored.

Results: An AR-related gene set, comprising 19 genes (*ARRB2*, *BUD31*, *DAB2*, *DDX5*, *EP300*, *FOXP1*, *HDAC1*, *HDAC6*, *HEYL*, *PARK7*, *PHB*, *PIAS2*, *PRMT2*, *RNF14*, *RNF6*, *SFRP1*, *SIRT1*, *SMARCA4* and *TRIM68*), was developed. Clustering analysis with this gene set further divided cases into two molecular subtypes (subtypes 1 and 2), AR mRNA expression of subtype 2 was significantly higher than that of subtype 1 in both cohorts ($p < 0.0001$ for both). This AR-related genomic subtype was significantly associated with oestrogen receptor and human epidermal growth factor receptor 2 status in METABRIC and TCGA cohorts. In METABRIC cohorts, 91% of luminal B were classified as subtype 2 and 85% basal-like BC were classified as subtype 1. The overall survival of subtype 2 was significantly worse than that of subtype 1 in both cohorts (METABRIC: HR 1.23, 95% CI 1.08–1.41, $p = 0.0023$; TCGA: HR 1.48, 95% CI 1.03–2.04, $p = 0.037$).

Conclusions: This study demonstrates that AR is associated with a specific transcriptomic profile with potential prognostic value. These finding suggests that AR associated signaling pathway may play an important role in the tumour aggressiveness for luminal type breast cancer patients.

No conflict of interest.

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Axillary lymph node involvement may be predicted by breast cancer subtype: a single center experience

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Introduction: The aim of our study was to evaluate the association between the different breast cancer subtypes (BCSs) and axillary lymph node (ALN) involvement and to analyze the clinical records of our Breast Unit.

Materials and Methods: We performed a retrospective analysis of our clinical records between 2003 and 2013. All the early breast cancers were included and divided into 5 different BCSs based on: estrogen receptors, progesterone receptors, Ki-67 value and HER2 status according to St Gallen 2013 classification. For each cancer the anatomo-pathological features and lymph node involvement were evaluated at definitive histological examination (macrometastasis). Statistical analysis was performed using the Kruskal-Wallis test.

Results: 2551 cases were treated: 37% Luminal A-like, 40% Luminal B-like Her2 negative, 8% Luminal B-like Her 2 positive, 6% Her 2 positive

Table (abstract 296)

	Luminal A-like	Luminal B-like (Her2 negative)	Luminal B-like (Her2 positive)	HER2 positive (non luminal)	Triple negative	p
N0	713 (75%)	621 (62%)	102 (50%)	85 (51%)	141 (63%)	p < 0.0001
N1	160 (17%)	218 (22%)	44 (22%)	32 (19%)	43 (19%)	
N2-3	76 (8%)	171 (17%)	58 (28%)	49 (29%)	38 (17%)	
LN tot	1.2 (±4.2)	2.6 (±6.6)	3.7 (±6.6)	3.5 (±6.4)	3.1 (±8.7)	p < 0.0001
Età	65 (±14)	64 (±14)	59 (±15)	61 (±15)	60 (±16)	p < 0.0001
Diametro mm	16 (±26)	20 (±16)	25 (±18)	25 (±19)	26 (±19)	p < 0.0001
Grade %						
I	43.4	16.4	4.7	0.6	0.9	p < 0.0001
II	44.6	46.4	34.7	14	12.6	
III	12	37.2	60.6	81.2	86.5	
Ki-67	11 (±5)	24 (±13)	30 (±14)	37 (±17)	53 (±25)	p < 0.0001
LVI %						
No	81.4	69.2	66.8	68.6	74.4	p < 0.0001
Int/focale	14	18.4	17.4	17.2	14.8	
Massive	4.6	12.4	15.8	14.2	10.8	
Bcl-2%						
Pos	96.4	80.7	55.3	7.8	15.6	p < 0.0001
Neg-Int	3.6	19.3	44.7	92.2	84.4	

(HER2+) and 9% Triple negative (TN). We noted significantly statistical differences in: lymph node involvement, number of involved lymph nodes involved, age, diameter, Ki-67 value, LVI status and Bcl-2 (all p < 0.0001). TN showed: absence of macrometastatic lymph node involvement in 63.5% of our cases, greater G3 nuclear grading, high Ki-67, absence of LVI. The HER2 + showed: greater lymph node involvement, more lymph nodes involved.

Conclusions: In our experience, according to different studies published, breast cancer showed anatomopathological characteristics and lymph node involvement statistically different with respect to the different BCS. In spite of the worst prognosis and the most aggressive behavior, TN showed less nodal involvement and less LVI. The HER2+ showed greater nodal involvement with more than 4 lymph nodes involved and more LVI. The different BCSs, besides having an important prognostic value, are predictive of the presence of a possible lymph node involvement and might be used to guide axillary management decision.

No conflict of interest.

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Micro-morphological regression patterns of tumors and lymph nodes following neoadjuvant chemotherapy for breast cancer with follow-up analysis: a new scoring system with implication into practice

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Background: One of the main advantages of neoadjuvant chemotherapy (NACT) for breast cancer (BC) is an early initiation of systemic control of disease. However, the effectiveness of NACT does not correlate with the result of standard micro-morphological regression (RG) analysis, thus disease is in some cases not well controlled or even progressed. The main aim was to categorize the micro-morphological markers of RG and the baseline characteristics of tumor that identify patients at high risk of NACT failure.

Material and Methods: 153 patients with BC (stages I–III) underwent NACT and RG evaluations of the tumor (T) and lymph nodes (LN) between Feb 2003 and Mar 2014 in the academic BC unit. 95% of patients received an institutional core biopsy (CB); and all underwent surgery, and a LN procedure. After completion of NACT and surgery, all the T and LNs underwent histological tissue processing incl. hematoxylin-eosin and immunohistochemical staining. After micro-morphological analysis, RG patterns were divided into 8 grades for T (from –2 to 5) and 7 grades for LNs (from –2 to 4). Summing the grade points for T and LNs generated the Neo-Pat-Score (NPS). The NPS totals, ranging from a min. of –4 (massive progression) to a max. of 9 points (complete regression, 3/4/5 points for T + 3/4 points for LN), were referred to survival data (event-free, EFS and overall survival, OS) and compared with the Residual Burden Cancer Score (RBCS) as the reference test.

Results: The median age of the patients was 49.5 years (range: 25–84). The breast conserving rate was 36.7%. 138 (87%) cases were NST. The frequency of complete responses was 36.6% for in situ components, 24.4% for LN metastases, 19% for invasive T, and 12.4% for lymphangitic carcinomatosis (LC). The predominant grade values of RG in T, LNs, and the NPS were +2 (22.15%), 0 (30.8%), and +1 (17.1%), respectively. The NPS was well correlated with RBCS (p < 0.001). NPS scores were significant predictors of RFS (p < 0.05) and OS (p < 0.001). Among baseline histopathological cancer characteristics assessed in CB, only LC had an impact on NACT failure irrespective of molecular subtype (LC correlated with RG in T and NPS but not with RG in LNs). After completion of NACT no change or de novo occurring LC followed by peripheral progression of invasive cells in T, invasion of cancer cells without scar formation in LNs, and de novo occurring in situ components in T were the indicators of disease progression and early relapse of BC.

Conclusions: LC in primary tumor is a factor of resistance to NACT in LNs. LC identified in CB should make clinicians cautious about applying NACT. Predictors of progression should compel clinicians to recommend a rapid switch off current treatment sequence either to primary surgery or, in the context of clinical trials, to a possible intensification of systemic and personalized therapies.

No conflict of interest.

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Relationship between VEGF-A and PD-L1 expression in primary breast cancer

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Background: Vascular endothelial growth factor-A (VEGF-A) is a major potent positive regulator of angiogenesis, the effects of which on cancer growth and development have been well documented. Recently, it has been reported that anti-VEGF therapy has the important effect of enhancing anti-tumor immunity in various cancers. In this study, we investigated the relationship between VEGF-A expression and immunological factors, including degrees of stromal tumor-infiltrating lymphocytes (TILs) and programmed cell death ligand 1 (PD-L1) in breast cancer.

Material and Methods: Invasive carcinoma tissues of 97 breast cancer patients who underwent surgery without preoperative therapy were examined. Grade of stromal-TILs was immunohistochemically (IHC) evaluated using the criteria of the International Working Group for TILs in BC: low (10–20%), intermediate (20–40%) and high (50–90%). VEGF-A and PD-L1 positive were evaluated by IHC. The relationships between VEGF-A expression and expressions of TILsor PD-L1 were investigated.

Results: Among the 97 patients, 37 (38.1%) had positive VEGF-A expression in the primary tumor. We divided the cases into two groups based on the expression of VEGF-A. The analysis revealed that positive expression of PD-L1 was significantly associated with VEGF-A expression (29.7% vs

10.0%, p = 0.014) in the primary tumor. Among the cases with positive PD-L1, 36.7% of VEGF positive cases had low TILs in the primary tumor, while none of negative VEGF-A cases had low TILs in the primary tumor.

Conclusion: The present study demonstrated that VEGF-A expression in breast cancer may be reflective of the expression of PD-L1 in the tumor. VEGF-A may act as negative regulator of TILs in the PD-L1 positive BC. In light of our results, VEGF-A may be predictive of immunological features and be a useful biomarker for immuno-targeting therapy among patients with breast cancer.

No conflict of interest.

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Gene expression profiles in premenopausal women with HR+ HER2− early breast cancer

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Background: Early breast cancer (EBC) is not a single disease but consists of several clinically relevant molecular subtypes. Within hormone receptor positive (HR+), HER2 negative (HER2−) disease, different luminal subtypes (A vs. B) impact on outcome and response to endocrine therapy. Gene expression signatures predicting risk of recurrence are already part of clinical management. Gene profiles correlated with important tumor pathways such as metastasis and progression, immune response or proliferation also correlate with clinical outcome and therapy response. Premenopausal patients often have poorer prognosis compared to postmenopausal patients. Even though the principle for treating premenopausal patients is consistent with that for postmenopausal patients, the molecular properties of breast cancer in young patients demand special attention in planning the therapeutic strategy. Nevertheless, most studies on gene expression, in particular for risk estimation, focussed on postmenopausal patients. The purpose of our project is to determine gene expression profiles of tumor samples from premenopausal patients with HR+, HER2− EBC. The gene expression profiles will then be correlated to response to therapy response and patient outcome.

Material and Methods: We comprised a collective of 162 premenopausal EBC patients (77 with and 85 without relapse) treated at the LMU breast center over a ten-year follow-up period. Diagnostic, therapeutic, and recent follow-up data were documented and prepared for statistical analysis. Tissue specimens were prepared for laboratory analysis which include a gene expression profiling using a custom-made pan-cancer code set (n = 745 genes) and the Nanostring nCounter® analysis. Gene expression data will be compared with conventional immunohistochemistry subtyping as well as histopathological factors that can be used as surrogates for certain pathways (pan cancer pathways, pathways for tumor progression and tumor immunology, etc.).

Results: Median patient age was 43.98 years of age (range 29–50). The two patient groups (with/without relapse within 10 years) differed with regard to clinical parameters: grade (2.06 ± 0.07/2.29 ± 0.06, $p = 0.024$), tumor diameter (26.62 mm ± 2.11/21.89 mm ± 2.67, $p = 0.033$), percentage of lymphnode metastasis [0.18 (range 0–1)/0.078 (range 0–0.92), $p = 0.001$] (Table 1).

Table 1 Patients' clinical parameters

	With relapse (n = 77)	Without relapse (n = 85)	*p*-value
Age at diagnosis	43.64 ± 0.58 (30–50)	44.29 ± 0.49 (29–50)	0.510
Grade	2.06 ± 0.07 (1–3)	2.29 ± 0.06 (1–3)	0.024
Tumor size (mm)	26.62 ± 2.11 (1–130)	21.89 ± 2.67 (2–110)	0.033
Nodal status	0.1844 (0.00–1.00)	0.0783 (0.00–0.92)	0.001

Conclusion: The project is ongoing. Updated results will be presented at the conference.

Funding: The first author is funded by China Scholarship Council.

No conflict of interest.

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Circulating tumor associated cells in breast cancers are resistance educated towards prior anthracycline treatments

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Background: Doxorubicin and Epirubicin are two anthracycline agents commonly used in treatment of breast cancers. However, chemoresistance towards these agents and subsequent treatment failures are commonly reported. There are presently no means for real-time monitoring of innate and acquired chemoresistance. Repetitive invasive biopsies to obtain tumor tissue for in-vitro chemoresistance profiling (CRP) or viable tumor are not feasible. We describe a non-invasive approach for CRP using peripheral blood Circulating Tumor Associated Cells (C-TACs).

Materials and Methods: We obtained 15 mL peripheral blood from 1034 known cases of breast cancers, among whom 353 were therapy naïve and 681 were pretreated. Viable C-TACs were enriched and harvested from PBMCs using an epigenetically active media that selectively kills normal cells and simultaneously confers survival benefit on apoptosis-resistant cells of tumorigenic origin. Surviving cells (C-TACs) confirmed by immunostaining (EPCAM+, CK+, CD45±, GCDFP+). Viable C-TACs were seeded into multi-well plates and treated with Doxorubicin or Epirubicin and surviving C-TAC fraction was measured to determine % cell-death and chemoresistance.

Results: Among therapy naïve patients (n = 353), innate resistance towards Doxorubicin and Epirubicin was observed in 44% and 46% of samples respectively (overall innate resistance = 45%). Among pretreated patients (n = 681), acquired resistance towards Doxorubicin and Epirubicin was observed in 81% of samples.

Conclusion: Our study demonstrates the feasibility of CRR profiling of C-TACs in therapy naïve and pretreated patients. Adoption of C-TAC – CRR profiling can non-invasively provide real time oversight towards treatment selection, monitoring of drug resistance and timely therapeutic course correction.

Conflict of interest:
Ownership: Rajan Datar is the Founder of Datar Cancer Genetics Limited.
Other Substantive Relationships: Ajay Srinivasan, Dadasaheb Akolkar, Darshana Patil, Revati Patil, Sanket Patil, Vishakha Mhase, Vineet Datta, Sachin Apurwa and Sushant Pawar are full time employees of Datar Cancer Genetics Limited.

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Real-time non-invasive chemoresistance profiling of circulating tumor associated cells in breast cancers to determine resistance towards mitotic inhibitors

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Background: Paclitaxel, Docetaxel and Vinorelbine exert anti-tumor activity by interfering with microtubule dynamics, leading to mitotic arrest. Though these agents are commonly used in treatment of breast cancers, therapy failures are noted due to innate and acquired chemoresistance. Real-time monitoring of chemoresistance towards such treatment agents is an unmet clinical need since conventional methods for chemoresistance profiling (CRP) necessitate invasive biopsies to obtain viable tumor tissue. We evaluated the utility of peripheral blood Circulating Tumor Associated Cells (C-TACs) for real-time non-invasive CRP in breast cancers.

Materials and Methods: We obtained 15 mL peripheral blood from 1034 known cases of breast cancers, among whom 353 were therapy naïve and 681 were pretreated. Viable C-TACs were enriched and harvested from PBMCs using an epigenetically active media that selectively kills normal cells and simultaneously confers survival benefit on apoptosis-resistant cells of tumorigenic origin. Surviving cells (C-TACs) confirmed by immunostaining (EPCAM+, CK+, CD45±, GCDFP+). Viable C-TACs were seeded into multi-well plates and treated with Paclitaxel, Docetaxel or Vinorelbine. Surviving C-TAC fraction was measured to determine % cell-death and chemoresistance.

Results: Innate resistance towards Docetaxel, Paclitaxel and Vinorelbine was observed in 42%, 59% and 56% of samples respectively in therapy

naïve patients' samples. Acquired resistance towards Docetaxel, Paclitaxel and Vinorelbine was observed in 78%, 72% and 66% of pretreated patients' samples.

Conclusion: Our study demonstrates the feasibility of CRR profiling of C-TACs in therapy naïve and pretreated patients. Adoption of C-TAC – CRR profiling can non-invasively provide real time oversight towards treatment selection, monitoring of drug resistance and timely therapeutic course correction.

Conflict of interest:
Ownership: Rajan Datar is the Founder of Datar Cancer Genetics Limited. Other Substantive Relationships: Ajay Srinivasan, Dadasaheb Akolkar, Darshana Patil, Revati Patil, Sanket Patil, Vishakha Mhase, Vineet Datta, Sachin Apurwa and Sushant Pawar are full time employees of Datar Cancer Genetics Limited.

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BRCA variant classification of ClinVar submitter content from ENIGMA, ARUP laboratories and German cancer consortium compared to MH BRCA® and correlation with response to PARP inhibition in MH GUIDE®

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Background: Germline mutations in *BRCA1* and *BRCA2* genes confer a high risk for the hereditary breast and/or ovarian cancer (HBOC) syndrome, whereas both germline and somatic mutations are predictive biomarkers for PARP inhibition. MH BRCA® classifies variants based on ACMG guidelines. Clinical interpretation of NGS results by MH GUIDE® provides clinicians with treatment recommendations to cancer based on expert curated biomarker knowledge.

Material and Methods: MH BRCA® was compared to ClinVar submitter content from ENIGMA, the international consortium of investigators on clinical significance of BRCA1/2 variants, the ARUP laboratories, a clinical testing lab of the university of UTAH, and the German Cancer Consortium (combined total of 7840 BRCA1/2 variants). In each validation dataset the concordance-rate was calculated, and discordant variant interpretations were analyzed. Finally, based on functional evidence for DNA damage response, we assessed the ACMG classification with the predicted response to PARP inhibition by MH GUIDE®.

Results: In three independent validation datasets, MH BRCA® demonstrated a concordance-rate between 74 and 99%. Subset analysis of the *pathogenic/likely pathogenic* variants showed almost 100% concordance of MH BRCA® with clinically assessed pathogenicity (4975 out of 4976 variants). Moreover, in the ARUP laboratories dataset, a re-classification of variants of uncertain significance (VUS) was found in 32 out of 342 variants (9%). The analysis of the ENIGMA dataset revealed that 9 variants are either re-classified from VUS or change their classification from *likely benign* to *likely pathogenic* based on functional evidence provided by the proprietary variant annotation database of Molecular Health. Last, we assessed the accordance of MH BRCA® variant classifications with treatment-decisions in MH GUIDE® regarding PARP inhibition. The comparison demonstrated a complete coverage of pathogenic classified variants with predicted response to treatment. Interestingly, low-efficacy of PARP inhibition due to moderately impaired homologous recombination repair activity was predicted in a subset of variants classified as pathogenic due to hypomorphic BRCA1/2 mutations.

Conclusion: We showed that MH BRCA® provides a standardized ACMG-guided process for assessment of pathogenicity by concordant classification of pathogenic BRCA1/2 variants with ClinVar submitter content of ENIGMA, ARUP laboratories and the German Cancer Consortium. Moreover, we identified clinically relevant *likely pathogenic* BRCA1/2 variants due to re-classification in accordance with the ACMG-guided assessment using in-house expert curated variant annotations. In addition, we showed that the contextualization of BRCA1/2 variants classified as *pathogenic* with MH GUIDE® supports the treatment strategy of PARP inhibition.

Conflict of interest:
Other Substantive Relationships: All authors/co-authors are employees of Molecular Health GmbH.

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Interaction of PAFAH and beta-catenin in BRCA1 mutant breast cancer

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Background: Aberrant Wnt/beta-catenin signaling is a well-established characteristic of breast cancer implicated in tumorigenesis and metastasis, whereas platelet-activating factor acetylhydrolase (PLA2G7/PAFAH) is not well understood in breast carcinogenesis so far. This study analyzes the functional relationship between PAFAH and beta-catenin in breast cancer tissue.

Material and Methods: PLA2G7/PAFAH expression was determined in five breast cancer cell lines on mRNA- and protein-level. Beta-catenin staining was performed in MDA-MB-231 (TNBC, BRCA1 wildtype) and HCC1937 (TNBC, BRCA1 mutant) cell lines before and after siRNA knockdown of PAFAH. Cell viability and proliferation were analysed via MTT and BrdU assay after PAFAH knockdown. PAFAH and beta-catenin expression was analyzed in BRCA1 wildtype and BRCA1 mutant breast cancer tissue by immunohistochemistry using the IR-scoring System.

Results: mRNA and protein expression of PLA2G7/PAFAH were significantly higher in HCC1937 cell line than in BRCA1 wildtype cell lines. HCC1937 cells showed a distinct membranous beta-catenin staining compared to the BRCA1 wildtype cell line MDA-MB-231 that showed cytoplasmic/nuclear staining. After siRNA knockdown of PAFAH, HCC1937 cells lost this specific staining pattern. Viability and proliferation of HCC1937 cells were significantly improved after PAFAH knockdown. In breast cancer tissue, nuclear PAFAH and membranous beta-catenin staining showed a strong correlation ($cc = 0.794$, $p < 0.001$) with higher expression of both in BRCA1 mutant cases (both $p < 0.001$).

Conclusions: Our data suggest a functional relationship between PAFAH and the Wnt/beta-catenin pathway in BRCA1 mutant breast cancer and may help to improve the understanding of breast cancer carcinogenesis.

No conflict of interest.

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A Breast 3D model as a possible tool for non-invasive tumour localization in breast surgery

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Background: For tumour location and surgical planning physicians need to convert 2-D information into a 3D approach. Wire guided surgery is the most common method for preoperative localization of breast cancer lesions. Other localization methods can also be used, such as radioactive seeds, carbon tattooing or ultrasound guided clips, but they are all invasive procedures. In this work, we aimed at building an individualized 3D digital breast model integrating the breast torso and tumor location through MRI/3D fusion algorithms to help in pre-operative tumour location without the use of invasive procedures.

Material and Methods: Patients with Tis/T1-T3 breast cancer proposed for breast conservative treatment at the Champalimaud Clinical Centre between April 2017 and January 2019 were assessed for inclusion in the current study. Selected patients were proposed for image capturing with 3D torso surface scans in the standing position with hands on hips; breast MRI with gadolinium contrast was performed – patient in prone position with arms up.

An image acquisition protocol was designed and applied to a validation group to acquire breast Magnetic Resonance Imaging (MRI) and 3D surface scan data using surface markers on the patient's breasts and torso. Breast MRI/3D surface scan fusion algorithms (a second-stage free form deformation versus biomechanical model (BM)) with pose transformation were applied to simulate patient-specific 3D digital breast models with quantitative analysis of breast morphology and algorithm validation.

Results: A total of sixteen patients were selected and included in the current study. Of these, seven patients were included in the validation group.

Thirty-two (16 bilateral) patient-specific 3D digital breast models were simulated. The single-breast MRI/3D fusion algorithm performance with a second- stage free form deformation increased tumour location accuracy compared to a biomechanical simulation and was not affected by variances in breast volume. Best target registration error (TRE) performance (18.5 ± 3.88 mm) was observed with the inclusion of the BM of pose transformation, but tumour locations were consistently worse (80% of the cases) than fusion results without BM (TRE of 26.26 ± 6.61 mm).

Conclusions: A patient-specific digital breast model integrating the breast torso and tumour location was created and validated with a MRI/3D surface scan fusion algorithm. The spatial computing applied to this dataset of breast cancer patients, merging digital and physical anatomic structures of the breast, including tumour in a digital 3D breast model, could pave the way for a new non-invasive pre-operative localization technique through augmented reality.

No conflict of interest.

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Application of culture-based assays to human malignant breast tissue can infer tumour microbiota composition

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High-throughput 16S rRNA sequencing (HTS) has recently been used to describe the microbial communities of *in-vivo* compartments that were up until that point described as "sterile." Among these is the human breast, the microbiome of which was described by our group in patients with and without breast cancer. The impression of the healthy and malignant mammary microbiome to date has been informed primarily by 16S metabarcoding data, and only sparingly by culture-based assays, which may lead to an imbalanced view of the tumour microbiota.

Here, we designed a culture-based assay to capture as many bacteria as possible from human breast tissues. Preclinical validation was completed in murine tumour and liver tissues before application to human specimens. Consent was obtained from 44 male/female patients with breast cancer. Fresh tissues and swabs were cultured immediately on several types of agar. Cultured colonies were Sanger-sequenced.

Culture data reflected relatively low bacterial diversity in all samples plated. Four genera were isolated across all tumour and normal adjacent specimens, the most common of which were coagulase-negative Staphylococci and Corynebacteria. Some tumour tissue isolates were not found in normal adjacent tissue, and vice versa; however, absolute numbers of bacteria recovered were low. 14/38 patients were in fact culture-negative across all samples. Our data suggest that the true profile of the breast microbiota may be considerably less diverse than what high-throughput data indicate. We are currently investigating machine learning and HTS data in parallel with our culture data to investigate the probable origin of these bacteria.

No conflict of interest.

Genetics

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Characterization of 331G/A polymorphism of rp gene and identification of viral oncogene HMTV virus as genetic markers for the improvement of breast cancer management in Cameroon

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Background: Breast cancer is a real public health problem in Cameroon, where more patients with this cancer usually die a year after diagnosis, as it is still based on histological examination, mortality due to cancer is far from decreasing. Since cancer is an accumulation of molecular changes, the +331 G/A polymorphism of PgR gene (progesterone receptor) and viral oncogene HMTV (Human Mammary Tumor Virus) has been recently considered as a molecular markers associated with breast cancer. Due to that, we fixed our objectives to characterize these markers by semi-nested PCR to understand etiological factor of that cancer in Cameroon.

Method: We carried out a case control study, in which 26 cases diagnosed positive for breast cancer at the CHU of Yaounde were recruited through the identification of archived biopsies. Blood samples were also collected from 20 women recruited using a questionnaire and a inform concern sign by each of them. +331 G/A polymorphism in the PgR gene was identified using NlaIV endonuclease by PCR-RFLP, and HMTV viral oncogene by hemi-nested PCR. The data were analyzed using Microsoft Excel and SPSS v20.

Results: We got a mean age of 57,73 +/– 9,87 in our cancerous group with the predominance of infiltrant duct carcinoma at grade II of SBR. An Odd Ratio of 1.268 with Confident Interval of 95% 1.004–1.664 proving that there is a significant association between 331G/A mutation and breast cancer with P-value of 0.026, obtained by comparing the mutant group (AA) 28.5% and wild genotype (GG). In addition, 3 cases were detected with the HMTV virus, one was found in the cancer group and two in the control group.

Conclusion: These results indicate that, HMTV could predispose to breast cancer, beside 331 G/A polymorphism is an associated risk factor of that cancer.

No conflict of interest.

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Non-BRCA hereditary gene mutations in the Mongol breast cancer patients of Russia

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Background: Breast cancer (BC) is the most prevalent female malignancy worldwide. In Russians, who were descended primarily from Slavic ancestors (newcomers), a strong founder effect was observed for the *BRCA1* 5382insC allele, which account up to 90% of all known BC-associated mutations in this population. To date, despite a significant burden of cancer and limited access to genetic cancer risk assessments there are a limited number of reports on the inherited gene mutations associated with BC among ethnic groups in Russia. The present study aimed at identifying mutations of BC-associated genes in 73 unrelated ethnically diverse BC patients (Mongoloid race) of Russia.

Methods: Seventy-three BC patients with young-onset and/or bilateral and/or familial BC were included in the study. The median age of the patients at the time of BC diagnosis was 41 years (range 25–51 years). Genomic DNA isolated from blood samples was used to prepare libraries using a capture-based target enrichment kit (Hereditary Cancer Solution™, SOPHiA GENETICS, Switzerland) covering 27 genes (*ATM, APC, BARD1, BRCA1, BRCA2, BRIP1, CDH1, CHEK2, EPCAM, FAM175A, MLH1, MRE11A, MSH2, MSH6, MUTYH, NBN, PALB2, PIK3CA, PMS2, PMS2CL, PTEN, RAD50, RAD51C, RAD51D, STK11, TP53* and *XRCC2*). Next-generation sequencing (NGS) was performed on NextSeq500 System (Illumina, USA). The study was conducted in accordance with the Helsinki Declaration (1964). The Ethics Committee of the Cancer Research Institute approved the study, and all participants provided written informed consent.

Results: Seventy-three unrelated ethnically diverse BC patients were negative for *BRCA1/2* mutations (*BRCA1* 5382insC, *BRCA1* 185delAG, *BRCA1* 4153delAG, *BRCA1* T300G, *BRCA1* 3875delGTCT, *BRCA1* 2080delA, *BRCA1* 3819delGTAAA, and *BRCA2* 6174delT). Fourteen patients had pathogenic mutations (14/73, 19%) and one (1/73, 1.4%) had likely-pathogenic mutation. Of these, 8/73 (11%) had mutations in *BRCA2* and 6/73 (8%) were in other genes: *ATM* (2), *MUTYH* (1), *PTEN* (1), *RAD51D* (2). In addition, we found 46 SNVs among which 5 were pathogenic, 6 were conflicting interpretations of pathogenicity and 35 SNVs were of unknown significance (variant of unknown significance, VUS). Six VUS were detected in *BRCA1/2* whereas 29 VUS were in other genes. As expected, VUS were more frequent in non BRCA1/2 genes.

Conclusions: This report is the first to describe highly pathogenic germline variants in the *BRCA2* (rs483353122), *PTEN* (rs786201044), *RAD51D* (rs137886232), *ATM* (rs866521873, rs780619951) genes in unrelated ethnically diverse patients (Mongoloid race) of Russia with young-onset and/or bilateral and/or familial BC. Further research is warranted to confirm the impact of mentioned above variants on the risk of BC in ethnically diverse patients of Russia.

The reported study was funded by RFBR according to the research project 18-29-09046.

No conflict of interest.

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Association of germline genetic variants with breast cancer survival in patient subgroups defined by standard clinic-pathological variables

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Background: Given the high heterogeneity of breast tumors, associations between germline variants and survival that may exist within specific patient subgroups could go undetected in a pooled set of breast cancer (BC) patients. Therefore, we investigated the association between common inherited genetic variants and breast cancer survival within patient subgroups based on known prognostic factors.

Material and Methods: Analyses were based on 91,686 female BC patients of European ancestry from 70 studies participating in the Breast Cancer Association Consortium. Cox regression models were used to assess associations between individual common germline genetic variants and 15-year BC-specific survival. We performed genome-wide association analyses within 13 groups of BC patients based on age at diagnosis, tumor grade, Estrogen Receptor status, Progesterone Receptor status, the human epidermal growth factor receptor 2 status, and type of systemic treatment. All models were stratified by country. To assess the noteworthiness of the observed associations, we used a Bayesian false discovery probability (BFDP) measure, setting the prior probability of true association to 0.0001 and choosing the prior distribution of the log hazard ratio representing a variant effect size to follow a Normal distribution centered at 0 with standard deviation equal to 0.2. For each significant association, we tested whether the expression of the nearest gene correlates with survival using KMplotter.

Results: We identified five genome-wide significant associations within the group of patients diagnosed with a grade 3 tumor, all located on chromosome X and in strong linkage disequilibrium. The most significant variant was rs5934618, situated in an intronic region of the TBL1X gene. The risk allele G was associated with increased risk of dying compared to the reference allele A (HR [95% CI]: 1.39 [1.24, 1.56], P = 1.7E−08). The BFDP for this variant was 0.02, suggesting a robust association with outcome. The result remained substantially unchanged when we accounted for age at diagnosis, additional tumor characteristics and treatment with (neo)adjuvant chemotherapy. Furthermore, the expression of the TBL1X gene was associated (HR (95%CI) for high vs low expression: 1.45 (1.16–1.81), P = 0.0009) with breast cancer survival specifically in grade 3 patients. We did not find *genome-wide significant* associations or noteworthy associations (BFDP < 0.15) in other patient subgroups after adjustment for additional prognostic factors.

Conclusions: We found one locus to be strongly associated with breast cancer survival within grade 3 tumors. Our data provided limited evidence for the existence of additional genetic variants associated with breast cancer survival in more homogeneous patient groups. A remaining challenge is the limited power due to the low number of events.

No conflict of interest.

314 Poster

Prevalence of germline BRCA pathogenic variants in a monoinstitutional cohort of patients with triple negative breast cancer

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Triple negative (TN) breast cancer (BC) is an uncommon and aggressive subtype of BC associated with early disease recurrence and short survival. In literature, prevalence of BRCA mutations in TNBC patients may vary from 9 to 32%. The prevalence of BRCA germline mutations has been systematically evaluated in this setting of patients at our center.

Between 2014–2019 BC patients and unaffected women with a familial history accessed to the Familial Cancer Services at the Oncology Unit of «Vito Fazzi» Hospital in Lecce, and data were collected in a registry database. The eligibility for the BRCA test was assessed according to national and international guidelines. BRCA1 and BRCA2 testing was performed by complete sequencing of the genes using Next Generation Sequencing (NGS).

A total of 704 women with BC were eligible for the study analyses; of these, 480 had documented genetic test results. Germline BRCA mutations (N = 109) were identified in 108 cases (22.7%), including 74 BRCA1 (68.5%) and 32 BRCA2 32 (31.5%) mutations identified. Of the eligible 704 BC patients, 129 (18.3%) were TN. Among these, 47 (36.4%) were BRCA1/BRCA2 carriers. Specifically, the most frequent mutation identified was a BRCA1 frameshift variant (36.1%): c.5266dupC, while the second most frequent was the BRCA1 frameshift variant (14.9%): c.514delC. Among TNBC patients, 86 (66.6%) presented a family history of BC, while a family history of ovarian, prostate and pancreas cancer were found in 28 (21.7%), 21 (16.2%) and 12 (9.3%) cases, respectively.

In this study population, the prevalence of BRCA deleterious variants among TNBC patients appeared higher compared to available literature data, being 36.4%, regardless of family history and age. These patients should be referred to genetic counseling and testing regardless of age, and collection of family history may help to identify further patterns of cancer risk. Studies on larger samples are ongoing to confirm and explain these data.

No conflict of interest.

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Clinical pathological association with breast cancer gene analysis through next generation sequencing

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Purpose: The next generation sequencing technology has the advantages of high speed, high throughput and high accuracy. Because of these advantages, it is used in various cancer fields. Several gene pannels have been applied to breast cancer to assess risk and determine treatment direction accordingly. The purpose of this study was to improve the prognosis and future treatment of patients with breast cancer by applying NGS.

Method: From January 2018 to December 2018, we studied patients who underwent surgery at Kosin University Gospel Hospital. The study patients were from stage 1 to stage 3 of breast cancer. Patients who were not able to undergo surgery or who had more than stage 4 patients were excluded. This study included patients who underwent Neo-systemic therapy(NST). NGS was performed postoperatively. And in patients who underwent NST, NGS proceeded to pre-chemotherapy specimens.

Result: The expression of somatic mutation was different for each type of breast cancer. Most of them have been observed to have more than two mutations. It shows the expression ratios of each gene in Figure 2. Overall, TP53, PIK3CA, and ERBB2 showed high expression frequencies. Figure 1 shows the frequency of mutation incidence frequent in each type of patient.

Conclusion: Various types of somatic mutations are also expressed in breast cancer, and they are different according to each type. These various manifestations may be associated with the prognosis of breast cancer. Further studies are needed to determine for them.

No conflict of interest.

316 Poster

New germline RAD51D gene variant in the Mongol breast cancer patients

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Background: In recent decades, breast cancer (BC) is the most common malignancy in the Russian Federation. The population is descended primarily from newcomers (Slavic ancestors) and indigenous population (Mongoloid race). Currently, nothing is known regarding the molecular factors associated with increased risk of hereditary BC in the indigenous population of Russia. BC prevention models for indigenous population have not been developed yet. Our aim was to evaluate the frequency of hereditary mutations of *RAD50* and *RAD51D* genes in Mongol BC patients.

Methods: Seventy-three BC patients with young-onset and/or bilateral and/or familial BC were included in the study. The median age of the patients at the time of BC diagnosis was 41 years (range 25–51 years). Genomic DNA isolated from blood samples was used to prepare libraries using a capture-based target enrichment kit (Hereditary Cancer Solution™, SOPHiA GENETICS, Switzerland) covering 27 genes (*ATM, APC, BARD1, BRCA1,*

BRCA2, BRIP1, CDH1, CHEK2, EPCAM, FAM175A, MLH1, MRE11A, MSH2, MSH6, MUTYH, NBN, PALB2, PIK3CA, PMS2, PMS2CL, PTEN, RAD50, RAD51C, RAD51D, STK11, TP53 and *XRCC2*). Next-generation sequencing (NGS) was performed on NextSeq500 System (Illumina, USA). The study was conducted in accordance with the Helsinki Declaration (1964). The Ethics Committee of the Cancer Research Institute (Tomsk NRMC) approved the study, and all participants provided written informed consent.

Results: We have screened for *RAD50* and *RAD51D* germline mutations seventy-three *BRCA1*- and *BRCA2*-negative patients diagnosed with BC. Of these, 6/73 (8%) had mutations in *RAD50* and *RAD51D* genes and 12/73 (16%) were in other genes: *BRCA2(8), ATM* (2), *MUTYH* (1), *PTEN* (1). We identified nonsense mutation (2.7%, 2/73) of the *RAD51D* gene (c.757C>T, p.Arg253Ter, rs137886232, highly pathogenic) in two young unrelated BC patients. We also identified a variant of conflicting interpretations of pathogenicity in the *RAD51D* gene (rs145309168, MAF = 0,000 (ExAC)) in one Mongol BC patient aged 33. In three other unrelated Mongol BC patients, we identified a variant of conflicting interpretations of pathogenicity in the *RAD50* gene (rs200017020, MAF = 0, 0002 (ExAC)).

Conclusions: According to published data, mutations in the *RAD51D* gene are associated with a high risk of developing familial forms of ovarian and breast cancer that are not caused by germline mutations in the *BRCA1* and *BRCA2* genes. Further research is warranted to confirm the impact of mentioned above variants on the risk of BC in ethnically diverse patients of Russia.

The reported study was funded by RFBR according to the research project 18-29-09046.

No conflict of interest.

317 Poster

Use of multi gene-panel testing to detect hereditary breast cancer gene variants in patients attending to a breast cancer clinic, Peradeniya, Sri Lanka

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Background: Globally one in eight women develops breast cancer (BC) in the lifetime. As per the national statistics, 38.7% Sri Lankan women aged 39–46 years account for BC, which ranked first among all cancers in that age group. About 5–10% of Breast Cancer (BC) cases are clustered in families owing to germline mutations in genes other than *BRCA*1/2 leading to hereditary breast cancer. Genes in which germline mutations confer highly or moderately increased risks of cancer are called cancer predisposition genes (CPGs). Hereditary breast cancers occur in individuals with germline variants in various CPGs such as BRCA1, BRCA2, CHEK2, ATM, PALB2, TP53, PTEN, STK11, BRIP1, CDKN2A, BARD1, FANC1. Multi-gene panel testing for detection of clinically actionable genetic variants in CPGs are useful in routine clinical practice. This study aimed to describe the pattern of germline variants in a cohort of Sri Lankan patients using multi gene panel testing to assess the cancer risk in individuals. Ethical clearance was obtained from Ethics Review Committee of the Faculty.

Materials and Methods: Participants were selected and categorized into four groups according to the different criteria of BC such as patients with family history (13), sporadic BC patients (20), healthy individuals with a family history of BC (22) and healthy controls (05) in the age of 20–78 years. After providing pre-test counselling and obtaining written informed consent, blood samples were collected from sixty four participants and DNA extraction was performed. DNA samples were subjected to next-generation sequencing using multi gene panel to analyze 18 genes associated with BC using Ion Torrent PGM.

Results: In the study group, 16 were identified having pathogenic sequence variant (c.3113A>G pGlu1038Gly) in BRCA1 gene (six of sporadic BC patients, two of BC confirmed patients with family history, eight of healthy individuals with family history). Three patients (5%) identified with pathogenic missense variants in BRCA2 gene (c.6509A>G, p.Lys2170Arg) and one had frame shift mutation in PALB2 gene due to a deletion. One patient reported with benign variant in BARD1 (c.1075_1095del, p.Leu359_Pro365del) and drug response variant in TP53 (c.215C>G, p.Pro72Arg) genes. Pathogenic deleterious frame shift mutation (c.1592delT, p.Leu531Cysfs) in PALB2 gene was also found in two currently healthy participants with family history of BC.

Conclusion: As previously reported, BRCA1 gene variants are common (26%) in this study group. BRCA2 gene variants were present in 5% of the participants. About 5% identified with deleterious mutation in PALB2 gene. This study revealed that multi gene panel testing is useful to identify the subjects possessing the gene variants leading to hereditary breast cancer. Based on the results, low cost molecular test was developed for screening of at-risk family members.

No conflict of interest.

318 Poster

The risk of colorectal cancer associated with BRCA 1 and/or BRCA 2 mutation carriers: systematic review and meta-analysis

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Introduction: Carriers of the BRCA 1 and/or BRCA 2 mutation incur a lifetime risk of up to 85% for breast cancer and between 20 and 40% for ovarian cancer. Efforts to elucidate the lifetime risk of developing colorectal cancer with BRCA carrier mutations have demonstrated conflicting results. Consequently, there are no formal guidelines regarding the necessity for bowel screening for individuals with BRCA 1 and/or BRCA 2 mutations. A systematic review and meta-analysis was performed to determine the risk of colorectal cancer associated with BRCA carrier mutations.

Methods: Nine studies were included in the meta-analysis. The overall population of the study was 18,839, with 4,978 colorectal cancers identified. Primary outcome was overall incidence of BRCA mutation and colorectal cancer. Secondary outcomes included subgroup analysis of incidence in BRCA 1, BRCA 2, Ashkenazi Jews and age and sex matched BRCA mutation loss carriers.

Results: There was no statistically significant increase in the odds of having colorectal cancer in patients carrying a BRCA mutation (OR 1.03, 95% CI 0.80–1.32, p = 0.82) with no heterogeneity (I^2 = 0). Again, in studies adjusted for age and sex estimates, there was no increased odds of developing colorectal cancer (OR 1.08, 95% CI 0.69–1.0, p = 0.73), with no heterogeneity (I^2 = 0).

Conclusion: This meta-anlaysis found that colorectal cancer risk was not significantly elevated in BRCA1 and/or BRCA2 mutation carriers. Only one prospective cohort study has been performed on this subject to date. Much more robust evidence is required before recommending screening colonoscopies, which are not without risk, to BRCA1/2 mutation carriers.

No conflict of interest.

319 Poster

BRCA screening among Jewish community of Rome

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Background: Pathogenic variants (PVs) in *BRCA ½ (BRCA*) genes confer a high life time risk of developing breast and/or ovarian cancer. The percent of *BRCA* PVs in the general population is around 0.2%. However it can vary among different geographic areas and ethnic groups, as in the Ashkenazi Jewish community, where is observed at relatively high frequency (2%), with 3 different specific PVs due to a founder effect.

No information regarding the *BRCA* status are available nowadays among the Jewish community in Rome, one of most ancient community worldwide that settled after the Jerusalem temple destruction. For this reason, aim of the study is to perform germline *BRCA* screening among breast and/or ovarian cancers women from this community, including that of Sephardic origin settled in Rome in the past 50 years from Libyam.

Material and Methods: We enrolled 22 women for *BRCA* testing, so divided: 17 of Roman origin and 9 Sephardic from Libyan origin. The personal history was positive for ovarian and breast cancers in 3 and 24 patients, respectively and the median age at onset was 55,8 years. Only 7 patients met the current Regione Lazio guidelines criteria for genetic testing; 20 patient did not presented breast or ovarian family recurrence. After written consent, the samples were NGS screened for *BRCA* status. BRCA Devyser Kit (Devyser, Svezia) was used to analyzing the entire coding sequences of both genes. The sequencing process was carried out according to Illumina's protocols (Illumina, San Diego, CA, USA). Sequence data were processed using CE-IVD Amplicom Suite Software v.1.0 (SmartSeq s.r.l, Novara, Italy, www.smartseq.it). The study received approval from local Ethics Commettee.

Result: We found the *BRCA 2 c.7007 G > C*, p.(Arg2336Pro) PV among 3 out of 17 Jewish women of Rome origin, of which one affected by ovarian cancer and two by breast cancer; the same variant was reported in an unaffected woman from a family with HBOC history. All the carriers of this variant were family unrelated and no *BRCA PVs* were found among patients from Libyan origin. A women reported the PV c.6973C>T in BRCA 2 but she has been excluded from the study because not from Jewish side.

Conclusions: 15.3% of the subjects from Jewish Community of Rome were positive for *BRCA2 c.7007G>C* PV. We hypothesize that this variant would represent a founder mutation among the Jewish community in Rome. Further research is need in order to confirm this study.

No conflict of interest.

Lifestyle, Prevention including Secondary Prevention

320 Poster

Five-year follow-up results of aerobic and circuit training on bone mineral density in early breast cancer patients

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Background: Systemic breast cancer therapies interfere with bone turnover and predispose patients to cancer-treatment related bone loss. Breast cancer survivors are at an increased risk for osteoporosis and fracture compared with women in general.

The aim of this randomised clinical trial was to determine the preventive effect of weight-bearing jumping exercises and circuit training on bone loss among breast cancer patients.

Material and Methods: 573 early breast cancer patients aged 35–68 years and treated with adjuvant therapy were randomly allocated into a 12-month aerobic exercise program or a control group. 444 patients (78%) were included in the five-year analysis. The exercise intervention comprised weekly supervised step aerobics and circuit exercises as well as home training. [ST1] BMD at FN and LS were measured by dual energy X-ray absorptiometry and followed for five years. The amount of physical activity was estimated in metabolic equivalent hours (MET) per week. Physical performance was assessed by 2-km walking and figure-8 running tests.

Results: In premenopausal women, the 12-month exercise program prevented femoral neck bone loss during the intervention and two years thereafter but the difference between the group had disappeared at five years. The mean FN BMD change among the trainees and controls was −0.2% and −1.5% at one year, −1.1% and −2.1% at three years and −3.3% versus −2.4% at five years of follow-up, respectively. The exercise intervention had no effect on lumbar spine BMD changes in premenopausal women: LS BMD loss among the trainees and controls was −3.2% and −3.2% at three years and −5.1% and −4.7% at five years. In postmenopausal women, the exercise intervention had no effect on BMD changes at FN or LS.

Conclusions: The 12-month exercise program prevented femoral neck bone loss in premenopausal breast cancer patients during the intervention. The bone protective effect was maintained two years after end of the program but lost later in the follow-up.

No conflict of interest.

321 Poster

Age-, community-matched Body Mass Index and overall survival in patients with breast cancers

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Background: Obesity has been known as a risk factor for the development of breast cancer and also affects survival in women diagnosed with breast cancer. Although its relationship has been reported in Korea, age has been yet a major confounding factor to interpret the hypothesis. Aging is also a risk factor of obesity. We aimed to investigate the correlation between the body mass index (BMI) and overall survival of patients with a breast cancer compared with a public released standard Korean obesity index which was age-matched in a community general population.

Methods: We conducted a retrospective observational study from a single institute from January, 2014 to December, 2018. Among all 429 patients diagnosed and treated with breast cancer, we categorized them as three groups (low weight: BMI < 18 kg/m^2, normal: BMI < 25 kg/m^2, obesity: BMI ≥ 25 kg/m^2) stratified by stage. We also used Log Rank test comparing with standard Korean obesity index by age-, a community (Busan)- matched general population.

Results: Total 418 patients were finally enrolled. Mean duration of follow up was 33.3 months. Obesity, normal BMI and low BMI was 124(29.2%), 174 (41.3%), and 9 (2.1%) patients, respectively. BMI was correlated with age, patients with obesity was 19.3% (35/181) of women with less than 50 years, but 45.0% (109/242) of women with more than 50 years. According to Age-matched BMI index, patient with more than 50 percentile is 52.1%. Both overall survival was not significantly different among three BMI groups or age-matched BMI index (<50 percentile vs ≥50 percentile) stratified by stage.

Conclusions: According to BMI index with Age-matched general population, BMI of patient with breast cancer was relatively high. Obesity is not major risk factor of short term overall survival in Busan. Not only further studies need to lighten the relationship between obesity and long-term survival, but also intervention to reduce BMI needs to know its effects on breast cancer survival in Korea.

No conflict of interest.

322 Poster

An audit of chemoprevention provision in a breast cancer family history clinic

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Background: The family history clinic started offering Tamoxifen as a risk-reducing measure in 2015 in line with the NICE clinical guidance on Familial breast cancer. In 2017, following an amendment to the guidance, post-menopausal patients were also offered Anastrazole.

The purpose of this audit was to demonstrate adherence to the NICE guidelines. It was also hoped that any common themes in patients' reasons for declining chemoprevention would be identified in the audit process.

Method: The records of 1606 patients seen in the family history clinic since the introduction of chemoprevention were observed and the following questions asked.

- Was the patient suitable/eligible for chemoprevention?
- Was the patient offered chemoprevention?
- If eligible and not offered chemoprevention, what was the reason?
- If the patient was offered chemoprevention, what was the outcome?
- What reasons were given by patients for declining chemoprevention?

Results: A total of 366 patients were deemed eligible and suitable to be offered chemoprevention at their appointment. A further 3 patients had incomplete documentation and the assumption was made that they were eligible. A compliance rate of 99.19% was demonstrated in that 366 women were offered chemoprevention.

70 (19.13%) women accepted the offer of chemoprevention and a further 154 (42.08%) were still undecided at their most recent appointment. 142 (38.8%) women declined the offer of chemoprevention.

Of the 142 women who declined chemoprevention, the most common reason for declining it was concerns over the side-effects and risks of the treatment (30.28%).

A significant proportion of women took several appointments and discussions before making a final decision on chemoprevention.

Conclusion: We were able to demonstrate a satisfactory level of compliance with the NICE guidance on chemoprevention. The audit also demonstrated a higher level of uptake of chemoprevention than previously reported nationally.

Findings suggest more time should be allowed for answering questions and offering guidance on potential side effects and how they can be managed.

No conflict of interest.

323 Poster

Is socioeconomic status a barrier for individual breast cancer awareness in developing countries?

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Introduction: Though the causes Delayed diagnosis of breast cancer remains a major reason for higher breast cancer related mortality in

developing countries are multifactorial, low socioeconomic status and illiteracy is often thought of as one of the prime causes in women to pick up a breast lump and report to the health care system.

Aims: To assess and compare the awareness level about breast cancer in low and higher socioeconomic status.

Methodology: A study was undertaken in healthy non-affected population. Gr A (432 females below poverty line and thus designated as low socioeconomic status) and Gr B (439 females above this level) were included in the study. The age group ranged between 30 and 72 years. The awareness levels were assessed by objective oral questionaries by volunteers. A scoring was done based on the answers given. The questions included define, symptoms, biopsy leading to spread of cancer(misconception), investigations, treatment, body shape alterations, physicaldysabilities after treatment, source of knowledge, whom should be approached after diagnosis and curability. The hypothesis was tested using student T-test using SPSS software version 24.0.

Result: The mean score in GrAwas 4.4 whereas in Gr B was 4.7. Though the mean score in GrB was higher compared to Gr A, there was no statistical significance between two groups ($p > 0.05$). However, there was marginally higher knowledge about treatment in Gr B (4.6 vs 5.0) but it was also found statistically insignificant.

Discussion: The study highlights the fact that knowledge level is equal in all strata of the society and therefore is not the basic cause for delay in self-detection by the women in the society.

No conflict of interest.

324 Poster

Getting fit for surgery: Introducing a multi-modal prehabilitation programme for our breast surgical patients

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Background: The benefits of multimodal prehabilitation are still in its infant stages – there is emerging evidence to suggest that prehab can reduce the length of hospital stay in colorectal surgery patients. However, there is a lack of published data studying the effects of prehab amongst breast surgery patients. Medway NHS Trust has introduced a pilot prehabilitation programme in October 2018 for their breast cancer patients. The aim of this is to increase patients' physiological reserve with the outlook of better withstanding the stress of surgery, diminishing post-operative complications, and swiftly returning to their baseline.

Method: Multimodal prehabilitation was offered to patients undergoing breast surgery from October 2018 – they were assigned to an intervention or control group according to whether they accepted or declined prehabilitation. The prehab programme (intervention group) consisted of four interventions: high intensity interval training, high protein nutrition and supplements, smoking cessation and psychological support. To assess the impact of these interventions, questionnaires assessing functional capacity (SF-12), anxiety states (HADS) and shoulder pain (SPADI) were given to patients to fill out prior to and after prehabilitation. The length of hospital stay, complications and hospital readmissions were monitored for 30 days post-operatively.

Potential Impact of Study: We are faced with challenges to improve the outcomes for our cancer patients. Novel research is focussed on preventative medicine. If this pilot service is found to be of value to patients, prehabilitation can be cemented as part of the breast cancer treatment pathway.

No conflict of interest.

325 Poster

The effects of lifestyle modification, including dietary and physical activity interventions, on Anthropometric indices and Quality of life of patients with breast cancer: A systematic review and meta-analysis of clinical trials

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Background: Lifestyle modifications have been found to strongly reduce the side effects of breast cancer (BC). This is the first systematic review and meta-analysis assessing the effect of lifestyle modification including dietary and physical activity intervention on anthropometric indices and quality of life (QOL) of patients with BC.

Material and Methods: This study was prepared according to PRISMA checklist. We searched PubMed, Scopus, ISI Web of Science, Cochrane, central register for controlled trials and Google Scholar from database inception to June 2019 for relevant human controlled trials. Dietary intervention included any weight-loss diets or programs. Mean differences and standard deviations for each outcome were pooled using a random-effects model. Quality of evidence was evaluated using Cochrane Collaboration Risk of Bias tool and the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology. Publication bias and sensitivity analysis was performed using STATA.

Results: Forty-six trials (n = 4541 participants) were included in this meta-analysis. Seven studies had good quality, 19 and 27 studies had fair and poor quality. Duration ranged from 8 to 72 wks. Three trials included very large sample sizes. Twelve studies assessed only dietary interventions, while 34 trials assessed both dietary and physical activity interventions. We observed that lifestyle-modification intervention had significant reducing effects on body weight [42 trials, $n = 3947$ participants, weighted mean difference (WMD) = −3.430; 95%CI:−4.165, −2.695 kg; $P = 0.000$; $I^2 = 94.5\%$; P-heterogeneity = 0.000)], body-mass-index (BMI) (38 trials, $n = 3630$ participants, WMD = −1.645; 95% CI: −2.313, −0.978 kg/m^2; $P = 0.000$; $I^2 = 92.4\%$; P-heterogeneity = 0.000), body fat percent (BF%) (15 trials, $n = 1413$ participants, WMD = −3.927; 95% CI: −5.759, −2.095%; $P = 0.000$; $I^2 = 92.8\%$; P-heterogeneity = 0.000 and waist-to-hip ratio (WHR) (8 trials, $n = 749$ participants, WMD = −0.02; 95%CI: −0.032, −0.002 cm; $P = 0.025$; $I^2 = 0.000$; P-heterogeneity = 0.9) and a significant increasing effect on QOL (7 trials, $n = 436$ participants, standardized-mean-difference = 0.912; 95% CI: 389, 1.435; $P = 0.000$; $I^2 = 85.4\%$; P-heterogeneity = 0.000). Potential sources of heterogeneity were found to be different kinds of dietary (low-fat, low-carbohydrate, low-calorie diets or dietary educational programs) or different physical activity intervention, duration and different stages of disease or treatments of participants.

Conclusions: Although our data suggests promising effects of lifestyle modification intervention on QOL measures and anthropometric indices in patients with BC, research on other precise aspects of lifestyle modifications and their effects on breast cancer recurrence and the prevention of weight gain in patients newly diagnosed with BC, is highly needed. (This article is a part of ongoing meta-analysis registered at PROSPERO: CRD42018100628).

No conflict of interest.

326 Poster

Muscle quality is a prognostic factor for postoperative complications after DIEP-flap breast reconstruction

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Background: In this study we assessed whether muscle quality as expressed by skeletal muscle radiodensity (SMD) and relative muscle volume as expressed by skeletal muscle indexes (SMI) are independent prognostic risk factors for postoperative complications in women undergoing DIEP-flap breast reconstruction (BR).

Methods: All patients (n = 131) who received DIEP-flap BR at our tertiary center between 2010 and 2018 were retrospectively asked to sign informed consent for the use of their electronic medical records and images. By outlining anatomical skeletal muscle contours on the preoperative thoracoabdominal CT-scan at the level of the L3 vertebra, SMD and SMI were measured by two observers independently. For SMD, the average radiodensity of the muscle tissue was calculated in Hounsfield Units (HU). For SMI, the muscle surface was corrected for body length. Using multivariate logistic regression analyzes, the association between low SMD (<40 HU), low SMI (<41 cm^2/m^2) and complications Clavien-Dindo (CD) grade II and higher was evaluated and adjusted for BMI ≥ 30.

Results: Out of the 103 patients included in this study, 36% had a CD grade ≥II complication within 30 days of surgery. A total of 11% of patients had a pathological SMD below 30. In this study, women with SMD below the average of 40 HU had a higher risk for CD grade ≥II complications in general and CD grade ≥II complications at the reconstructed breast (46% versus

28%, ORadjusted = 2.75, 95% CI 1.2 to 6.4, p = 0.018 and 32% versus 11%, ORadjusted = 3.71, 95% CI 1.3 to 10.6, p = 0.014 respectively). No other risk factors were associated with an increased risk for CD grade ≥II complications after DIEP-flap BR (age, comorbidity, SMI, radiotherapy, timing of reconstruction).

Conclusions: Low muscle quality as expressed by SMD was found to be an independent prognostic parameter for the development of postoperative complications. This could assist in the decision-making process for high-risk women opting for DIEP-flap BR. It remains to be clarified whether improving SMD by prehabilitation may improve the complication rate.

No conflict of interest.

327 Poster

Estimating lung cancer and cardiovascular mortality in female breast cancer patients receiving radiotherapy

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Background: Our aim was to create clinical applicable risk assessment models to predict lung cancer and cardiovascular mortality in female breast cancer patients receiving radiotherapy.

Material and Methods: By integrating data of the PLCO cancer screening trial, the SCORE-risk charts and radiotherapy excess ratios we were able to create radiotherapy-induced lung cancer and cardiovascular mortality risk charts.

Results: These clinical applicable risk charts estimate individual current, 10- and 20-year risk of lung cancer and 10-year cardiovascular mortality based on lung and heart dose, age, systolic blood pressure, cholesterol, family history of lung cancer and smoking status including intensity, duration and cessation. Moreover it enables to quantitatively predict the effect of smoking cessation on future lung cancer probability.

Conclusions: Estimating radiotherapy-induced lung cancer and cardiovascular mortality might be useful to individualize radiotherapy and optimize lung cancer and cardiovascular prevention and screening in female breast cancer patients.

No conflict of interest.

328 Poster

Quality of life (QoL) post surgical treatment of breast carcinoma: A prospective study

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Background: Oncoplastic surgery, using plastic surgery's metods and techniques, has created a new route in breast surgery and breast cancer therapy with the target of oncologic outcomes comparable to traditional conservative surgery and better aesthetic results.

Several studies proved that a better cosmetic result improve psychological outcome.

The aim of this study is to evaluate oncologic outcomes and psychological impact on patients undergoing breast surgery with or without Oncoplastic technique, through an evaluation tool: Body Image after Cancer Questionaire (BIBCQ).

Material and Methods: From February 2018 to November 2018, we observed a sample of 60 patients, 30 of whom underwent conservative surgery with an oncoplastic approach and 30 without remodeling.

All treatment options were agreed by a multidisciplinary breast team.

All patients have been drawn the same morning as the surgery.

We evaluated oncological results in accordance with the state of resection margins.

To evaluate psychological impact we used two Questionnaires, one already well known and used in clinical practice, SF36, which is a patient's health self-assessment tool, the other one is BIBCQ.

BIBCQ is the only questionnaire currently existing and validated in the USA that is able to obtain informations about the quality of life of patients undergoing breast cancer surgery.

Results: Comparison of descriptive analysis of two study population show that patients submitted to Oncoplastic surgery tend to have more bodily attention (Vulnerability scale) t-2.697 p.009, less dissatisfaction in their physical appearance t-2,584 e p.012 (Dissatisfaction scale), more awareness of body changes (Transparency scale) con t-2.172 e p.034 as compared to the sample submitted to simple breast surgery.

Conclusions: Breast surgery affects an important part of woman's femininity, detecting a deterioration in the relationship with her body, partner or even in the relationship with family and friends.

Quality of life is of increasing importance in clinical oncology studies. When analysing publications concerning quality of life in breast cancer, however, the majority of the articles appear to study health status and not quality of life.

The small number of the sample used is due to the fact that this work is the beginning of a wider validation project of BBCQ in the Italian language, in order to use it in our clinical practice as an assessment tool and to let an improvement in our daily medical practice.

No conflict of interest.

Local Regional Treatment – Radiotherapy

329 Poster

Hypofractionated boost to the tumor bed in early breast cancer: Skin toxicity analysis

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Background: It has been prove that the use of tumor bed boost improves local control and is an important part of the breast conservation therapy. However the information of the use of a hypofractioned boost in the tumor bed is sparse, a revision is needed. We performed a retrospective analysis in our institution, evaluating skin toxicity and local control comparing Hypofractioned Boost (HB) versus Normofractioned Boost (NB).

Materials and Methods: We did a revision from April of 2015 to Juny of 2018, we selected a group of 96 patients of breast cancer was pT1pN0/mic and pT2pN0/mic in 82.3% and 17.7%, respectively. Treated with hypofractioned whole breast irradiation (WBI) in association with HB or NB were retrospectivelly analized, 49 patients were treated with normofractioned boost with 16 Gy in 8 fractions (2 Gy/fraction). Other group of 47 patients were treated with hypofractioned boost with 13.35 Gy in 5 fractions (2.67 Gy/fraction). Patient, tumor and treatment characteristics were evaluated. We examined skin toxicity with CTCAE versión 4; and statistical analyses were performed using SPSS versión 25, statistical significance was considered at a p-value of <0.05.

Results: With the media follow-up was 21.3 months (5–41). Media patient age was 57 years (35–82). In the univariate analysis there were no statistically significant differences between both groups were in patient characteristics (age at diagnosis, hormonal status). In the characteristics of the tumor (histological subtype, histological grade, tumor size, focality, hormonal receptors, expression Ki67 and HER2neu). In the characteristics of the surgery (post-surgery seroma, post-surgery hematoma). In the characteristics the treatment (hormonal treatment, monoclonal antibody or chemotherapy, irradiated breast volume, irradiated boost volume, technique with photons or electrons). We found differences in quadrant location where the boost is located (17 patients in quadrant superior normofraccionated boost vs 31 patient in hypofraccionated boost, p: 0.004) and to the post-surgery infection (4 patients in normofraccionated boost vs 1 patient in hypofraccionated boost, p: 0.01). No evidenced of acute skin toxicity exceeding G2 was observed. No evidence of late skin toxicity exceeding G1 was observed. No difference were found in acute or late skin toxicity between the two groups. No local recurrences were evident at the time of this publication.

Conclusions: Hypofractionated boost is a viable option in the management of conservative breast treatment. A longer follow up is needed to assess clinical outcomes and late toxicity.

No conflict of interest.

330 Poster

Exposure of the oesophagus in breast cancer radiotherapy: A systematic review of oesophageal doses published 2013–2018

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Background: Breast cancer radiotherapy has been shown to increase the risk of subsequent primary oesophageal cancer. It is unclear if avoidance of

the oesophagus is being considered routinely during radiotherapy treatment planning. This study aims to describe exposure of the oesophagus from modern breast cancer regimens.

Material and Methods: A systematic review of oesophageal doses from breast cancer radiotherapy regimens published during 2008–2018 was undertaken. Average mean oesophageal doses and average maximum oesophageal doses were described for different anatomical regions irradiated and techniques used. Oesophageal exposure from current modern regimens was compared to that received in previous decades.

Results: Seventy-three regimens from 16 countries reporting oesophagus doses were identified. The average mean oesophagus dose was 0.2 Gy (range 0.1–0.4) for partial breast irradiation, 1.5 Gy (Range 0.1–10.4) for whole breast/chest wall radiotherapy and 14.2 Gy (range 1.1–29.3) with the addition of regional nodal irradiation. For regimens that included regional nodal irradiation, the average mean oesophageal dose was higher for IMRT (21.6 Gy static IMRT, 13.6 Gy rotational IMRT) than tangential radiotherapy (5.5 Gy) ($p < 0.001$). Overall, average oesophageal exposure from modern regimens was similar to that estimated from regimens used in previous decades.

Conclusions: Exposure of the oesophagus remains an issue in modern breast cancer radiotherapy. Routine avoidance of the oesophagus during treatment planning may reduce the number of women developing a subsequent primary oesophageal cancer in the future.

No conflict of interest.

331 Poster

Chronic toxicity after intraoperative electron radiotherapy as boost followed by whole breast irradiation

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Background: Breast conserving surgery (BCS) followed by postoperative whole breast irradiation (WBI) is the current standard for early stage breast cancer patients. In selected patients the tumor bed itself represents a region with higher probability of in-breast recurrence, thus an additional boost dose of 10–16 Gy significantly reduces local recurrence rates. Intraoperative electron radiotherapy (IOERT) offers several advantages, like direct visualization of the tumor bed, less inter- and intrafractional motion. Objective of this retrospective analysis of IOERT was to assess chronic toxicity and local recurrence.

Material and Methods: 43 patients recruited between july 2013 and september 2019 with IOERT boost during BCS were analyzed. IOERT was applied using the mobile linear accelerator Linac. The toxicity was assessed by CTCAE 4.0 at 6 months after the end of treatment.

Results: The median age was 65 years (40–90). Pathological tumor size was 16 mm (6–50). 88.4% (38) of the patients had invasive ductal carcinoma. 51.2% (22) presented histological grade II. 48.8% (21) were Luminal A like, 23.3% (10) Luminal B like, 14% (6) HER2 positive, 14% (6) triple negative. All patients received IOERT boost with a total dose of 10–12 Gy, prescribed to the 90% isodose. Three patients converted from IOERT exclusive to IOERT boost due to histopathological characteristics. WBI with normofractionated (50 Gy) or hypofractionated (40.05 Gy) regimens was aplicated in those patients. 83.7% (36) of the patients received adjuvant hormone therapy. 44.2% (19) received chemotherapy treatment. The median follow-up was 55 months (5–80). Grade 3–4 fibrosis was not evidenced as chronic toxicity. Grade 1–2 fibrosis was evidenced in 14% (6) patient. 4.7% (2) patients presented with fat necrosis. 7% (3) presented seroma. 4.7% (2) had localized pain. 2.3% (1) presented localized hematoma. 2.3% (1) presented localized edema. We had no local recurrence in IOERT boost. The 4.7% (2) patients presented distant recurrence.

Conclusions: IOERT boost during BCS is a safe treatment option with low chronic toxicity. IOERT as boost is an effective treatment.

No conflict of interest.

334 Poster

Early invasive ductal breast cancer: Review after 5-year median follow-up of the first 681 patients treated by partial breast irradiation with intraoperative electron radiation therapy

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Objectives: Intraoperative electron radiotherapy (IOERT) can be used to treat early breast cancer during the conservative surgery. The primary endpoint of this prospective phase II study is the evaluation of this treatment in terms of local control. Early complications and cosmesis will also be analyzed.

Patients and Methods: At Jules Bordet Institute, from February 2010 till July 2016, 681 consecutive patients underwent partial IOERT of the breast. Inclusions criteria were unifocal invasive ductal carcinoma, age ≥40 years (median age was 61, range 40–89), stage T0-T1N0, pathological size ≤20 mm, sentinel lymph node free (in frozen section and immunohistochemical analysis). A 21 Gy dose was prescribed on the 90% isodose line in the tumor bed with the energy of 6 to 12 MeV (Mobetron®- intraOp Medical).

Results: At a 5-year median follow-up (0.9 to 111 months), 24 patients presented an ipsi lateral relapse (3.2%) among which 8 in-quadrant (true recurrences). (1%). Thirty-four patients died (5%) among them 6 (0.9%) due to breast cancer, 11 (1.6%) due to another cancer and 17 (2.5%) due to another reason. Acute toxicity rate was low (grade I: 2.7%, grade II: 2.6%), similar to a conventional treatment. The cosmetic result was considered by the clinicians to be very good or good in more than 87%.

Conclusions: The rate of breast cancer local recurrence after IOERT is very low and comparable to published results. Our preliminary analyzes did not reveal classic criteria of increased risk of relapse as described in ESTRO and ASTRO recommendations. However, BRCA mutation and/or personal history of breast cancer seems to be significant. Free margins at the surgery are imperative as well as a watchful preoperative workup (MR is performed for every patients). The complication rate is low and the cosmetic results evaluated by the physicians are considered as good or very good in the vast majority of cases.

No conflict of interest.

335 Poster

The effect of a decision aid for breast cancer patients deciding on their radiation treatment

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Trial abbreviation and ID: BRASA-trial (***NCT03375801***).

Background and Objective: The choice for Radiotherapy (RT) after breast surgery can be a so-called preference sensitive decision in selected patient groups: in these patients, RT lowers the recurrence risk, but does not improve survival. Therefore shared decision making (SDM) on RT, taking into account their personal preferences, is indicated. We developed a patient decision aid (PtDA) to support patients and their clinicians in the process of SDM. The aim of the study was to evaluate the effect of the PtDA on decisional conflict and SDM process measures.

Material and Methods: We performed a pre- and post-intervention study. 103 clinicians of 14 radiotherapy centers in the Netherlands participated in the study.

Population: We included 214 breast cancer patients in the pre- and 189 in the post-intervention arm.

Intervention: The PtDA was developed for 4 categories of breast cancer patients with a doubtful indication of RT after surgery. The implementation of the PtDA was adapted to the logistics of the participating sites.

Outcome Measures: Patients were asked to complete validated questionnaires: decisional conflict scale, SDM-Q9, CollaboRATE, and a knowledge test, immediately after they had made their decision (T = 1) as well as three months after (T = 2). In addition, the actual chosen treatment was registered.

Analysis: Differences between pre- and post-intervention groups were analysed with independent t-tests.

Trial Status: Patients were included between December 2017 and July 2019.

Trial Sponsors: This study was sponsored by the Dutch cancer society, KWF MAC2014-7024.

Results: We found no difference in patient characteristics between the pre- and post-intervention arm. Decisional conflict was similar for both groups, both at T = 1 and T = 1 (27.3 vs 26.2, and 27.9 vs 26.8, respectively). In addition, experienced SDM, measured with the SDM-Q9 and CollaboRATE at T = 1 were comparable between both groups (74.7 vs 73.6 and 88.9 vs 88.6 respectively). The use of the PtDA also did not affect the choice for more or less treatment at group level. The only significant

difference we found was on the knowledge-test, with a higher score in patients in the post-implementation arm (7.4 out of 11 points vs 6.1 out of 11).

Conclusions: Use of the PtDA did result in better knowledge, suggesting a better informed choice. We found no differences in decisional conflict and on perception of SDM, between the pre-and post-implementation arms. The relatively low level of decisional conflict in the pre-intervention arm might be explained by increased awareness among the professionals for SDM already in the pretest phase of the trial. Implementation of only a PtDA might be insufficient to achieve improvement in experienced SDM.

No conflict of interest.

337 Poster

Results of locoregional radiotherapy or axillary dissection in breast cancer with pN0(i+) and pN1mi nodal disease

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Background: Clinical significance and treatment value of detection of isolated tumor cells (pN0(i+) = 0.2 mm and below) or micrometastasis (pN1mi = 0.2–2 mm) in sentinel lymph node biopsy (SLNB) in early-stage breast cancer is still controversial. Randomized studies have shown that advanced axillary lymph node dissection (ALND) need not be performed. However, radiotherapy (RT) fields that should be irradiated are not clear. In our study, advanced axillary treatments (dissection or RT) were evaluated retrospectively in patients with N1mi and N0(i+) detected by SLNB, and the effects of local/regional recurrence (LRR) and survival were analyzed.

Material Method: Patients who underwent surgery for diagnosis of early stage breast cancer and who were found to have N1mi or N0(i+) by SLNB were included in the study. Neoadjuvant chemotherapy recipients and patients with any lymph node macrometastasis were not included. Histopathological features of the tumor, surgical treatment details and dose and field data were recorded for patients who underwent RT. Statistical analysis of the collected data was performed using SPSS 22.0. Chi-square tests were used for qualitative comparisons and Kaplan-Meier method was used for survival analysis. Significance was evaluated below $p < 0.05$.

Results: 116 patients were examined. The N0(i+) patient rate was 23% and the N1mi rate was 77%. The axilla approach was left at the SLNB level in 95 patients (82%) and the mean number of removed lymph nodes were 3 (min 1-max 10). ALND was added in 21 patients (18%) and the mean number of removed lymph nodes were 20 (min 10-max 39). Surgical form of the breast was breast conservation (BCS) in 69 patients (59%) and simple mastectomy or skin/nipple sparing in 47 (41%). Adjuvant RT was performed for all patients who underwent BCS and in 12 (26%) patients who underwent total mastectomy and SLNB. Of the 81 patients who underwent RT, 46 (57%) were irradiated only at breast or chest wall (B/CW), 18 (22%) with addition of Level 1-2 lymph nodes to B/CW, 11 (14%) with further addition of supraclavicular fields to B/CW plus Level 1-2 lymph nodes and 6 (7%) with addition of internal mammary lymph nodes to B/CW and all peripheral lymph nodes.

There was no difference in LRR between total mastectomy/SLNB (n = 26), total mastectomy/SLNB and RT (n = 12) and total mastectomy/ALND (n = 9) groups. There was, again, no difference in terms of LRR between only breast RT after BCS/SLNB (n = 32), BCS/SLNB and breast+lymphatic RT (n = 25), and only breast RT after BCS/ALND (n = 12).

Systemic metastasis developed in 2 of 116 patients (2%). Disease-free survival rate was 98%. Breast cancer was not the cause of death for the cases.

Conclusion: LRR rates are very low in cases with N1mi and N0(i+) detected in early stage breast cancer. ALND or addition of lymphatics to the radiotherapy area after SLNB does not affect LRR results.

No conflict of interest.

338 Poster

Prospectively registered acute toxicity in breast cancer patients undergoing adjuvant intensity modulated proton therapy

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Purpose: In selected breast cancer (BC) patients, proton therapy (PrTh) has the potential to lower radiation doses to heart, lung and contralateral breast (CLB) compared to photon therapy. However, higher skin toxicity using PrTh has been reported in literature. We prospectively evaluated acute toxicity in breast cancer patients treated with robust intensity modulated proton therapy (IMPT).

Methods and Materials: In 20 consecutive BC patients selected for PrTh, acute toxicity (radiation dermatitis (RD) and dysphagia scored according to CTCAE version 4.0) was prospectively registered. We applied 40.05 Gy in 15 fractions of 2.67 Gy for elective local (n = 4) or locoregional (n = 16) radiotherapy, with a simultaneous integrated boost up to 53.4 Gy to the tumour bed or residual lymph nodes in 10 of these patients. The Clinical Target Volume (CTV) and organs at risk were delineated on a free breathing CT. The CTV was clipped 5 mm under the skin after breast conserving surgery, 3 mm after mastectomy and 0 mm in case of cT4d. Robust IMPT plans were made around the CTV using Raystation with a Monte Carlo algorithm for the Mevion machine. Two to 4 beam directions were used with a set-up uncertainty of 0.5 cm and a range uncertainty of 3%. Coverage of the CTV in the voxel wise minimum plan, based on 28 scenario's, had to fulfill V95%(CTV)≥98%. No dose constraints were used for the skin structure (SS) (defined as the first 5 mm from the outer contour from the unclipped CTV) and the esophagus (E). Dose (D) parameters (Dmax E, Dmean SS, Dmax SS and Volume(V)95%(cc) of SS) were collected.

Results: Follow-up was at least 2 weeks after the last fraction. RD grade 3 was present in 10% (2/20) of the patients. The grade of RD seemed to be related to Dmax SS, but not to Dmean SS and V95% (Table). Acute dysphagia was observed in 8/15 (53%) patients in whom the periclavicular nodes were included, with a mean Dmax E of 35.0 Gy vs a mean Dmax E of 33.7 Gy in patients without dysphagia. 4/8 patients had grade 2 dysphagia with a mean Dmax E of 37.0 Gy vs 35.4 Gy for the other 4 patients who experienced grade 1 dysphagia.

Table

	N (% of all patients)	Average Dmax in Gy (range)	Average Dmean in GY (range)	Average V95% in cc (range)
Any skin toxicity	20/20 (100%)	45.0 (40.4–54.0)	40.6 (37.9–44.0)	96.0 (42.4–175.3)
Grade 1	2/20 (10%)	41.3 (40.3–42.3)	39.3 (38.1–40.5)	107.9 (64.5–151.4)
Grade 2	16/20 (80%)	45.8 (40.4–54.0)	40.8 (37.7–44.0)	93.5 (42.4–175.3)
Grade 3	2/20 (10%)	47.2 (41.7–52.8)	40.3 (38.2–42.3)	103.0 (89.8–116.2)

Conclusion: Acute radiation dermatitis grade 3 was observed in 10% of the BC patients treated with adjuvant robust IMPT. In BC patients with radiotherapy to periclavicular nodes 53% experienced acute dysphagia. The toxicity grade for radiation dermatitis and dysphagia seems to be correlated with the Dmax in the skin and esophagus, respectively.

No conflict of interest.

Optimal Diagnosis

339 Poster

Magnetic resonance imaging: Role in the response to neoadjuvant therapy of breast cancer

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Background: Nowadays the residual tumor after neoadjuvant treatment (NACT) is evaluated by magnetic resonance (MR). Our study has the main objective of estimating MR imaging (MRI) accuracy in finding a complete response to neoadjuvant chemotherapy and estimating the correlation between the size of the residual tumour mass appreciated with MRI after NACT and the size of the residual disease evaluated by post-operative histological examination.

Material and Methods: The study, therefore, is composed of 55 patients who were subjected to neoadjuvant therapy. At the end of the treatment, an

MR was performed. Subsequently, they underwent surgery. Then we restrospectively investigated the correspondence of the complete answers to the treatment evaluated first at the MRI (iCR) and then through the post-operative histological examination (pCR). Subsequently, we divided the sample of patients into three groups: luminal A/B (HER2 negative), triple negative (TN), HER2 positive. Finally, by examining patients in whom there was no iCR and/or pCR, we evaluated the correlation between the size of the residual tumour mass shown on MRI and those shown by the postoperative histological examination.

Results: MRI, in predicting a Complete Response (RC), has a sensitivity of 55%, a specificity of 86%, a VPP of 50% and a VPN of 88%. The analysis shows that for luminal subtypes the use of magnetic resonance imaging leads to non-specific and heterogeneous responses with a high number of false positivities in the face of a histological examination that shows a pCR. The other two subgroups, on the other hand, are more similar to each other in terms of predictivity of imaging with a comparable percentage of false positives and negatives. What distinguishes them, however, is the greater specificity of resonance in the HER2+ group with 71% compared to 33% in the triple-negative group, although among the latter imaging has shown greater sensitivity (90% vs 64%). The correlation between the size of the residual tumor seen through MRI and the size shown by the post-surgical histological examination is very low (0.23) in the group of luminals.

Conclusions: MRI is sensitive but not very specific, leading in 50% to the risk of over-treating patients and in 12% of cases to under-treating them. In the stratification by subtype, it has also emerged that this method could be useful and more reliable in the evaluation of the response of HER2+ and triple-negative tumors; instead, it is considered unreliable in the evaluation of luminal subtypes, where a histological examination is also necessary.

No conflict of interest.

340 Poster

Deep learning enables fully automated mitotic density assessment in breast cancer histopathology

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Background: Mitosis counting is an important part of breast cancer grading, yet known to suffer from observer variability. Advances in machine learning enable fully automated analysis of digitized glass slides. The present study evaluated automatic mitosis counting and demonstrated applicability on triple negative breast cancers (TNBC).

Material and Methods: In entire scanned H&E slides of 90 invasive breast tumours, a deep learning algorithm (DLA) fully automatically detected all mitoses and determined the hotspot (area with highest mitotic density). Subsequently, two independent observers assessed mitotic counts on glass slides according to routine practice, and in the computer-defined hotspot.

Next, automated mitotic counting was performed in our TNBC cohort (n = 597). Multivariable Cox regression survival models were expanded with dichotomized mitotic counts. The c-statistic was used to evaluate the additional prognostic value of every possible cut off value.

Results: Automatic counting showed excellent concordance with visual assessment in computer detected hotspots with intraclass correlation coefficients (ICC) of 0.895 (95% CI 0.845–0.930) and 0.888 (95% CI 0.783–0.936) for two observers, respectively. ICC of fully automated counting versus conventional glass slide assessment were 0.828 (95% CI 0.750–0.883 and 0.757 (95% CI 0.638–0.839), respectively (Table 1).

In the TNBC cohort, automatic mitotic counts ranged from 1 to 269 (mean 57.6) in 2 mm^2 hotspots. None of the cut off values improved the models' baseline c-statistic.

Table 1 Linear weighted kappa scores and intra class correlation coefficients for mitotic scores between observer I, observer II and the CNN.

	Kappa	Intra class correlation coefficient (ICC)
Observer I glass versus CNN	0.604 (95% CI 0.477–0.731)	0.828 (95% CI 0.750–0.883; p < 0.001)
Observer II glass versus CNN	0.609 (95% CI 0.484–0.734)	0.757 (95% CI 0.638–0.839; p < 0.001)
Observer I hotspot versus CNN	0.654 (95% CI 0.530–0.777)	0.895 (95% CI 0.845–0.930; p < 0.001)
Observer II hotspot versus CNN	0.794 (95% CI 0.691–0.896)	0.888 (95% CI 0.783–0.936; p < 0.001)

Conclusion: Automatic mitosis counting is a promising complementary aid for mitoses assessment. Our method was capable of fully automatically locating the mitotic hotspot in tumours, and was capable of processing a large series of TNBC, showing that mitotic count was not prognostic for TNBC even when attempting alternative cut off points.

Conflict of interest:
Advisory Board: Jeroen van der Laak is member of the scientific advisory boards of Philips, the Netherlands and ContextVision, Sweden and receives research funding from Philips, the Netherlands and Sectra, Sweden.

341 Poster

Prone, stereotactic, vacuum-assisted breast biopsy

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Background: Stereotactic VAB is the gold standard in the biopsy guidance of nonpalpable breast lesions which cannot be detected on ultrasound. The aim of this study is to learn about prone, stereotactic, vacuum-assisted core biopsy (PS VAB) systems through our experience:

- Basic concept, types, future advancements
- Utilization
- Advantages and disadvantages
- BI-RADS lesions

Material and Methods: Between 2010–2019, 1600 cases were documented, 90% due to microcalcifications. System: guidance-table combo and biopsy device. The patient lies prone, her breast is compressed. After targeting, sampling/excision is done under local anaesthesia with 7–9 G needles from multiple angles. Markers may be used at the end of the procedure to mark the site of the biopsied lesion.

Results: 53.4% B2, 10.8% B3 and 35.2% B4-5 lesions in concordance to the literature. Enough sample for the extremely precise diagnosis leads to 55% less surgeries and 75% less two-step surgeries. Digital breast tomosynthesis might further facilitate targeting, sampling and might broaden the scope of lesion identification. This is currently under investigation.

PS-VAB in particular, compared to seated variants, offers more comfort to the patient, meanwhile eliminating collapses and promoting effortless, precise targeting shortening diagnostic workup. No specific preparation is needed from the patient, even anticoagulation-therapies are not necessary to be suspended.

Conclusions: VAB is the gold standard in lesions that are not palpable and cannot be detected on ultrasound (mostly microcalcifications).

Provides enough sample for the extremely precise preoperative diagnosis.

- Can be therapeutic (papillomas, radial scars, smaller fibroadenomas)
- Site markers can be used, when necessary (might migrate)
- Surgeries are reduced by 55%, two-stage surgeries by 75%
- Prone systems are more comfortable and eliminate collapses, while promoting precise targeting
- Few prone systems are operating in Hungary (only one with tomosynthesis), it is expensive and underfinanced (2400 cases annually, 200 financed)

No conflict of interest.

343 Poster

The relative eosinophil count in breast cancer as an emerging prognostic biomarker

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Background: Cancer outcome appears to be affected by circulating immune cells in several tumor types. The role of peripheral eosinophils was widely studied in melanoma, while less data are available for breast cancer (BC) so far. In a previous study, we showed an association between baseline relative eosinophil count (REC), pathological complete response and survival rate in triple negative and hormone receptor negative/HER2 positive breast cancer. In this retrospective study we analyzed the role of REC in all breast cancer subtypes at time of diagnosis and during follow-up.

Material and Methods: Stage I-III BC patients (pts) treated between 1999 and 2018 were included in the study. REC and relative lymphocyte count (RLC) at seven different timepoints were collected. The pts were divided into two groups according to REC, using 1.5% as threshold, and according to RLC,

using 17.5% as threshold. The co-primary endpoints were the BC specific survival (BCSS) and the time to treatment failure (TTF) according to REC. The secondary endpoints were: BCSS and TTF according to RLC, the association between REC and RLC with relapse; the variation of REC during follow-up and at relapse. Statistical analysis was done with SPSS v25 software.

Results: Overall 930 early BC pts were included in the study. The median age of the whole cohort was 61 years (25–97). The pts were well balanced according to the TNM stage in the group REC-low (393 pts) and in the group REC-high (597 pts): 30.5% and 32.9% stage I; 45.3% and 45.1% stage II; 22.6% and 21.4% stage III respectively; 1.4% unknown. After a median follow-up of 91 months (range 1–245) we observed a benefit in TTF (HR 0.610–95% CI 0.458–0.812, p 0.001) and BCSS (HR 0.632–95%CI 0.433–0.923, p 0.018) in REC-high *vs* REC-low group. A survival benefit was observed also in the RLC-high *vs* RLC-low group (TTF: HR 0.421–95% CI 0.262–0.677, p 0.001; BCSS: HR 0.350–95% CI 0.2–0.614, p 0.001). A lower rate of relapse was observed in the REC-high *vs* REC-low group (17.1% *vs* 24.7%, p 0.005) and in the RLC-high *vs* RLC-low group (19.4% *vs* 35.8%, p 0.004). We observed a lower median REC at baseline before surgery (1.8% and 1.4% in pts without and with relapse respectively), compared to the median value after surgery (2.7% and 2.5% respectively), that remain stable until 10 years of postsurgical follow up in cancer free pts. A decrease in median REC was detected at time of relapse (1.5%). All the differences observed in the groups of pts with and without tumor recurrence were statistically significant ($p < 0.0001$), suggesting a role of the presence of cancer in the modulation of eosinophil count.

Conclusions: REC could be a new promising, affordable and accessible predictive and prognostic biomarker in all BC subtypes. Mechanistic studies, ongoing in our laboratory, are needed to understand eosinophils' physio-pathological role.

No conflict of interest.

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Diagnostic work-up in women suspect for breast cancer in the Netherlands

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Introduction: The goal of this study is to outline the hospital-based work-up during the diagnostic care pathway of women suspect for breast cancer in the Netherlands and to identify factors which influence this diagnostic work-up.

Method: Two cohorts have been analyzed: the "benign" cohort (n = 30,334 women suspect for breast cancer from ten hospitals) and the "malignant" cohort (n = 2,236 breast cancer patients from five hospitals). Hospital-based financial data in combination with tumor data (malignant cohort) from the Netherlands Cancer Registry was used. Patterns within the diagnostic care pathway were analyzed for both the benign and malignant cohort. For the women with finally diagnosis of breast cancer factors influencing the number of diagnostic care activities number of days until diagnosis of breast cancer were identified in the malignant cohort using multivariable Poisson regression models. To determine the factors influencing the number of days until diagnosis of breast cancer in the malignant cohort multivariable Cox regression models were used.

Results: Patients finally diagnosed with malignant disease had their diagnosis less often in one day (62% versus 67%) and on average had an equal number of average hospital visits (1.6) and a higher average number diagnostic care activities (4.7 versus 2.6) compared to patients with benign breast lesions. Of patients with malignant disease receiving triple-diagnostics, 87% were diagnosed during their first hospital visit. Factors influencing the number of diagnostic care activities were: individual hospital (IRR ranged between 0.89, 95%CI 0.84–0.95 to 1.22, 95%CI 1.16–1.29), higher age at diagnosis (continuous; IRR 0.998, 95%CI 0.996–0.999), palpable tumor (yes vs no; IRR 0.96, 95%CI 0.93–1.00), metastasis suspect lymph nodes (cN2 vs cN0; IRR 1.3, 95%CI 1.0–1.7; cN3 vs cN0; IRR 1.16, 95%CI 1.0–1.3), localization (central vs inner quadrant; IRR 0.93, 95%CI 0.88–0.99) and histology (other vs ductal; IRR 0.92, 95%CI 0.86–0.99). Factors influencing the number of days until (malignant) diagnosis were: hospital (IRR ranged between 1.12, 95%CI 1.09–1.35 and 1.3, 95%CI 1.19–1.42), higher BIRADS score (2/3 versus 0/1/unknown IRR 0.79 95%CI 0.66–0.95), detected by screening (yes vs no IRR 1.13, 95%CI 1.04–1.22), metastasis (cM1 vs cM0; IRR 0.70, 95%CI 0.54–0.91), and cT stage (cT2 vs cT1 IRR 1.16, 95%CI 1.05–1.28).

Conclusion: The diagnostic work-up of patients finally diagnosed with malignant disease demanded more time and diagnostic care activities than for those with benign lesions and was influenced by hospital, tumor and patient characteristics. This knowledge can improve the diagnostic care pathway and decrease variation.

No conflict of interest.

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Is sentinel lymph node biopsy necessary in the setting of microinvasive DCIS?

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Background: Breast cancer treatment guidelines recommend the surgeon perform a sentinel lymph node biopsy (SLNB) for patients with ductal carcinoma in situ (DCIS) who have a high risk of invasive cancer or for whom a mastectomy is planned.

Material and Methods: Our retrospective review evaluates patients diagnosed with DCIS or DCIS with microinvasion who were clinically node negative and had SLNB from 2005–2017. A diagnosis of DCIS does not routinely merit SLNB. However, a diagnosis of DCIS with microinvasion is considered a more aggressive form of DCIS and surgeons at our institution routinely perform SLNB in this setting, even though the patients are clinically node negative. SLNB is performed due to the concern for possible understaging of DCIS at the time of core needle biopsy in order to exclude the possibility of occult axillary metastatic disease. Our hypothesis is that metastatic disease is not routinely diagnosed in patients with DCIS with microinvasion. SLNB is not without morbidity; the literature quotes about a 5% chance of postoperative lymphedema (McLaughlin et al. J Clin Oncol. 2008 Nov 10;26(32):5213–9).

Results: At this time in our ongoing data collection, we have looked at a total of 75 patients who had DCIS with microinvasion and 56 patients who had DCIS only. Sixty four (85.3%) of patients with DCIS with microinvasion had SLNB. Sixteen patients (28.6%) with DCIS only had SLNB, which we surmise was due to surgeon preference. The SLNB results for the 64 patients with DCIS with microinvasion are as follows: 89.1% were pN0, 3.1% were pN0i, 3.1% were pN1mi, and 4.7% were pN1a. Both pN1mi and pN1a are considered clinically significant metastatic disease to the axillary lymph nodes. Of the 75 patients who had DCIS with microinvasion, 92.2% of the patients did not have clinically significant axillary metastatic disease. Of the 16 patients who had DCIS only and SLNB, none had axillary metastatic disease.

Conclusions: Given the low rate of significant metastatic disease to the axillary lymph nodes, even in the setting of DCIS with microinvasion, our preliminary results support our hypothesis that SLNB could be omitted in these patients. These results correlate with Roozendaal's study of 910 patients in the Netherlands (Breast Cancer Research Treatment 2016 156:517–525); Roozendaal's study found that 79.5% of the patients with DCIS with microinvasion were pN0, 4.9% were pN0i+, 6.6% were pN1mi, and 9% were pN1. Clinical relevance: Our results support the omission of SLNB for patients with DCIS with microinvasion; this will reduce the morbidity of postoperative side effects such as lymphedema in this patient population. Additionally, even though there were few patients with DCIS who underwent SLNB, this study reinforces the fact that these patients should not have SLNB.

No conflict of interest.

347 Poster

Reconsidering the management of palpable DCIS: a single institution audit

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Background: Ductal carcinoma in situ (DCIS) identified by screening mammography accounts for 20% of breast cancer diagnoses, and microinvasion (DCIS-M) is found in 5%–10%. There are no defined treatment guidelines for palpable DCIS or DCIS-M. The role of screening

mammography is now being questioned across the world and in the developing world with no national screening programs, women with DCIS present with a palpable lump in the breast. We conducted a retrospective audit of women with DCIS treated at our institution to classify palpable DCIS and DCIS-M as distinct clinical stages and emphasize the need for a change in management of 'palpable DCIS'.

Methods: Annually we register approximately 1700 new cases of early breast cancer of which DCIS and DCIS-M constitutes less than 1%. Between 2005–2016 we registered 784 cases of with DCIS, DCIS-M and early invasive cancer with extensive intraductal component (EIC) at our centre. A retrospective analysis of these cases was performed.

Results: Of the 784 patients case records reviewed, 113 (14.4%) had Tis, 87 (11.1% of all early cases and 43.5% of DCIS) had T1mic, the rest had invasive cancer with EIC, of which 46 (5.9%) were T1a, 28 (3.6%) were T1b, 146 (18.6%) were T1c and 364 (46.4%) were T2. The median age at presentation was 48 years, median clinical tumour size was 3 cm; 740 (94.4%) presented with palpable breast lumps.

At a median follow up of 86 months, the disease free survival was 95.6% for Tis, 96.6% T1mic, 90.5% T1 and 82.7% T2 ($p = 0.00$). On follow up distant recurrences were noted in 5 (4.4%) patients with Tis, 3 (3.4%) with T1mic, 21 (9.5%) with T1 and 63 (17.3%) with T2, ($p = 0.00$). Limited use of adjuvant chemotherapy in Tis and T1mic may have contributed to the high distant recurrences in that group. Also palpable Tis, T1mic and T1a had higher percentage of HR negative compared to those with larger invasive tumours.

	Tis (N%)	T1mic (N%)	T1a (N%)	T1b (N%)	T1c (N%)	T2 N(%)
cT>2 cm	63 (55.8)	68 (78.2)	28 (60.9)	6 (21.4)	1 (0.7)	363 (99.7)
Palpable lump	85 (75.2)	81 (93.1)	39 (83)	28 (100)	144 (98.6)	363 (99.7)
Nipple discharge	26 (23)	6 (6.8)	7 (14.9)	0 (0)	2 (1.3)	1 (0.3)
Hormone receptor positive (HR +ve)	60 (53.1)	18 (20.7)	18 (38.3)	15 (53.6)	92 (63.0)	218 (60.6)
Her2+ve	31 (27.4)	41 (47.1)	13 (27.7)	08 (28.6)	27 (18.5)	93 (25)
Axilla+ve	6 (5.3)	9 (10.3)	9 (19.1)	9 (32.1)	50 (34.2)	184 (50.7)

Conclusions: DCIS presenting in palpable lesions poses a clinical dilemma for the use of adjuvant therapy. In our cohort 43.5% of the palpable DCIS showed evidence of microinvasion with high risk of distant recurrence compared to screen detected DCIS. We thus need to reconsider grossing techniques to accurately identify foci of invasion, redefine DCIS-M based on number and size of foci of invasion and explore the possible role of adjuvant chemotherapy in treating large palpable DCIS.

No conflict of interest.

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Evaluation of FES (16α-[18F]-fluoro-17β-estradiol) PET for (re)staging of patients with clinical (locally) advanced or locoregional recurrent estrogen receptor positive breast cancer

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Background: Staging is of great importance for patients with breast cancer in order to make the right therapeutic decisions. The current standard for staging, [^{18}F]FDG PET/CT, might not be the most optimal technique for detection of (distant) metastases in estrogen receptor positive (ER+) breast cancer due to its low metabolic activity rate. The current retrospective study aimed to evaluate the value of [^{18}F]FES PET/CT for (re)staging of patients with clinical (locally) advanced breast cancer or locoregional recurrent (LRR) ER+ breast cancer.

Methods: 26 patients with clinical (locally) advanced or LRR ER+ breast cancer were included. A visual analysis was performed by comparing lesions detected on conventional imaging ([^{18}FDG PET/CT, CT, MRI, bone scan) with lesions detected on [^{18}F]FES PET/CT. Furthermore, a semi-quantitative analysis was performed for each [^{18}F]FES+ lesion to determine the maximum standard uptake value (SUV_{max}). A $SUV_{max} > 1.5$ was considered positive.

Results: For visual comparison, [^{18}F]FES PET/CT and conventional imaging was available for 19 patients. In 14/19 (74.4%) patients [^{18}F]FES PET/CT detected lesions that were not visible on conventional imaging. In 3/19 (15.8%) patients [^{18}F]FES PET/CT failed to identify lesions that were found on conventional imaging. Semi-quantitative analysis was performed for [^{18}F]FES PET/CT scans of 18 patients. Median SUV_{max} of primary tumour lesions was 2.90 (IQR: 2.30–5.05). For locoregional lymph node and distant metastases the median SUV_{max} was 3.05 (IQR: 2.41–4.04) and 3.32 (IQR: 2.74–4.84), respectively.

Conclusion: The present study suggests that in a substantial number of patients [^{18}F]FES PET/CT identified lesions that were not detected with conventional imaging. Therefore, [^{18}F]FES PET/CT can be a valuable addition to current imaging modalities for (re)staging of patients with clinical (locally) advanced or LRR ER+ breast cancer.

No conflict of interest.

349 Poster

MRI accuracy in each immunophenotype to evaluate axillary tumour load after neoadjuvant treatment

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Background: Defining MRI accuracy to evaluate axillary tumour load after neoadjuvant treatment (NAT) in cN1 tumours could be of use to establish the need of further axillary imaging before deciding which intervention to perform in this setting (sentinel node or axillary node clearance). Our hypothesis was that MRI accuracy in this situation varied depending on the tumour immunophenotype (IP).

Material and Methods: We performed a retrospective review of prospectively entered data of our institutional Tumour Registry. Data on patients submitted to neoadjuvant treatment between 2009 and 2018 were retrieved. To calculate MRI accuracy to establish axillary tumour load after NAT, we deducted the number of lymph nodes suspected to be neoplastic described in the MRI report from the number of lymph nodes confirmed to be neoplastic in the pathology report: we considered that axillary tumour load was correctly estimated if the difference was 0, overestimated if the difference was negative and underestimated if the difference was positive. We calculated if accuracy differences between IP were significant with the Xi2 test. We also calculated sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of MRI to establish axillary complete response, taking the pathology report as the gold standard. All the calculations were made for each IP (Luminal A, Luminal B Her2 negative, Luminal B Her2 positive, Her2 enriched and Triple Negative) and for overall.

Results: We included 153 patients in the study. MRI correctly estimated axillary tumour load in 31.3% (5/16) of Luminal A, in 42.9% (30/70) of Luminal B Her2 negative, in 51.7% (15/29) of Luminal B Her2 positive, in 53.8% (7/13) of Her2 enriched and in 56% (14/25) of Triple Negative tumours; the differences were significant ($p = 0.007$). Overall, MRI correctly estimated 46.4% (71/153) of the tumours. PPV and NPV were 0.33 and 0.75 for Luminal A, 0.35 and 0.74 for Luminal B Her2 negative, 0.72 and 0.50 for Luminal B Her2 positive, 0.85 and 0.33 for Her2 enriched and 0.43 and 1 for Triple Negative tumours, respectively.

Conclusion: MRI performs differently in each IP when it comes to evaluating residual axillary tumour load after NAT. The IP should be considered when deciding which imaging procedures should be performed after NAT and before surgery.

No conflict of interest.

352 Poster

Development of a qPCR based ER signaling pathway activity test predictive for response to endocrine therapy in ER IHC positive breast cancer patients

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Background: While generally ER IHC positive breast cancer patients receive endocrine treatment, not all of them respond. A test to predict therapy

response with higher specificity is needed to avoid endocrine overtreatment and to consider alternative therapies. To this end, we developed computational models to assess functional activity of signal transduction pathways (Verhaegh et al., Cancer Res 2014; Inda et al, Mol Cancer Ther 2019), based on interpreting mRNA expression levels of the respective pathways' direct target genes, and showed differences between ER protein expression and actual activation of the ER signaling pathway. For a broader application of these computational models, we here present RT-qPCR tests for a quantitative and reproducible assessment of ER signaling pathway activity.

Materials and Methods: We developed PCR primers and probes for a subset of target genes of the original ER pathway model and measured expression levels in a number of samples with known pathway activity status. These were used to calibrate a computational PCR model, resulting in an OncoSignal PCR test that reports a quantitative ER signaling pathway activity score. This test was applied on independent test samples of breast cancer cell lines deprived of estrogens, after addition of estradiol, and after addition of estradiol and fulvestrant. Reproducibility was assessed on replicate experiments, and by building an equivalent microarray model using the same calibration samples and gene subset, comparing scores on a collection of 120 samples measured on both platforms. Clinical patient data was analyzed using both tests.

Results: In triplicate MCF7 cell line experiments, the OncoSignal ER activity scores went up from 10 ± 1 on deprived samples to 42 ± 2 on 1 nM estradiol stimulated samples, and went down again to 27 ± 3 and 5 ± 0.4 after subsequent addition of 10 nM and 100 nM fulvestrant, respectively. On a set of 120 cell line and patient samples, the OncoSignal microarray test showed a good concordance with the PCR test, with a correlation of 0.92 ($p < 2.2e-16$). The microarray test confirmed that not all ER positive breast cancer patients have an active ER pathway (scores ranging from 7 to 63), and that ER signaling pathway activity is associated with better clinical outcome in an adjuvant setting (GSE6532 & 9195, n = 160).

Conclusions: We developed broadly applicable tests to assess ER signaling pathway activity in a quantitative manner on individual samples, which was verified on independent test samples with known activity status. The tests showed good reproducibility on repeat experiments, and between PCR and microarray measurements. ER pathway activity in ER positive patients is associated with clinical outcome and enables better therapy selection for individual patients. Further clinical evaluation and development of an equivalent RNA sequencing based test are ongoing.

Conflict of interest:
Corporate-sponsored Research: The authors are all employees of Philips, and the work presented here has been funded by Philips as part of its research and development program.
Other Substantive Relationships: Philips holds related patent WO2013/011479 (granted), on which MAI, HvO and WV are listed as inventors.

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Enhanced axillary assessment using contrast enhanced ultrasound (CEUS) before neo-adjuvant systemic therapy (NACT) in breast cancer patients identifies axillary disease missed by conventional B-mode ultrasound that may be clinically relevant

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Background: Accurate axillary assessment prior to NACT is important for treatment planning. De-escalation of axillary surgery after NACT in patients with pre-treatment lymph node (LN) metastases is becoming more widespread but there are concerns about patient selection. CEUS can be used to augment conventional B-mode ultrasound and improve metastatic LN detection.

Material and Methods: Between August 2009 and October 2016, 288 NACT patients were identified from a prospective database; 58 were excluded (distant metastases/endocrine therapy) and 19 had incomplete data. 211 underwent NACT followed by surgical treatment; 110 had malignant axillary lymph nodes (LN) identified by B-mode ultrasound + core biopsy before treatment (Group A). 101 had a normal B-mode axillary ultrasound +/– benign core biopsy and then underwent enhanced axillary assessment using intradermal microbubbles and CEUS with core biopsy of sentinel lymph nodes (SLN). In 2 cases the procedure failed. Malignant SLN were identified in 35 cases (Group B) and 64 patients had a benign SLN core biopsy (Group C) prior to starting NACT. All patients with pre-treatment malignant LN/SLN underwent axillary lymph node dissection (ALND) after NACT. Follow up data was collected until May 2019.

Results: The median age of Group A patients was 49, median pre-NACT size 35 mm, 85% were IDC, 54% G3, 60% ER+, 40% Her-2+, 22% triple negative, 95% had FEC-T and 89% completed NACT. At the end of NACT: 26% of Group A patients had a tumour PCR, 63% had residual malignant axillary LN with a median nodal burden of 3 macrometastases. 1 patient had a local recurrence and 5 systemic relapse. The median age of Group B patients was 52, median pre-NACT size 37 mm, 69% were IDC, 40% G3, 74% ER+, 34% Her-2+, 9% triple negative, 97% had FEC-T, and 97% completed NACT. At the end of NACT: 11% of Group B patients had a tumour PCR, 63% had residual malignant LN with a median nodal burden of 2 macrometastases. 5 had systemic relapse. The median age of group C patients was 49, median pre-NACT size 32 mm, 98% IDC, 72% G3, 47% ER+, 30% Her-2+, 36% triple negative, 94% had FEC-T and 90% completed NACT. At the end of NACT: 23% had a tumour PCR and 8% had metastatic SLN with a median LN burden of 1 macrometastasis. 2 patients had local recurrence and 6 had systemic relapse.

Conclusions: Enhanced axillary assessment with CEUS before NACT is a useful test that identifies a group of patients with axillary metastases that are missed by conventional B-mode ultrasound (Group B). Of these, 63% had LN metastases found in the ALND after NACT. Without CEUS, these patients may have been erroneously classed as progressive disease because they were designated as N0 by pre-NACT B-mode ultrasound. CEUS is a reproducible test that could be repeated after NACT to aid the selection of exceptional responders suitable for limited axillary surgery.

No conflict of interest.

355 Poster

More precise mitotic count and estrogen/progesteron (ER/PR) scoring system impact on grading in pre- and post-neoadjuvant primary breast cancer: morphological, clinical and radiological assessment

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Background: Breast cancer molecular subtypes (Luminal A and B, Triple negative, Her2-enriched) together with histology-based parameters (i.e. grading) are pivotal in understanding how tumor response is related to relapse risk and would help clinicians make decisions about additional treatment options after neoadjuvant chemotherapy (NCT). Different methods can be used to assess ER/PR status (Allred score, H score, semiquantitative score). Mitotic index (MI) can be performed on conventional histology or by using immunohistochemistry for phosphohistone H3 (PHH3). Clinical response evaluation could include various imaging methods, i.e. echography (US), mammography (MX) and magnetic resonance (MRI). We assessed the accuracy of different methods to assess ER/PR status and more precise mitotic count using immunohistochemistry both in pre-NCT core biopsy and post-surgical breast specimen to predict pathologic response after NCT administration.

Materials and Methods: We retrospectively evaluated 28 patients who underwent NCT after breast cancer diagnosis. All pre-NCT core biopsies and post-NCT surgical specimen were independently reviewed by three pathologists for ER/PR status using three different scoring system, according to CAP (Allred score, H score, semiquantitative score). MI were assessed on conventional hematoxylin & eosin slide and by using PHHE immunohistochemistry. All cases were evaluated on pre-NCT core biopsy and on surgical specimen post-NCT. Imaging data were independently reviewed for every patient on US, MX and MRI. All histological/immunohistochemical parameters were correlated to clinical and imaging data.

Results: Mitotic index was significantly higher when evaluated by PHH3 (mean 26.39 ± 17.73 vs 6.11 ± 6.67; $p < 0.001$) and 14 cases were upgraded (1 case from G1 to G2; 13 cases from G2 to G3) on core biopsy. On surgical specimen, 3 cases were upgraded (from G2 to G3), but MI was not statistically significantly different (mean 17.60 ± 22.24 vs 31.33 ± 29; $p = 0.2$). Statistically significant differences were found comparing MI on H&E between core biopsy and surgical specimen (6.11 ± 6.67 vs 17.60 ± 22.24; $p = 0.01$) whereas PHH3 count was not statistically significantly different (mean 26.39 ± 17.73 vs 31.33 ± 29; $p = 0.7$). Twelve cases (12/28; 43%) with pathological complete remission after NCT had statistically

significant higher ki-67 (58.75 ± 15.43 vs 41.19 ± 17.26; $p < 0.001$) and lower ER expression when evaluated with Allred and H score (83.75 ± 119.56 vs 179.69 ± 137.28; $p = 0.03$ and 2.83 ± 3.56 vs 5.25 ± 3.69; $p < 0.05$).

Conclusions: Maybe due to specimen artifact on core biopsy, MI is largely underestimated in conventional H&E and Allred and H score can better stratify ER/PR expression than semiquantitative visual score. PHH3 and different ER/PR scoring system can be easily used in diagnostic routine workout and can help to predict pathological complete response to NCT.

No conflict of interest.

Rehabilitation/Survivorship

357 Poster

Scalp cooling system to prevent alopecia: Effectiveness, psychological effects and feasibility

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Background: In order to counter the alopeciatic effect of some chemotherapies (CT), oncology centres have started using scalp-cooling devices. Recent literature demonstrates considerable interest in investigating its real effectiveness, the reasons for dropouts, and the effects on the emotional states and on patients's quality of life (M.G.S. Salvo, 2010). This study aims to assess the efficacy of scalp- cooling devices in preventing CT – induced alopecia. Secondary outcomes: i) the feasibility of scalp cooling introduction in terms of timing and of resources involved; ii) to investigate change of psychological distress and health-related quality of life in scalp cooling treatment.

Material and Methods: This prospective no-profit study was conducted from March 2016 to July 2018. (approved by Ethical Commitee: N.43/2015). Inclusion criteria: women with different types of oncological pathology, no alopecia, age ≥18 years and ECOG performance status 0–1, who were scheduled to alopecic CT. Exclusion criteria: alopecia pre-CT, history of treatment with CT and contraindications due to other diseases. Hair loss (HL) was evaluated by patient self-assessment and by the physician according to the Dean's scale at half and at end of treatment. A Dean's scale score of 0–1 (i.e. HL ≤ 50%) was considered a success. Patients completed questionnaires (TD, HADS, QLQ-30 e BR-23) before, at half and at end of CT. 47 women, (mean age 55 ± 11) of whom 62% with breast disease, adhered to the study. 79% completed scalp-cooling treatment, while 21% discontinued after half-treatment.

Results: Scalp cooling was effective in preventing CT-induced HL in 35 of 37 patients (94.6%) who concluded treatment. With carbo-taxol scheme, initial loss was followed by stabilization and thickening during the second half of chemotherapy. There was a fair agreement between patients and staff evaluation on HL (weighted Cohen's Kappa = 0.27). Long refrigeration times determine the need for health workers to be present on two shifts. We found statistically and clinically significant improvement in the emotional state (distress, social role, cognitive functions, and pain) at mid-treatment with results stabilized till the end of CT. In patients with psychological support, this improvement was achieved during the whole treatment.

Conclusions: The study showed very positive results as regards the effectiveness of the scalp-cooling and a tipical trend of alopecia with carbo-taxol. Patients overestimate HL respect to operators' evaluations: it could be useful to carry out psychoeducation and information activities. To set up the scalp-cooling procedure in a stable way is necessary that the structures must be organized for full time opening. The results on emotional dimensions prove the importance to plan psychological support actions, halfway through the CT pathways.

No conflict of interest.

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Patient-reported outcome measures used for reporting late effects in postmenopausal breast cancer survivors and compared to general symptoms in a Danish female age matched population

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Background: Survival rates for breast cancer (BC) are increasing due to improved surgery and multimodality oncological treatment, leading to growing interest in treatment-related late-effects (LEs). The aim of the present study was to explore LEs using Patient-Reported Outcome Measures in postmenopausal BC survivors in standard follow-up care. The results were compared to age- and gender-matched data from the general Danish population.

Material and Methods: Postmenopausal BC survivors in routine follow-up care between April 2016 and February 2018 were asked to complete the EORTC QLQ-C30 questionnaire prior to their routine consultations with oncologists at the Department of Oncology, Aarhus University Hospital, Denmark. When completing questionnaires, patients were at different time intervals from completion of primary treatment, allowing for a cross-sectional study of reported side effects at different time intervals from primary treatment. The time intervals used in the analysis were year 1, 2, 3, 4, 5, and 6+ after surgery. The results were compared with reference data from the general Danish female population. Between-group differences are presented as effect sizes (ESs) (Cohen's *d*), with values of 0.2, 0.5, and 0.8 considered small, medium, large, respectively. Furthermore, Minimally Important Differences (MIDs) established for the EORTC QLQ-C30 were used for interpreting results.

Results: A total of 1089 BC survivors participated. Compared with the reference group, BC survivors reported better Global Health Status in year 3 and 5 after surgery corresponding to $d = 0.25$ (95% CI 0.08–0.42) and 0.24 (95% CI 0.06–0.41). Poorer outcomes in BC survivors compared with the reference group were found for cognitive functioning (year 1, 2, 3, 4, and 6+ after surgery), fatigue (year 1 and 2 after surgery), insomnia (year 2 and 3 after surgery), and social functioning (year 1 after surgery) with ESs ranging from 0.30 to 0.41 for cognitive functioning, 0.30 to 0.35 for fatigue, 0.25 to 0.40 for insomnia, and 0.20 for social functioning. For the remaining outcomes, no ESs exceeded 0.17 in either direction. Differences exceeding MIDs were only found for cognitive functioning year 1, 2, 3, 4 and 6+ after surgery and for role functioning year 1 after surgery, both with poorer outcomes in BC survivors compared to the reference group.

Conclusion: Postmenopausal BC survivors' scores on the QLQ-C30 were generally similar to those found in the general Danish female population, although BC survivors reported better Global Heath Status, poorer cognitive functioning, and higher levels of fatigue and insomnia. Differences exceeding the MID were primarily found for self-reported cognitive function.

No conflict of interest.

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Evaluation of the use of primary and hospital care in long-term breast cancer survivors: A longitudinal study based on real-world data

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Background: Long-term breast cancer survivors are those women who survive at least 5 years after primary breast cancer diagnosis. Cancer

survivors' follow-up is an essential phase of cancer care presenting new challenges for healthcare organizations in terms of the role of every health professional and the characteristics and frequency of visits and tests performed. The aim of this study is to analyze the patterns of utilization of health care services in long-term breast cancer survivors and to compare them with those in women without history of breast cancer.

Material and Methods: Observational study on a retrospective cohort of five Spanish regions. Women with a diagnosis of breast cancer and a survival period greater than ≥5 years were identified, as well as a sample of women, matched by age and administrative health area, without a cancer diagnosis. N = 19328 women (6512 cases/12816 controls). The use of primary and hospital care was assessed during the follow-up period: 2012–2016. Healthcare visits were identified using electronical medical records. Visits to both primary and hospital care were classified by type of visit (Primary care, admission, outpatient visit, diagnostic tests), health professional and medical specialty.

Results: The mean age at diagnosis of breast cancer was 59 years and 87% were invasive tumors. The mean number of visits per year to Primary Care was higher in the survivor group than in the group of women without breast cancer (16.8 vs 13.2 visits respectively) as well as the imaging tests (2.2 vs 1.4 tests). Among cases, 85.5% of women visited at least once the hospital and medical oncology was the most visited medical specialty (23.3%).

Table 1 Healthcare services use in the SURBCAN cohort by participating areas

	Long-term breast cancer survivors (n = 6512)	Women without history of breast cancer (n = 12816)
Age at the beginning of follow-up mean (sd)	68.6 (12.8)	68.5 (12.7)
Age at diagnosis mean (sd)	59.2 (11.8)	–
Vital status n (%)		
Alive	5662 (87.4)	11758 (92.4)
Exitus	819 (12.6)	966 (7.6)
Follow-up time n(%)		
5–10 years	4872 (74.8)	–
≥10 years	1640 (25.2)	–
Extent of the primary tumor n(%)		
Invasive	3544 (87.3)	–
In situ	517 (12.7)	–
Annual Visits to Primary Care mean (sd)	16.8 (19.6)	13.2 (13.7)
Type of professional visited (%)		
Physician	15.1 (17.7)	11.7 (11.6)
Nurse	12.6 (19.7)	10.8 (15.3)
Other	18.5 (12.7)	10.1 (13.5)
Tests per patient per year mean (sd)	2.2 (2.6)	1.7 (1.5)
Type of test mean (sd)		
Imaging test	2.2 (2.6)	1.4 (1.4)
Lab tests	2.1 (1.8)	2.0 (1.7)
Annual Visits to Hospital mean (sd)	11.8 (16.8)	–
Annual visits to medical oncology mean (sd)	7.4 (17.2)	–

Conclusions: Long-term breast cancer survivors use health services more than women of the general population. The next steps are to study whether this use is in agreement with specific follow-up recommendations for breast cancer survivors.

No conflict of interest.

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Mobile health (mhealth) to improve quality of life in breast cancer survivors: study protocol for randomized controlled trial

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Background: Breast cancer is the most common female cancer worldwide. In India it is the number one cancer among women. These women have to undergo extensive form of treatment which results in side effects such as fatigue, sexual dysfunction, shoulder and arm morbidity, which adversely affects women's quality of life. To support these women during their survivorship period, appropriate strategies should be taught to these women so that they can manage their problems own. With advancement of technology, e-health supported with mobile health (m-health) provides promising platform to BCS to acquire knowledge and interactions with the health care providers. The aim o this study to develop mobile application for delivering information to BCS and to evaluate its efficacy for improving their post treatment QoL.

Methods/Design: In phase I, mixed method approach was adopted for the assessment of the symptoms faced by BCS. For phase II, Prospective Randomized Open labeled with Blinded End point assessment trial design will be used. Patients will be eligible if: on follow up after 3 months of completion of hospital based treatment, their diagnosis is of stages I, II, or IIIA breast cancer; they had access to the Internet and smartphone. A research team consist of oncology specialist, psychiatrist, physical therapist, PhD student and oncology nurse of PGIMER, India designed the program. This is the first mobile app in India mainly focus on the first three survivorship problems of the breast cancer patients. This app will be available in Hindi, English and Punjabi. For the fatigue management, physical therapy along with tips to manage fatigue is included. For sexual dysfunction, sensate focus exercises along with pelvic floor exercises and for arm and shoulder morbidity, lymphatic drainage, strengthening and resistance exercises with complex decongestive therapy were included in the mobile app. The control group will be asked to maintain their usual routine. Study endpoints will be assessed after 3 months and after 6 months. The primary outcome will be QoL measured by The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 version 3.0 and breast module.

Sample Size Calculation: The sample will consist of 154 participants (77 in each group), which provide 90% power (5% significance) for improving health related QoL 15%, (global health status). In anticipation of 10% possible losses during follow up, 170 participants will be recruited in the study.

Conclusion: This study investigates the feasibility and effectiveness of a mhealth on the quality of life in patients with breast cancer. If this treatment option is effective, mhealth systems could offer a choice of supportive care to cancer patients during their survivorship phase.

Trial registration number (2018/06/014638).

No conflict of interest.

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Preoperative systemic treatment in breast cancer patients. Does the site of response matter?

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Background: Pathologic complete response (pCR) after preoperative systemic treatment (PST) has been used as an independent prognostic factor in breast cancer (BC). Nevertheless, there is some controversy regarding site of pCR and its effect on outcomes. The objective of this study was to determine the impact of site of response on disease-free (DFS) and overall survival (OS) in breast cancer patients with clinically positive axilla receiving PST as their first treatment.

Matherial and Methods: From a prospectively maintained database, 646 patients diagnosed with T1-T3 N0-3 infiltranting breast cancer underwent PST from January 2011 to April 2019. Cox regression curves were used to evaluate differences in OS/DFS. Univariate and multivariate analyses were performed to analyze clinical and pathological factors that influence OS and DFS.

Results: Of the 646 patients, 380 patients (59%) had a clinically biopsy proven positive axilla and it was the group included in the analysis. Mean age was 53.99 years (27–95). Most of the patients had T2 tumors (61.48%) and cN1 (75%) at diagnosis. pCR was achieved in 68 patients (17.89%). According to molecular subtypes, rates of pCR were significantly higher for patients with HER2-positive and triple-negative tumors (46.7 and 28.1%, respectively) compared to Luminal A (0%) or Luminal B tumors (4.55%), p < 0.001. Regarding site of response, 73 (19.21%) achieved an axillary pCR, 16 patients (4.21%) achieved a breast pCR and 223 (58.68%) obtained a partial

pathologic response (pPR). Univariate analysis showed that women achieving a pCR at any site were younger that the ones with pPR (51.5 vs. 55.8 years, p = 0.003). Nuclear grade was higher in patients achieving any type of pCR (p < 0.001). T status at diagnosis was similar across the groups. With respect to the type of surgery, we find no differences in the rates of breast conservation among the groups, but patients achieving pCR or axillary pCR were more prone to receive a sentinel lymph node biopsy instead of an axillary clearance (p < 0.001).

There were no differences in DFS or OS when comparing patients with pCR (breast and axilla) vs axillary pCR vs. breast pCR (p = 0.30), although there were differences when pPR was included, with patients with pPR having worse outcome (p = 0.05). Mean follow-up was 37 months (range, 0.5–90 months).

Multivariate analysis showed that initial N3 lymph status was a significantly predictor of worse prognosis.

Conclusions: Achieving a pCR in any of the sites is associated with improved OS/DFS compared to pPR. We find no differences in outcomes whether a pCR is achieved at the breast, axilla or both sites. Initial cN3 status at diagnosis remains an independent risk factor for worse OS/DFS.

No conflict of interest.

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Use of oral complementary-alternative medicine (OCAM) and fatigue among early breast cancer (BC) patients (pts)

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Background: Use of OCAM varies widely among cancer pts, ranging 20–80%. Efficacy of OCAM for cancer-related symptoms including fatigue is controversial, while some interactions with standard anticancer therapy were reported. We aimed to describe factors associated with use of OCAM, particularly its relationship with self-reported fatigue in BC pts.

Materials and Methods: We used a multicenter, prospective, longitudinal cohort (CANTO/NCT01993498) to identify 5237 pts with stage I-III BC. Use of OCAM was defined as taking homeopathy or herbal/other dietary supplements and was collected by dedicated nurse practitioners at BC diagnosis (dx), year-1 and year-2 post-dx. Fatigue, pain, insomnia (EORTC-C30 questionnaire) and other symptoms were assessed at dx. We evaluated the association of use of OCAM, defined as use at dx vs. starting post-dx vs. never use, with pts characteristics, including fatigue reported at dx, using multivariable multinomial logistic regression models.

Results: Mean age was 56 years (SD 11), 38% pts had a college degree or higher, 49% had stage I BC and 54% and 80% received chemo (CT)- and endocrine-therapy (ET), respectively. Very few pts refused to undergo standard CT (0.8%) and ET (1.2%). At dx, the mean fatigue score was 28 (SD 24). 61% and 28% pts reported at least some anxiety symptoms and hot flashes, respectively. Overall, 23% pts (n = 1204) reported ever use of OCAM (92% used homeopathy, 11%, 24% and 23% pts used vitamins/minerals, herbal supplements or other types of dietary supplements, respectively). Of them, 51% already used OCAM at dx and 49% started post-dx. In multivariable analyses, older age (ORs [95% CI] for 1-year increase = 1.02 [1.01–1.03], p = 0.002) and college degree or higher (ORs [95% CI] vs. primary school = 1.80 [1.27–2.56], p = 0.001) were associated with use of OCAM at dx, whereas anxiety symptoms (ORs [95% CI] vs. absent = 1.24 [1.01–1.53], p = 0.047) and receipt of CT (ORs [95% CI] vs. not = 1.40 [1.11–1.77], p = 0.005) were associated with starting use of OCAM post-dx. There was a significant association between reporting higher fatigue scores at dx and use of OCAM, both among pts that used OCAM at dx (adjusted OR for 10 unit-increase in fatigue = 1.05 [95% CI 1.01–1.09], p = 0.036) as well as among those that started use of OCAM post-dx (1.04 [95% CI 1.01–1.09], p = 0.046). No association was found between use of OCAM and burden of other symptoms, including pain, insomnia and hot flashes.

Conclusions: One-in-four pts in this large study declared to use OCAM between dx and year-2 post-dx, almost all reporting use of homeopathy. Half of OCAM users declared to have started to use OCAM post-dx, particularly those with anxiety and those treated with CT. Despite the lack of solid evidence supporting its benefit on fatigue, pts who report more severe fatigue at dx seemed to be more likely users of OCAM.

No conflict of interest.

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What signals cancer survivorship when revealed during the job application process to employers?

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Background: Scholars have shown that the share of cancer survivors returning to the labor market is significantly lower after cancer survivorship. Moreover, stigma and workplace discrimination are identified as prominent challenges to employment after cancer. Identifying discrimination – however – is one thing, tackling it – is another. To combat labor market discrimination against cancer survivors effectively, one needs to understand its driving factors. In other words, to design adequate *interventions*, one has to gain insights into which employers discriminate against job candidates with a cancer history, and more importantly *why* these employers discriminate against them.

Material and Method: To this end, we conduct a vignette experiment in which we *empirically investigate the dominant signals related to a history of cancer* by employers. By asking HR-professionals and recruiters from Belgium, Germany, Netherlands, UK, and USA to evaluate the profiles of five fictive job candidates regarding a fictive vacancy, we are able to identify the different signals and attitudes related to a history of cancer. The fictive profiles *randomly* differ in six characteristics: (i) gender, (ii) age, (iii) striking period of non-employment on the résumé (ranging from 0 months to 24 months), (iv) time of occurrence of non-employment period (from 0 to 5 years ago), (v) stated reason for non-employment period (cancer diagnosis, depression, personal reasons, or no reason provided), and (vi) extracurricular activities. The stated reason for non-employment being history of cancer is then the variable of main interest for our study. The participants of the study make hiring decisions based on the given set of candidates (probability of invitation to a job interview). Secondly, they score the candidates with respect to key perceptions of the candidates' abilities, candidates' behavioural traits, and perceived potential implications for the workplace.

Preliminary results: Preliminary analyses indicate that a history of cancer *lowers* the probability of being invited to a job interview when compared to job candidates without a period of non-employment. The pilot study finds that a history of cancer signals lower physical abilities, lower autonomy, and lower stress tolerance of the candidate. Next to this, when compared to the group with mental illness (depression) as the stated reason for non-employment, cancer survivors have a higher probability of being invited to a job interview, with higher cognitive, emotional, and social abilities as main signals. Lower physical abilities remain an important signal to employers, however. The results of the study indicate the information that cancer survivors have every interest in disclosing during their job application process and what signals need to be addressed.

No conflict of interest.

Risk Factors

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The REMAR (Rhein-Main-Registry)-Study: Prospective evaluation of oncotype DX® Assay in Addition to Ki-67 for adjuvant treatment decisions in early breast cancer

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Background: The 21-gene Recurrence Score® (RS) assay predicts the likelihood of chemotherapy benefit and 10-year risk of distant recurrence. Thus, this test might be useful to guide adjuvant treatment decisions in HR+/HER2– early breast cancer (EBC). The Oncotype DX® Test clinical utility was validated worldwide in major trials including more than 63,000 patients. There are only few studies that investigate the correlation of Ki67 with tumor grade and RS result. The REMAR-Study was designed to assess this correlation as a prospective, non-interventional, multicenter and non-randomized study.

Methods: From 9/2016 to 2/2019, 617 patients from 15 certified breast cancer centers were recruited. 567 patients were eligible for analysis. Eligible female patients were ≥18 years, hormone-receptor positive (HR+), HER2–, eBC and N0/1, pT1-3, nuclear grade 1-3, Ki67:10–40%, cM0.Ki67 and nuclear grade as centrally assessed blinded to the local testing. The central pathology assessments had no influence on the treatment recommendation. As primary objective changes of the treatment recommendations pre- vs. post- RS assay were analysed. The proportion of patients for whom the treatment recommendation changed was assessed overall and by select groups. McNemar's test was used to compare the proportion of patients' recommended chemo-hormonal therapy pre- vs. post-assay. The Pearson product-moment correlation was used to compare RS with local and central Ki67.

Results: 403/567 (71.1%) patients were N0/N1mic and 164/567 (28.9%) had 1–3 positive nodes. Treatment recommendation changed for 190/567 (33.5%, 95% CI: 29.6% to 37.6%) of the cases based on the RS result. In 116/179 patients with an initial recommendation for chemo-endocrine therapy, the post-RS recommendation changed to endocrine therapy alone (64.8%, 95% CI: 57.3% to 71.8%). For the 388 cases with an initial recommendation for endocrine therapy only, 74 (19.1%, 95% CI: 15.3% to 23.3%) changed to combined chemo-endocrine therapy. RS was weakly correlated with local Ki67 and moderately correlated with central Ki67. We observed an association between central grade and RS, with the median RS of 13 for low, 17 for intermediate and 34 for high grade. Regarding the correlation between central tumor grade and RS, we observed a wide range of RS 0-59 for the central intermediate tumor grade. Furthermore, the central low tumor grade was correlated with the RS in the range of RS 3-28.

Conclusion: Our results show that Oncotype DX® has a significant impact on treatment decisions in order to avoid chemotherapy for patients with HR+, HER2– eBC resulting in a 23.5% reduction of chemotherapy recommendations. A substantial therapy change was evident in 33.5% of the cases. This confirms that Oncotype DX® might be useful to optimize individual treatment recommendations in luminal-B eBC.

Conflict of interest:
Advisory Board: Amgen, AstraZeneca, Celgene, Eisai, Genomic Health, Lilly, MSD, Novartis, Pfizer, Roche, Tesaro, Myriad.
Corporate-sponsored Research: Genomic Health.
Other Substantive Relationships: Lecture fees: Amgen, AstraZeneca, Celgene, Clovis, Eisai, Genomic Health, Hexal, Lilly, MSD, Novartis, Pfizer, Roche.

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Change in trend in various clinico-pathological factors and treatment profile of breast cancer patients in developing countries: A tertiary cancer center experience

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Background: Breast cancer management has undergone a seismic revolution in last decade with immense benefit to patients; it is encouraging to see how we have remained abreast of new developments in breast cancer management over that time. However sheer impact of this upon current trends in diagnosis and management of disease, are largely unknown. We aimed to assess & evaluate change in spectrum in socio-demographic profile and management of breast cancer over a decade within a specialist tertiary of a medical college hospital.

Methods: Data of 1432 breast cancer patients for last ten years were recorded retrospectively at department of radiotherapy SMS medical college Jaipur with respect to baseline patient, tumour, treatment characteristics; and change in spectrum was analysed.

Table 1 Results

Factors	2007/08	2009/10	2011/12	2013/14	2015/16	P-Value
Age						0.064
<40	29.5	28.3	31.7	33.8	36.4	
>40	70.5	71.7	68.3	66.2	63.6	
Mean	52.67	50.09	50.74	48.55	48.85	
Menopausal status						**0.011**
Pre	35.9	42.8	30.3	40.6	42.5	
Post	64.1	57.2	69.7	59.4	57.5	
Stage						**0.021**
I	5	6	5.5	7.1	9.2	
II	15.1	16.3	21.8	23.7	22.7	
III	65.5	62.1	52.8	49.6	47.7	
IV	14.4	15.6	19.9	19.6	20.4	
Hormone receptor						**0.034**
ER &/or PR+	75.5	72.1	67.4	63.2	58.5	
ER & PR-	24.5	27.9	32.6	36.8	41.5	
Surgery						**<0.001**
Nil	4.3	10.2	14	15.6	17.2	
Simple Mastectomy	24.5	21.7	15.1	9.8	5	
BCS	8.6	9.6	16.2	18.1	22.9	
MRM	62.6	58.5	54.7	56.5	54.9	
Chemotherapy						**<0.001**
Nil	3.6	5.4	10.3	10.6	13.9	
NACT→Adjuvant	12.9	17.5	23.6	31	35.6	
Adjuvant only	83.5	77.1	66.1	58.4	50.5	
Chemotherapeutic agents						**<0.001**
CMF/CEF/CAF	71.6	64.1	55.7	47.4	41.9	
AC→T	28.4	35.9	44.3	52.6	58.1	
Adjuvant Radiotherapy						0.051
Palliative	19.4	19.3	21.4	22.2	28.1	
Radical	80.6	80.7	79.6	77.8	71.9	
Technique						**0.007**
Co-60	78.4	74.1	67.5	65.2	64.3	
Linear accelerator	21.6	25.9	32.5	34.8	35.7	

Results: Significant decline was observed in post menopausal status, hormone receptor positivity, advanced stage at presentation; whereas significant increase was observed in breast conservative, neoadjuvant, Taxane based chemotherapy and radiotherapy with advanced technology. There was increasing trend of young age at presentation, but was not statistically significant.

These trends are likely to be the result of cancer awareness due to increasing education, access to diagnostic modalities, increasing therapeutic advances, adequacy of treatment services available to different parts of society.

Conclusions: The challenge in developing countries is to provide a comprehensive service in diagnosis and treatment of breast cancer; it is incumbent upon us to adapt our practice patterns in light of emerging knowledge, continuous reviews of literature and to deliver quality care in accordance with best available evidence. This will require training of a team of health professionals dedicated to breast health; advocacy can also play a role here in galvanizing political will to meet this challenge.

No conflict of interest.

370 Poster

Implication of atypical supraclavicular F18-fluorodeoxyglucose uptake in patients with breast cancer: Relationship between brown adipose tissue and TILs, PD-L1

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Background: It has been reported that F18-fluorodeoxyglucose (FDG) uptake in the neck and supraclavicular lesions represents activated brown adipose tissue (BAT). We previously reported that the presence of atypical FDG uptake in neck and supraclavicular lesion was associated with HER2 expressions and was an independent prognostic factor for breast cancer. In this study, we investigated the relationship between BAT activity detected by FDG-PET and immunological factors, including degrees of tumor-infiltrating lymphocytes (TILs), and programmed cell death ligand 1 (PD-L1), which have been suggested as prognostic factor in BC.

Material and Methods: Invasive carcinoma tissues of 95 breast cancer patients who underwent surgery without preoperative therapy were examined. Grade of stromal-TILs was immunohistochemically (IHC) evaluated using the criteria of the International Working Group for TILs in BC: low (10–20%), intermediate (20–40%) and high (50–90%). PD-L1 positive were evaluated by IHC. We reviewed the distribution and intensity of atypical FDG uptake in the neck and/or supraclavicular region, which is defined as BAT. The intensity of FDG uptake was graded as follows: 1-weak, 2-moderate, and 3-intense. The relationships between BAT activity and expressions of TILs, and PD-L1 were investigated.

Results: Among the 95 patients, 37 (38.9%) showed grade 1 intensity of BAT activity, 42 (44.2%) showed grade 2, and 16 (16.8%) showed grade 3. The high intensity of BAT activity was significantly related with positive HER2 expression. High degree of TILs and positive expression of PD-L1 were relatively higher in patients with weak atypical BAT activity. The average age and BMI were not statistically significant factors.

Conclusion: In the present study, the presence of atypical FDG uptake in neck and supraclavicular lesion, which may represent active BAT, may be associated with the grades of TILs and expression of PD-L1 in the tumor. High TILs is to be better prognostic factor, however, high expression of PD-L1 is to be a poor prognostic factor. From our findings, BAT activity detected by FDG-PET may be predictive of immunological features among patients with breast cancer.

No conflict of interest.

371 Poster

Relationship between FDG uptake and platelet/lymphocyte ratio in patients with breast invasive ductal cancer

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Background: Cancer progression and prognosis are affected by the host's inflammatory response in the tumor microenvironment. Accordingly, inflammation-based prognostic indicators such as neutrophil/lymphocyte ratio (NLR), and platelet/lymphocyte ratio (PLR) have been investigated in breast cancer. PET using F18-fluorodeoxyglucose (FDG) is a non-invasive whole-body imaging technique used to evaluate various kinds of malignancies, including breast cancer. FDG uptake is influenced by many factors, including inflammation, and we previously reported that FDG-uptake was associated with NLR. However, yet no published study, to our knowledge, has assessed the association between FDG uptake and PLR in breast cancer cases, even though both represent inflammation. In this study, we investigated the relationship between FDG uptake and PLR.

Methods: We retrospectively investigated the cases of 143 consecutive invasive ductal carcinoma patients who had undergone surgery and FDG-PET preoperatively. The median SUVmax was 2.5 (range 0–10.5). Thus, we divided the cases into two groups based on the value of SUVmax; low (<2.5) and high (≧2.5). The median PLR was 130 (range = 67.5–387.8). The cases were divided into two groups based on PLR: low (<130) and high (≥130). The relationships between SUVmax or PLR and clinicopathological features were investigated.

Results: Among the 143 patients, 73 (51.0%) had high SUVmax in the primary tumor. The analysis revealed that large tumor size, high nuclear grade, the presence of lymphovascular invasion, high C-reactive protein (CRP) and high PLR and high NLR were significantly associated with high SUVmax in the primary tumor. There were significant associations between SUVmax and PLR. Among the 143 patients, 74 (51.7%) had high PLR. The analysis revealed that large tumor size, the presence of node metastasis, the presence of vascular invasion, high NLR and high SUVmax were significantly associated with high PLR. We demonstrated that preoperative high SUVmax in primary breast cancer is effective for predicting poor prognosis among patients with breast cancer, however, PLR was not associated with recurrent disease in patients with breast cancer.

Conclusions: We have demonstrated that the finding of a high preoperative SUVmax in primary breast cancer is effective for predicting poor prognosis among patients. PLR is independently associated with SUVmax, but it is not associated with recurrent disease in patients with breast cancer. Among those with SUVmax and/or PLR in the primary tumor, it may be reflective of the tumor microenvironment, and further study are warranted to evaluate how FDG uptake influences the tumor microenvironment and disease recurrence.

No conflict of interest.

372 Poster

Role of immunohistochemical determination of Bcl-2 and p53 expression in identifying hormone receptors positive/Her 2 negative (Luminal-like) high-risk breast cancer patients

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Introduction: Tumors expressing hormonal receptors (HR) are generally associated with better outcome than Her2 positive and triple negative cancer, but they also include a group of high-risk tumors in terms of survival who would benefit from a more aggressive treatment. Specific genomic tests have been proposed to identify these patients but are not so far universally applied. On the other hand, immunohistochemical bioprofiles, integrated with clinical-pathological data, are commonly used in everyday practice to identify high-risk cases in order to offer the most appropriate treatment.

Materials and Methods: We analyzed the data of 1141 cases of HR positive/Her2 negative breast cancer treated at our Breast Unit (Policlinico di Sant'Orsola, Bologna) between 2003 and 2013 for which follow-up was available. Estrogen and progesterone (PR) receptors, Ki67, Her2, bcl-2 and p53 expression are routinely determined by IHC at our center. Tumors were classified in luminal A like and B like/Her2 negative based on the new St. Gallen criteria. Uni- and multivariate analysis were performed to evaluate how these parameters affected disease free survival (DFS) and distant recurrence free survival (DRFS). Median follow-up was 82 months.

Results: PR, Ki67, p53 and bcl-2 expression were all associated with worse DFS and DRFS in the univariate analysis, but only high Ki67% and low or intermediate bcl-2 expression significantly correlated to worse outcome in the multivariate analysis (Table 1). Bcl-2 status affected significantly DFS and DRFS in luminal A and luminal B/Her 2 negative tumors. After separating cases with total absence of p53 expression (p53-null) from those with significant nuclear accumulation (generally associated with mutation), p53-null was independently associated with worse DFS. P53 status also correlated to a worse DRFS in luminal A tumors, with the subgroup of p53-null associated with the worst DRFS.

Table 1

	DFS		DRFS	
	OR (IC 95%)	*p*	OR (IC 95%)	*p*
PR	1.22 (0.93–1.60)	*0.151*	1.26 (0.92–1.73)	*0.015*
Ki67	2.30 (1.74–3.07)	*<0.001*	2.51 (1.81–3.51)	*<0.001*
Bcl-2	1.96 (1.44–2.66)	*<0.001*	1.97 (1.38–2.80)	*<0.001*
P53	1.07 (0.77–1.48)	*0.68*	1.28 (0.88–1.83)	*0.192*
P53-null	1.62 (1.01–2.61)	*0.045*	1.68 (0.96–2.83)	*0.07*

Conclusions: integration of bcl-2 and p53 IHC determination into the ER/PR/Ki67/Her2 bioprofile improves the identification of HR+/Her2 negative high-risk patients. Bcl-2 alteration is an independent factor associated with worse outcome in terms of DFS and DRFS. P53 status could also be an

important tool to identify high-risk patients with luminal A like breast cancer, which have generally a better long-term outcome. While recognizing the limitations of IHC, the integration of Bcl-2 and p53 into the IHC bioprofile, combined with the clinical and pathological characteristics of the tumor, can be an extremely useful tool in tailoring the most appropriate therapy in a multidisciplinary setting.

No conflict of interest.

373 Poster

Evaluation of FISH of ER-positive breast cancer with low-HER2 expression could improve their survival

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Background: Several prognostic and predictive biomarkers for decision-making regarding neo-adjuvant (NAC) and adjuvant treatment in estrogen receptor (ER)-positive breast cancer patients have been developed. However, their ability to predict patient prognosis and treatment outcomes is poor. Hence, validated markers for predicting prognosis and treatment outcomes need to be developed. Expression of human epidermal growth factor receptor 2 (HER2) is evaluated by immunohistochemistry (IHC), and its gene amplification by Fluorescence in situ Hybridization (FISH) is not always examined. In our hospital, HER2 FISH has been assessed in almost all patients including those with HER2 status 0 and 1 (i.e., low-HER2 expression). Moreover, anti HER2 chemotherapy is administered if the patient's status is low-HER2 FISH-positive. In this report, we retrospectively investigated the ratio and characteristics of low-HER2 FISH-positive patients and compared their recurrence-free survival (RFS) with that of luminal A FISH-negative patients to examine whether evaluation of HER2 FISH in luminal A breast cancer could improve survival.

Material and Methods: We examined 849 patients who underwent surgery in our hospital from 2013 to 2016. In the survival analysis, patients who underwent surgery from 2013 to 2014 were chosen, because these patients have survived ≥5 years, without recurrence. Patients' data were extracted from electronic records at our hospital.

Results: Twenty-two (2.6%) patients were low-HER2 FISH-positive. Among them, 15 (1.8%) were ER-positive and 7 (0.8%) were ER-negative. Moreover, while 584 patients (68.8%) were ER-positive and low-HER2 FISH-negative, 57 patients (6.7%) were ER-positive and HER2-positive FISH-positive and 62 patients (7.3%) were ER and HER2-negative FISH-positive. Among the 22 low-HER2 FISH-positive patients, 7 were below 50 years and 15 were over 50 years. Twenty-one patients (95.4%) had invasive ductal carcinoma and one (4.6%) had invasive lobular carcinoma. Fifteen patients (68.1%) were treated using standard chemotherapy; among them, 5 patients (22.7%) were treated by NAC using a combination of standard chemotherapy and anti-HER2 therapy. All the ER-positive patients were treated with endocrine therapy. Among the 271 patients who underwent surgery between 2013 and 2014, the RFS rate of ER-positive and low-HER2 FISH-positive patients were 100% whereas that of ER-positive and low-HER2 FISH-negative patients was 96.9%. There was little difference in RFS rate between both groups terms of luminal A type.

Conclusion: Considering that there has been no recurrence so far in ER-positive and low-HER2 gene amplification patients, it has been suggested that evaluation of FISH in such patients can improve the RFS.

No conflict of interest.

374 Poster

Does concomitant DCIS affect the clinical outcome in breast cancer patients with invasive ductal carcinoma: An Asian perspective

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Background: Ductal carcinoma in situ (DCIS) is an established precursor to invasive ductal carcinoma (IDC) and its coexistence with IDC appear to favour reduced biological aggressiveness. Its prognostic implication and ability to affect clinical outcome has been controversial with no prior Asian studies. This study aims to be the first to explore if concomitant DCIS affects the clinical behavior in terms of disease progression and overall survival among Asian patients with IDC.

Material and Methods: Stage I to III breast cancer patients with histologically proven invasive ductal carcinoma, diagnosed and treated in a single institution from 1 June 2004 to 30 June 2014 were identified from a prospectively collected database and included in this study. Statistical analyses were conducted using x^2 test, independent T-test, multivariate logistic regression and Kaplan-Meier test.

Results: A total of 818 patients were identified, including 224 and 594 patients with isolated IDC and IDC with coexisting DCIS respectively. IDC with concomitant DCIS was more likely to be associated with smaller tumour (median: 22 mm, $p <= 0.01$), estrogen receptor positivity ($p = 0.001$) and progesterone receptor positivity ($p < 0.001$). On the other hand, isolated IDC was found to be associated with Stage 3 disease ($p = 0.001$). The median follow-up was 9 years. Patients with isolated IDC were 1.6 times more likely to develop disease progression (95% CI: 1.1–2.3, $p = 0.027$). The 5 year breast cancer specific survival for patients with isolated IDC and those with IDC + DCIS was 91.2% and 93.6% respectively ($p = 0.635$).

Conclusions: Being the first Asian study, our results are consistent with recent published Western literature. The presence of a DCIS component in IDC among our patients is found to be associated with favourable clinicopathological features, suggesting reduced disease aggressiveness. Hence, patients with concomitant DCIS are less likely develop disease progression, though the overall 5 year breast cancer specific survival was not found to be statistically significant in our study.

No conflict of interest.

375 Poster

Breast cancer patients undergoing delayed deep inferior epigastric perforator (DIEP) flap reconstruction differ from their matched controls by a higher socioeconomic status and better overall survival

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Background: Breast cancer patients selected for deep inferior epigastric perforator flap (DIEP) reconstruction have higher overall survival (OS) and breast cancer-specific survival (BCSS) rates when compared with patients undergoing mastectomy without delayed reconstruction. We aimed to investigate underlying selection mechanisms potentially explaining observed survival differences.

Material and Methods: This matched cohort study primarily investigated the risk of recurrence and death in all patients undergoing DIEP flap reconstruction at Karolinska University Hospital between 1999 and 2013. Incidence density matching was based on year of and age at mastectomy, tumour stage and lymph node status, and excluded patients receiving any type of delayed reconstruction. For the current analysis, socioeconomic data and comorbidity scores (Categorized into a Charlson Comorbidiry Index, CCI) were obtained from the Swedish Board of Health and Welfare and Statistics Sweden. Uni- and multivariable Cox proportional hazards regression analyses were carried out to assess the associations of socioeconomic factors and comorbidity with OS and BCSS.

Results: 254 DIEP reconstructions were matched to 729 controls. Patients undergoing DIEP were less often singles (24.8 vs 31.1%, $p = 0.024$), belonged less often to the low income group (24.1 vs 36.5%, $p < 0.001$), had less often primary school as the highest education (11.4 vs 16.2%, $p = 0.026$) and were less often unemployed or retired (21.7 vs 28.0%, $p = 0.018$). DIEP patients had a significantly lower CCI than controls ($p = 0.032$).

Despite adjustment for clinical and socioeconomic covariates and CCI, the previously observed overall, as well as, breast cancer specific survival advantage for the DIEP group persisted. Further independent risk factors were lower age at mastectomy (HR 1.61, 95% CI 1.06–2.43), receiving radiotherapy (HR 1.50, 95% CI 1.00–2.23), higher CCI score (HR 66.99, 95% CI 16.24–276.31), being single (HR 1.46, 95% CI 1.023–2.078), and being retired or unemployed (HR 1.95, 95% CI 1.23–3.10). Data on BMI and smoking were insufficiently available and could represent further selection mechanisms.

Conclusion: A higher socioeconomic status distinguishes patients undergoing DIEP flap reconstruction from those who do not, and significantly affects survival. The impact of socioeconomic status on breast reconstruction should be minimal in a national health care system providing equal economic health care support for all citizens, and our findings therefore call for further analyses into potential inequalities.

No conflict of interest.

376 Poster

Clinical prediction models for patients diagnosed with breast cancer: A systematic review

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Background: Clinical prediction models provide insight in the probability of an event based on the combination of multiple predictor variables. Predicted probabilities may support clinical decision making. It is currently uncertain how many prediction models exist to support decision making in breast cancer care, which outcomes can be predicted, and which predictor variables are necessary to predict these outcomes. We aimed to systematically review prediction models that may be used to guide clinical decision making in patients who have been diagnosed with breast cancer.

Methods: Medline and Embase were searched systematically to identify existing prediction models published between January 2010 and September 2019. Studies reporting on the development or update of models predicting outcomes in patients diagnosed with breast cancer were included. Data extraction was performed according to the CHecklist for critical Appraisal and data extraction for systematic Reviews of prediction Modelling Studies (CHARMS). The potential risk of bias was assessed using the Prediction model Risk Of Bias ASsessment Tool (PROBAST).

Results: After screening 16004 studies on title and abstract, 913 studies were selected for full text screening where 553 studies were excluded for the full analysis. A total of 360 studies were included, reporting on 516 models. Numerous models predict similar outcomes (Table 1), but often differed on 1) the outcome definition (i.e. lymph node involvement (LNI) can comprise sentinel LNI and/or non-sentinel LNI), 2) the intended use of the model (i.e. model eligible only for triple negative breast cancer), and 3) the predictor variables used to predict the outcome (i.e. clinical or genetic). The majority of the models (>75%) were considered to contain high risk of bias on the PROBAST analysis domain. Approximately 25% of the models failed to report sufficient information to reproduce the model.

Table 1 Number of models per outcome

Outcome	N (%) total = 516
Overall survival	165 (32.0%)
Breast cancer specific survival	40 (7.8%)
Recurrence free disease	111 (21.5%)
Lymph node involvement	103 (20.0%)
Pathologic complete response	38 (7.4%)
Complication or adverse event	28 (5.4%)
Lymphedema	14 (2.7%)
Menses recovery	7 (1.4%)
Surgical margin	5 (1.0%)
Quality of life	4 (0.8%)
Healthcare expenditure	1 (0.2%)

Conclusions: The number of available prediction models for breast cancer is abundant. Models often require the same predictor variables to calculate the same outcome. Still, the clinical utility of most of these models remains unclear as a substantial number of models were not reported according to established reporting guidelines or showed methodological flaws in the development and validation of the model. Development of new models is undesirable before current promising models have been thoroughly assessed on their impact in clinical practice.

No conflict of interest.

377A Poster

Factors affecting locoregional recurrence rate of breast conserving surgery in patients with neoadjuvant chemotherapy

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Background: Breast conserving surgery(BCS) is preferred over traditional mastectomy for better cosmetic and non-inferior oncological outcome. BCS is best indicated for early stage breast cancer with relatively small tumor size. Neo-adjuvant chemotherapy(NAC) helps downstaging locally advanced breast cancer and increase the possibility for BCS. However, recent meta-analysis from the Early Breast Cancer Trialists' Collaborative Group (EBCTCG) showed a higher locoregional recurrence(LLR) rate in the NAC group than in the adjuvant chemotherapy group. Thus, the aim of this study was to retrospectively explore the factors affecting the LRR rate in breast cancer patients receiving BCS after NAC.

Materials and Methods: During 2005–2017, we retrospectively collected 1047 breast cancer patients underwent BCS or mastectomy after NAC in Chang Gung Memorial Hospital, Linkou. We obtained information about patient and tumor characteristics, chemotherapy regimen, clinical tumor response, tumor molecular subtypes and pathology complete response (pCR) status, type of surgery and recurrence retrospectively.

Results: A total of 1047 patients underwent NAC, 22.2% patients (n = 232) achieved pCR while the other were non-pCR (77.8%, n = 815). The BCS rate is 41% (n = 432) and the rest of patients received mastectomy (59%, n = 615). The median follow-up time is 45 months. During the follow-up period, 22.9% patients experienced tumor recurrence (n = 240), in which 8.6% was LRR (n = 90). The LLR rate in BCS group is 14.3% (n = 35) while in mastectomy group is 13.2% (n = 55). Amount the BCS group who had LLR, 4.3% (n = 6) is pCR vs 10.0% (n = 29) is non-pCR, ($p < 0.05$). Further investigation according to the breast cancer molecular subtype showed HER-2 overexpressing non-pCR group has significantly increased in LRR as compared with HER-2 overexpressing pCR group (22.2% vs 6.3%, $p < 0.05$) in post-NAC BCS patients. Triple-negative non-pCR group also noted a significant increase in LRR rate as compared with triple negative pCR group (0% vs 20.4%, $p < 0.005$) in post-NAC BCS patients. There was no LRR rate difference in between pCR and non-pCR groups of luminal type breast cancer.

Conclusions: The status of pathological response after NAC is related to the risk of developing LRR. LRR rate was higher in non-pCR group after NAC with BCS, especially in the HER2 positive and triple negative breast cancer. Therefore, both the status of pathological response and molecular subtype have to be taken into careful consideration when choosing candidates for BCS after NAC.

No conflict of interest.

377 Poster

Circulating tumour DNA as a prognostic biomarker in predicting breast cancer outcomes: Systematic review and meta-analysis

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Background: Fragmented DNA is constantly released into the circulation by apoptosis and necrosis of both cancerous and non-cancerous cell. When it is released by cancer cells, it is specifically known as circulating tumour DNA (ctDNA). We performed a systematic review and meta-analysis to determine the clinical utility of ctDNA as a prognostic biomarker in predicting breast cancer outcomes.

Methods: A meta-analysis of nine relevant studies was performed. Primary outcome was the association of ctDNA with breast cancer disease free survival/relapse free survival. Secondary outcomes focused upon a subgroup analysis of the survival implications of ctDNA detection in early breast cancer and metastatic breast cancer. Statistical analysis was performed using Revman 5.

Results: Nine studies reported on 661 cases in total. ctDNA detection (both pre and post treatment) was significantly associated with worse disease free survival (DFS) (HR 3.53, CI 1.47–8.49, P = <0.00001). ctDNA detection was significantly associated with a reduction in disease free survival in the early breast cancer subgroup (HR 8.32, CI 3.01–22.99, P = <0.0001). ctDNA in the metastatic group was not associated with significance (HR 1.86, CI 0.43–1.34, P = 0.61). Pre and post-treatment plasma sample collection was analysed in both early and metastatic groups. Pre-treatment plasma detection of ctDNA was significantly associated with reduced DFS (HR 3.30, CI 1.98–5.52, P = <0.00001). Post-treatment sampling of ctDNA failed to achieve statistical significance (HR 4.31, CI 0.14–136.23, P = 0.41).

Conclusion: Circulating tumour DNA is an important prognostic biomarker of reduced breast cancer disease free survival. Detection of elevated plasma ctDNA can predict patients at high risk of relapse and therefore may provide an excellent method to stratify risk and personalize patient follow-up.

No conflict of interest.

Screening

378 Poster

Evaluation of synthesized 2D mammography visibility with same pixel pitch as full-field digital mammography

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Background: Compared with Full-Field Digital Mammography (FFDM) + Digital Breast Tomosynthesis (DBT), synthesized 2D Mammography (s2D) + DBT can reduce the radiation dose. However, s2D reconstructed from DBT data of binning processing has a lower spatial resolution. The binning processing is a technique that adjacent pixels together for minimizing time required for DBT reconstruction. The binning processing may cause problems such as appearing artifacts and diagnosing small lesion. A non-binning processing s2D with same pixel pitch as FFDM was created to address these challenges. The aim of this study was to compare the visibility between FFDM and non-binning processing s2D.

Material and Methods: Both visibility (FFDM and s2D) regarding mimic lesions (specks, masses and fibers) within the heterogeneous phantom of each thickness (20, 40, and 60 mm) were assessed at Paired-comparison Scheffé's methods by ten readers.

This was an IRB-approved protocol of retrospective study. A total of 186 abnormal lesions (147 cases; mean age 48, range 20–85) were evaluated that show findings of microcalcification, mass, and architectural distortion classified as BI-RADS 3, 4, or 5 were selected. Four readers evaluated the visibility of image quality review (sharpness and contrast) for each lesion in FFDM and s2D images and selected better or equivalent.

And compare the Mean Glandular Dose (MGD) for cases in both DBT + FFDM and DBT + s2D.

Results: Results of comparing the visibility of s2D and FFDM with the same phantom thickness, specks and fibers were significantly higher in FFDM than s2D at all thicknesses (yardstick analysis, all $p < 0.05$). The visibility of the masses differed depending on the phantom thickness.

There were 81 calcifications, 69 masses, and 36 architectural distortions. The result of selecting better visibility, FFDM was 46.2%, s2D was 30.0%, and the equivalent was 23.8%. Compared with results by 70 malignant lesions and 116 normal or benign lesions. By malignant/normal or benign, FFDM was 42.5%/48.5%, s2D was 32.5%/28.4%, and the equivalent was 25.0%/23.1%. Compare with malignant and normal or benign, the difference visibility between s2D and FFDM was no significant (logistic regression analysis, $p = 0.1352$). Results by each lesion, calcification/mass/architectural distortion, FFDM was 51.9%/52.2%/22.2%, s2D was 32.4%/18.8%/45.8%, and the equivalent was 15.7%/29.0%/31.9%.

The average of MGD was that DBT + FFDM was 3.10 mGy and DBT + s2D was 1.66 mGy.

Conclusions: Even with same pixel pitch in FFDM and non-binning processing s2D, the visibility of FFDM was superior, especially calcification and mass. Although s2D is not performed alone in clinical practice, image appearance differs both s2D and FFDM, so it is important to be careful in interpretation with s2D.

No conflict of interest.

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Patterns of treatment and outcome of ductal carcinoma in situ for population-based screened women

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Purpose: To evaluate patterns of care in treatment and outcome of ductal carcinoma in situ (DCIS) of the breast in the Netherlands since the introduction of the national screening programme. Treatment trends are interpreted against the background of the ongoing debate considering overdiagnosis and overtreatment.

Methods: Patterns of care in DCIS were studied in 28,339 women aged 50–74 years from January 1990 until January 2018 per 2-year screening cohort.

Results: The incidence of DCIS increased from 488 women (1990–1991) to 3,599 (2016–2017). Breast conserving surgery (BCS) increased from 30.2% to 73.3% ($p < 0.001$). For patients treated with BCS, radiotherapy use increased from 36.7% in 1990–1991 to 89.5% 2012–2013 and subsequently decreased to 77.7% in 2016–2017 ($p < 0.001$). The proportion of patients undergoing sentinel lymph node biopsy (SLNB) increased from 2.2% in 1998–1999 to 64.3% in 2014–2015 and subsequently decreased to 57.2% in 2016–2017 ($p < 0.001$). Of all low grade DCIS 21.9% underwent SLNB compared to 45.3% in intermediate 69.6% in high grade DCIS ($p < 0.001$). When divided by type of breast surgery, 67.1% of all patients who underwent a mastectomy received a SLNB, compared to 43.7% of the patient who underwent BCS ($p < 0.001$).

Conclusions: Over the years, DCIS is increasingly diagnosed in women aged 50–74 year, though stabilizing since 2011. Gradually less extensive surgery is used, with fewer mastectomies and axillary lymph node dissections. Interestingly, the trend of de-escalation continues with less use of radiotherapy after BCS and of SLNB.

No conflict of interest.

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Feasibility and comparison study of augmented breast self examination vs. conventional breast self examination rural Indian women for early detection- results of POC study

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Background: A steep and alarming raise of breast cancer cases, contributing to 19–34% of all malignancies across various Indian geographies is a major health concern. While one reasons is lifestyle, other significant factors include lack of awareness and cultural reasons. 2/3 cases presenting in locally advanced or metastatic setting reflects the same. This scenario compounded with nonexistent national breast cancer screening programs is alarming and warrant widespread awareness campaigning. Breast self-examination (BSE) is easy cost effective way for early detection. With recent technical advances, which are simple to use (https://selfdiagnostics.com/breastlight-breast-examination-device/), we used indigenous developed devise for augmented Breast self examination (aBSE) and used in exploring the feasibility of the same and compare with conventional BSE and Clinical breast examination (CBE).

Materials & Methods: This data was compiled from breast cancer screening camps from various NGOs like FCG, Cognitive care foundation and grace cancer foundation (https://www.guinnessworldrecords.com/world-records/largest-simultaneous-self-examination-for-breast-cancer/). The video&visuals prepared by physician for BSE&aBSE was displayed followed by interactive session by volunteers for period of 15 minutes to answer questions. 20:1 random check was done to elicit the understanding and adoption of techniques as per instruction manual. Participants were observed and supervised by trained personnel during the process followed by CBE and the results were documented.

Results: BSE was successfully trained for 6814 women across 32 camps between 2018 – 2019. 95% (approx) understood accurately the right method of BSE. Re-training was felt necessary in 32%. aBSE was done for 686 (10% approxi) subjects. When randomly taken sample was compared aBSE significantly detected 90.6%, 100% of lesions which were detected by CBE and BSE. There are 12% more suspicious lumps were unearthed after aBSE after conventional BSE. Comparison of CBE is 100% with aBSE. Of all the camps we could detect 281 new lumps among participants, which were referred for mammographic evaluation at medical centers and malignancies were detected in 108 participants, which indicates high impact of such training programs in rural India.

Conclusion: Our study proves that it is feasible and effective to do BSE and aBSE in rural Indian population for early detection. It is simple to implement education programs in all health camps for BSE and aBSE (indigenous developed breast light like device). The detection rate of 1.6% of all screened population was quite high especially in the rural areas where medical facilities are poor and have better clinical outcomes. The aBSE was well accepted among rural women and can improve on conventional breast self examination and is comparable with clinical breast examination.

No conflict of interest.

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Breast Cancer Screening in undeveloped country. How precision medicine will help?

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Background: Breast cancer screening has always been a challenging task in underdeveloped countries like Pakistan. We believe that during this era precision medicine for breast cancer is the most accurate approach in prevention, diagnosis and treatment of the disease. Several kinds of genetic and nongenetic tests for breast cancer are available that can help personalised therapy. Our study aims to find the role of precision medicine in breast cancer screening.

Materials & Methods: The study was conducted in Sir GangaRam Hospital, Lahore. 500 patients were included in the study. Informed consent was obtained. For our risk-based screening approach, we selected the Breast Cancer Surveillance Consortium (BCSC) model. Variables typically include demographics (age, race/ethnicity), reproductive history, menopausal status, family history, breast biopsies, benign breast disease, single nucleotide polymorphisms and mammographic density.

Results: The Breast Cancer Surveillance Consortium risk model will be used to calculate a woman's 5-year risk and will be modified by a polygenic risk score based on 76 SNPs. For women age 40 to 49 years, screening is recommended when their five-year risk equals or exceeds that of the average woman age 50 years. Women will be recommended to go for annual screening due to the precipitating factors such as dense breast or oestrogen receptor negative breast cancer. Carriers of genetic mutations will receive screening recommendations guided by their mutation type and family history.

Conclusion: Our main goal is early detection and prevention of cancer. Personalized screening may be the way forward in preventing breast cancer, but this can only be determined within the setting of a randomized controlled trial. We have provided the evidence base underlying our proposed risk assessment process and the risk thresholds used to inform individualized screening recommendations.

No conflict of interest.

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Current status for breast density notification in Japan

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Background: Mammography is recommended as a population based screening, and is implemented by municipalities in Japan. As with other Asian races, the percentage of dense breasts is high among young women, but the notification method varies depending on the municipality. Breast density notifications are already legislated in USA, but gaining understanding of the participants and increasing additional tests such as ultrasonography and MRI are in problem. Since there was no investigation regarding the notification of dense breast, the actual situation regarding the notification of breast density in Japan were investigated.

Method: In 2018, a questionnaire survey of all 1741 municipalities regarding breast cancer screening in the previous year were conducted. The survey items were breast density notification of breast composition, recommendation after notification, and recommendation content.

Results: The number of valid responses from municipalities was 1664. Of these, 99.8% were provided with mammography. Breast density notifications were made in 15.7% of municipalities. 46.2% recommend a specific method for handling after notification, including ultrasonography, medical examinations, and breast awareness.

Conclusions: Breast density notification is not recommended in Japan. However, due to the influence of the USA, some municipalities have already been notified, but the subsequent response has not been shown, and it is left to the judgment of the each clinic or hospital. If this situation continues, there are concerns about an increase in unnecessary tests and an increase in medical costs. Since the scientific basis for additional testing has not yet been established, it is not recommended to notify uniformly about breast density at this time.

No conflict of interest.

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Patients' experience with mammography and attitude towards targeted breast ultrasound as initial imaging technique for the evaluation of focal breast complaints

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Background: Mammography is historically used as the initial imaging technique for women with focal breast complaints that visit a hospital's radiology department. However, the value of mammography in this setting is questionable, as according to most guidelines, regardless of the outcome of the mammogram, ultrasound will follow. This study focuses on patients' experience with mammography and on their opinion on performing a breast ultrasound only for the assessment of their complaints.

Material and Methods: This study is conducted within the context of the Breast Ultrasound Study (BUST), in which the standard order of the breast examination was reversed. The radiologist first performes a target ultrasound which is always followed by mammography. The radiologists' conclusion of the ultrasound alone is compared to the conclusion after both examinations, to investigate whether performing ultrasound only may suffice from a medical point of view. Findings of this study are currently being analyzed.

After breast imaging, participants were asked to fill out a questionnaire, including questions on pain and stress experienced during mammography and whether they would already be comforted if the ultrasound showed clearly benign findings.

Results: A total of 778 patients responded to the questionnaire. They ranged in age from 30 to 88 years old ($M = 47$, $SD = 11.08$). In 83% of the cases, the complaint of the woman was a palpable lump. After correcting for missing answers, 17.9% of the respondents reported no burden of the mammography at all, while 13.5% reported the burden to be severe. In between, 35.7% of the patients experienced the burden to be small and 32.9% moderate. As for the pain, 14% of the patients reported no pain at all, 38.1% thought the mammography was slightly painful and 35.7% that it was moderately painful. Only 12.2% experienced intense pain. Out of the 720 patients that responded to the question, 641 reported that they would be satisfied with ultrasound diagnostics only (89%).

Conclusions: Most patients with focal breast complaints experience at least a slight to moderate burden due to the mammography and almost all patients experience some degree of pain, varying from slight to very severe pain. These findings, in combination with the fact that a great majority of the patients would already be comforted when the ultrasound shows a benign outcome, underscore possibilities for implementation of target ultrasound as an initial imaging technique in women with focal breast complaints, when the main analysis of BUST shows this approach to be safe.

No conflict of interest.

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Communication of biopsy results: A breast radiologist task?

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Background: To determine the patient preference receiving breast biopsy results communication.

Material and Methods: A 11 point survey has been administered to all patients of Centro di Senologia della Svizzera Italiana (CSSI) from September 2018 to October 2019. The survey has been designed and revised by Quality Control and administered to patients undergoing any biopsy performed in breast imaging department in Lugano, e.g. fine needle, core or vacuum-assisted biopsy. The survey was written in Italian, most spoken language in Ticino. The anonymous survey data were collected and stratified by patient's age, language spoken, preferences about the professional involved in the diagnosis communication, and its method.

Results: 66 survey were collected. Patients were all females, median age 55 (20–92); 61% married, 15% singles, 11% divorced, 5% widows, 9% marital status not declared. Almost all the patients declared a good understanding of the Italian language, 13.6% were non-native Italian (mainly with German mother tongue). 28 patients declared to have a superior education, 44% declared to have a secondary school education. 89.5% of patients identified their family doctor as their trusted doctor for.

54.5% indicated the gynecologist. Almost all the patients had clear that the procedure would've been performed by a radiologist. The most requested patients' medical professional as first choice to share the biopsy result was the trusted doctor (44%), one patient out of three preferred to meet with the radiologist, in both cases the radiologist was indicated to be the first or second choice from 30 and 31 women respectively. 70% of the patients preferred to meet the doctor in person, 26% preferred a phone call and 3% preferred to be notified via email. The majority of women indicated their preferences to receive the result on time, on top of making questions and trusting the doctor to communicate the result.

Conclusions: All patients knew that a radiologist would perform the upcoming invasive procedure. A limited number of patients in a single site has been involved. Male patient preferences were not included, due to the lack of patients in the observational period. The radiologist is the medical professional chosen to give the biopsy result from 1/3 to half patients, even if in previous questions it wasn't acknowledged to be a trusted doctor, at the level of a family doctor or a gynecologist. Patients still prefer to meet the doctor in person, even if they would receive the result as soon as possible.

No conflict of interest.

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Cost-effectiveness of digital mammography screening in the Netherlands: An extensive evaluation of 920 strategies

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Background: The benefits and harms of breast cancer screening programmes have been debated. Recent improvements in treatment as well as changes in screening performance may shift the balance between benefits and harms and might imply that current strategies may not be the most optimal. In addition, some countries are facing capacity issues. Therefore, this cost-effectiveness study evaluates optimal screening intervals in the Netherlands.

Material and Methods: Using a microsimulation model, the cost effectiveness of 920 breast cancer screening strategies with varying starting age (between 40 and 60), stopping age (between 64 and 84), and interval (annual, biennial, triennial and quadrennial) were simulated. The number of quality adjusted life years (QALYs) and net costs (in €) per 1,000 women were predicted (3.5% discounted) and incremental cost-effectiveness ratios (ICERs) were calculated to compare screening scenarios.

Table 1 QALYs gained and net costs per 1,000 women (3,5% discounted) and ICERs of strategies on the efficiency frontier

Strategy	QALYs gained (per 1,000 women)	Additional costs (per 1,000 women, 3.5% discounted)	ICER
Biennial 50-74	72.0	268,473	Dominated
Quadrennial 60-64	16.7	34,083	2,044
Quadrennial 56-64	27.1	56,351	2,129
Quadrennial 53-65	37.2	80,558	2,394
Quadrennial 52-64	38.8	84,762	2,730
Quadrennial 52-68	43.4	99,496	3,200
Quadrennial 50-70	50.1	56,351	3,674
Triennial 48-69	63.1	186,821	4,805
Triennial 48-72	65.7	200,340	5,365
Triennial 47-71	67.7	210,851	5,726
Triennial 46-73	71.5	236,265	6,388
Triennial 44-71	75.2	261,981	6,947
Triennial 44-74	77.0	275,095	7,073
Biennial 44-72	92.1	397,337	8,112
Biennial 43-73	96.0	431,623	8,754
Biennial 42-74	99.3	467,115	10,728
Biennial 41-75	102.4	503,798	12,008
Biennial 40-76	105.3	542,016	13,285
Annual 41-75	131.8	1029,897	18,403
Annual 40-75	135.1	1093,597	18,864
Annual 40-76	135.7	1105,482	19,944
Annual 40-78	136.6	1127,665	27,199
Annual 40-79	136.8	1137,974	44,491
Annual 40-81	137.2	1157,036	46,438
Annual 40-82	137.3	1165,691	93,080
Annual 40-83	137.4	1173,771	93,433
Annual 40-84	137.5	1181,296	95,626

Results: In total, 26 strategies covering all four intervals were on the efficiency frontier. For a willingness-to-pay threshold of €20,000/QALY gained, the annual 40-76 screening strategy would be optimal (Table 1). However, this strategy resulted in more overdiagnoses and required a high screening capacity. The current strategy in the Netherlands, biennial 50-74, was estimated to cost €268,473 and gained 72.0 QALYs per 1,000 women and was dominated. The triennial 46-73 strategy resulted in a similar amount of QALYs gained (71.5), while the costs were lower (€236,265), the amount of overdiagnoses was comparable, and the required screening capacity was lower.

Conclusions: Screening for breast cancer triennially between ages 46 and 73 can reduce costs without decreasing benefits or increasing harms compared to the current strategy.

No conflict of interest.

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Organisational characteristics of informed decision-making implementation in mammography screening programmes in 28 European countries

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Material and Methods: Data was collected via an online survey distributed to screening programme coordinators in Europe. Responses provided to the survey questions addressing the official policy of the programmes towards informed decision making, plus the strategy for implementation and evaluation were used to compute using a Multiple Correspondence Analysis to facilitate a Hierarchical Cluster Analysis of the mammography screening programmes into comparable groups.

Results: 35 responses were received representing independent mammography screening programmes from 28 different European countries. 27 respondents reported that the programme provides information to women on the benefits and harms of mammography screening and that a policy is in place for facilitating informed decision-making for women offered screening. Heterogeneity was reported towards the modalities used to implement the policy with 10 programmes stating that decision aids are used in practice to support informed choice. Only one programme reported an attempt to measure the proportion of women who have made an informed decision. The cluster analysis identified three emerging categories of programmes: established programmes distinguished by either reporting a policy specific to mammography screening and resources directed to implementation; established programmes with a general policy, applicable to other screening programmes, and the lack of administrative support to monitor implementation; and emerging programmes without a defined policy and few information provided to women regarding the benefits and harms of mammography screening. No statistically significant differences in participation rates amongst the two categories with a policy.

Conclusions: The data indicates a broad adoption by mammography screening programmes in Europe of the principle of supporting informed decision-making defined by either a specific or general policy directive. Validated best practices of how to develop, implement and evaluate a specific policy to promote informed decision-making, with culturally appropriate and responsive tools for measurement of informed choice, would provide much needed support cancer screening programmes to ensure that they help women make an informed choice.

No conflict of interest.

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Breast incidentalomas. How often do they are? – A 5-year Greek hospital experience

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Background: Aim of the study is to evaluate the rate of referrals to the breast unit due to incidental breast findings on thoracic CT.

Materials & Methods: Thoracic CT examinations that were performed at Hippokrateio General Hospital, Athens, Greece and the correspondent radiological reports were retrospectively reviewed from 1 January 2014 to 31 December 2018. Patients with previous breast surgery, either for malignant or benign disease, were excluded from the study. The breast findings that were incidentally identified were masses, calcifications, architectural distortions and breast tissue enlargement.

Results: During this 5-year period 6,013 thoracic CT scans were performed for various pneumological conditions. Fifty-one patients (0.9%) had incidental breast lesions and subsequently prompted to the breast unit for further assessment. The most common breast incidentaloma was a mass comprising almost half of the cases, followed by calcifications and breast tissue enlargement (25, 10 and 8 patients respectively). Architectural distortion was incidentally diagnosed in five cases whereas calcified mass was found in three patients. In 7 cases (13.7%) patients were men, five of whom were diagnosed with uni- or bilateral breast tissue enlargement.

Conclusions: Breast incidentalomas found on thoracic CT scans are an uncommon but substantial entity, that need further assessment with more specific breast imaging modalities. The most common finding is a breast mass and almost 1 in 8 of incidentalomas are seen in men.

No conflict of interest

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YouTube as a source of information for breast-examination for patients and healthcare professionals: content, quality and reliability

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Introduction: YouTube is one of the most visited websites on the internet and contains a multitude of health information of varying quality. In an era where patients are increasingly seeking health related guidance by turning to social media (SoMe), providing reliable information on SoMe, specifically YouTube, may improve anxiety and positively influence and encourage regular breast self-examination. Our aim was to assess the quality and characteristics of the most viewed and relevant videos on YouTube related to breast-examination including its techniques and guidance.

Method: A search of YouTube was made using the keywords of "breast" and "self-examination." The videos were categorised by two of the authors (KR, TC) as useful information or misleading information. To evaluate the quality of the videos, a 5-point global quality scale was used (GQS: 1 = poor quality, 5 = excellent quality), for reliability a 5-point DISCERN scale was used, and for content an 8-point scale (higher points indicated greater reliability and better content). The 100 most viewed videos were identified and user interaction analyzed. Video upload source was classified as patient, individual health care professional (HCP), hospital/professional association or charity.

Results: Of the 100 videos initially included in the study, 13 (13%) were classified as useful and 87 (87%) as misleading information. The reliability, content and quality scores of the videos in the useful information group were higher ($p < 0.05$). The length (in seconds) of the videos in the useful information group (median 327, IQR 231–512) was longer than that of those in the misleading information group (median 173, IQR 94.8–231) ($p < 0.001$). The majority (75.6%) of the videos in the misleading information group had been uploaded by an individual user. The number of views per day of the videos in the misleading information group (median 85.4, IQR 25.5–318) was greater than that of the videos in the useful information group (median 44.2, IQR 24.3–168) ($p = 0.36$).

52 videos were uploaded by patients, 9 by hospitals, 32 by HCPs and 7 by charity channels. Patient uploaded videos had significantly more comments ($P = 0.001$), with 95% of comments on patient videos being users requesting further information or thanking the user for the guidance. No video obtained a perfect score using our critical appraisal tools. Videos from professional bodies and charities scored higher points than those by patients ($p = 0.002$).

Conclusion: Although there are many videos related to breast self-examination on YouTube, a significant proportion of these contain misleading, inaccurate information. Therefore, for public information, there is a need for high quality videos with accurate information to be made by universities, healthcare organisations and doctors to be uploaded to YouTube.

No conflict of interest.

POSTERS B
Advanced Disease

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Metastatic breast cancer: A retrospective review

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Background: Metastatic breast cancer remains a treatable, yet incurable disease. These patients have different healthcare requirements to patients with early breast cancer due to unique disease characteristics and outcomes. The information provided to them must be tailored accordingly. This review will aim to analyse the demographics, survival and disease characteristics of those diagnosed with metastatic breast cancer and further compare recurrent to *de novo* metastatic disease.

Methods: All patients newly diagnosed with metastatic breast cancer at the Beatson West of Scotland Cancer Centre from January 2015 to August 2019 were identified (n = 160) and the relevant data was extracted from patient records for analysis. Data were analysed using Microsoft Excel, SPSS and STATA.

Results: The mean age at primary diagnosis was 62.5 years, and 67.2 years at secondary diagnosis. Overall, 53% of patients died, with a median overall survival time of 17 months. Those who presented as an emergency admission had increased risk of death compared to other modes of presentation (HR = 2.58, 95%CI: 1.57–4.23), while those with any comorbidity had increased risk compared to those with no known comorbidity (HR = 2.15, 95%CI: 1.3–3.57). Patients with triple negative tumours had increased risk of death (HR = 2.42, 95%CI: 1.47–3.98).

Differences between *de novo* and recurrent metastatic disease groups were observed at presentation and site of metastases. Most *de novo* metastases were detected during staging of a primary tumour (67.3%) while those with recurrent metastases presented most as an emergency admission (36.6%). Patients with recurrent disease were more likely to have pleural metastases (23.1%) compared to *de novo* disease (5.4%, p = 0.004).

Conclusions: Unsurprisingly, those with comorbidities, emergency metastatic presentation and triple negative tumours all have poorer survival outcomes. The negative impact of comorbidities on survival of metastatic breast cancer patients specifically, has not been reported before. Reassuringly, age did not appear to impact survival, suggesting that treatments are not denied based on age alone.

According to previous reports, approximately 25% of the metastatic breast cancer population have *de novo* metastatic disease but 35% of this cohort had *de novo* metastatic disease. This raises the question, are fewer patients relapsing after treatment of early disease or are more patients being staged and we're now seeing a stage shift?

More than 60% of patients with recurrent metastatic disease presented as emergency admissions and GP referrals. This indicates effective monitoring in primary care, however, it also highlights that more recurrences presented as unscheduled events than scheduled, follow up appointments. The increase in pleural metastases in recurrent metastatic disease a finding not yet recorded in the literature to the best of our knowledge.

No conflict of interest.

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The impact of advanced or metastatic breast cancer or its treatment on productivity, energy, and physical activity among palbociclib participants of the MADELINE study

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Background: MADELINE is an observational, multicenter study of women with HR+/HER2- advanced or metastatic breast cancer (aBC/mBC) who were followed for 6 months to evaluate patient reported quality of life (QOL) after initiating palbociclib combination therapy or other approved treatment in the US. Patient-reported outcome data was collected via a custom-developed mobile application at daily, weekly, and cycle-based intervals. A

subset of QOL measures collected were evaluated to determine the impact of aBC/mBC or its treatment on productivity, energy, and physical activity in patients treated with palbociclib.

Material and methods: Patients indicated weekly how aBC/mBC or its treatment interfered with family/social life and limited productivity, physical activities and energy on a 5-point scales ("Not at all", "A little bit", "Moderately", "Quite a bit", "A great deal") as well as employment status. Daily pain and fatigue severity were measured on an 11-point scale (0–10, 10 being worst possible pain/fatigue) and averaged to create weekly scores. Patient demographic and clinical data including adverse events was recorded in an eCRF. The relationship between weekly productivity limitation ("not at all" or "a little bit" vs. "moderately" to "a great deal") and neutropenia (yes/no), pain (<2 vs ≥2), and fatigue (<2 vs ≥2) was evaluated using generalized linear logistic models.

Results: Twenty-five sites contributed 139 patients (median [range] age 60 [34, 82]; white: 83%; ECOG 0–1: 87%). About half of patients (49%) were employed at baseline and employment status was generally stable over time when excluding missing data and early withdrawals. Most patients across the first week of all cycles indicated aBC/mBC or its treatment limited or interfered physical activity, energy or stamina, mood or emotions, productivity, family life, and social life "Not at all" or "A little". These findings were similar regardless of experience with neutropenia. The overall odds ratio (95% CI) for pain and fatigue severity >2 vs. severity ≤2 on productivity limitation from aBC/mBC or its treatment of was 5.8 (3.3, 10.2) and 8.2 (4.8, 14.0) respectively.

Conclusions: The majority of patients treated with palbociclib in the MADELINE study indicated aBC/mBC or its treatment limited productivity, energy, and physical activity "Not at all" or "A little". Employment was stable across cycles for patients remaining in the study. While results suggest a low level of pain and fatigue in the study, there was a significant effect on productivity limitation with higher levels of pain and fatigue associated with higher limitations on productivity. Neutropenia was not associated with higher limitations on productivity.

Conflict of interest:
Ownership:
Pfizer Inc (Shareholder/Stockholder/Stock options): Zhan L, Mitra D, McRoy L
Other Substantive Relationships:
RTI Health Solutions (employee) who were paid consultants to Pfizer in connection with the research and development of this abstract: Richardson D, Reynolds M, Odom D, Hollis K
Pfizer Inc (employee): Zhan L, Mitra D, McRoy L
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Pfizer Inc (paid consultant): Hargis J

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The prevalence of depression symptoms among advanced breast cancer patients: A systematic review and meta-analysis

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Background: Depression in patients with advanced breast cancer is serious comorbidity that affects the quality of life for patients, and their survival rates. This study aims to systematically review current literature with data on the prevalence of depression symptoms in metastatic and recurrent breast cancer patients, examine the pooled mean prevalence of depression symptoms and potential sources of heterogeneity.

Materials and Methods: An extensive systematic review of PubMed, Web of Science, Scopus, ScienceDirect, Google Scholar, American Doctoral Dissertations and Open Grey databases, and following reference list hand-search was performed to retrieve studies from January 2005.

Results: We identified 11 eligible studies that assessed 1223 patients on the presence of depression symptoms, and 465 patients met the criteria. According to the random-effects model, the pooled mean prevalence of depression was 38.23% (95% CI [30.92; 45.83]; I^2 = 87%; Q (df = 10) = 77.89, p-val < 0.01). Patients with metastatic stage had a slightly higher prevalence of depression symptoms compared to recurrent breast cancer patients.

Table 1 Pooled mean prevalence of depression in advanced breast cancer patients and subgroup analysis results

Random-effects model	k	
PMPD	38.23% (95% CI [30.92; 45.83]; I^2 = 87%; Q (df = 10) = 77.89, p-val < 0.01)	11
Sub-group analysis: PMPD by cancer type		
recurrent (local, regional or distant) breast cancer patients	36.64% (95% CI [19.07; 56.20]; I2 = 0%; Q (df = 1) = 0.04; p = 0.85)	2
metastatic breast cancer patients	38.59% (95% CI [30.19; 47.34]; I2 = 90%; Q (df = 8) = 77.8; p < 0.01)	9
Subgroup analysis: PMPD by income level of the country		
upper-middle	48.39% (95% CI [32.31; 64.63]; I^2 = 93%; Q(df = 1) = 14.04; p < 0.01)	2
High	35.79% (95% CI [28.20; 43.74]; I^2 = 80%; Q(df = 8) = 39.36; p < 0.01)	9

CI = confidence intervals; I^2, percentage of variability in the effect sizes which is not caused by sampling error; k = number of studies; PMPD = pooled mean prevalence of depression;

Conclusion: Prevalence of depression symptoms among advanced breast cancer patients is high. It is important to improve psychological prevention methods to decrease the occurrence of depression, as breast cancer patients start receiving care from primary diagnosis, and offer continuous support and treatment to meet their psychological needs.

No conflict of interest.

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The global prevalence of anxiety among advanced breast cancer patients: A systematic review and meta-analysis

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Background: Anxiety in patients with metastatic or recurrent breast cancer is a common psychological comorbidity. This study aims to systematically review the current literature on observational studies with data on the prevalence of anxiety in metastatic and recurrent breast cancer patients, examine the pooled mean prevalence of anxiety and potential sources of heterogeneity.

Materials and methods: An extensive systematic review of PubMed, Web of Science, ScienceDirect, Google Scholar, and Open Grey databases, and following hand-search of the reference list of the included studies was performed to retrieve studies from January 1990 until May 2020.

Results: We identified 16 eligible studies that assessed 1284 patients on the presence of anxiety using structured interviews and two self-report inventories. Most of the studies had a cross-sectional design and a consecutive sampling method. In total, 371 patients met the criteria for anxiety. According to the random-effects model, the pooled mean prevalence of anxiety was 29.93% (95% CI [23.22; 37.09]; I^2 = 86%). Studies that reported the prevalence of anxiety in the last fifteen years had the same rate as the studies that were published in the fifteen years before that. The prevalence of anxiety reported according to the results of the structured interview was significantly lower than the prevalence rate reported with the Hospital Anxiety and Depression Scale inventory.

Table 1 Pooled mean prevalence of depression in advanced breast cancer patients and subgroup analysis results

	Random-effects model	k
PMPA	29.93% (95% CI [23.22; 37.09]; I^2 = 86%, p-val < 0.0001)	16
Sub-group analysis: PMPA by the years that the studies were conducted		
2005–2020	30.35% (95% CI [20.07; 41.68], I^2 = 83%, p < 0.01)	8
1990–2004	29.55% (95% CI [19.30; 40.91], I^2 = 87%, p < 0.01)	8
Subgroup analysis: PMPA by the anxiety evaluation method		
BAI	61.29% (95% CI [34.88; 84.64])	1
Interview	20.75% (95% CI [11.98; 31.03], I^2 = 59%, p < 0.03)	6
HADS	32.15% (95% CI [24.41; 40.40], I^2 = 85%, p < 0.01)	9

BAI = Beck Anxiety Inventory; CI = confidence intervals; HADS = Hospital Anxiety and Depression Scale; NA = not applicable; PMPA = pooled mean prevalence of anxiety; I^2, percentage of variability in the effect sizes which is not caused by sampling error; k = number of studies

Conclusion: Around one-third of patients with advanced breast cancer are diagnosed with anxiety. Breast cancer patients' high psychological needs have to be recognized and met not only at primary diagnosis but also at recurrence and progression of the disease.

No conflict of interest.

505 Poster

Systematic review of impact of intra-operative ultrasound in breast conserving surgery in early breast cancer

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Background: Breast conservation (BCS) is the standard surgical procedure for early breast cancer. It is a challenge for surgeons to achieve adequate excision of lesion with clear margins and acceptable cosmesis. To remove precisely the volume of tissue required, continuous intra-operative ultrasound (IOUS) had been used during BCS. We reviewed its effectiveness to obtain clear margins, low excision volume and better cosmetic outcome.

Methods: Three bibliographic databases (MEDLINE, CINAHL, Cochrane Library online) were searched for relevant published and unpublished literature from their inception until December 2019. The randomised controlled trials of impact of IOUS on excision volume, margin status and cosmetic outcome were reviewed, and meta-analysis was done for margin status and narrative summary was done for other outcomes.

Results: This study included 4 articles in the systematic review. Overall, 207 patients with IOUS and 192 patients with palpation guided (PGS) BCS were included in the study. The standardised mean difference of excision volume for 2 trials was −0.31(−0.62, −0.00) and −0.50 (−0.85, −0.16) with p value of 0.048 and 0.004. There was no significant volume difference in remaining two studies. The positive margin rate was significantly reduced with IOUS guidance. The pooled OR was 0.19 (95%CI: 0.09, 0.41) with no heterogeneity among studies (p = 0.72, I^2 = 0%). *The COBALT study showed* significant better cosmetic outcome with ultrasound guided BCS (OR = 0.53, 95%CI: 0.28, 0.99, p = 0.048). The remaining three studies, p value of >0.05 suggesting that there was no significant difference in satisfaction between IOUS and PGS. The post-operative follows up was varied from 2 weeks to 41 months among included RCTs. Therefore, interpretation of combined cosmetic outcome was not possible. The overall cosmetic outcome favoured satisfaction in ultrasound guided BCS groups although there was no statistical significant.

Conclusion: This study suggests that use of IOUS provides statistically significant less positive margin without significant difference in excisional volume. Overall, satisfaction exceeds dissatisfaction with ultrasound guided breast conserving surgery. However, there is insufficient evidence to support the better cosmetic outcome in IOUS group. Further research will be needed to compare the actual cosmetic outcome differences between groups.

No conflict of interest.

506 Poster

Effect of the COVID-19 pandemic on use of bone-modifying agents for metastatic breast cancer in a UK Oncology centre

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Background: Bone-modifying agents (BMAs) prevent skeletal-related events (SREs) in breast cancer patients with bone metastases. Our centre uses mainly zoledronic acid (ZA). Denosumab is permitted, due to its high cost, only with a documented indication such as renal failure. ASCO/CCO guidelines have responded to Phase 3 trial evidence showing non-inferiority of 12-weekly ZA compared to 3 or 4-weekly, which may reduce adverse events (AEs) and cost. We report on patterns of prescription in our centre and how it has changed due to COVID-19.

Materials and methods: Data was retrospectively collected on patients who received BMAs in two separate three-month periods (Oct-Dec 2019 and Apr-Jun 2020, total n = 389) including choice of BMA, frequency of administration, concurrent systemic therapy, and incidence of SREs and AEs. We searched the electronic prescribing record, outpatient letters, radiotherapy record and blood tests for each patient.

Results: Of the patients receiving BMAs in period one, 88% were on ZA and 13% on denosumab. Of those on denosumab, the majority (79%) had a documented indication, of which the most common (68%) was poor renal function. Mean total duration of BMA therapy was 22 months, during which 26% received radiotherapy to the bone. We found 3 cases of osteonecrosis of the jaw (ONJ), no osteonecrosis of the auditory canal (ANAC), and no atypical femoral fractures (AFF) out of the patients still receiving BMAs in period one. 32% experienced hypocalcaemia, defined as any reading below the laboratory reference range since starting BMA therapy.

In period two, 11% fewer patients received BMAs. There was a large variation in intervals prescribed within period one (Table 1) and a marked shift thereafter. The percentage of patients on 12-weekly treatment rose from 45% to 66%. The change resulted in a saving of approximately £1300 in medication cost and 60 hours of nursing time. If all patients were on 12-weekly dosing, this could save approximately a further £2400 and 120 nursing hours per year. Hypocalcaemia occurred in 8.5% of patients during period one and 7.0% during period two.

	Period one N = 205	Period two N = 183
ZA	88%	84%
Denosumab	13%	16%
4-weekly	24%	6%
6-weekly	13%	10%
8-weekly	17%	18%
12-weekly	45%	66%
Other frequency	2%	0%
Concurrent chemotherapy	30%	34%

Conclusions: Despite strong evidence supporting use of 12 weekly ZA, local practice was slow to change. During COVID-19 it became necessary to minimise exposure of patients to hospital. This resulted in a rapid shift in practice; leading to reduced treatment burden, less hypocalcaemia, liberation of nursing time and cost saving in the COVID-19 period and beyond.

No conflict of interest.

507 Poster

Patterns of treatment and outcomes in real world elderly patients with metastatic oestrogen receptor positive (ER+) breast cancer receiving the CDK4/6 inhibitor Palbociclib and endocrine therapy

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1. Advancement in the treatment of metastatic oestrogen receptor positive (ER+) breast cancer has led to the introduction of CDK4/6 inhibitors such as Palbociclib (PAL), which are associated with reversal of endocrine resistance and delayed necessity for chemotherapy. Clinical trials to date have demonstrated improved survival outcomes for patients on these agents. We evaluated outcomes with PAL plus endocrine therapy in a real-world setting and compared their efficacy in the elderly patients aged ≥65 years.
2. Retrospective review of a prospectively maintained multicentred institutional database of patients with ER+, human epidermal growth factor

receptor 2 negative (HER2-) advanced breast cancer who were commenced on PAL between January 2010 and September 2019. Data analysed included demographics, disease characteristics, treatments, toxicities, response rates and survival outcomes. Inferential statistical analysis was completed using frequency table calculations, Cox proportional hazard model for univariate analysis and Kaplan Meier curves for survival data and time to event data.

3. We identified 271 pts, median age was 60 years (31–88) and divided them into 2 patient cohorts. 38% of pts (n = 103) were ≥65 years (Group 1) with a median age of 72 years (65–88) and 62% of pts (n = 168) were younger than 65 (Group 2) with a median age of 53 (31–64). There was no significant difference in progression free survival (PFS) between the two groups. 8 months (6.4–11.7) in group 1 vs 10 months (7.3–12.7) in group 2. Median OS was 29 months with group 2 exhibiting a longer OS 34 months (19.4–48.6) vs 22 months (14.7–29.3), however this was not statistically significant (p = 0.221). Among the 271 pts, 33.2% (n = 90) were diagnosed with de novo metastatic disease. 11.8% (n = 32) in group 1 and 21.4% (n = 58) in group 2. OS was greater in both groups compared to relapsed disease and greatly improved in de novo metastatic patients in group 2, 59 months (28.6–89.4) vs 13 months (10.8–15.2). Among 71 pts treated with PAL in the 1st line overall response rate (ORR) was 56% (n = 40). 22.5% (n = 16) Group 1 and 33.8% (n = 24) in group 2. The median PFS was 35 months (95% confidence interval [CI], 17.2–52.8) in all pts, with a median PFS of 21 months in group 2 vs not reached in group 1. The most frequent grade 3 toxicities were neutropenia (40%), anaemia (4%), fatigue (3%) and thrombocytopenia (2.5%). The rate of febrile neutropenia was 2.5% and mostly observed in group 2. Dose reductions occurred in 40%, with the most common reason being neutropenia and was similar for both groups. Treatment was discontinued in 3% due to toxicity.
4. Palbociclib plus endocrine therapy appears to be safe and well-tolerated in a real-world elderly population and is associated with favorable survival outcomes comparable to younger patients and to those seen in clinical trial settings.

No conflict of interest.

508 Poster

The value of shear-wave elastography for prediction of tumor-infiltrating lymphocytes in patients with breast cancer

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Introduction: Tumor-infiltrating lymphocytes (TILs) has been known to be a useful marker for predicting the treatment response and survival in breast cancer. However, little is known about whether SWE can predict the TILs. We aimed to investigate the relationship between elasticity values measured by SWE and TILs.

Method: Pre-treatment shear-wave elastography was performed in 797 patients who underwent surgery followed by adjuvant therapy at Gangnam Severance Hospital from January 2016 to March 2020. The patients were assigned into two groups: the high TILs group (≥50%) and the low TILs group (<50). The cutoff points of elasticity values (maximum stiffness, 166.15; mean stiffness, 156.05; minimum stiffness, 126.25; elasticity ratio, 7.88) were determined as the maximum area under curve value using receiver operating characteristics curve for predicting high TILs.

Results: Of the whole cohort, 101 (12.7%) patients had high TILs and 696 (87.3%) patients had low TILs. All elasticity values were significantly higher in patients with low TILs compared to those with high TILs. In the multivariable analysis, all high elasticity values, including the maximum stiffness (OR 0.249; 95% CIs, 0.144–0.432, P < 0.001), mean stiffness (OR 0.232; 95% CIs, 0.129–0.416; P < 0.001), minimum stiffness (OR 0.413, 95% CIs, 0.243–0.704; P = 0.001) and the elasticity ratio (OR 0.464; 95% CIs, 0.271–0.794; P = 0.005) were independent predictive factors for low TILs after adjusting clinic-pathologic factors. Moreover, the maximum stiffness was independent predicitive factors for low TILs across the subtypes (HR+HER2: OR 0.427, 95% CIs, 0.200–0.913, P = 0.028; HER2+: OR 0.345. 95% CIs, 0.143–0.831, P = 0.018); and TNBC: OR 0.170, 95% CIs, 0.053–0.544, P < 0.001, respectively).

Conclusion: The elasticity values were inversely associated with the TILs measured in the surgical specimen. Our results suggest that SWE can be a useful diagnostic tool for the TILs level in patients with breast cancer.

No conflict of interest.

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Real world evidence of palbociclib use in metastatic hormone positive HER negative metastatic breast cancer in Indian population

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Background: Hormone positive, HER-2 negative metastatic breast cancer (HR+/HER2- MBC) had always been challenging to treat. With the addition of Cyclin-dependent kinase 4/6 (CDK4/6) inhibitors to the treatment armamentarium, these patients have not only shown improvement in progression free survival (PFS) and response rates (RR) but also overall survival (OS) has improved in both the lines compared with endocrine therapy (ET) alone. Since 2017, in India, the combination of CDK4/6 inhibitors with ET is standard therapy in HR+/HER2- MBC. Several randomized control trials have already shown clear benefit of this combination, however real world descriptive studies supporting use of Palbociclib in Indian patients is lacking. Herein we present largest real world data from Indian population combining patients from two institutes from New Delhi, India.

Methods: HR+/HER2- MBC patients who received palbociclib with hormonal agent either Aromatase inhibitors or Fulvestrant between February 2017 and May 2020 from two private institutes were retrospectively analyzed. The primary endpoint was to determine the progression free survival while secondary end points were to look for the toxicity profile and response rates.

Results: A total of 188 patients were included in the final analysis. Median age of the patients was 58.5 years (32–85 years). Altogether, 57% patients were premenopausal, while 43% were postmenopausal. 82% patient had visceral disease while 17% patients had bone only disease. In the study, 115 (61%) patients received palbociclib with Aromatase inhibitors either Letrozole or Anastrazole in the first line whereas 73 (39%) patients received it in the second line with Fulvestrant. All premenopausal women received ovarian suppression or ovarian ablation (OS/OA). The median PFS in first line was found to be 20.2 months while in second line it was 12 months. The objective response rate was 80% and 47.9% in first and second lines, respectively while 7 out of 115 and 2 out of 73 patients achieved complete remission in first & second line respectively. Dose interruption was required in 28 (14.9%) patients due to toxicity while 9 (4.8%) patients required dose reduction while 4 (2.7%) patients required drug discontinuation due to very poor tolerance. In terms of toxicity, 88% patients had all grade neutropenia while only 20% patients had grade 3–4 neutropenia. However, there was no incidence of any febrile neutropenia. 9 % patients had other non hematological grade 3–4 side effects.

Conclusions: The present real world data of palbociclib use in Indian population suggest similar effectiveness to previously published real world evidences and is standard of care in first and second line treatment of HR+/HER2- MBC.

No conflict of interest.

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Real world treatment patterns and clinical outcomes associated with palbociclib combination therapy in nine european countries: Results from the IRIS study

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Background: Palbociclib (P) was the first cyclin-dependent kinase (CDK 4/6) inhibitor for HR+/HER2- advanced/metastatic breast cancer (ABC/MBC) approved in Europe, in combination with an Aromatase Inhibitor (AI) or Fulvestrant (F). The multi-country Ibrance Real World Insights (IRIS) study was initiated to evaluate real-world palbociclib use.

Materials and methods: Retrospective chart review of HR+/HER2- ABC/MBC patients (pts) who received P+AI or P+F in 9 European countries conducted between July 2019 – April 2020. Data captured included clinical characteristics, treatment patterns and clinical outcomes. Progression free rate (PFR) and survival rate (SR) estimated via Kaplan Meier analysis at 12 and 24-months. Analyses stratified by clinical characteristics such as age, ECOG at palbociclib initiation, visceral status and time from initial BC to ABC/MBC diagnosis.

Results: Medical records of 1723 pts receiving palbociclib combinations were abstracted across 9 EU countries by 238 physicians. Overall 982 pts

received P+AI (94.2% 1st line; 5.8% ≥2nd line) and 741 pts received P+F (51.1% 1st line; 48.9% ≥2nd line). Mean (SD) age at palbociclib initiation was 62.3 (10.6) years for P+AI and 64.0 (10.0) years for P+F pts. Most pts had a performance status (ECOG) at palbociclib initiation of 0 or 1 (P+AI: 86.4%; P+F: 87.7%). Of those pts with metastatic disease (P+AI: n = 906; P+F: n = 661), 49.2% P+AI and 48.7% P+F pts had visceral disease; 43.5% P+AI and 39.5% P+F pts had bone only metastases.

Median follow-up duration from palbociclib initiation was 10.5 months for P+AI and 8.0 months for P+F patients. Overall 80.3% P+AI and 77.5% P+F pts were still on treatment at the time of data collection. Of those initiating at 125 mg/day (P+AI: n = 922, 93.9%; P+F: n = 668, 90.1%), dose reductions occurred in 18.8% P+AI and 11.9% P+F pts. The 12- and 24-month PFR and SR across lines of therapy are presented in Table 1. Pts receiving P+F 1st line had higher PFR and SR than those receiving 2nd line or later. PFR and SR outcomes were favorable across subgroups including pt age, ECOG score at palbociclib initiation, visceral status and time from initial to ABC/MBC diagnosis.

Table 1. Clinical outcomes data for P+AI and P+F by line of therapy

	P+AI 1st line n = 925	P+F 1st line n = 379	≥2nd line n = 362
n†	924	379	362
12 month PFR, %	88.90%	81.00%	78.90%
24 month PFR, %	63.10%	48.90%	48.80%
n†	919	362	353
12 month OS, %	97.40%	97.60%	97.30%
24 month OS, %	90.60%	92.70%	86.40%

†Reduced pt base where dates for time to progression or death not recorded in medical records.

Conclusions: In 9 European countries, palbociclib demonstrated real-world efficacy by favorable PFR and SR at 12 and 24-months; results are consistent across countries and pt subgroups. Low levels of dose reductions were observed suggesting both combinations are well tolerated. More mature data required for longer-term patient outcomes.

Conflict of interest:
Ownership:
Pfizer Inc (Shareholder/Stockholder/Stock options): Zhan L, Mitra D
Other Substantive Relationships:
Adelphi Real World, who were paid consultants to Pfizer in connection with the research and development of this abstract (employee): Mycock K, Hart K, Taylor-Stokes G, Milligan G, Atkinson C
Pfizer Inc (employee): Zhan L, Mitra D

Advocacy

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Patients' willingness to travel further to have their cancer surgery at a Centre of Excellence

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Background: In the UK there are trends for centralising complex surgery in high-volume centres. Evidence to support this trend are perceived benefits for patients, staff & health economy. In 2012, 5 hospitals in Northeast London were merged as a single NHS trust, serving 2 million people. A new surgical strategy was approved to establish several Surgical Centres of Excellence across the 5 sites. This resulted in patients being required to travel further to have their surgery at the relevant centre.

Aims: To randomly survey the opinions of a group of patients from Newham Borough of London attending breast clinics at 2 different hospitals, on their willingness to undergo surgery at a Centre of Excellence rather than the local hospital.

Methods: A questionnaire-based study of a convenience sample of patients with multi-ethnic backgrounds attending symptomatic breast clinics in East London. The questionnaire was adapted from a 2007 IPSOS MORI national survey. Completion of survey was taken as consent for inclusion in the study.

Results

Table 1 Responses (n = 60)

In which of the scenarios would you be willing to be treated at a hospital further than your local hospital	Yes %	No %	Don't Know %
If the hospital had all specialists involved in your treatment on one site	91.7	3.3	5
If the hospital had shorter waiting times	88.3	3.3	8.3
If the hospital had better standards of care	83.3	6.7	10
If the hospital had better 5 year survival rates after cancer treatment	81.7	3.3	18.3
If you needed to have an operation & the hospital offered surgery that meant you would be in hospital for 4 days rather than 10	81.7	1.7	16.7
If the hospital had a lower risk of complications after surgery	80	8.3	11.7
If the hospital had less chance of cancelling your surgery at short notice or on the day	71.7	13.3	15
If the hospital had a lower risk of death in the month following a major operation for cancer	73.3	10	16.7
If the hospital provided treatment with fewer side effects	76.7	6.7	16.7
If treatment involved daily trips to the hospital for up to 6 weeks	46.7	28.3	25
If the hospital provided better information for patients & carers	75	10	15
If the hospital provided new therapy & research including clinical trials	78.3	6.7	15

Conclusions: The majority of patients across the communities in East London were willing to travel further than their local hospital for a single visit if they had better quality of care & fewer post-surgical complications. Patients were reluctant to travel to a further hospital if it they were required to travel repeatedly for up to 6 weeks. Our results support those of similar national surveys. Further studies are required to address the concerns of those who were reluctant to travel further and explore issues such as ease of transportation, language barriers, mobility & other relevant factors.

No conflict of interest.

512 Poster

Breast cancer among immigrants: An Irish experience

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Background: Immigrants represent a large, increasing and vital segment of the Irish population. No data exists regarding the epidemiology of breast cancer in this cohort. To treat patients effectively it is important to understand the epidemiology of this population and factors that will have a negative impact on their prognosis. We performed a retrospective study to investigate the demographic and clinical characteristics of women who have immigrated to Ireland.

Material and methods: Patients diagnosed with breast cancer whose case was discussed in the regional Breast Cancer Multidisciplinary team meeting from January 2018 to August 2019 were identified. Electronic medical records were retrospectively reviewed. Data pertaining to patients not born in Ireland was compared in an unmatched analysis with the first 80 Irish born patients diagnosed during this period. Chi-square was used to determine statistical analysis.

Results: 60 patients were identified as immigrants, accounting for 12.5% (60/480) of those diagnosed. Median age at diagnosis was 43 (range 30–80), with 18 countries of birth represented. 36 patients (60%) originated from countries where English is not the first language. 13 patients (12%) did not speak English and required a translator. All of these patients experienced delays in commencing or continuing treatment. 80 Irish patients were identified, median age 63 (range 31–92). There was no difference between stage at presentation; 66% of the immigrant population presented with Stage I or II disease, comparable to 60% of the Irish population (p = 0.42). Of those eligible for cancer screening; 1 patient (5%) of the immigrant population was diagnosed through screening, compared with 4 (18.2%) of the Irish population. The immigrant population were more likely to have HER2+ (10% versus 4% p = 0.89) or triple negative breast cancer(17% versus 10% p

= 0.24). The Irish population were more likely to have hormone-receptor positive breast cancer (86% versus 73%, p = 0.06).

Conclusion: Immigrants to Ireland represent a significant cohort (12.5%) of breast cancer patients in the south of the country, with a wide range of countries and 5 continents represented. Immigrants present with similar stage disease, and may experience delays in treatment when compared to an Irish cohort. Our results highlight aspects of patient care that require further optimisation to improve patient safety and outcomes.

No conflict of interest.

513 Poster

Primary endocrine treatment for older women with early-stage hormone receptor-positive breast cancer. Real-World experience from a single UK cancer centre

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Background: Upfront surgery is the gold standard of treatment for early-stage breast cancer (EBC) in fit older women. It reduces the risk of local recurrence and the associated morbidity and has a positive impact on overall survival. However, primary endocrine treatment is commonly used for older women with co-morbidities that are considered medically unfit for surgery. We aim to present data for older women treated with endocrine therapy alone.

Materials and methods: We collected data retrospectively from electronic patients' records from 01/2014 until 12/2019. Forty-one women aged >70, with hormone-receptor-positive EBC, were treated with aromatase inhibitors as definite treatment and never undergone breast surgery. Patients characteristics: The median age was 82 (ranging from 73 to 102). All patients had resectable tumours (stage I–III), including 8 women with positive axilla (clinical and radiological), and all of them were initially treated with aromatase inhibitors. 27 of the patients had more than two co-morbidities and were considered unfit for surgery. Atrial fibrillation, hypertension, COPD, type II Diabetes, chronic kidney disease and dementia were among the more often medical conditions. 8 women had a second primary tumour at the time of diagnosis, either metastatic or early stage, which was considered a medical priority in terms of treatment. Eight women finally declined surgery when co-morbidities were optimized and decided to continue with endocrine treatment. Tumour characteristics: 40/41 had a high ER (expression QS > 7) and 29/41 had a high PR expression (QS > 7). The majority were grade II (31/41), and most of them were of ductal histology (33/41). 8/41 tumours were grade III, and 3/41 were HER2 positive, never received anti-HER2 treatments.

Results: The median duration of treatment was 28 months, ranging from 2 to 70 months. End of treatment date was either the date of disease progression or death from any cause. 15/41 patients had radiological partial response to endocrine treatment, 4/41 had complete radiological response, and 3/41 had stable disease. 6 patients progressed while on ET. 5/6 had local progression and were subsequently treated with a switch to another ET and/or radiotherapy. One patient had distant metastatic disease and received chemotherapy. Radiological follow up was missing for 13 patients, but 12 of them had documented clinical response based on physician's assessment (PR or SD), thus increasing the rate of disease control up to 85,3% (CR, PR, SD radiologically confirmed or clinically documented).

Conclusions: Although surgical resection of early-stage hormone-receptor-positive BC is the optimal treatment for fit older women >70 years old, supported by multiple trials and meta-analysis, endocrine monotherapy could still be considered an acceptable option for "frail" or patients who refuse to have surgery.

No conflict of interest.

Basic Science and Translational Research

514 Poster

Analysis of fractal dimension allows identification of malignancies in breast tissue histopathological images

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Background: Histopathological analysis remains as the gold standard diagnosis of breast cancer (BC) and benign tissue alterations. Nevertheless, despite training and standardization, it is considered operator-dependent and subject to errors. Recent works have shown that image processing algorithms are useful in identifying either benign or malignant alterations on tissues. Fractal dimension analysis is a computational image processing technique that allows assessing the degree of complexity in patterns. Therefore, it may represent a powerful tool in the investigation of alterations in biological systems. This technique has successfully differentiated normal and pathological images in histo- and cytopathology; radiology; and melanomas. In the present study, we have evaluated this tool in the histopathological diagnosis of BC.

Material and methods: Two datasets of H&E slides available for research were employed: A) Breast Cancer Histopathological (BreakHis - UFPR); and B) Grand Challenge on Breast Cancer Histology. Set A contained 2480 images from 24 patients with benign alterations, and 5429 images from 58 patients with BC; we analysed images in the 40× and 400× magnifications. Set B comprised 100 images of each type: normal tissue (N), benign alterations (B), *in situ* carcinoma (IS), and invasive carcinoma (IC), not assigned to patients. All images were analysed with the FracLac algorithm in the ImageJ computational environment; all statistical analyses were performed with the box count fractal dimension (Db). One-way Welch ANOVA was employed to interrogate statistical differences on all means. A ROC curve was also calculated from set B.

Results: Upon visual inspection, images on set B were considerably more homogenous concerning staining. The set A images on 40× magnification displayed differences when comparing: all benign images × all malignant ($p = 0.0003$) as well as when comparing mucinous and papillary carcinomas to benign images ($p = 0.0009$ and $p = 0.0261$). However, no statistical difference was found when analysing the 400× images. On set B, the Db values were significantly different when comparing: 1) N × I; 2) B × IS; 3) N × IC; 4) B × IC; and 5) N and B × IS and IC (all $p < 0.0001$).

Conclusions: The Db values allowed differentiating normal tissue and benign alterations from BC tissue. The statistical difference among the 40× images from set A corroborates with previous findings; furthermore, this magnification allows visualizing whole tissue architecture. Greater difference was found on set B, which may be both due to the homogenous staining and greater resolution. The totality of the data indicates that Db may be employed as a parameter when developing future clinical algorithms for computer-aid in the histopathology service when analysing of BC slides, as well as to feed artificial intelligence algorithms.

No conflict of interest.

515 Poster

APOBEC driving genomic evolution in ER+/HER2- breast cancer

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Background: Cytidine deaminase apolipoprotein B mRNA-editing enzyme, catalytic polypeptide-like (APOBEC) has been identified as an important

mutagenic factor in multiple cancers. APOBEC induces specific mutations, which potentially contributes to tumor progression and/or therapy resistance. To learn how APOBEC mutagenesis impacts tumor evolution in ER+/HER2- breast cancer (BC), we determined which APOBEC-associated amino-acid (AA) changes are more frequently observed than expected in primary and metastatic breast tissue, in which genes these occur, and which of these alterations are enriched in primary breast cancer (pBC) compared to metastatic lesions.

Material and methods: We defined all possible AA-changes that can result from APOBEC related single base substitutions (SBS) on the coding strand of the genome, i.e. SBS2 and SBS13, thereby creating a theoretical distribution of expected APOBEC mutations. This theoretical frequency was compared to the observed frequency of AA-changes in pBC (BASIS cohort, WGS, n = 325) and two metastatic BC (mBC) cohorts (CPCT02, WGS, n = 425; Razavi, targeted NGS using MSK-IMPACT targeted gene panel; n = 1918; all cases endocrine resistant) using a permutation/bootstrap method.

Results: In pBC, SBS2 mutations resulting in E > K and Q > X(stop) AA-changes were significantly enriched and recurrently identified in specific genes. As reported previously, E > K mutations were most prominently identified in the helical domain of *PIK3CA*. Q > X mutations, which are likely to inactivate the gene, most frequently occurred in *CDH1, TP53* and *MAP3K1*. In pBC, SBS13 mutations resulting in AA-changes E > Q, Q > E and L > F were enriched when compared to the theoretical distribution but these mutations did not recur in specific genes. When compared to pBC, AA-changes E > K (SBS2), E > Q and S > X (SBS13) were significantly enriched in mBC. Of those, recurrent E > K mutations were present in *PIK3CA* and recurrent E > Q mutations were present in *ESR1*, although to a lesser extent. In endocrine resistant mBC, Q > X (SBS2) and S > X (SBS13) mutations in *KMT2C*, *ARID1A* and *NF1* emerged as a result of differential selection under endocrine treatment. Remarkably, L > L AA-changes were enriched in mBC when compared to the theoretical distribution but these mutations were likely bystanders as they were mainly observed in large genes and in samples in which E > K and Q > E mutations co-occurred.

Conclusions: We demonstrate that APOBEC leads to alterations in genes known to be able to act as a driver in early and mBC and further facilitates endocrine resistance in mBC. Our results underscore the importance of APOBEC mutagenesis in the genomic evolution of BC.

No conflict of interest.

516 Poster

Tumor-stroma ratio is associated with Miller-Payne and pathological response to neoadjuvant chemotherapy in HER2-negative early breast cancer

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Background: The tumor-stroma ratio (TSR) has proven to be a strong prognostic factor in breast cancer, demonstrating better survival for patients with stroma-low tumors. Since the role of TSR as a predictive marker for neoadjuvant chemotherapy outcome is yet unknown, this association was evaluated for HER2-negative breast cancer in the prospective DIRECT and NEOZOTAC trials.

Methods: The TSR was assessed on 375 hematoxylin and eosin-stained sections of pre-treatment biopsies. Associations between the TSR and chemotherapy response according to the Miller-Payne (MP) grading system, and between the TSR and pathological response were examined using Pearson's chi-square, Cochran-Armitage test for trend and regression analyses.

Results: A stroma-low tumor prior to neoadjuvant chemotherapy was significantly associated with a higher MP score ($p = 0.005$). This relationship remained significant in the estrogen receptor (ER)-negative subgroup ($p = 0.047$). The univariable odds ratio (OR) of a stroma-low tumor on pathological complete response (pCR) was 2.46 (95% CI 1.34–4.51, $p = 0.004$), which attenuated to 1.90 (95% CI 0.85–4.25, $p = 0.119$) after adjustment for relevant prognostic factors. Subgroup analyses revealed an OR of 5.91 in univariable analyses for ER-negativity (95% CI 1.19–29.48, $p = 0.030$) and 1.48 for ER-positivity (95% CI 0.73–3.01, $p = 0.281$).

Conclusions: A low TSR on pre-treatment biopsies is significantly associated with a higher MP score and pCR rate. Therefore, the TSR is a promising biomarker in predicting neoadjuvant treatment outcome. Incorporating this parameter in routine pathological diagnostics could be worthwhile to prevent overtreatment and undertreatment and should be investigated further.

No conflict of interest.

517 Poster

Monitoring clinical patterns in early and advanced breast cancer in Europe through population-based cancer registries data

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Background: Population-based cancer registries (CRs) collect data that enable computation of cancer incidence in a well-defined area. Moreover, most registries collect more extensive information such as data on stage and treatment (in particular first course of anticancer therapy), which can be used to assess and compare different care pathways. The current analysis reports on treatment by stage patterns for female breast cancer in Europe.

Material and methods: 829,247 female breast cancer cases from 20 CRs (based in 13 European countries) included in the European Cancer Information System (ECIS) and having submitted data on stage and treatment were analysed. Proportions of cases by first course anticancer therapy type – surgery (SG), radiotherapy (RT), systemic therapy (ST), by stage, age, period and region were calculated. Regions were defined according to the United Nations Statistics Division Geoscheme. Out of 13 countries, 3 are in Western Europe, 2 in Northern Europe, 4 in Eastern Europe and 4 in Southern Europe. Patients with stage I TNM (Union for International Cancer Control) were defined as early breast cancers, while patients with stage IV were defined as advanced cases.

Results: Treatment for stage I patients aged 19–74 years in 1999–2005 was SG alone (22%), SG+ST (13%) SG+RT (31%), SG+RT+ST (32%). SG alone decreased to 18%, while SG+RT+ST rose to 37% in 2006–13. High geographical variability was observed: in Eastern Europe SG alone was 31%, SG+ST 17%, SG+RT 24%, SG+RT+ST 23% in 2006–13 in Western Europe SG alone was 12%, SG+ST 13%, SG+RT 31%, SG+RT+ST 43%. For age group 75+ in 1999–2005 SG (37%) and SG+ST (20%) were higher than in 19–74 old patients, while SG+RT (17%) and SG+RT+SG (15%) were lower. SG decreased to 31%, SG+RT+ST rose to 20% in 2006–13. Untreated patients were 3% in both periods. For the regional comparison, in 2006–13 SG alone was 50% in Eastern Europe versus 25% in Western Europe; SG+RT+ST was 9% in Eastern Europe, while it was 24% in Western Europe. In 2006–13 for 19–74 old stage IV patients SG alone was 7%, ST alone 29%, SG+ST 18%, SG+RT+ST 14%, no treatment 9%. For patients aged 75+ years, SG was 11%, ST 30%, SG+ST 12%, SG+RT+ST 7%, no treatment 15%.

Conclusions: Variability in first course treatment patterns was observed by stage, age, period and European region. Clinical information from CRs can provide important support for monitoring clinical care patterns and informing policy, allowing comparison of levels of compliance according to national and international recommendations.

No conflict of interest.

518 Poster

BluePrint molecular subtyping recognizes single and dual subtype tumors with consequences for therapeutic guidance

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Background: BluePrint (BP) is an 80-gene molecular subtyping test that classifies early breast cancer into functional Luminal, HER2, and Basal types[1]. BP Luminal type is further stratified into A- and B-type using MammaPrint, the 70-gene test for Low and High Risk of distant relapse[2]. The BP subtype of a patient is determined by a score for each subtype based on the expression of the BP signature genes. In regular diagnostics, tumor samples with a "single BP subtype" have the highest score for that specific subtype, and lower scores for the other subtypes. However, a small proportion of tumors also exhibit a secondary subtype with a relatively high score, i.e. a "dual subtype".

Methods: BP microarray data of 9573 samples with ER, PR, and HER2 IHC/FISH status were available. Samples were classified using BP scores into single or dual subtypes based on a Maximum Allowable Difference

(MAD). These MAD values were derived of 95th percentile statistics from a distribution of repeated control sample measurements. For a dual subtype, two BP subtype scores fall within the corresponding MAD range. Full genome data was available for 7985 samples for gene expression analysis. Differential expression analysis (DEA), and pathway analysis were performed using R packages "limma" and "GSEA" respectively.

Results: Of the 9573 tumor samples, ~98% were classified as single subtype and ~2% were classified as dual subtype. The two most frequently occurring dual subtypes were Luminal B/Basal subtype (N = 96) and Luminal B/HER2 subtype (N = 87).

Tumors classified as dual Luminal B/Basal subtype show positivity for ER and no amplification for HER2 as measured by IHC/FISH. DEA analysis between Luminal B/Basal and Basal samples showed a 3-fold up-regulation of the genes AGR2 and ESR1, which are well defined as indicators for poor outcome[3] and therapeutic resistance[4], respectively.

Tumors classified as dual Luminal B/HER2 subtype had characteristics of both Luminal B and HER2 subtypes, including ER, PR and HER2 amplification as measured by IHC/FISH. DEA of this dual subtype with the single HER2 subtype showed regulation of pathways indicating higher ER response and lower MAPK and Akt activation. MAPK and Akt possess ER inhibiting capabilities and their down-regulation allows for co-expression of ER and HER2 which is linked to increased resistance to targeted therapies[5].

Conclusion: In BP diagnostic testing, the majority of samples analyzed with BluePrint show a single functional subtype, however, a small proportion of samples display a dual BP subtype. DEA shows that these BP dual subtypes have specific genomic characteristics that might help understand the biology of these tumors and further improve their treatment recommendations.

No conflict of interest.

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519 Poster

Genetic variability of PON1 and NT-proBNP levels after breast cancer radiotherapy

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Background: Radiotherapy enables good long-term local control and survival in early breast cancer patients. However, some patients experience acute or late adverse events that may decrease their quality of life. Cardiotoxicity of radiotherapy represents one of the important late adverse events. N-terminal pro-B-type natriuretic peptide (NT-proBNP) is one of the biomarkers for the evaluation of suspected heart failure. Genetic factors can also contribute to the interindividual variability in the occurrence of adverse events. Because radiation leads to increased production of reactive oxygen species and oxidative stress, our aim was to evaluate the association of polymorphisms in antioxidant enzyme paraoxonase 1 (*PON1*) with NT-proBNP levels after radiotherapy, as a marker of cardiotoxicity in breast cancer patients.

Materials and methods: We included in our study 101 HER2-positive early breast cancer patients treated with adjuvant radiotherapy. Systemic oncological treatment was prescribed according to local clinical guidelines. The NT-proBNP level was measured at a follow-up visit after the treatment. DNA was isolated from buccal swabs and all patients were genotyped for *PON1* rs854560 and *PON1* rs662 polymorphisms using competitive allele-specific PCR. Association of polymorphisms with NT-proBNP level was evaluated using nonparametric tests and logistic regression.

Results: Median follow-up after radiotherapy was 4.0 (2.6–5.4) years. Median NT-proBNP was 90 (56–157) ng/l and 36 (35.6%) patients had increased NT-proBNP (above 125 ng/l). Carriers of at least one polymorphic *PON1* rs854560 allele had lower NT-proBNP levels (P = 0.048), while carriers of at least one polymorphic *PON1* rs662 had higher NT-proBNP levels (P = 0.007) compared to carriers of two wild-type alleles. Carriers of at least one polymorphic *PON1* rs854560 allele were less likely to have increased NT-proBNP (OR = 0.34; 95% CI = 0.15–0.79, P = 0.012), while carriers of at least one polymorphic *PON1* rs662 were more likely to have increased NT-proBNP (OR = 4.44; 95% CI = 1.85–10.66, P < 0.001). The association remained significant after adjustment for clinical parameters (P = 0.017 and <0.001, respectively). Additionally, *PON1* AG haplotype was associated with the highest NT-proBNP levels (P = 0.036) and significantly increased risk for increased NT-proBNP (OR = 5.48; 95% CI = 2.10–14.29, P < 0.001).

Conclusions: Polymorphisms in *PON1* were associated with significantly different NT-proBNP levels. In the era of personalized medicine, they could serve as biomarkers for predicting heart-related treatment outcome after radiotherapy in breast cancer patients.

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No conflict of interest.

520 Poster

Normative BREAST-Q data from a Dutch population-based cohort

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Background: The BREAST-Q, a patient-reported outcome measure for cosmetic and reconstructive breast surgery, is widely used in both clinical research and practice. The aim of this study was to collect and describe normative data of the BREAST-Q from a Dutch population sample.

Materials and methods: Flyers with QR-codes, WhatsApp, and one academic center's Facebook and LinkedIn platforms were used to direct participants to self-complete an online version of 4 domains of the preoperative BREAST-Q Breast-Conserving Therapy module. Six age groups (20–29, 30–39, 40–49, 50–59, 60–69 and ≥70 years) were constructed. Normative BREAST-Q domain scores were compared between age groups using the Kruskal-Wallis test. Multivariable regression analyses were used to assess associations between age, prior non-breast cancer-related breast surgery and BREAST-Q domain scores.

Results: 9037 questionnaire responses were analyzed. Mean age for the overall group was 44 years ± SD 13, with most respondents representing the 40–49 and 50–59 age groups. Overall, the mean BREAST-Q domain scores were 64.24 ± SD 18.60 ("Satisfaction with Breasts"), 71.95 ± SD 15.93 ("Psychosocial Wellbeing"), 89.54 ± SD 12.48 ("Physical Wellbeing") and 60.38 ± SD 15.37 ("Sexual Wellbeing"). Significant score differences were found between age groups for the 4 domains ($p < 0.001$). "Satisfaction with Breasts" was significantly higher ($p = 0.002$) and "Physical Wellbeing" was significantly lower ($p < 0.001$) in patients who had prior (non-breast cancer-related) breast surgery. Multivariable linear regression analyses revealed age to be a significant predictor for "Satisfaction with Breasts" ($\beta = -0.07$, $p < 0.001$), "Psychosocial Wellbeing" ($\beta = 0.10$, $p < 0.001$) and "Physical Wellbeing" ($\beta = 0.07$, $p < 0.001$). Prior non-breast cancer-related surgery was a particular strong predictor for "Physical Wellbeing" ($\beta = 3.54$, $p < 0.001$), "Satisfaction with Breasts" ($\beta = -2.75$, $p < 0.001$) and "Sexual Wellbeing" ($\beta = -1.30$, $p = 0.03$).

Conclusion: Normative Dutch BREAST-Q data enables future comparisons in breast-related satisfaction and quality of life issues of Dutch breast cancer patients against their age-matched peers.

No conflict of interest.

521 Poster

New potential therapeutics based on natural polyphenol and SASP inhibitor combination for treating cutaneous sequelae following radiotherapy and chemotherapy in breast cancer patients

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Chemotherapy and particularly radiotherapy result in adverse cutaneous effects in breast cancer patients, leading to a clinical burden comprising

chronic skin lesions and healing impairment, reducing the quality of life of these individuals.

Dermal fibroblasts were isolated from breast cancer patients that had undergone radiotherapy and/or chemotherapy in order to investigate potential mechanisms involved in wound healing failure. Experimental techniques comprised carboxyfluorescein dye injection/transfer, western blot, quantitative real time polymerase chain reaction, immunofluorescence and wound healing scratch assay.

The results showed phenotypic changes associated with alterations in connexin43 (Cx43), a protein component of the intercellular communication channels called gap junctions. Our findings report an increase in Cx43 levels in dermal fibroblasts from patients undergoing radio/chemotherapy in comparison with healthy untreated ones, but decreased gap junction-mediated intercellular communication (GJIC). These changes correlated with accumulation of beta-galactosidase positive senescent cells. Fibroblasts isolated from irradiated skin biopsies and those obtained from healthy untreated skin that were then experimentally irradiated in a lineal accelerator showed the same phenotypic changes and increased senescence levels, as determined by cytochemical detection of β-galactosidase activity and gene and protein expression of senescence factors p53 and p21, as well as senescence-associated secretory phenotype (SASP) components MMP-3, IL-1ß and IL-6. Treatment with the olive-derived phenolic compound oleuropein significantly reduced Cx43 levels, restored GJIC and significantly attenuated cellular senescence. Combination therapy with the pan-p38 MAPK SASP inhibitor doramapimod (BIRB 796®) decreased SASP production and significantly improved irradiated fibroblast migratory capacity in *in vitro* wound healing assays.

These data provide a two-molecule combinational approach that can potentially contribute to ameliorate secondary cutaneous effects of radiotherapy and chemotherapy in oncological patients by reducing senescent cells accumulation and SASP production, as well as restoring GJIC in dermal fibroblasts.

No conflict of interest.

522 Poster

Fatty acid inhibition reduces MYC expression in triple-negative breast cancer

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Background: Triple negative breast cancer (TNBC) is a clinically aggressive subtype of breast cancer that is associated with the over-expression of oncogenic transcription factor c-MYC (MYC). MYC drives cell growth by increasing proliferation, metabolism, and protein synthesis. Overexpression of MYC is also linked to tumor immune evasion. Because clinical-grade small molecule inhibitors against MYC remain elusive, our lab and others have worked to understand ways to therapeutically target MYC-specific cellular processes. Our group discovered that fatty acid oxidation (FAO) is an important source of energy production in TNBC, and disruption of fatty acid oxidation leads to cell death in MYC over-expressing TNBC tumors, but not in tumors with low MYC expression. Critically, how FAO inhibition specifically changes cellular signaling in MYC high tumors is unknown.

Materials and methods: To answer this question, we used MCF10A-MYC cells, a human mammary epithelial cell line engineered to overexpress MYC, to study cell proliferation and changes in protein expression upon FAO inhibition. Cell proliferation was measured on a BioTek's Cytation 5 Live Cell Analysis System. Protein expression was measured by western blot.

Results: We first confirmed that etomoxir, a small molecule inhibitor for carnitine palmitoyl transferase I (CPT1), inhibited cell proliferation in MCF10A-MYC cells. We found etomoxir treated MCF10A-MYC cells had a decrease in cell proliferation compared to the vehicle treated cells. Furthermore, the MCF10A-MYC cells displayed lower levels of MYC protein expression following treatment with etomoxir, but MYC expression did not change with etomoxir in parental MCF10A cells.

Conclusions: Our preliminary findings suggest etomoxir downregulates MYC expression, warranting further studies on FAO inhibition in TNBC as a potential target for combination therapeutics in this subtype of breast cancer. Future studies will examine how MYC is downregulated and whether targeting MYC with Etomoxir, or perhaps other drugs that inhibit FAO, may be rationally combined with other therapeutics such as immunotherapy.

No conflict of interest.

Follow up

523 Poster

The effect of postoperative complications on survival and recurrence after surgery for breast cancer: A systematic review and meta-analysis

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Background: This systematic review investigated the impact of complications on long term outcomes for patients with primary invasive operable breast cancer.

Methods: A systematic review and meta-analysis was performed using appropriate keywords, and meta-analysis using a random effects model completed.

Results: Ten retrospective cohort studies, including 37657 patients were included. Five studies identified a relationship between wound complications, infection and pyrexia and recurrence or recurrence-free survival. Risk of recurrence, 1-year and 5-year recurrence-free survival and overall survival were related to complications, particularly for patients with poor Nottingham Prognostic Index. Five studies failed to demonstrate a relationship between complications and prognosis. Complication was found to significantly affect 5-year recurrence-free survival (HR 1.48 95% CI 1.02–2.14, p = 0.04) but not recurrence (HR 2.39, 95%CI 0.94–6.07, p = 0.07), with a high degree of heterogeneity among analysed studies (I^2 = 95%).

Conclusions: Further research is needed to quantify the effects of postoperative complication on prognosis following surgery for breast cancer.

No conflict of interest.

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Patient-reported healthcare utilization among Medicare beneficiaries with HR-positive, HER2-negative early breast cancer

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Background: This study assessed healthcare utilization among female Medicare beneficiaries with hormone receptor-positive (HR+), human epidermal growth factor receptor 2-negative (HER2-) early breast cancer (BC) and similar matched women without breast cancer.

Material and methods: A retrospective cohort study was conducted using the Surveillance, Epidemiology, and End Results (SEER) Consumer Assessment of Healthcare Providers and Systems (CAHPS) Data Resource to characterize HRU among HR+/HER2- stage I-III BC patients aged ≥18 years between 2010 and 2013. Information from longitudinal patient surveys and SEER cancer registry records were collected. Patient-reported healthcare utilization in the prior 6 months was analyzed, including visits to personal and specialist physicians, routine care, hospitalizations, and the number of prescription medicines filled. BC cases were matched to up to five female Medicare beneficiaries as non-cancer controls by age, survey year, race/ethnicity, education, mode of survey, and SEER region of residence. Differences in healthcare utilization were compared within 6-month intervals (1–6, 7–12, 13–18, and 19–24 months) after diagnosis using chi-square tests for categorical variables and Wilcoxon rank-sum tests for medians of continuous variables.

Results: In a cohort of 889 patients with HR+/HER2- early-stage BC [mean age 73 years; standard deviation 8 years], most patients were diagnosed with AJCC stage I (65%) grade 1–2 (82%) disease, were node-negative (78%), had a tumor size <2 cm (74%), and received breast-conserving surgery (64%). Matched non-cancer controls (n = 4,167) were

similar to BC cases with respect to the number of comorbidities, Medicare subsidy status and dual eligibility. Within the first 6 months and between 7 and 12 months, the number of visits to a personal doctor, specialists, routine care, and any hospitalizations were greater for BC cases than matched non-cancer controls (all p-values <0.05). Healthcare utilization during 13–18 and 19–24 month periods was greater among BC cases for number of visits to a specialist and for routine care (p-values <0.001); differences between patients with BC and controls were not observed for hospitalizations (p = 0.68), visits to personal physician (p = 0.15), or prescription medications (p = 0.05) by months 19–24 post-BC diagnosis.

Conclusions: Compared to non-cancer controls, patients diagnosed with HR+/HER2- non-metastatic BC reported higher healthcare utilization in the first two years after diagnosis. However, differences attenuated in the second year, indicating the burden of treatment and follow-up lessened over time.

Conflict of interest:
Ownership:
Pfizer Inc (Shareholder/Stockholder/Stock options): Cueto J, Mitra D, Law E
Other Substantive Relationships:
University of Illinois at Chicago (employee): Calip G S, Hoskins K F, Zhou J, Deng H, Naing K, Nabulsi N, Hubbard C C
Boston University School of Medicine (employee): Ko N Y
Pfizer Inc (employee): Cueto J, Mitra D, Law E
Pfizer Inc (paid consultants): Calip G S, Hoskins K F, Ko N Y, Zhou J, Deng H, Naing K, Nabulsi N, Hubbard C C

525 Poster

Standard treatment in very old breast cancer patients. Recommended or not recommended?

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Background: As older patients with breast cancer are often not included in clinical trials, we currently have a limited number of specific recommendations available for their management. In this paper, we are presenting a single-center study describing the influence of older age on breast cancer treatment and prognosis.

Material and methods: This study is a retrospective analysis of patients older than 75 years treated between January 2010 and December 2018. We evaluated the effect of under-treatment (UT), defined as any deviation from the guidelines based on cancer stage and biological sub-type, on overall survival (OS), local recurrence-free survival (LRFS), systemic recurrence-free survival (SRFS) and disease-free survival (DFS), stratified by age (75–85 yrs and >85 yrs). This analysis was performed using the log-rank test.

Results: Among all cases we treated, we selected 408 patients. Of these, 356 were aged 75–85 yrs, and 52 were aged >85 yrs. Moreover, 201 patients were UT (156 patients in the 75–85-year group, and 45 patients in the >85-year group). In all patients >75 years, worse OS (p < 0.001), LRFS (p = 0.008) and SRFS (p = 0.042) were observed in the under-treated group as compared to the treated (T) group, while DFS showed no changes. UT appeared to have no impact on DFS also when the two age groups were considered separately (p = 0.567 and p = 0.152). When the two groups were considered separately, OS and LRFS appeared to be not affected by UT in the >85 yr group (p = 0.476 and p = 0.834, respectively), but to be worse in the 75–85 yr UT group (p < 0.001 and p = 0.007, respectively). Moreover, while a worse SRFS was noticed in the >85 yr UT group (p = 0.031), it did not appear to be affected by UT in the 75–85 yr group (p = 0.119).

Conclusions: Comparison between T and UT patients showed that adherence to the standard of care improved OS, LRFS and SRFS, as described in literature. Indeed, in the most elderly patients, OS is not affected by UT. Therefore, in these patients, a minimum therapy could be recommended, in accordance with performance status, without consequences on prognosis.

No conflict of interest.

526 Poster

A prospective analysis of patient-reported outcomes within breast cancer surgical treatment strategies

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Background: Although patient-reported outcomes (PROs) are increasingly assessed within breast cancer care, there is limited knowledge about short-term PRO scores following various surgical treatments. This study sought to investigate short-term PRO scores in breast cancer patients after either breast-conserving therapy (BCT) or conventional mastectomy.

Methods: Breast cancer patients, who had undergone surgical treatment at the Erasmus University Medical Center between October 2015 and July 2019, were included. PROs were measured from prior to surgery to one year postoperatively using the BREAST-Q, EORTC-QLQ-C30 and EORTC-QLQ-BR23 questionnaires. Multiple imputation was used to account for missing responses. Within surgical treatment strategies, PRO domain scores at different follow-up points were compared with repeated measures ANOVAs.

Table 1 Baseline characteristics of all breast cancer patients (N = 213), according to surgical strategy

	All patients (N = 213)	Missing/ Unknown, N (%)	BCT (N = 143)	Conventional mastectomy (N = 70)	p-value
Age, median [IQR]	58 [47–67]	3 (1.4)	58 [47.3–67]	59 [47–70]	0.57
Smoking (past/ current), N (%)	23 (10.8)	3 (1.4)	17 (11.9)	6 (8.6)	0.35
BMI, N (%)		3 (1.4)			0.61
<25	80 (37.6)		49 (34.3)	31 (44.3)	
25–30	96 (45.1)		68 (47.6)	28 (40)	
30–35	28 (13.1)		19 (13.3)	9 (12.9)	
>35	6 (2.8)		4 (2.8)	2 (2.9)	
ASA-classification, N (%)		3 (1.4)			0.43
1	78 (36.6)		55 (38.5)	23 (32.9)	
2	118 (55.4)		77 (53.8)	41 (58.6)	
3	13 (6.1)		8 (5.6)	5 (7.1)	
Menopausal status, N (%)		3 (1.4)			0.10
Pre-Menopause	49 (23)		31 (21.7)	18 (25.7)	
Peri-Menopause	31 (14.6)		26 (18.2)	5 (7.1)	
Post-Menopause	130 (61)		83 (58)	47 (67.1)	
Gene Mutation Carrier, N (%)	8 (3.8)	105 (49.3)	5 (3.5)	3 (4.3)	0.02

Results: 213 breast cancer patients were included: 143 (67%) underwent BCT and 70 (33%) conventional mastectomy. A significant improvement in "Body Image" at 12 months follow-up (Δ T0-T12 = +6.57, p < 0.01) was observed for patients following BCT, while "Physical Wellbeing" (Δ T0-T12 = –11.00, p < 0.001), "Physical Functioning" (Δ T0-T12 = –7.87, p = 0.002) and "Sexual Wellbeing" (Δ T0-T12 = –18.00, p < 0.001) had significantly declined. Significantly reduced median "Satisfaction with Breasts" (Δ T0-T12 = –8.00, p = 0.04) and "Psychosocial Wellbeing" (Δ T0-T12 = –7.00, p = 0.03) scores were reported at one year following conventional mastectomy.

Conclusions: Most significant differences in PRO domain scores were observed in patients following BCT. The course of PROs during follow-up may help both patients and clinicians to better understand the impact of (surgical) treatment for breast cancer, and manage expectations.

No conflict of interest.

527 Poster

A review of subsequent breast cancers detected on mammographic surveillance following Vacuum Assisted Excision for lesions of uncertain malignant potential (B3) with atypia

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Background: There is a spectrum of lesions that fall into the category of 'uncertain malignant potential' (B3). These lesions are often associated with atypia, insitu or invasive carcinoma. Therefore, once these lesions are discovered on biopsy, it necessitates the need to ensure adequate sampling to exclude focal carcinoma. Vacuum Assisted Excision (VAE) has become the management of choice of B3 lesions <3 cm which meet criteria as set out by NHSBSP B3 guidelines. Because B3 lesions with atypia confer a risk for a future breast cancer, it is important to ensure mammographic follow up following VAE to allow early diagnosis of a potential subsequent cancer. Our departmental protocol for surveillance of VAE/Vacuum Assisted Core Biopsy histology demonstrating atypia is annual mammography for 5 years, followed by return to routine biennial screening thereafter.

Material/methods: We conducted a retrospective review of all VAE cases performed in our screening centre over a 5 year period in women aged 50–68 years old, who underwent mammographic surveillance for excised lesions of

uncertain malignant potential (B3) with atypia. Of this group, we identified cases of subsequent cancers which were detected using consensus review on annual surveillance mammography.

Results: Between 2015 and 2020, a total of 264 women underwent VAE in our screening centre as a result of B3 histology from core/vacuum assisted biopsy of a screen detected lesion. Of these 264 women, 128 women (48%) demonstrated atypia on biopsy and/or VAE histology and it was recommended for them to undergo annual mammographic surveillance for 5 years, followed by return to routine screening. A total of 104 women (39%) demonstrated benign histology on VAE and could return to routine screening. Diagnostic surgery was required in 13 women (5%) and therapeutic surgery for upgrade to malignancy was required in 19 women (7%). Of the 128 women who have been undergoing annual surveillance for atypia, 4 women have had a subsequent cancer detected on surveillance (2 in the same breast near site of excision and 2 in the contralateral breast). 1 woman had cancer detection on her first year of surveillance, 2 women had cancer detection on their second year of surveillance and 1 woman had cancer detection on their third year of surveillance.

Conclusion: Breast lesions with atypia confer an increased risk of future malignancy. In our cohort of women who underwent annual mammographic surveillance following VAE for B3 lesions with atypia, 3% developed a subsequent cancer. Half of these subsequent cancer cases occurred in the same breast as the site of the previous B3 with atypia and half occurred in the contralateral breast. This demonstrates the importance of close mammographic surveillance following VAE for lesions with atypia, not just focussing on the site/side of previous VAE, but also in the contralateral breast.

No conflict of interest.

528 Poster

Impact of COVID-19 on Breast clinic follow ups – a new way forward?

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Background: The global pandemic of coronavirus disease 2019 (COVID-19), caused considerable change to working practices in breast units across the UK. Prior to March 2020, at the Princess Royal University Hospital (PRUH), Kings College NHS Trust, Kent, almost daily face to face breast clinic follow ups occurred. This consisted of patients with both benign and malignant conditions. It encompassed post investigation/operative results, pre-operative planning, benign follow ups and 5 year surveillance patients. On March 23rd 2020 the UK went into official lockdown. The effect on breast elective follow up practice was swift. There was a move to cancellation and triaging of the majority of our follow ups, with replacement of face to face with telephonic or virtual consultations.

The aim of this study was to review the change of the follow up pattern, comparing pre and post COVID-19 setup, could this effect the future of follow up consultations at PRUH?

Material and methods: A comparison of all patients attending PRUH breast unit outpatients in January 2020 (pre COVID-19) for follow up and with those attending in April 2020 (post COVID-19). Categories analysed included numbers of patient attendances, patient demographics, type of follow up, and original diagnosis. All data was collected from clinic lists and electronic patient record notes and analysed using Excel version 16 (365).

Results: 368 patient follow ups were booked into clinic in Jan 2020 with 25 not attending (DNA's), overall 343 attendances. 59 patient follow ups were booked in April 2020 with 6 DNA's, overall 53 attendances. The mean age in January was 57 and in April 51. Sex distribution in January F:M 336:7 (98%:2%) was similar to that in April F:M 51:2. In January 65% of cases were malignant and 60% in April. Benign/B3 diagnosis were 35% in January and 20% in April.

	5 year surveillance	Benign f/up	Post Biopsy Results	Post Investigation Results	Post Operative Results	Pre Operative Planning	Primary Endocrine f/up
Pre COVID – April 2020	134(39%)	15(4%)	26(8%)	79(23%)	68(20%)	16(5%)	5(1%)
Post COVID – April 2020	5(9%)	7(13%)	14(26%)	15(28%)	11(21%)	2(3%)	0(0%)

Summary of follow up types

Conclusions: Impacts of COVID have been widespread in our practice. Our results show a significant reduction in face to face appointments. Further evaluation of this model will show if this is sustainable. Patient satisfaction will also have to be taken into account and assessed. Implementation of 5 year post cancer treatment surveillance without a clinical follow up (open access follow up) is becoming a standard practice in many breast units. Social distancing in the waiting areas has been one of the limiting factors for face to face consultations. Options of video/telephone consultations are a possibility, although clinical review is sometimes necessary.

No conflict of interest.

Genetics

529 Poster

The psychosexual effects of risk reducing bilateral salpingo-oophorectomy in female BRCA1/2 mutation carriers: A systematic review

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Introduction: Breast and ovarian cancer account for approximately 15000 deaths per year in the United Kingdom. It is estimated that up to 20% of these cases have an inherited genetic aetiology. The most common genetic mutation occurs in the *BRCA1* or *2* genes. For women with mutations in these genes, or a high incidence of breast and/or ovarian cancer in their family, risk-reducing bilateral salpingo-oophorectomy (RRBSO) may be offered to eliminate the risk of primary ovarian cancer. In pre-menopausal women this results in immediate onset of surgical menopause. Women experience menopausal symptoms including hot flushes, vaginal dryness, loss of libido and dyspareunia. This article sought to explore the psychosexual impacts of risk reducing bilateral salpingo-oophorectomy in the published qualitative literature.

Methods: PubMed, Medline, Web of Science and PsycInfo were searched for qualitative papers that looked at the impact on RRBSO on individuals who were pre-menopausal at the time of surgery. Studies were quality assessed and data was extracted. Thematic synthesis of the results was performed.

Results: Of 143 papers identified in searching, 5 qualitative papers were identified relating to interviews with 115 women after RRBSO published between 2000 and 2012. The quality of the papers was moderate. Five different themes were identified related to individual experiences with RRBSO; (1) information needs, (2) psychological impact, (3) psychosexual impact, (4) partner support and (5) hormone replacement therapy (HRT). Women felt under prepared for the impact of the surgery and felt that their information needs were not sufficiently met. The psychological impact of the surgery was generally positive with women expressing a sense of relief after taking control of their cancer risk. The psychosexual impact was more negative and many women experienced difficulty with the changes they encountered post-surgery which lead to dissatisfaction with their sexual relationships. Partner support was varied and women often felt supported pre-surgery but then expressed frustration as their partners could not understand why their sex life had changed following the surgery. For some women HRT was able to significantly reduce the negative impact of the surgery. Other women were unable to take HRT due to side effects or their perceived increased risk of breast cancer and so they felt that the surgery had a hugely negative impact on their life.

Conclusion: Individual experiences of RRBSO were varied and influenced by multiple factors but psychosexual problems were common, often caused significant distress to the women and her partner and were often poorly explained before surgery. There is a need for better counselling both pre- and post-surgery to ensure that women are aware of the side-effects of the surgery and how to mitigate and manage them.

No conflict of interest.

530 Poster

Frequency and spectrum of mutations in the BRCA1, BRCA2, PALB2, P53, PTEN, CHEK2, CDH1 genes in women from 3 cities of Colombia

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Background: Germline mutations in the BRCA1 and BRCA2 genes confer a life time risk of 40–80% of developing breast cancer, while mutations in TP53, PTEN CDH1, PALB2, CHEK2 confer moderate to high life time risk for this disease. It is important to detect these mutations in order to give genetic counseling and specific treatment. There are a few high frequency mutations in Colombia: A1708E (BRCA1), 3450delCAAG y 3034delACAA (BRCA2). The aim of this study is to determine the frequency and spectrum of mutations in 7 genes in women with breast cancer unselected living in three cities of Colombia.

Material and methods: 135 patients with breast cancer unselected between the ages of 25–77 were recruited in 6 health centers from Medellin, Cali and Barranquilla. DNA was extracted from blood samples by salting out; then exons and 20 nucleotides in the intron-exon boundaries of the BRCA1, BRCA2, PALB2, P53, PTEN, CHEK2 and CDH1 genes were sequenced by next generation sequencing on the ion torrent platform. Raw signal data were analyzed using Torrent SuiteTM ®, The pipeline included Quality control, read alignment to human genome 19 reference (with TMAP), quality control of mapping quality, coverage analysis, and variant calling using the torrent variant caller 5.0–7 (SNVs and INDELs) and GATK (for SNVs). The variants were annotated with the Ion reporter software and classified according to the following databases: Clinvar, Leiden Open Variation Database and Wintervar. The new variants were classified using Intervar. Pathogenic mutations were confirmed by sanger sequencing. The carriers received genetic counseling by an oncogenetist.

Results: Six pathogenic mutations (frequency of 4.4%) were found in these patients: BRCA1: C.5186C>A, C.178C>T and C.213-12A>G, BRCA2: C.7007+1G>A y C.631+3A>G and TP53: C.586C>T. one variant of uncertain significance showed pathogenic evidence in silico (CHEK2: C.497A>G) and it was found in three cases.

Conclusions: This is the first study in Colombia that evaluates genes different from BRCA1 and BRCA2 in unselected cases in Colombia, and the frequency of pathogenic mutations was 4.4%. three mutations were found in splicing sites, so it is important to include these sites in the sequencing. Here, we report 4 new pathogenic mutations for the Colombian population. The mutation C.497A>G has a great pathogenicity in silico, it should be validated in vitro for his reclassification.

No conflict of interest.

531 Poster

Positive correlation between high breast cancer incidence and ancestry in Colombian population

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Background: Breast cancer is the most frequent cancer in women in the world, however, breast cancer incidence varies substantially world-wide. This disparity can be caused by exposure to reproductive, environmental, lifestyle risk factors, and genetic factors among which is genetic ancestry associated with breast cancer risk. The genetic ancestry is a factor that can influence the risk of many diseases, because of genetic admixture among ancestral source populations from Africa, the Americas and Europe. Colombian population have a trihybrid gentic structure that reflects a early mixed of ancestral populations (indigenous amenricans, europeans and africans), and in the conuntry has been reported a high heterogenety in the breast cancer incidence rates. In this study we investigated how genetic ancestry in admixed colombian population may correlated with the distribution of the breast cancer incidence and mortality rates.

Materials and methods: This study included genetic information of 849 women from 4 departaments of Colombia, the average of ancestry was estimated using a 102 Informative Markers panel in the ADMIXTURE program. Additionally we did a systematic review following the Cochrane handbook for imformatión of ancestry the others departaments. The incidence and mortality information was obtained from last report of National Cancer Institute of Colombia.

Results: High incidence rates have the similar distribution pattern as the ancestral component. We found a significant correlation between european ancestry and highest breast cancer rates (R2 = 0,422 p = 0,0025) in colombian population, in comparison with the others ancestral components (indigenous americans (R2 0,022 p 0,53 and africans R2 0,122 p 0.13). The trend is the same for mortality rates and the ancestrals compounds.

Conclusions: This study evidence the association between Europen ancestry and high breast cancer incidence rates in the colombian population, one a advantage is the employment of genetic data, compared to other ecological studies where they use self-report of ancestry. In the future, this results will can be considered in the design and employment of strategies for identifying susceptible populations and try to reduce the breast cancer incidence rate in Colombia.

No conflict of interest.

Lifestyle, Prevention including Secondary Prevention

532 Poster

Effects of organised mammography screening on breast cancer care in specialist breast units in Aachen, Germany since 2008

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Background: Two specialist breast units were established in the Region of Aachen, Germany in 2004. Organised mammography screening was introduced in 2008. This study investigates the impact of the screening program on breast cancer stage distribution and diagnosis and treatment of affected women.

Materials and methods: All breast cancer cases treated in the two specialist breast units (University Hospital-Luisenhospital Aachen and Marienhospital Aachen) were documented by data entry into the EUSOMA QT database (Quality Treatment Audit System) since January 1, 2004. Screening-detected breast cancers were compared to conventionally diagnosed cases with respect to stage at diagnosis, surgical and adjuvant treatment in two-year periods since the beginning of the organised screening program.

Results: Between 2004 and 2019, a total of 7.536 breast cancer cases were treated in the two specialist breast units in Aachen. Since the introduction of the screening program, an increase in the number of cases with a steady decline of advanced stages at diagnosis was observed. The proportion of lesions >2 cm (pT2-pT4) decreased from 18.7% (Round 1) to 10,5% in Round 6 (2018–2019) among 944 screening-detected breast cancers. Also in the remaining 2.016 conventionally diagnosed cases among women of the same age-group, a decline of advanced stages >2 cm was noted from 42% (2008–09) to 27,5% (2018–19).

Table 1 Number of Breast Cancer Cases treated in two specialist breast units in Aachen 2004–2019 by type of diagnosis

Total breast cancer cases 2004–2019	Breast cancer cases since start of organised screening 2008	Screen-detected breast cancers	Conventionally diagnosed breast cancers (all age-groups)	Conventionally diagnosed breast cancers (age-group 50–69 years)
17.5367	5.721	944	4.777	2.016

Improvement of diagnostic quality was reflected in less radical treatment approaches with respect to breast conserving treatment and systemic therapy. The indication for adjuvant chemotherapy more than halved from 41% (Round 1) to 20% (Round 6) in screen-detected cancer cases and also declined from 54% to 43% in the conventionally diagnosed breast cancers among women of the same age-group.

Conclusions: A notable impact on stage distribution at diagnosis and less aggressive treatment choices for women with breast cancer was shown after implementation of the organised breast cancer screening program. Even for non-participants a continuous decline of advanced stages at diagnoses and resulting benfits with higher rates of breast conserving surgery and less systemic chemotherapy were observed. The beneficial effects of organised breast screening programs is demonstrated also in long-term clinical breast cancer care data.

No conflict of interest.

533 Poster

A dedicated osteoporosis service improves bone health standards for aromatase inhibitor associated bone loss in Breast Cancer patients

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Background: Aromatase inhibitors (AI's) are the gold standard adjuvant treatment for post-menopausal women with oestrogen-receptor positive breast cancer (BC) but accelerate bone loss and increase fracture risk.

NICE guidelines recommend all post-menopausal patients starting adjuvant aromatase inhibitor therapy should undergo measurement of baseline bone mineral density (BMD) with Dual Energy X-ray Absorptiometry (DEXA) with a follow up scan at 24 months if medium or high fracture risk or clinically indicated.

We present a re-audit of our unit's compliance with national bone health standards following the introduction of a separate dedicated service run by an Osteoporosis nurse specialist and Elderly Care physician in November 2013.

Materials and methods: Local trust audit approval was obtained. We performed a retrospective study of 200 consecutive BC patients commenced on an AI between 1st September 2016 and 31st May 2017.

Number of patients undergoing baseline scan and 24 month follow up scan were recorded.

Results: 198/200 (99%) underwent a baseline scan. 168 of the 187 (89%) indicated follow up scans were performed. Of the 61 patients initially deemed low risk, 50 underwent a repeat scan as this was felt to be clinically indicated. Of these, 10 patients progressed placing them in the medium risk group on subsequent scan.

Conclusions: Since our initial audit in 2010 we have improved our baseline DEXA scan rate from 54% to 99% and our 24 month follow up scan rate from 28% to 89%.

More work is required to help clinicians further stratify low risk patients and avoid unnecessary DEXA scans.

No conflict of interest.

534 Poster

Patients reported outcomes (PRO) in breast conserving treatment

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Background: Early breast cancer patients have a high survival due to improvement in treatments and sreening programs. It is very important to focus how treatments impact in their quality of life.

The objetive of this study is to determinate whether the type of radiotherapy technique after breast conserving therapy has an impact on patient-reported satisfaction and quality of life, as well as provide reliable and valid evidence regarding patient outcomes.

Material and methods: We analyzed 169 consecutive patients with early breast cancer after conservative treatment between 2017 and 2019.

Breast-Q questionnaire® (postoperative conservative therapy module) was provided to patients 6 months after the end of the radiotherapy.

We compared two different radiotherapy techniques, acelerated partial breast irradiation (APBI) with brachytherapy in one 18 Gy fraction and external beam radiotherapy (EBRT), hypofractionated in 15 fractions plus a boost of 3 fractions.

We used the W - Wilcoxon signed-rank test to compare the patient satisfaction after different treatments.

Results: 84% of patients were treated with external beam radiotherapy and 16% with brachytherapy in one 18 Gy fraction.

70% of patients were treated with selective sentinel node biopsy and 18% with lymphadenectomy and 12% no axillary treatment. 24,9% of patients treated with EBRT received axillar plus infra-supraclavicular nodes.

We only found statistically significant differences in the radiation adverse events, with a median of 78 (EBRT) versus 89 (APBI), p 0,027.

Conclusions: Patients treated with APBI with brachytherapy had higher levels of satisfaction with the treated breast than those who received external beam radiotherapy.

All patients eligible for APBI should be considered to be treated with brachytherapy.

No conflict of interest.

535 Poster

Survival benefit of surveillance for postoperative metastasis in breast cancer patients

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Introduction: The surveillance for postoperative metastasis in asymptomatic breast cancer patients has been a debate. The purpose of this study is to analysis survival benefit of surveillance for postoperative metastasis in breast cancer patient.

Methods: We conducted a retrospective study of metastatic breast cancer patients who underwent breast surgery between 2010 and 2014 in Samsung Medical Center. A total 316 breast cancer patients with distant metastasis were identified. The patients were divided into two groups based on the way of metastasis detection, whether surveillance (asymptomatic group) or patient's symptom (symptomatic group); the asymptomatic group had 204 patients (64.6%) and the symptomatic group had 112 patients (35.4%).

Results: Characteristics of the patients between the two groups were well balanced. Mean age was 46.0 years. Breast conserving surgery was performed 51.9% and axillary lymph node dissection was performed 73.1%. Invasive ductal carcinoma was 92.7% and stage II was 42.7%. There were significantly more patients with hormone receptor (HR) -positive in asymptomatic group (69.7% vs 53.6%, p = 0.013). There were significantly more patients who received neoadjuvant chemotherapy (28.4% vs 42.0%) or radiotherapy (76.0% vs 90.2%) in symptomatic group. In multivariate analysis for overall survival, the hazard ratio for symptomatic group was higher than that for asymptomatic group. When stratified by subtype, luminal subtypes and triple-negative breast cancer subtype showed significantly better prognosis in asymptomatic group than symptomatic group, whereas HER-2 subtype showed no significant difference.

Conclusion: Breast cancer patients who were diagnosed distant metastasis before symptom occurs had better prognosis than patients with symptom. When stratified by tumor subtype, asymptomatic patients with luminal subtype or triple-negative breast cancer subtype had better prognosis than symptomatic patients, whereas HER-2 subtype had no significant difference. Our findings recommend the need for surveillance in breast cancer patients.

No conflict of interest.

Local Regional Treatment – Radiotherapy

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Single pre-operative radiation therapy – with delayed surgery for low risk breast cancer (SPORT-DS)

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Background: Treatment of early-stage invasive breast cancer is rapidly evolving. Breast-conserving surgery followed by several weeks of adjuvant radiotherapy is the current standard of care. A novel approach using single-

fraction neoadjuvant radiotherapy is under study. We sought to investigate the rate of pathologic response and postoperative toxicities related to delaying surgery after neoadjuvant radiotherapy.

Methods: Women 65 years of age or older with a new diagnosis of stage I unifocal luminal A breast cancer were eligible for inclusion. A single 20 Gy dose of radiotherapy to the primary breast tumor was given, followed by breast-conserving surgery 3 months later. The primary endpoint was the pathologic response rate assessed by microscopic evaluation using the Miller-Payne system. The secondary endpoint was the incidence of radiation toxicity, graded according to the Common Terminology Criteria for Adverse Events (CTCAE). The toxicity was planned to be assessed at 6 weeks, 4 months, 12 months and yearly for up to 5 years after radiotherapy.

Results: To date, 13 patients have been successfully treated and had completed the 4-month follow-up. Median age of patients was 71 years (range: 65–83 years). Neoadjuvant radiotherapy resulted in a tumour pathologic response in 11 of 13 patients with a median residual cellularity of 1% (range: 0–10%). At the 4 months' toxicity assessment, 10 patients developed grade 1 toxicities (dermatitis, telangiectasia, fibrosis, breast pain, breast swelling and chronic mastitis), and 3 patients developed grade 2 toxicities (dermatitis, fibrosis and skin or wound infection). No grade 3 or higher toxicities were noted.

Conclusion: This study demonstrates that delaying surgery after a single fraction of neoadjuvant radiotherapy can lead to a high level of pathologic response in most patients and is relatively well tolerated with acceptable toxicity. Continued follow up of our patients and subsequent larger trials are needed to better assess the late radiation toxicities as well as the optimal fractionation and timing of this novel technique in the management of early-stage breast cancer.

Trial registry number: NCT03917498

Trial status: Recruiting

Trial sponsor(s): Hôpital Maisonneuve-Rosemont

No conflict of interest.

537 Poster

Dosimetric impact of an AI-based delineation software satisfying international guidelines in breast cancer radiotherapy

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Background: Delineation is time consuming in radiation oncologist's daily life and prone to inter-expert variability. Automatic delineation (AD) allows time saving, practice harmonization and may result in qualitative improvement. The objective of this study was to evaluate, based on a retrospective monocentric cohort of breast cancer patients treated before 2015, the clinical impact of the use of an Artificial Intelligence (AI)-based solution for organs-at-risk (OAR) and target volume delineation, respecting international guidelines.

Material and methods: A CE-marked solution for AD harnessing a unique combination of anatomically preserving and deep learning delineation concept was developed. Using transfer learning, the model was tuned to respect the 2015 ESTRO guidelines, through the integration of 256 cases randomly selected from the HYPOG-01 trial. Forty-four patient cases were retrieved for which 3D-conformal radiotherapy (3D CRT) was prescribed. For each case, AD was generated and minor corrections were applied when necessary. Dosimetric maps used in clinic were then transferred without plan re-optimization on the AD to evaluate the dosimetric relevance of the delivered plans. Dosimetric values were compared using a Wilcoxon test. Qualitative evaluation consisted in scoring each plan as A (Dosimetry accepted), B (Minor correction required) or C (Dosimetry rejected) based on the HYPOG-01 dosimetric constraints.

Results: Dosimetric objectives were met with AD and manual delineations (MD) for all OARs as shown in Table 1 for 50 Gy prescription. The majority (91%) of thoracic wall treatments included axillary and internal mammary nodes (IMN). All of them were scored as "B" or "C" in AD configuration as 3D CRT was responsible for field junction undercoverage. 3/26 cases of 50 + 16 Gy prescription were scored as "C" in AD. These cases included axillary nodes treatment without MD, showing that this region was underdosed in clinical practice.

Table 1. Dosimetric comparison between MD and AD for 50 Gy prescription (mean dose; standard deviation) (n = 11) – ND: Not Done

	Manual Delineation	Auto Delineation	p-Value (Wilcoxon test)
CTV Breast			
D95 (Gy)	38.01 (9.44)	37.62 (12.48)	0.58
D2 (Gy)	54.45 (0.96)	54.70 (1.17)	0.06
Dmean (Gy)	49.16 (2.00)	49.23 (2.22)	0.41
Volume (cm3)	399.49 (195.09)	386.49 (204.51)	0.21
CTV Level 3 (D95, Gy)	ND	41.98 (3.64)	
CTV Level 4 (D95, Gy)	ND	44.02 (2.82)	
CTV IMN (D95, Gy)	ND	18.10 (9.09)	
Ipsilateral lung			
V20 (%)	21.75 (5.18)	17.40 (3.34)	0.10
Dmean (Gy)	11.31 (2.04)	11.67 (2.08)	0.10
Heart			
V20 (%)	2.98 (2.23)	2.78 (1.96)	0.41
V40 (%)	1.27 (1.70)	1.74 (2.23)	1.00
Spinal cord			
Dmax (Gy)	5.96 (6.03)	5.18 (4.23)	0.67

Conclusions: Even if dose plans were performed before ESTRO recommendations, dose constraints were respected for all OARs. Axillary nodes delineation should improve coverage of target volumes and AD could contribute to this coverage improvement.

No conflict of interest.

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Effects of adjuvant breast radiotherapy delivered over one week (+/– sequential hypofractionated tumour bed boost): Prospective observational study confirming acceptable acute skin toxicity

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Purpose: For patients requiring adjuvant breast radiotherapy the landmark FAST-Forward trial has recently shown that delivering 26 Gy in 5 fractions over one week is non-inferior to the moderately hypofractionated schedule 40 Gy in 15 fractions delivered over 3 weeks, both in terms of acute and late toxicity and 5-year local tumour control. This study aims to confirm the pattern of acute skin toxicity resulting from this treatment regimen as well as reporting the acute skin toxicity rates associated with the addition of a sequential boost.

Methods: This multicentre prospective observational study included consecutive patients who attended for adjuvant breast radiotherapy and received 26 Gy in 5 fractions over 1-week (± sequential hypofractionated tumour bed boost) April–July 2020. Acute skin toxicity was recorded during virtual consultations the week of treatment (baseline) and 1, 2, 3, and 4 weeks post-treatment using CTCAE v4.03 scoring criteria. To allow comparison, the primary endpoint was as per the FAST-Forward trial: the proportion of patients with grade $\geqslant$3 toxicity at any time from the start of radiotherapy to 4 weeks after completion of radiotherapy. Toxicity was compared between patients who received a boost and those that did not.

Results: During this period 75 patients underwent the adjuvant breast 26 Gy in 5 fractions over a week radiation regimen. Of these 9 patients (12%) underwent a sequential hypofractionated boost. 66/ 75 (88%) patients completed at least 4 out of 5 acute toxicity assessments. Not one patient (0/ 66) reported moist desquamation not confined to skin folds or minor bleeding (grade 3 toxicity), 19/ 66 (28.8%) reported, brisk erythema, moist desquamation confined to skin folds or breast swelling (grade 2 toxicity) and 14/66 (21.2%%) reported faint erythema or dry desquamation (grade 1 toxicity). The highest frequency of grade $\geqslant$2 toxicity occurred at week 1 (20%) following completion of 26 Gy in 5 fractions but by week 4 this had reduced to 3%. A Fisher's exact test showed no statistically significant difference in grade 2 toxicity between the boost group and those who did not receive a boost ($p = 0.422$).

Conclusion: This study further confirms the safety and tolerability of delivering adjuvant breast radiotherapy 26 Gy in 5 fractions over 1-week in terms of acute skin toxicity, even followed by a sequential hypofractionated boost.

No conflict of interest.

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Patient Reported Outcomes Version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE) for patients undergoing radiotherapy for breast cancer: A single-center prospective registry experience

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Background: While advances in breast radiotherapy (RT) are commonly studied with respect to clinician-reported adverse events (CTCAE), implications from a patient perspective require consideration. We report one of the first analyses of PRO-CTCAE for BC patients with curative intent RT from a large, single-institution prospective registry.

Methods: PRO-CTCAE questionnaires were administered at baseline, end-of-treatment, 3, 6, 12 months, then annually for all patients treated with curative RT. Patients must have a baseline and at least one post-RT survey. Patient, treatment, toxicity, and outcome characteristics were extracted from the registry. Logistic regression was utilized for univariate (UVA) and multivariate (MVA) analyses.

Results: Three-hundred thirty-one (331) patients were analyzed from 2016–2019. Majority of the baseline patient/tumor characteristics included the following: ECOG 0 (66%), hormone receptor + (80%), Her2 + (23%), right-sided (50%), lumpectomy (75%), invasive ductal carcinoma (86%), pathologic T1–2 (94%), N0 (71%), grade 1–2 (66%). Radiotherapy characteristics include: photon RT (85%), boost (40%), whole breast RT (77%), lymph node RT (36%), median dose 40 Gy. Grade 2+ ("Moderate" or worse bother/severity) PRO-CTCAE occurred in 247 (75%) and grade 3+ ("Severe" or worse bother/severity) in 106 (32%). MVA revealed that grade 2+ and 3+ PRO-CTCAE were associated with ECOG $\geq$1 ($p = 0.01$, 0.02) and increasing dose per fraction with grade 3+ PRO-CTCAE ($p < 0.01$).

Conclusions: Moderate to severe PRO-CTCAE are common for patients undergoing RT for BC with curative intent and appears present more often than CTCAE in the literature. Further study is warranted to correlate PRO-CTCAE with recorded CTCAE and the implementation of PRO-CTCAE in clinical practice.

No conflict of interest.

Local Regional Treatment – Surgery

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Sentinel node after NeoAdjuvancy in node-positive breast cancer. SANA multicentric study

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Background: Targeted Axillary Dissection (TAD) in Node-Positive breast cancer patients treated with Neoadjuvant Chemotherapy (NAC) seems to be a good technique in order to avoid Axillary Lymph Node Dissection (ALND) for patients achieving a good response. Our goal was to validate TAD in our population and compare false-negative rates(FNR) of this technique according to molecular subtypes.

Material and methods: Prospective multicentric study of patients T1-3 N1-2 M0 with histological nodal metastases confirmation. Positive axillary node was clipped before NAC. All patients underwent SLNB and selective removal of the clipped node whether guided by ultrasound or by the localization of an additional iodine-125 or magnetic seed inserted before surgery. After TAD, all patients underwent complete ALND. The TAD FNR was compared with those obtained with either SLNB and the clipped node removal only, as well as regarding molecular tumor subtypes.

Results: Between Feb-2016 and Feb-2020, 153 patients met the inclusion criteria. Final assessment is based on 128 women that underwent axillary surgery after NAC. The majority of tumors were ductal carcinomas (89.1%) with histological grade II(64.8%). The mean size by magnetic resonance image (MRI) was 38.9 mm. Distribution by molecular subtypes: LuminalB-like Her2 negative(50.8%); LuminalB-like Her2 positive(19.5%); LuminalA-like (4.7%); Her2 positive non luminal(12.5%) and Triple negative (TN) (12.5%). Pathological response was different depending on molecular profiles (see Table 1).

Table 1 *Pathological Complete Response

Molecular subtype	n Tumor pCR*	%	n Axila pCR*	%
Luminal A-like (n = 6)	0	0	0	0
Luminal B-like Her2 – (n = 65)	6	9.2	7	10.7
Luminal B-like Her2+ (n = 25)	13	52	15	60.0
Her2 Positive (n = 16)	15	93.7	16	100
Triple Negative (n = 16)	10	62.5	12	75.0

SLNB identification rate(IR) was 91.4%. In 62.4% of patients, 2 or more SLN were obtained. In 33 patients, either SLN or clipped node couldn't be detected so that TAD IR was 74.2%. A seed placed before surgery by an expert radiologist improved the clipped node detection rate from 73.3% to 94.9% compared by ultrasound detection solely. The clipped node was non concordant with any SLN in 24.2%. The FNR was 7.8% (IC 95; 3.4%–17%) for clipped node; 8.7% (IC 95; 4%–17.7%) for SLNB and 1.7% (IC 95; 0.3–9.0%) for TAD. TN and Luminal B Her2 positive tumors resulted in an FNR of 0% (IC 95%; 0%–49%). FNR in HER2 positive tumors was not assessable because of its axillary CPR, achieving a Negative Predictive Value of a 100%.

Conclusions: TAD predicts the pathological axillary response with optimal FNRs especially in Her2 positive and TN tumors. Nevertheless, it is a demanding procedure which requires a multidisciplinary team. The use of seeds improves substantially this technique.

No conflict of interest.

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Clinical significance of the failure of sentinel lymph node mapping in patients with non-advanced invasive breast cancer – single-centre analysis

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Background: A failure of sentinel lymph node (SLN) mapping during sentinel lymph node biopsy (SLNB) is usually an indication for axillary lymph node dissection (ALND) usually involving dissection of axillary lymph nodes in the level I. However, according to recommendations of some scientific associations, it is not always necessary. This proves that significant differences still exist, when optimum management is concerned in the event of a failure of SLN identification.

The aim of this paper was to evaluate the clinical importance of the failure of SLN identification during SLNB performed to spare axillary lymph nodes.

Material and methods: 5396 patients with invasive breast cancer qualified for SLNB, treated in a period 01.2004–06.2018. All cases of the failure of SLN identification and reasons underlying this situation were analysed retrospectively.

Results: In 196 (3.6%) patients SLN was not identified (group I), and this resulted in a simultaneous ALND. 48.5% patients from this group were diagnosed with cancer metastases to lymph nodes (vs 23.6% patients with SLN removed – group II, $p < 0.00001$) – stage pN1 in 44.2% of the cases,

stage pN2 in 22.1% of the cases, and stage pN3 in 33.7% (in group II – 73.4%, 19.5% and 7.1%, respectively), with a presence of extracapsular infiltration in 68.4% patients (vs 41.7% – in group II) and with a significantly higher percentage of micrometastases in group II (17.0% vs 3.2% in group I).

In group I, the metastases in the axillary cavity were located at a lower level in 89.5% patients, at a middle level in 62.1% patients, and in lymph nodes of the axillary apex in 38.9% (in group II: 100%, 16.4% and 10.9% respectively; $p < 0.0001$). Metastatic lesions were diagnosed in at least 4 lymph nodes in 54.7% patients from group I (vs 26.6% in group II; 0.0233).

Other variables, for which statistically significant differences between compared groups were found included patients' age and a value of body mass index (BMI) (in both cases, $p < 0.00001$), primary tumour size (in clinical evaluation: $p = 0.0250$, and in pathological evaluation: $p = 0.0217$), a percentage of G3 cases ($p = 0.0425$), luminal HER2(-) type ($p = 0.0012$) and presence of vascular invasion, previous surgical treatment of a breast, and a failure of SLN mapping in preoperative lymphoscintigraphy ($p < 0.00001$).

Conclusions: The failure of intraoperative sentinel lymph node mapping indicates a significantly increased risk of breast cancer metastases to the axillary lymph nodes. At the same time, it can also indicate higher cancer stage and its increased aggressiveness (pN evaluation, percentage of G3 cases, and presence of extracapsular infiltration and intravascular metastatic tumour emboli). For this reason, in such situation performance of axillary lymph node dissection still appears to be the approach most advantageous for patients.

No conflict of interest.

543 Poster

Feasibility trial of lymph node marking using both clip and carbon dye in cN1 patients submitted to neo-adjuvant chemotherapy to improve accuracy of axillary surgical staging in ycN0 patients after treatment

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The actual trend to use chemotherapy in the neoadjuvant setting, with high rates of pathologic complete responses, raises questions about de-escalation of locoregional treatment. Sentinel lymph node biopsy (SLNB) in biopsy-proven node positive patients (cN1) who have a clinical complete response after neoadjuvant chemotherapy (NAC) is still controversial. Trying to minimize false negative results of SLNB procedure some groups have been using different markers (metallic clips, guide wires, iodine seeds, etc) to tag positive lymph nodes before NAC and facilitate their retrieval during surgery. The objective of this feasibility study was to test the use of carbon dye as a marker and the role of double marking with a clip to improve accuracy of axillary staging with SLNB.

The first phase of the study started in July 2016 and consisted of cT1-T3, cN1, M0 patients scheduled to receive NAC. Exclusion criteria were lobular histology, prior axillary surgery and clinical N2/3. The biopsied positive node was marked with carbon dye at diagnosis (Neotarget node). After an interim analysis we changed protocol in order to do a double marking procedure and started the second phase in March 2019. The biopsy-proven positive node (Neotarget node) was marked at diagnosis with a clip and after NAC a carbon dye tag was done. In patients with axillary complete response (ycN0), a targeted axillary staging was done with the removal of the sentinel nodes using dual tracer technique and of the previously marked node. All patients had complimentary axillary dissection.

Thirteen patients underwent the first version of the protocol (Cohort 1) with a single carbon dye marking of the biopsy-proven metastatic node at diagnosis and 18 patients were submitted to the second version of the protocol (Cohort 2) and underwent double marking with clip and carbon dye. Although only one node has been marked with carbon dye at diagnosis, more than one node was removed and classified as Neotarget node in 67% of Cohort 1 patients and in 22% of Cohort 2. Also in 38% of Cohort 1 patients and 17% of Cohort 2 there was no identification by the surgeon of lymph nodes tagged with black ink. In Cohort 2, clip identification by surgical specimen radiography allowed the identification of the tagged node in 17/18 (94%) of cases. In one patient the clipped node was not retrieved during targeted axillary procedure, but was present at the complimentary axillary dissection specimen. In another patient the clipped node was not a sentinel lymph node, but was ink tagged.

The introduction of double marking by clipping the metastatic node and verifying their removal by surgical specimen radiography, using carbon ink as a tracer, allowed the identification of the metastatic node in 94% of cases, proving to be an simple and economic targeted axillary dissection procedure without relevant complications.

No conflict of interest.

544 Poster

Sentinel lymph node biopsy in early breast cancer: Experience from a tertiary care facility in India

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Background: Sentinel lymph node biopsy (SLNBx) is a standard of care in early breast cancer. In India, SLNBx has been slow in uptake. Only in recent years, centres in big cities have adopted it. A retrospective analysis of a prospectively maintained database of SLNBx procedures at Max Superspecialty Hospital, Vaishali, India has been carried out.

Materials and methods: Data of all patients undergoing SLNBx from April 2018 to June 2020 has been analysed. Over this period, 164 patients underwent 167 SLNBx procedures.

Results: Majority of patients had T1 and T2 tumors (19.2% and 67.7%). Axillary assessment was by clinical examination, ultrasound (104/167), MRI (57/167), and PET CT scan (62/167). FNAC of axillary nodes was carried out in 18 patients.

Breast conservation surgery was carried out in 87 cases and mastectomy in 80 cases. SLNBx using dual tracer (technetium labelled radiocolloid and methylene blue dye) was used for 165 procedures. Two patients had only blue dye based SLNBx. SLNBx was successful in 164 cases (98.2%). Intraoperative frozen section was performed for nodal assessment and decision about axillary surgery.

Number of nodes reported on frozen section ranged from 1 to 12 with a mean of 4.6 nodes. Forty three (26.2%) patients had positive nodes on frozen section, 35 with macrometastases (81.4%) and 8 with micrometastases (18.6%). Positivity rate of SLNs showed no relation to the number of nodes reported on frozen section (31.6% for 1–3 nodes, 23.4% for 4 or more nodes). Forty two out of 43 patients (97.7%) underwent completion axillary surgery at the same time. In two patients, paraffin section of the sentinel nodes showed micrometastases while the frozen section examination was negative.

Out of the 42 patients with positive sentinel nodes who underwent ALND, 13 patients had non sentinel node metastases (31%). For macrometastases in the sentinel nodes, non-sentinel nodes were involved in 31.4% (11/35) while for micrometastases, non-sentinel nodes were involved in 28.6% (2/7) patients.

On final pathological assessment, 6 patients had DCIS. Based on immunohistochemical assessment (ER, PR, HER2neu, Ki67) and FISH testing for equivocal HER2 IHC results, the biological profile was luminal (113/157 or 72%) with 23% luminal A, 42% luminal B, 7% luminal unspecified, HER2 enriched (17/157, 10.8%) and TNBC (27, 17.2%).

Conclusions: Sentinel lymph node biopsy using dual tracer has a high success rate in an Indian tertiary care set up. Methylene blue is easily available, cheap and associated with good success rate. Frozen section examination of nodes is reliable and allows single stage treatment of the axilla.

Lack of nuclear medicine facilities and frozen section facilities in peripheral hospitals are barriers to wider application of the sentinel node procedure in India and solutions are required for this to increase access to the procedure.

No conflict of interest.

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Application of ACOSOG Z0011 patient selection criteria to an Indian breast cancer cohort undergoing sentinel lymph node biopsy

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Background: Sentinel lymph node biopsy (SLNBx) is a standard of care in early breast cancer. Previously, completion axillary surgery was offered for all patients with positive sentinel nodes. Publication of ACOSOG Z0011 trial results has led to change in practice in the developed world. In India, there is hesitation about implementing this approach and majority of patients still undergo axillary dissection if sentinel nodes are involved. We have tried to apply the selection criteria for the ACOSOG Z0011 trial to a cohort of breast cancer patients that underwent SLNBx at Max Superspecialty Hospital, Vaishali, India and assess the potential impact of this approach.

Materials and methods: Data of all patients undergoing SLNBx from April 2018 to June 2020 has been analysed. Over this period, 164 patients underwent 167 SLNBx procedures.

Results: Out of the 167 cases, 3 patients had failed SLNBx. Of the remaining 164 procedures, 80 were total mastectomy and 84 were breast

conservation procedures (conventional or oncoplastic). Out of this group, 53 patients had Tumor size 0.1 to 3.0 cm. Out of this 22 were T1 and 31 were T2 (up to 3 cms). When immunohistochemical profile is taken in consideration, 12 patients are excluded for being HER2 enriched, triple negative or Luminal B HER2 positive.

In the remaining group of 41 patients, 12 patients (29.3%) had sentinel nodes reported metastatic on frozen section, 9 being macrometastases and 3 being micrometastases. Completion axillary dissection was carried out in all 12 patients at the same time. Only 1 out of these 12 patients had additional tumor deposit in the non-sentinel nodes. Of the patients with micrometastases or a single macrometastasis (7 patients), none had non-sentinel node involvement. Of the remaining 5 patients with 2 or 3 nodes involvement in sentinel nodes, 1 patient had micrometastatic involvement of a single non-sentinel node.

Conclusions: In this cohort of patients undergoing SLNBx at our hospital, patients with tumors up to 3 cms in size, Luminal A or Luminal B HER2 negative IHC profile and undergoing breast conservation surgery constituted 25% (41/164)of all patients having SLNBx. Out of these, patients with micrometastases or single macrometastasis in the sentinel node on frozen section did not have non sentinel node metastases and can be safely considered for omission of completion axillary dissection. This would affect the treatment of 7 patients out of this cohort of 164 patients. With progressively earlier diagnosis, this ratio should improve.

No conflict of interest.

546 Poster

Audit of surgical de-escalation following revised UK guidelines for margins and completion axillary clearance at a single UK teaching hospital

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Background: There has been a global trend for surgical de-escalation in the management of breast cancer. There has been widespread acceptance that 'no tumour at ink' is adequate following breast conservation surgery (BCS) for invasive malignancy and also that completion axillary clearance (cANC) is not required in all women with a positive sentinel node biopsy (SLNB). UK National Guidelines for surgical margins and axillary management were updated in 2018 to reduce axillary completion clearance indications but UK margin guidelines still advocate a margin of ≥2 mm for invasive disease. This study assess margin re excision and cANC rates before and after revised UK guidelines were issued.

Materials and methods: A retrospective, consecutive audit of invasive breast cancers in a single UK teaching hospital between 2 time periods: Jan–March 2017 (before guidelines changed) and Jan–March 2019 (after guidelines changed). Data on rates of cavity re excisions, completion mastectomies and cANCs and their indications were collected. Rates were compared using Chi^2.

Results: Between 1st Jan–31st March 2017, 74 invasive and insitu breast cancers were diagnosed. There were 86 diagnosed between Jan-March 2019. The median age of the 2 cohorts were similar (63, range 31–94 in 2017, 61.6, range 39–87 in 2019). Median tumour sizes were similar (2017: 23 mm, 2019: 21.8 mm). Multiple ipsilateral breast cancers were more common in the 2019 group (2019: 7.8%, 2017: 1.13%). The primary mastectomy rate was higher (30/86,35%) in 2019 compared to (14/74,18.9%) in 2017; p = 0.024.

More women underwent BCS (55/74, 82%) in 2017 compared to (55/86,64%) those in 2019. The margin re excision rate was 20/55, 36% in the 2019 group of which only 4/20 were for margins of between 0 and 2 mm clearance and the remainder were for tumour at inked margins. In 2017 13/61, 21% had re-excision with 2/13 had margins of between 0 mm and 2 mm clearance and 11 for tumour at ink. The difference in margin re excision rates between the two groups was not significant (p = 0.084). Residual disease was seen in a third of these cases in both groups.

Axillary macro-metastases were diagnosed on SLNB in 11/64(17%) cases in 2017 and 14/70(20%) in 2019. Of these, 90% (10/11) in 2017 and 64% (9/14) in 2019 had cANCs. Marginally higher number of women had no further axillary treatment in 2019 (p = 0.430).

Conclusion: The rate of surgical re excision has not reduced following revision of UK guidelines, which may reflect that UK guidelines do not recommend acceptance of 'no tumour at ink' whereas European and US guidelines do. This would have reduced the number of re-excisions by 19% in 2019. There does appear to be de-escalation of axillary surgery.

No conflict of interest.

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Effects of COVID-19 pandemics in a Breast unit

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Background: COVID-19 pandemics caused a fear all around the world. Avoidance from hospitals caused a reduction in routine controls and screening programs.

In this study, we explored differences in the diagnosis and treatment process of breast cancer (BC) patients in our hospital during pandemics.

Material and methods: The declaration of COVID-19 pandemics was on March 11, 2020. Between March 11 and June 1, 2020, social isolation suggestions caused most people to beware of hospitals. Since June 1, normalization in social life has started in our country.

We aimed to compare the pandemic period (March 11, 2020–June 1, 2020) with a previous similar period of 82 days (December 21, 2019–March 10, 2020) for applications, diagnoses, operations, and treatment options of BC patients in our hospital.

Results: With the declaration of pandemics, patients who applied to outpatient clinics noticeably decreased. Patients who had BC diagnosis were 250 before and 146 after pandemics. The rate of patients referred to neoadjuvant treatment was similar, 13.6%, and 12.3% of newly diagnosed patients, respectively. During pandemics, there was a significant decrease in operations.

	Before pandemics (December 21, 2019 – March 10,2020)	During pandemics (March 11, 2020 – June 1,2020)
Application to outpatient clinics	28705	5872
Application to breast unit	8686	2793
Number of breast cancer patients	1660 (19.1%)	760 (27.3%)
Breast cancer diagnosis	250 (2.8%)	146 (5.2%)
Neoadjuvant treatment	34 (13.6%)	18 (12.3%)
Wire guided biopsy	77	27
Breast cancer operations (total)	216	128
Mastectomy	103 (47.6%)	85 (66.4%)
Breast Conserving Surgery	75 (34.7%)	40 (31.25%)
Sentinel Lymph Node Biopsy	142 (65.7%)	93 (72.6%)
Axillary Dissection	47 (21.7%)	57 (44.5%)
Operations after neoadjuvant treatment	29 (13.4%)	27 (21.1%)

Conclusion: Our hospital is a reference center for cancer patients, which classified as a non-infected hospital that does not hospitalize confirmed COVID-19 patients. The increased BC diagnosis rate shows that most patients who came to our hospital already had a disease or need treatment.

Breast cancer screening programs could not be worked effectively during pandemics, and routine diagnostic imagings were deferred. Therefore the number of patients who had early BC diagnosis with wire localization and biopsy significantly decreased.

The number of BC operations after neoadjuvant treatment did not change because treatments were already planned. On the other hand, the increased rate of these operations in all BC surgeries may be caused an increase in mastectomy and axillary dissection rates during pandemics. Furthermore, the rate of patients referred to neoadjuvant treatment did not change, which means there was no difference in our treatment approach for BC patients and no extra delays for surgery.

No conflict of interest.

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Surgery of the primary tumour in women with metastatic breast cancer at diagnosis in England and Wales – how do treatment rates vary at an individual and regional level?

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Background: Surgery to the primary tumour in women with metastatic breast cancer (MBC) has traditionally been reserved for palliative purposes, and European guidelines suggest it should be performed on an individualised basis[1]. A lack of consensus on the effectiveness of a procedure can lead to treatment variation in clinical practice. We examined what proportion of women with MBC aged 50+yrs received surgery to the primary tumour, and explored what patient and clinical characteristics influence receipt of surgery, as part of the National Audit of Breast Cancer in Older Patients (NABCOP).

Methods: Details of the NABCOP are available at www.nabcop.org.uk. Data on women aged 50+yrs newly diagnosed with MBC at diagnosis between January 2014 and December 2018 in England and Wales were obtained from national cancer registry datasets linked to routine hospital episodes. Receipt of surgery up to 3 years from diagnosis was examined using Kaplan Meier estimates, both nationally and between Cancer Alliances. The relationship between patient/tumour factors and time to surgery was analysed using log rank tests and a flexible parametric regression model (FPM).

Results: Between 2014 and 2018, 7316 women aged 50+yrs with MBC at diagnosis were identified. Overall, 18.7% women had surgery to the primary tumour within 1 year from diagnosis. Having surgery at 1 year was more common among younger women (50–59 yrs vs 80+yrs: 29.8% vs 8.6%, adjusted HR 1.79), those with T1/T2 tumours (T1/T2 vs T3/T4: 33.1% vs 20.8%, adjusted HR 1.72), and positive nodal stage (N0 vs N+: 19.3% vs 29.1%, adjusted HR 1.54). Rates of surgery within 1 year from diagnosis reduced over time, from 23.7% in 2014 to 15.7% in 2018, but to a greater degree among women aged 50–69 yrs (34.8% in 2014 to 21.1% in 2018) compared with women aged 70+yrs: 15.6% to 11.5%. Overall rates of surgery varied from 11.6% to 32.2% between the 20 Cancer Alliance/regions across England and Wales.

Conclusions: Almost 20% of women aged 50+yrs with MBC at diagnosis received breast surgery within 1 year from diagnosis, but this varied between regions in England and Wales, and the use of surgery has decreased in recent years. Research is required to understand why treatment variation exists as well as to generate better evidence on the value of surgery in patients with MBC.

No conflict of interest.

Reference

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549 Poster

A review of localization techniques in breast surgery – is wire free the future?

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Background: In the UK the gold standard for localisation of impalpable breast lesions including cancers, is the image guided hook wire localiser and has been since its development in the 1970's. Localisation methods have changed and advanced since this inception. The technique of wire localisation has both advantages and disadvantages. In recent years novel wire free techniques, using probe and marker/seed based systems, (e.g. Magseed®, SCOUT®, and LOCalizer™) have been developed to not only localise impalpable breast lesions but negate the disadvantages of wire localisation. The aim of our review was to compare the variety of techniques used to localise breast lesions from their origins to the most recent advancements.

Material and methods: A comprehensive review of available data in the form of published articles with the related topic using Pubmed, OVID, Cochrane databases, book chapters and information from manufacturer's websites. Key words used for database searches included impalpable breast tumours; localisation techniques; wire free technique; Magseed; SAVI SCOUT and LOCaliser.

This was a narrative review comparing the disadvantages and advantages of each technique, wire based or wire free.

Results: Novel wire free techniques are effective, safe, with non-inferiority and feasibility compared to wire localisation confirmed in multiple studies. Margin re-excision rates, deployment and retrieval rates are also comparable to wire localisation techniques.

Conclusions: The future of localisation of non-palpable breast lesions is heading toward non-wire technology, wire localisation may then be reserved for special cases. It simplifies patient pathways, surgical planning and also decreases patient anxiety.

No conflict of interest.

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Nonradioactive surgical guidance with radiofrequency identification technology for locating nonpalpable breast lesions; Initial experiences of the RFID Localizer I Trial

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Background: In breast conserving surgery accurate intraoperative lesion localization is essential for adequate surgical margins while sparing surrounding healthy tissue to achieve optimal cosmesis. Radiofrequency identification (RFID) technology may offer a viable non-radioactive, non-wire alternative.

Purpose: To evaluate the feasibility of RFID surgical guidance for localization of nonpalpable breast cancer.

Methods: The first 50 procedures of the RFID Localizer I trial were evaluated. A RFID LOCalizer™ (Faxitron, Hologic) tag (10.6 × 2 mm) was placed using ultrasound guidance up to 30 days preoperatively. The RFID tag was inserted percutaneously through a small skin incision with a preloaded 12-gauge sterile needle applicator. A two-view mammography was performed to confirm correct position of the RFID tag. At breast conserving surgery the surgeon localized the RFID tag using a handheld reader device. Duration of the placement- and surgical procedure was recorded. Histopathology results were collected to calculate the percentage of radical excisions. This percentage was compared to the NABON standard (min. 90 % radical excisions).

Results: Between April and December 2019, a total of 50 women underwent RFID tag placement in two hospitals. Median time of placement took five minutes (IQR 3–10) from start incision for needle access, to deposition of the marker. Median time between tag placement and surgery was seven days (IQR 4–11). In five patients the placement failed due to dislocation during retraction of the needle. In 46 patients the RFID system was used to guide surgical excision. Retrieval of the lumpectomy specimen took on median time 17 minutes (IQR 12–20), recorded from the moment of incision. Histopathology showed clear resection margins in 43/46 patients (93% | 95% CI 0,98–1,23). Re-excision was indicated in one patient (Invasive lobular carcinoma).

Conclusion: RFID surgical guidance offers non-radioactive non-wire localization of non-palpable breast cancers, first results show an acceptable radical excision rate according to the current NABON standard.

Table 1 Overview of results from 50 RFID tag placement procedures, 46 RFID-guided breast conserving surgery procedures and histopathological results.

Radiology, n (percentage)	Total n = 50
Shortest distance marker-tumor on mammography in mm, median (IQR)	2 (0–5)
Number of days of RFID tag in situ, median (IQR)	7 (4–11)
Duration of placement procedure in minutes, median (IQR)	5 (3–10)
Number of successful placement procedures	44 (88%)
Surgery, n (percentage)	Total n = 46
Identification rate	46 (100%)
Duration of surgery in minutes, median (IQR)	17 (12–20)
Post-operative wound infection	1 (2%)
Pathology, n (percentage)	Total n = 46
Radical excision rate	43 (93%)
Re-excision rate	1 (2%)
RFID marker retrieved	50 (100%)
Dominant tumor size in mm, median	10 (6–14)

No conflict of interest.

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Imaging and clinical predictors for nipple-areola complex (NAC) involvement in breast cancer patients undergoing Nipple-Sparing Mastectomy (NSM)

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Background: In the last decade NSM has emerged as a new and secure type of mastectomy in the therapeutic setting, including both primary and post-neoadjuvant therapy.

Assessing tumor distance to NAC by magnetic resonance imaging (MRI) may help physicians in surgery programming when patients elected to NSM are evaluated. We aimed to identify radiological and clinical predictors for NAC involvement.

Methods: Breast cancer patients scheduled for NSM were selected from hospital's surgical database from Jan 2012 to Dec 2019. Both intraoperative nipple-base biopsy frozen section and posterior H/E stain pathological exam was performed in all cases. We analyzed separately in situ carcinomas and invasive cancer cases. Clinical features (tumor size, nodal involvement, molecular subtype, LVI, response to NAC) and imaging results (tumor size by MRI, extended microcalcifications, multifocality and/or multicentricity, mass vs. no mass enhancement, nipple to lesion distance) were correlated with pathological NAC assessment.

Results: A total of 102 patients with median age 51,37 years were included. 79 were invasive breast cancer and 23 were in situ carcinoma. NAC infiltration was recorded in 11 patients (10.78%), 9 patients in the invasive group and 2 patients in the in situ group.

In the in situ group mean tumor size was 39.81 mm (SD 20.11; range 2–78) and the only variable with a positive statistical trend for NAC infiltration was no-mass enhancement in MRI (p 0,085).

In the invasive group, mean tumor size was 30,29 mm (SD 20.35; range 10–112) and 45 patients (56.96%) received neoadjuvant chemotherapy. Histology was reported: 66 patients (83.54%) ductal carcinoma, 5 patients (6.32%) lobelar carcinoma and 8 patients (10.12%) others. Molecular subtypes were: Luminal A 35.44% (28 patients); Luminal B 32.91% (26), LuminalB/Her2 11.39% (9), Her2 3.79% (3) and TNBC 16.45% (13). Neoadjuvant chemotherapy administration (p 0.034), MRI assessment after chemotherapy with complete and/or response greater than 50% (p 0,010) and low Residual Cancer Burden (p 0.039) were predictive for NAC preservation. Tumor to nipple distance <2 cm (p 0.046) was associated to NAC involvement. There was also a trend for NAC infiltration in luminal subtype (p 0.073) compared to HER2 and triple negative breast cancers.

After an average follow-up of 38,7 moths (SD 18.33; range 2–76), 1 patient died for causes other than breast cancer, 3 patients still remain metastatic and no loco-regional recurrences has been reported.

Conclusions: NSM is an oncological safe surgical procedure and alternative to conventional mastectomy. In cases with non clinical or imaging NAC involvement pathologic infiltration is uncommon. Special attention is required if tumor-nipple distance is less than 2 cm and for invasive luminal tumors with poor response to treatment.

No conflict of interest.

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Radio-Frequency Identification (RFID) Tags for localisation of impalpable breast cancers results in reduced waiting times for patients on day of surgery

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Background: The new localisation technique of Hologic LOCalizer Radio-Frequency Identification (RFID) Tags for impalpable breast cancers has several advantages over current methods, including the option to be placed anytime prior to surgery and no radioactivity-related protocols. Our unit is the first in the UK to begin using this new technology.

Traditional wire placement means patients must arrive early on the day of surgery resulting in extended waits and potential delays to the flow of the operating list.

Materials and methods: We conducted a retrospective study of patients undergoing either wire-guided or RFID tag localised wide local excision (WLE) for breast cancer on all day operating lists since the introduction of this new technique in our unit in June 2019. Interval time between arriving in hospital and entry to anaesthetic room were recorded and compared.

Results: During this 6 month period, we identified 149 patients. 59/149 (39%) underwent wire guided WLE. The mean interval was 309 minutes (range 69–559 m). 90/149 (61%) underwent RFID WLE with an mean wait of 203 m (range 31–540 m). 38/59 (64%) of the wire group waited more than 4 hours compared to 29/90 (32%) in the RFID tag group.

Conclusions: RFID tags reduce waiting times for patients on the day of surgery and allow more flexibility when planning operating lists.

With continued integration and familiarisation with this new technique, waiting times can be reduced even further with more effective list planning.

Conflict of interest:
Corporate-sponsored Research:
One of the authors (R Milligan) received an honorarium for delivering an educational seminar on the LOCalizer system sponsored by Hologic at the British Society of Breast Radiology Annual Scientific meeting 2019

553 Poster

Breast-conserving surgery under local anaesthesia is a safe and effective option for local control in an increasingly frail population

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Background: The NHS is faced with a rapidly expanding elderly population and its associated burden of co-morbid disease.

Incidence of breast cancer increases with age with older patients more likely to have oestrogen receptor positive cancers that can be treated with primary endocrine therapy (PET).

Breast conserving surgery (BCS) under local anaesthesia (LA) provides an alternative for local cancer control in those unfit for general anaesthesia or those unsuitable to receive PET.

Materials and methods: We conducted a single-centre retrospective study of patients undergoing wide local excision (WLE) for treatment of breast cancer performed under local anaesthesia between January 2017 and December 2019. Patient demographics, tumour biology and complications were recorded. Margin status was used as a surrogate marker for local recurrence.

Results: We identified 12 patients with an average age of 82 years, all underwent; day case procedures. Ischaemic heart disease was the most commonly encountered co-morbidity. Four patients underwent surgery due to disease progression on PET. The average estimated pre-operative tumour size was 19 mm (range 4–30 mm); 11/12 of these were of invasive ductal type. All patients had clinically normal lymph nodes and no sentinel lymph nodes biopsies were performed. One small haematoma occurred which was managed conservatively. Two patients had at least one positive margin. In one case this could not be surgically improved.

Conclusions: Performing BCS under LA represents a very small proportion of our overall cancer work. Surgeons should consider offering this option to their patients when faced with unfavourable tumour biology or advanced frailty.

No conflict of interest.

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Use of Hologic LOCalizerTM radiofrequency identification (RFID) tags to localise impalpable breast lesions and axillary nodes: Experience of the first 150 cases in a UK breast unit

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Background: Guidewires for a long time represented the standard localisation method for impalpable lesions prior to breast conserving surgery but alternative methods are now available.

We recently became the first UK centre to utilise the Hologic LOCalizerTM (radiofrequency identification) RFID tag system, and report the outcomes of our first 150 patients, including the first reported use of RFID tags in the axilla.

Materials and methods: Data collected prospectively from the first tag insertion (12th June 2019) until the 150th consecutive patient had undergone surgery (excision date 9th Jan 2020).

Results: A total of 177 tags were inserted to malignant lesions in 150 women. Tags were inserted an average of 7.8 days before surgery. 126 tags were targeted to a single lesion in one breast only; the remainder of tags were targeted to multiple lesions in the same or contralateral breast, multiple lesions involving both breasts, and axillary lymph nodes. In addition, two cases involved using two tags for bracketing microcalcification. All except three tags were satisfactorily deployed at their initial intended target. The majority of target lesions were masses (n = 142, mean size 13.8 mm), with a

range of other targets including post-vacuum assisted biopsy cavities, marker clips following post-neoadjuvant chemotherapy, architectural distortions, and clipped metastatic lymph nodes. All tags were successfully retrieved at surgical excision. Re-excision rate was 8.7%. There were no tag-specific surgical complications.

Conclusions: The RFID tag system demonstrates many advantages over guidewires, and is effective at targeting axillary lymph nodes and multiple sites within the same breast.

Conflict of interest:
Corporate-sponsored Research:
Two of the authors (R Milligan, A Leaver) received an honorarium for delivering an educational seminar on the LOCalizer system at the British Society of Breast Radiology meeting 2019. This was sponsored by Hologic

Optimal Diagnosis

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Correlation of ultrasound elastography of breast lesions with histopathology and immunohistochemistry: Looking for prognostic significance

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Background: With widespread research going into breast cancer genomics and its association with imaging, a quest to correlate radiological features of breast lesions with histopathology and immunohistochemistry is reiterated. Ultrasound Elastography is an advanced imaging tool for making an objective decision in the benign-malignant characterization of breast pathologies. The aim of the study is to correlate a semiquantitative Ultrasound Elastography parameter (Strain ratio) with clinical and pathological parameters of breast lesions.

Materials and methods: After obtaining approval from the Institutional Ethical Committee, a prospective cross-sectional study was conducted over 1.5 years from March 2018 to August 2020. Female patients referred for evaluation of breast lesions were included in the study after obtaining informed written consent. After excluding the patients without a pathological diagnosis, 190 breast lesions from 135 patients were included in the study. The lesions were assessed by Ultrasound Elastography (GE Logiq S8, USA) using a high-frequency linear probe (9–12 MHz). Strain ratio (SR) was obtained and was correlated with pathological diagnosis using the chi-square test and with clinical and pathological parameters like size, the histological grade of the tumor, malignant involvement of axillary lymph nodes, and immunohistochemistry status of the lesion using univariate analysis with SPSS version 23. P-value of <0.05 was considered significant.

Results: SR correlated well with pathological diagnosis (p: 0.000). The mean SR of breast lesions in the study population was 5.67 ± 3.88. A higher mean SR was found in the malignant group with invasive carcinoma being the most common malignant lesion (mean SR 8.18 ± 3.90). Fibroadenoma was the most common benign lesion (mean SR of 2.8 ± 2.44). The SR correlated significantly with parameters like size, the grade of the tumor, and malignant involvement of axillary lymph nodes ($p < 0.05$). The correlation of strain ratio of the malignant lesions (total 100 in our study) was significant with Ki67 values (p 0.03). No significant correlation was found with ER, PR, and Her2neu status.

Conclusion: Strain ratio is a semiquantitative ultrasound Elastography parameter that correlates well with clinical and pathological parameters as well as Ki67 values. Hence its use for prognostic significance in Breast carcinoma may be established in the future with larger-scale multicentric studies.

No conflict of interest.

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Role of Ultrasound Elastography in characterization of breast lesions: Does it really count?

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Background: To compare the diagnostic performance of Ultrasound Elastography, Ultrasonography (Greyscale & Colour Doppler) and Digital Mammography in the characterisation of breast lesions using Pathological diagnosis as Gold standard.

Materials and methods: After obtaining institutional ethical committee approval, a prospective cross-sectional study was conducted from February 2018 to August 2019 on female patients presenting with breast pathologies. After excluding patients in whom pathological evaluation was not possible or those who declined consent,190 breast lesions from 135 consecutive patients were included in the study. The lesions were classified as benign and malignant using ACR BI-RADS score (cut off 3) for Mammography and Ultrasonography. Strain Elastography (GE Logiq S8, Linear Ultrasound Probe: frequency- 7 to 11 MHz) parameters used to classify breast lesions were Tsukuba score (cut off 3) and Strain Ratio(SR) (cut off 4 obtained by Receiver operator characteristic (ROC) curve analysis). A novel Comprehensive score incorporating Tsukuba + Ultrasonography BIRADS score (USGplusElasto) was computed using logistic regression. Using SPSS version 23.0, ROC curve analysis was used to compare the diagnostic modalities considering Pathological diagnosis (FNAC or biopsy) as the gold standard.

Results: Mean age of the study population was 43.60 years. Imaging modalities had a significant association with Pathological diagnosis (chi-square test: p-value <0.001). ROC curve analysis showed a maximum area under the curve with combined USGplusElasto Score (0.917) followed by Tsukuba score (0.875), Strain Ratio (0.863), Mammography (0.770) and Ultrasonography (0.760). Elastography showed more specificity (Tsukuba:84.09%, SR:79.55%) and accuracy (Tsukuba:87.37%, SR:86.84%) as compared to Mammography and Ultrasonography (values mentioned in table 1) with comparable sensitivity.

Table 1 Comparison of the Diagnostic Modalities in the study using Pathological Diagnosis as Gold Standard

	Tsukuba Score	Strain ratio	Ultrasonography	Mammography
Sensitivity	90.20%	93.14%	**99.02%**	98.02%
Specificity	**84.09%**	79.55%	55.68%	56.06%
Positive Predictive Value	**86.79%**	84.07%	72.14%	77.34%
Negative Predictive Value	88.10%	90.91%	**98%**	94.87%
Positive Likelihood Ratio	**5.67**	4.55	2.23	2.23
Negative Likelihood Ratio	0.12	0.09	**0.02**	0.04
Accuracy	**87.37%**	86.84%	78.95%	81.44%
Area under Curve of ROC Curve Analysis	**0.875**	0.863	0.760	0.770

Conclusion: Ultrasound Elastography was found to be more specific and accurate than traditional imaging tools in the characterisation of breast lesions. These results are consistent with existing Literature, thus reiterating its usefulness as a potential problem-solving tool in equivocal breast lesions in the routine clinical scenario.

No conflict of interest.

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Visual versus automatic measurement of mammographic breast density (MBD)

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Background: Study the visual and automatic measurement of mammographic breast density (MBD) and its implications in diagnostic of tumor size and if it has implications as a prognostic factor

Material and methods: Study the visual and automatic measurement of mammographic breast density according to the breast imaging data system (BI-RADS) in 212 patients with invasive unifocal breast cancer (not microinvasive) who did not perform neoadjuvant chemotherapy and surgery before.

Analyze the tumor size globally and with the BIRADS mammographic breast density categories, comparing the histological tumor size, versus the clinical size, ultrasound size, mammographic size and size of the magnetic resonance, a regression is made to study which test values the size better, and the correlation of MBD with prognostic factors (RE, RP, HER2, Ki67, p53).

Results: The comparison of Visual MBD and Automatic MBD, visual MBD 2 the MBD Automatic matches in 40.6% (41/101), in 58.4% (59/101) the MBD is 1, the visual MBD 3 matches with DMR 3 automatic in 32,1% (9/28), in the MBD 3 automatic 64.3% (18/28) is lower ($p < 0,001$). When comparing Visual DMR and Automatic MBD, visual MBD 2 the MBD Automatic matches in 40.6% (41/101), in 58.4% (59/101) the MBD is 1, the visual MBD 3 matches with MBD 3 automatic in 32,1% (9/28), in the MBD 3 automatic 64,3% (18/28) is lower ($p < 0,001$). The study of BMI with MBD, a BMI > 30 there are 0 cases MBD BIRADS 4 (visual and automatic), BMI 15–29,9 there are 0 cases MBD BIRADS 4 automated and 4 cases (14,8%) with MBD BIRADS 4 visual. MBD is not correlated ($p = ns$) with prognostic factors (ER, PR, HER2, Ki67, Histological Grade). The study of size using linear regression shows us a better estimate with less variability with ultrasound and magnetic resonance. ($\bar{x} + 1,96\ \sigma$)

Conclusion: Visual measurement overestimate MBD versus automatic measurement according BIRADS categories. Ultrasound and magnetic resonance estimate tumor size better with less variability. MBD is not related to tumor prognostic factors.

No conflict of interest.

558 Poster

Development of a multiplexed protein panel using a targeted proteomics approach for the study of CDK4/6 inhibitors resistance in hormone receptor positive breast cancer

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1. Hormone receptor positive breast cancer represents approximately 70% of all breast cancer cases. These patients are treated with endocrine therapies which improves survival and allows a cure in early stages. Recurrent disease, metastatic dissemination and drug resistance limit the survival of patients. The limitations regarding endocrine therapy have prompted the search for new therapeutic targets, such as CDK4/6 Inhibitors(CDK4/6I). Despite the improved disease control that CDK4/6Is offer, not all patients respond to these drugs and most patients whose tumors respond to CDK4/6I eventually develop acquired resistance. No proven biomarkers of CDK4/6I efficacy exist to date, and there is a need for diagnostic tools that could stratify patients to save costs and the burden of unnecessary therapy. Our aim is to perform a quantitative evaluation of marker proteins with a developed multiplexed panel using targeted mass spectrometry(MS)-based proteomics for 25 proteins from the CDK/RB/E2F-pathway which have been shown in the literature to be central to CDK4/6I resistance.
2. We developed Multiple Reaction Monitoring(MRM) MS methods for the 25 target proteins using synthetic heavy-isotope-labeled standards with the aim of creating MRM assays to enable specific, sensitive and precise quantitation of these proteins in small amounts of samples. We developed a high resolution peptide fractionation system using high-pH micro-flow liquid chromatography(LC) which is required to overcome the problem of small samples amounts while improving analytical assay sensitivity in the analysis of complex biological matrices such as biopsies. The MCF-7 human breast cancer cell line was used as model during method development. Proteins from cell lysates were reduced, alkylated and digested with trypsin. The resulting peptides were micro-flow fractionated into 70 fractions and the developed nano-LC-MS MRM assays were used for peptide detection and quantification. Data were analyzed using Skyline.
3. Our developed micro-flow fractionation method allowed us to work on limited amounts of samples (60ug), and increased the possibility to detecting low abundance proteins such as cell cycle components. Using the MCF-7 cell model, we are able to identify and quantify 17 proteins out of the 25 from our panel: Cdk1-2-4,CyclinB1-D1-D3-E1,Rb1, E2f 3-4-5, Esr1,Top2a,Tyms,Ezh2,Mki67, Birc5.
4. We have developed a highly specific MS-based multiplexed assay with peptide standards targeting 25 proteins relevant to CDK4/6I breast cancer treatment. Our micro-flow fractionation method increased assay sensitivity and allows for the analysis of small sample amounts. In the future we will apply this workflow to samples such as Patient Derived Xenografts models, breast cancer tissues and FFPE samples in order to identify the predictive value of these potential biomarkers for responsiveness to CDK4/6i.

No conflict of interest.

559 Poster

Multidisciplinary team meeting and EUSOMA quality indicators in breast cancer care during COVID-19 outbreak in North-Eastern Italy. When the going gets tough, the tough gets going!

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Background: It is widely accepted that multidisciplinary team meetings (MTM) ensure higher quality of care and improved survival in breast cancer (BC) patients. During the COVID-19 outbreak in Northern Italy, in the large territory of ULSS6 "Euganea" (province of Padova, nearly one million people and 3 local hospitals: Cittadella – CTD, Camposampiero – CSP, Schiavonia -SCH) since the end of February 2020, SCH were turned into "COVID-19 hospital" and BC cancer patients were then transferred to CTD in order to underwent surgery. Prior to COVID-19 outbreak, MTM took place weekly, while during the COVID-19 emergency, MTM were largely suspended.

Material and methods: This was a retrospective observational study including patients newly diagnosed BC, discussed in pre- and/or post-therapeutic MTM between March 1st, 2019 and May 1st, 2019 compared to the same period of 2020, during COVID-19 emergency. EUSOMA quality indicators were evaluated and compared in order to establish the impact of COVID-19 outbreak in breast cancer patients' management in absence of MTM.

Results: Despite COVID-19 emergency, the time passed from the first diagnostic procedure to surgery/CT treatment was nearly the same in the two periods (41 ± 14 days in 2019, range 18–92 days versus 37 ± 19 days in 2020, range 15–107 days; $p = 0.3$). The only parameter which drastically changed was the proportion of patients to be discussed in MTM (p adjusted for false discovery rate = 0.002). However, the absence of MTM was substituted by a more point-to-point communication (oncologists/surgeons/radiologists directly communicating with the others) did not loosen the straight organization of the procedures, as showed by the adherence to the most part of EUSOMA quality indicators

Conclusions: The presence of MTM in a beast unit is a powerful mean to assess quality in breast cancer patients' management. The well-established adherence to EUSOMA criteria and to standard procedures allowed us to maintain the high quality of breast cancer care and management, even during the COVID-19 outbreak in the Veneto region.

No conflict of interest.

560 Poster

Breast referral management and outcome during COVID 19 Pandemic – A UK experience

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Background: The new respiratory illness commonly referred to as "corona virus" and officially called COVID-19 has changed life and delivery of health care worldwide. In UK it has resulted in major changes as not only halted the breast screening but also forced the breast unit to undergo reconfiguration for safety of patients and staff. The risk of becoming seriously ill from COVID-19 is low for most people. However, it's very important to know that people being treated for breast cancer may have a higher risk of severe illness if they get COVID-19. We conducted this observational study to assess the impact of COVID 19 on breast referral and breast cancer management.

Material and methods: We collected the data both retrospectively and prospectively from 16 March 2020 to 15 June 2020, while England was facing lock down restrictions. Total number of breast clinics scheduled, were 116 with 818 slots in Croydon University Hospital. We included 479 patients, 469 new referrals to breast clinic and 10 breast cancer patients referred back following neo adjuvant treatment. All new referrals were offered telephonic consultation (TC) prior to their face to face consultation (F2F) on the scheduled appointment day, within 2 weeks, 4–6 weeks and >12 weeks. All health care staff involved in direct care of these patients were provided with personal protective equipment (PPE) and guidelines.

Number of new referrals	469
TC	All
TC + discharge	92
F2 F	112
F 2 F in 2/52	151
F2F in 4–6/52	60
F2 F >3/12	54
B 3	11
New breast cancer	35
Post NACT	9
Post neo RT	1
Recurrent cancer/sarcoma	9
Primary Surgery	14
Bridging-ET	17
Primary ET	1
NACT	2
Neo RT	1

NACT – Neoadjuvant chemotherapy
Neo RT- Neo radiotherapy

Results: Out of 479 patients, 92 were discharged after TC due to low risk referral, 112 patients had F2F consultation on scheduled day, 151 within 2 weeks and 60 within 4–6 weeks after TC. 54 patients had their F2F appointments rescheduled after 3 months due to co-morbids. During this 3 months period, we diagnosed 35 new breast cancers, 5 recurrent cancer and 4 patients with sarcoma/malignant phyllodes. Primary surgery was performed in 14/35 patients with new cancer diagnosis, while 17 had bridging endocrine therapy prior to surgery. 10 patients had surgery following neoadjuvant treatment (chemotherapy in 9 and radiotherapy in 1). Total of 41 patients underwent surgery and COVID test was performed in all except 2 patients with one positive test result in whom surgery was deferred until converted negative. All patients had day case surgery with no adverse outcome noted.

Conclusions: After required reconfiguration in both clinics and theatre settings and following precautions and guidelines we found it safe to manage patients referred with breast symptoms or diagnosed with breast cancer during COVID-19 restrictions.

No conflict of interest.

561 Poster

Traumatic fat necrosis of the breast: a review of the spectrum of appearances of the 'great mimicker' of breast carcinoma

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Background: It can be extremely difficult to confidently diagnose fat necrosis of the breast given its variety of appearances and often striking resemblance to breast carcinoma. We rely on a correlation with a definite clinical history of trauma (accidental, biopsy-related or surgical) to that exact site, however even in this context it can be difficult to definitively outrule a co-incidental breast carcinoma/recurrence. This often leads to histological sampling of the region in question, despite a clear history of a traumatic insult to this site. We aim to review classic imaging characteristics of fat necrosis of the breast to aid radiological diagnosis.

Materials/methods: Using mammography, ultrasound and MRI, we demonstrate several examples of fat necrosis of the breast from both accidental and iatrogenic/surgical aetiologies.

Results: We exhibit both the typical and atypical features of breast fat necrosis which would cause concern and necessitate the need for histological sampling. We demonstrate its range of appearances on mammogram: from reassuring radiolucent oil cyst with curvilinear calcification to more indeterminate asymmetric mass-like density. We show its sonographic range, including focal regions of hyperechogenicity, cystic areas with peripheral hyperechogenicity and more indeterminate focal heterogeneity. On MRI, we demonstrate how the presence of fat signal or fat suppression within a lesion and enhancement of granulation tissue surrounding a non-enhancing central mass can also suggest fat necrosis versus malignancy.

Conclusion: Traumatic Breast Fat necrosis has a myriad of appearances on mammogram, ultrasound and MRI, presenting a dilemma for definitive radiological diagnosis. We present this spectrum of imaging characteristics and discuss the more atypical features which would necessitate histological confirmation.

No conflict of interest.

562 Poster

Advancing the age limit for core biopsy for U2 ultrasound lesions – are we ready?

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Introduction: In November 2019 the Royal College of Radiologists (RCR) suggested that a higher age cut-off of 30 years, as opposed to 25, may be appropriate in assessment of a lump when a fibroadenoma, lipoma or hamartoma is suspected, and a needle biopsy may not be required. We assessed whether this change in practice could be safely implemented, supported by local data and if we could adopt this in a multi-ethnic inner-city population.

Method: A retrospective audit of patients aged between 25- and 30-years undergoing core biopsy for well-defined U2 lesions from December 2018 to December 2019. Review of electronic health records for clinical grading and assessment, ultrasound and histology reports.

Results: There was a total of 46 female patients with a mean age of 27 years. All patients had benign clinical findings, P2. All ultrasound reports were U2, a fibroadenoma was mentioned in 25, and a well-defined lesion in 21. Histology confirmed B2 pathology in 40 cases (87%)[fibroadenoma in 28, benign changes 4, stromal fibrosis 3, inflammation 2, hamartoma 2 and sclerosing adenosis 1.] Four cases were B1 (9%) [minor benign changes] and 2 (4%) were B3, phyllodes cannot be ruled out. The latter 2 were excised with a final pathology of a cellular fibroadenoma in one case and a benign phyllodes.

Conclusion: Our retrospective data suggests that to raise the biopsy threshold to 30 years would potentially miss a clinically significant diagnosis in only 2% of cases. However, further prospective audit is required before adoption of the new recommendation.

No conflict of interest.

Rehabilitation/Survivorship

563 Poster

Fear of death among young breast cancer patients during adjuvant endocrine therapy

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Background: The diagnosis of breast cancer has a huge impact in so many young women. It makes the person encounter psychological and social challenges, particularly fear of death or recurrence. This type of fear can cause physical and mental disorders affecting the quality of life of young women with breast cancer. An increase in anxiety symptoms has been also noted with endocrine therapy. Thus, recognising and identifying factors that may be related to this issue is essential in order to draw new strategies to help our patients.

Aim: Evaluating the prevalence of fear of death in young breast cancer patients during adjuvant endocrine therapy by using some topics of the *Functional Assessment of Cancer Therapy* (FACT) for patients with breast cancer version 4 questionnaire.

Patients and methods: This cross-sectional study included 70 young breast cancer patients who started adjuvant endocrine therapy at three Portuguese institutions: Centro Hospitalar Universitário do Algarve, Centro Hospitalar Entre Douro e Vouga and Hospital Espírito Santo - Évora. Multiple linear regression analyses were used to test the association between each variable and fear of death while adjusting for the effects of other variable.

Results: The mean age of the patients was 41,6. All the patients received adjuvant chemotherapy. The mean time of endocrine treatment duration was 3,5 years.

We analyzed the answers of the question "I worry about dying": 20 patients answered "not at all", 20 "a little bit", 12 "somewhat", 14 "quite a bit" and 4 for "very much".

There were no significant associations between age, marital status, employment status, endocrine therapy, sexual life and death anxiety (p value>0.05). There was a significant relationship between accepting the disease and fear of death (p value <0.05). Thus, the level of fear of death was lower in patients that had accepted the disease; It was also lower in patients with good social and family support (p value <0.05).

Conclusion: There have been moderate levels of fear of death in the majority of the patients studied. The findings of the study indicate that a psychological approach in order to facilitate the acceptance of the disease may improve the quality of life of these patients. Health care professionals should also evaluate social and family support while treating these patients.

No conflict of interest.

Risk Factors

564 Poster

Dietary acid load and breast cancer risk: A case-control study in Uruguay

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Background: If endogenous acid–base balance is not well regulated, dietary acid load contributes to metabolic acidosis, which can lead to inflammation and cancer metastasis. However, there is limited epidemiologic evidence on the association between diet-dependent acid load and risk of cancer, particularly for breast cancer (BC). Also increased risk of recurrence among BC survivors was reported for high acid load. We carried out the present study with the aim of exploring its role on BC risk.

Material and methods: A case-control study was performed on 572 BC cases and 889 age-frequency matched controls, using a specific multi-topic questionnaire including a food frequency questionnaire on 64 items. Food-derived nutrients were calculated from available databases. Based on existing measures as potential renal acid load (PRAL) score and net endogenous acid production (NEAP) score, we assessed dietary acid load, using formulas that have been previously defined and used in recent epidemiologic studies on BC risk as well as on recurrence. Odds Ratios (ORs) and 95% confidence intervals were estimated by logistic regression, adjusting for dietary and other potential confounders. The equations included age, residence, education, body mass index, menopausal status, family history of BC, smoking intensity in pack-years, alcohol status, and energy intake as independent variables. Possible heterogeneities in the stratified analyses were explored through likelihood-ratio tests. The STATA software was used to make all calculations.

Results: We found direct associations between dietary acid load and BC risk. Highest quartiles of PRAL and NEAP were significantly associated (OR = 2.46 and OR = 1.78, respectively). Moreover, a positive family history of BC derived into even higher risks (OR = 6.14 and OR = 3.38 for highest PRAL and NEAP, respectively). In all cases the trend tests were highly significant (p for trend $\leq$0.001).

Conclusions: Since PRAL and NEAP scores are directly associated with meat intake and inversely associated with plant-based foods intake, results suggest that a low acid load dietary style may reduce BC risk, in agreement with studies focused on food groups and dietary patterns. Further studies are needed to clarify these points. The suggested associations with BC family history suggest possible gene-dietary interactions, which deserve to be explored.

No conflict of interest.

565 Poster

The Age Gap study: A prospective observational cohort study to determine the relationship between age, tumour stage and biology in older women with early breast cancer

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Background: Tumour stage and biology are known to vary with increasing age but little is known about variation within a cohort limited to older women (over age 70). The aim of this large multicentre observational study was to determine whether there is a correlation between patient age and tumour stage and biology.

Material and methods: A prospective, multicentre, comprehensive observational cohort of women over age 70 years with early breast cancer was recruited from 56 UK breast units. Detailed information at baseline on tumour stage (using the tumour, node, metastasis, TNM system), receptor status (ER, PgR, Her-2) and Oncotype DX score were collected. Tumour grade, nodal status, receptor status and Oncotype score were correlated with age subgroups (70–74, 75–79, 80–84, 85–89, 90+) using Chi squared. The Kruskal-Wallis test was used to examine differences in pre-operative (clinical) and post-operative (histopathological) mean tumour size.

Results: The study recruited 3414 women over age 70 with a median age of 77 (range 69–102). Both clinical tumour size (mean size age 70–74: 18 mm, age 90+: 31 mm, $p < 0.001$) and pathological tumour size (mean size age 70–74: 23 mm, age 90+: 36 mm, $p < 0.001$) significantly increased with age. Nodal involvement also increased with age with percentage node positive increasing from 14% to 21% between age 70–74 and 90+ age groups ($P = 0.003$). There were fewer grade 1 tumours in older age groups (p = 0.031). Tumour biology varied in line with previously published series with rates of Her-2 positivity falling with older age (9.9% age 70–74 versus 6.2% age over 90, p = 0.441), PgR positivity increasing with age (37% age 70–74 versus 43% aged over 90, P = 0.911) and ER positivity increasing with age (81% age 70–74 versus to 86% over 90). These differences were not statistically significant in this cohort. In women with ER+, node negative breast cancer eligible for an Oncotype DX test ™ only 3.5% were tested and no trend with age was therefore apparent either in rates of use, Oncotype Scores or clinical impacts.

Conclusions: The study confirms that tumours present later in older women which probably reflects the reduction in routine screening in this age group, reduced rates of screening self-referral, combined with reduced breast awareness. Tumour biology varies with few Her-2 positive cancers in older women, although the widely accepted increase in rates of ER positivity seen across the entire age spectrum is minimal within this limited older age range cohort. This stage shift may be a contributing factor to the inferior outcomes seen in older women.

No conflict of interest.

Supportive and Palliative Care Including End of Life Treatment

566 Poster

Quality of life of cancer patients at palliative care units in developing countries – systematic review of the published literature

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Background: Advanced cancer stage is detrimental to patients' quality of life (QOL), and should be mostly handled using palliative care (PC) strategies. Understanding factors that influence QOL of cancer patients in PC units in developing countries is necessary, but this information is limited. Therefore, this systematic review aims to summarize the evidence on this topic.

Material and methods: Following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, we registered our systematic review with PROSPERO (CRD42019142567). We systematically identified studies by searching electronic databases of MEDLINE, Embase, CINAHL, and Web of Science using the search terms: QOL, cancer, PC, and all developing countries` names. Studies with less than ten subjects, qualitative, pilot studies, reviews, abstract conferences, and a validation study of QOL instruments were excluded. We performed critical appraisal using the quality assessment scale for cross-sectional studies, the Newcastle-Ottawa Quality Assessment Scale for cohort studies, and the risk of bias assessment tool by the Cochrane collaboration for randomized control trials (RCTs) or quasi-experimental studies.

Results: Fifty-five studies from 15 developing countries in the African (n = 5 studies), Latin America and the Caribbean (n = 10), and Asian (n = 40) regions were included in the narrative synthesis. 65.4% were cross-sectional, 27.3% were cohort studies, 7.3% were RCTs or quasi-experimental studies. Over 30 QOL factors were studied with 20 different types of QOL instruments. While advanced cancer patients who were older, married/ever married, participated in additional care within PC, used complementary and alternative medicine (CAM), and practiced spirituality/religiosity showed higher QOL score, having a low educational level and high depression tended to decrease QOL.

Conclusions: Various factors affected QOL among cancer patients in PC. As patients valued CAM and spirituality/religiosity, its quality and safety aspects should be properly addressed. While there is a general need to develop PC provision further, recognizing patients' needs should be a priority. Other listed factors suggest the importance of social and spiritual support.

No conflict of interest.

567 Poster

Evaluation of optimal prophylactic antiemetic regimens for doxorubicin-cyclophosphamide chemotherapy

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Background: Chemotherapy-induced nausea and vomiting (CINV) is common with doxorubicin-cyclophosphamide (AC) chemotherapy. Recommended antiemetic regimens may incorporate neurokinin-1 receptor antagonist (NK1RA), 5-hydroxytryptamine type-3 receptor antagonist (5HT3RA), corticosteroid and dopamine antagonist. This post-hoc analyses compared 5 different antiemetic regimens which were tested in 3 prospective antiemetic studies among Chinese breast cancer patients who received (neo)adjuvant AC. The primary objective was to compare efficacies of doublet (5HT3RA/dexamethasone) with triplet antiemetic regimens (NK1RA/5HT3RA/dexamethasone) with/without olanzapine. The secondary objectives were to compare (1) netupitant- with aprepitant-based triplet antiemetic regimens; and (2) 1-day (D1) versus 3-day (D1–3) dexamethasone.

Methods: 304 patients were included: Group 1, ondansetron/dexamethasone (D1); Group 2, aprepitant/ondansetron/dexamethasone (D1); Group 3, aprepitant/ondansetron/dexamethasone (D1-3); Group 4, aprepitant/ondansetron/dexamethasone (D1-3)/olanzapine; Group 5, netupitant/palonosetron/dexamethasone (D1-3). Analyses were conducted on rates of Complete Response (CR; defined as 'no vomiting with no rescue therapy') and quality of life (QOL).

Results: CR rates in overall phase of cycle 1 AC were: Groups 1 vs 3 were 41.9% vs 38.3% (p = 0.6849); Groups 1 vs 4 were 41.9% vs 65.0% (p = 0.0107); Groups 1 vs 5 were 41.9% vs 60.0% (p = 0.0460); these were associated with better QOL. CR rates of Groups 3 vs 5 were 38.3% vs 60.0% (p = 0.0176); QOL was better in Group 5. CR rates of Groups 2 vs 3 were 46.8% vs 38.3% (p = 0.3459); QOL was significantly worse in Group 3.

Conclusion: Among Chinese patients who were uniformly receiving AC, aprepitant-containing triplets was not superior to doublet antiemetic regimen, while netupitant-containing triplets and the addition of olanzapine to aprepitant-containing triplets were superior to doublets. Netupitant/palonosetron/dexamethasone was superior to aprepitant/ondansetron/dexamethasone triplets. Protracted administration of dexamethasone provided limited additional benefit.

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Conflict of interest:
Corporate-sponsored Research:
Mundipharma supported the study design of NEPA6 but had no role in the present comparative analysis, data collection and analysis, decision to publish, or preparation of the manuscript. Madam Diana Hon Fun Kong Donation for Cancer Research had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.
Other Substantive Relationships:
W Yeo has been involved in CINV Network in Asia and has been a speaker on CINV, organized by Mundipharma.

Systemic Treatment

568 Poster

Efficacy and safety of neoadjuvant pertuzumab, trastuzumab and chemotherapy in non-metastatic HER2-positive breast cancer in the Asian population: a multicentre analysis

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Background: Pertuzumab combined with trastuzumab and chemotherapy is now the standard neoadjuvant treatment for non-metastatic HER2-positive early breast cancer (HER2+ BC). However, information on the efficacy of this combination in Asian population is sparse. This retrospective study aims to assess the clinical outcome of adding pertuzumab to trastuzumab and chemotherapy (PH/CTX) for stage II to III HER2+ BC in an Asian cohort.

Methods: A multi-centre, retrospective study on pre-treatment clinical stage II-III, HER2+ BC patients treated with neoadjuvant PH/CTX from January 2013 to June 2019 in six oncology centres in Hong Kong was performed. Demographic data, size, grade, tumor type, hormonal receptor (HR) status, concomitant chemotherapy used, cycles of systemic treatment and pathological complete response (pCR) rates were analyzed. pCR was defined as the absence of invasive or noninvasive cancer in breast and lymph nodes, i.e., ypT0ypN0.

Results: A total of 211 patients received neoadjuvant PH/CTX, median age: 52 year old (range: 26–83). 90 patients (42.7%) were in clinical stage II and 121 (57.3%) patients were in clinical stage III. 134 (63.5%) patients had HR+ tumors. The concomitant chemotherapy regimens included doxycycline-carboplatin (DC) (165, 78.2%), paclitaxel-carboplatin (TC) (33, 15.6%), and adriamycin-cyclophosphamide then doxycycline-carboplatin (AC-DC)

(13, 6.2%). The median number of cycles of neoadjuvant PH given was 6 (range 4–8).

197 patients had radical surgery after neoadjuvant PH/CTX (7 patients: refused operation; 7 patients had persistent inoperable disease or progression). 115 patients achieved pCR after neoadjuvant PH/CTX (overall pCR rate: 58.4%). pCR was higher in HR- tumors (HR+ vs. HR-: 52.3% vs. 70.8%, p = 0.014) and smaller tumors (OR: 0.99, 95% CI 0.97–1.0, p = 0.02). For the chemotherapy partner, adding anthracycline on top of taxane-based chemotherapy did not improve the pCR rate (pCR rate of DC: 57.1%; TC: 67.9%; AC-DC: 50%, p = 0.73).

Among 78 patients with clinically inoperable locally advanced disease, 69 patients (88.5%) had good response after neoadjuvant PH/CTX and underwent radical operation with clear resection margin; 41 patients (52.6%) achieved pCR. HR status, size of tumor, N stage, Ki-67 level or chemotherapy partner were not associated with pCR rate in locally advanced disease.

	Number of patients	Number with pCR	pCR rate
Overall	197	115	58.4%
Hormonal receptor – positive (HR+)	132	69	52.3%
Hormonal receptor – negative (HR-)	65	46	70.8%
Locally advanced disease	78	41	52.6%

Conclusion: Neoadjuvant PH/CTX was associated with a pCR rate of 58.4% in our Asian cohort. Results in locally advanced disease were promising. The conversion rate of initially inoperable disease to operable disease was high and the pCR rate was over 50%.

No conflict of interest.

569 Poster

ESR1 mutations in metachronous contralateral breast cancer

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Background: In metachronous contralateral breast cancer (CBC), the incidence of estrogen receptor positive (ER+) cancers is lower compared to the general population of breast cancers. This has been explained by the protective effect of endocrine therapy that a considerable number of these patients have had for their first breast cancer. In metastasis of ER+ breast cancers the incidence of mutations in the gene coding for the estrogen receptor (ESR1) is increased up to 15–25% compared to 1–2% of the primary tumors. These mutations develop under endocrine therapy and are associated with resistance to endocrine therapy. We hypothesized that the incidence of ESR1 mutations was also increased in metachronous CBC.

Material and methods: Metachronous CBC of patients with an ER+ first breast cancer were selected from our pathology files. DNA was isolated from formalin fixed paraffin embedded tissue and pyrosequencing of a hotspot region involved in the endocrine therapy resistance of the ESR1 gene (codon 536–538) was performed.

Results: A total of 89 patients were selected from our files with 92 CBC's. The mean age at the time of diagnosis of CBC was 66.1 years (std 10.9 years), the mean interval between the diagnosis of the first breast cancer and the metachronous CBC was 7.6 years (std 5.3 years), 38 (43 %) patients received endocrine therapy for their first breast cancer and all CBC's were ER+. We found 1 mutation (D538G)in the CBC's, i.e. in 1%.

Conclusion: The incidence of ESR1 mutations is not increased in CBC compared to the general population of breast cancers.

No conflict of interest.

570 Poster

Neoadjuvant endocrine treatment and clinical outcome in ER positive breast cancer – a single UK cancer centre experience

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Background: Neoadjuvant endocrine treatment (NET) is increasingly used in early stage ER positive breast cancer (EBC) mainly in post-menopausal patients. This approach shows response rates (RR) comparable to neoadjuvant chemotherapy for some patients but randomised trials are limited. We set out to review the RR in patients treated with NET at our UK centre.

Materials and methods: Records from the BC multi-disciplinary team meeting registry were reviewed to identify EBC patients treated with NET between 2014 and 2019. Clinical response, type of surgery and pathologic response were assessed.

Results: The medical records of 304 BC patients diagnosed between 2014 and March 2019 were reviewed.160 patients with 167 EBCs (7 bilateral cases) treated with ≥4 weeks of NET were included in this analysis; 9 were HER2 positive (5 diagnosed post-operatively). Mean age was 66 (40–92). 155 patients were post or peri-menopausal while 9 were pre-menopausal (3 unknown menopausal status).

NET consisted of: aromatase inhibitor (AI) (152, 2 with ovarian suppression (OS)), tamoxifen (6, 2 with OS) or a CDK 4/6 inhibitor with AI (9, 3 with OS). Median duration of NET was 3 months(1–29 months).

84 patients (50%) underwent mastectomy and 83 (50%) breast conserving surgery (BCS). In 26 (16%), breast surgery was combined with axillary node clearance (ANC) while in 12 (7%) a second surgery was required for ANC. One BCS required a subsequent mastectomy. Overall, 10 (6%) achieved a pathologic complete response (pCR). T downstaging was observed in 32 (19%), T upstaging in 41 (25%) and N upstaging in 33 (20%). Chemotherapy was given to 33 (21%) patients (2 pre-operatively); 5 of these received adjuvant HER2 targeted treatment.

114 patients were treated with <6 months of ET (median 2) and 53 for >6 months (median 8). Clinical response (PR+CR) in HER2 negative EBC with available imaging data (Table 1) was 44% in <6 months and 68% in >6 months NET. 4 (3.5%) cases treated for <6 months had a pCR and 6 (12%) in those treated for ≥6 months. pCR rates according to ER/PR expression (high expression = Quick score ER/PR ≥7; low expression = Quick score ER 6–8 and PR<7) were 8% (7/89) in high and 4% (2/50) in the low score group.

Table 1 Response rate according to NET duration

Imaging Response	NET <6 months (n = 39)	NET >6 months (n = 41)
CR	2 (5%)	3 (7%)
PR	15 (38%)	25 (61%)
SD	20 (51%)	12 (29%)
PD	2 (5%)	1 (2%)

CR = complete response; PR = partial response, reduction of ≥30%; SD = stable disease, PD = Progressive disease, increase of ≥20%.

Conclusion: NET is a suitable option for some patients with EBC to achieve tumour size reduction and undergo successful BCS but careful selection of patients is key. In our study 50% were able to have BCS and 6% had pCR following NET. Properly designed trials can identify the ideal candidates and the optimal duration of NET.

No conflict of interest.

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