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한국유방암학회
Korean Breast Cancer Society

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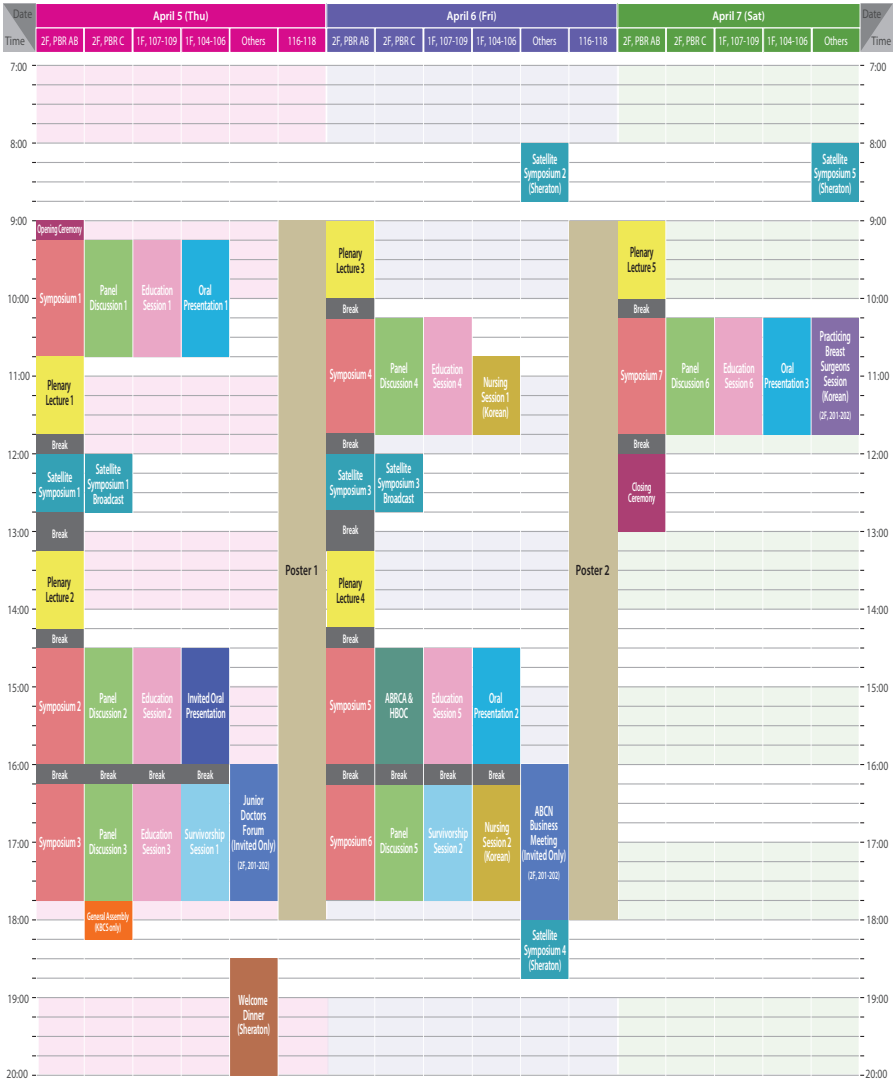

Program Details

Day 1 April 5 (Thu)

09:00-09:15 **Opening Ceremony** — Premier Ballroom AB

09:15-10:45 **Symposium 1** — Premier Ballroom AB

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Moderator Janice Sung
Memorial Sloan Kettering Cancer Center, U.S.A.

Day 1 April 5 (Thu)

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Samsung Medical Center, Korea

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Memorial Sloan Kettering Cancer Center, U.S.A.

Speaker Sung Hun Kim *65*
AUTOMATED BREAST US AS SUPPLEMENTAL SCREENING MODALITY IN WOMEN WITH DENSE BREASTS
The Catholic Univ. of Korea, Seoul St. Mary's Hospital, Korea

Speaker Woo Kyung Moon *66*
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Overcoming Resistance to HER2-directed Therapies

Moderator Ian Krop
Dana-Farber Cancer Institute, U.S.A.

Moderator Jung Sil Ro
National Cancer Center, Korea

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Moderator Ho Yong Park
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Moderator Louis Chow
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Moderator Funda Meric-Bernstam
The Univ. of Texas MD Anderson Cancer Center, U.S.A.

Moderator Woochul Noh
Korea Cancer Center Hospital, Korea

Speaker Soo Chin Lee *19*
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National Univ. Cancer Institute, Singapore

Speaker Seock-Ah Im *20*
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Seoul National Univ. Hospital, Korea

Speaker Funda Meric-Bernstam *21*
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The Univ. of Texas MD Anderson Cancer Center, U.S.A.

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Moderator Charles M. Perou
Univ. of North Carolina at Chapel Hill, U.S.A.

Moderator Woong-Yang Park
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Moderator David Chang
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Day 2 April 6 (Fri)

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Management of Febrile Neutropenia by Pegfilgrastim in the United States: Importance of Relative Dose Intensity and Control of Toxic Effects of Chemotherapy in Early Breast Cancer

Moderator Jin-Hee Ahn
ASAN Medical Center, Korea

Speaker Naoto Ueno *118*
MANAGEMENT OF FEBRILE NEUTROPENIA BY PEGFILGRASTIM IN THE UNITED STATES: IMPORTANCE OF RELATIVE DOSE INTENSITY AND CONTROL OF TOXIC EFFECTS OF CHEMOTHERAPY IN EARLY BREAST CANCER
The Univ. of Texas MD Anderson Cancer Center, U.S.A.

09:00-10:00 **Plenary Lecture 3** **Premier Ballroom AB**

The Role of Breast Surgery: Coping with the Present and the Future

Moderator Sung Hwan Park
Daegu Catholic Univ. Medical Center, Korea

Speaker Stephen Grobmyer *5*
THE ROLE OF BREAST SURGERY: COPING WITH THE PRESENT AND THE FUTURE
Cleveland Clinic, U.S.A.

10:00-10:15 **Break**

10:15-11:45 **Symposium 4** **Premier Ballroom AB**

Balancing Cosmetic Results and Oncologic Outcomes

Moderator Maria-Joao Cardoso
Champalimaud Foundation, Portugal

Moderator Hak Chang
Seoul National Univ. Hospital, Korea

Speaker Ho Yong Park *22*
INDIVIDUALIZED APPLICATION OF ONCOPLASTIC TECHNIQUES
Kyungpook National Univ. Chilgok Hospital, Korea

Speaker Eisuke Fukuma *24*
EVALUATION OF COSMETIC OUTCOME AND ITS PRACTICAL RELEVANCE TO REAL LIFE
Kameda Medical Center, Japan

Speaker Maria-Joao Cardoso *25*
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Champalimaud Foundation, Portugal

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10:15-11:45 | **Panel Discussion 4** | **Premier Ballroom C**

How Can We Better Treat Patients with Metastatic Disease?

Moderator	Eric P. Winer *Dana-Farber Cancer Institute, U.S.A.*	
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Moderator	Naoto Ueno *The Univ. of Texas MD Anderson Cancer Center, U.S.A.*	
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Moderator Soonmyung Paik
Yonsei Univ. College of Medicine, Korea

Speaker Mien-Chie Hung 7
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The Univ. of Texas MD Anderson Cancer Center, U.S.A.

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Moderator Fatima Cardoso
Champalimaud Clinical Centre, Portugal

Moderator Olivia Pagani
Oncology Institute of Southern Switzerland (IOSI), Switzerland

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Daerim St. Mary's Hospital, Korea

Moderator Ava Kwong
Queen Mary Hospital, Univ. of Hong Kong, Hong Kong

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Moderator Jin Zhang
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Moderator Joon Jeong
Gangnam Severance Hospital, Korea

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Moderator Tae Hyun Kim
Inje Univ. Busan Paik Hospital, Korea

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16:00-16:15 **Break**

16:15-17:45 **Symposium 6** **Premier Ballroom AB**

Various Options for Radiotherapy for Optimal Breast Cancer Care

Moderator Jiayi Chen
Ruijin Hospital, Shanghai Jiaotong Univ. School of Medicine, China

Moderator Chang-Ok Suh
Yonsei Cancer Center, Korea

Speaker Jayant S Vaidya *29*
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Univ. College London, United Kingdom

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Yonsei Univ., Korea

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Speaker Woo Joung Joung 112
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Speaker Eun Ju Lee 113
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Optimal Treatment Strategy for ER-positive, HER2-negative MBC - Implications from the Clinical Trial and Experience

Moderator Keun Seok Lee
National Cancer Center, Korea

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Moderator Jung Han Yoon
Chonnam National Univ. Hwasun Hospital, Korea

Speaker Giuseppe Curigliano *124*
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Univ. of Milano, European Institute of Oncology, Italy

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Recent Treatment Strategies for Advanced Breast Cancer Patients

Moderator Sung-Bae Kim
ASAN Medical Center, Korea

Speaker Fatima Cardoso *9*
RECENT TREATMENT STRATEGIES FOR ADVANCED BREAST CANCER PATIENTS
Champalimaud Clinical Centre, Portugal

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The Cancer Institute Hospital of JFCR, Japan

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Chang Gung Memorial Hospital, Taiwan

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Moderator Heung Kyu Park
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Program Details

Day 3 April 7 (Sat)

11:45-12:00	Break	
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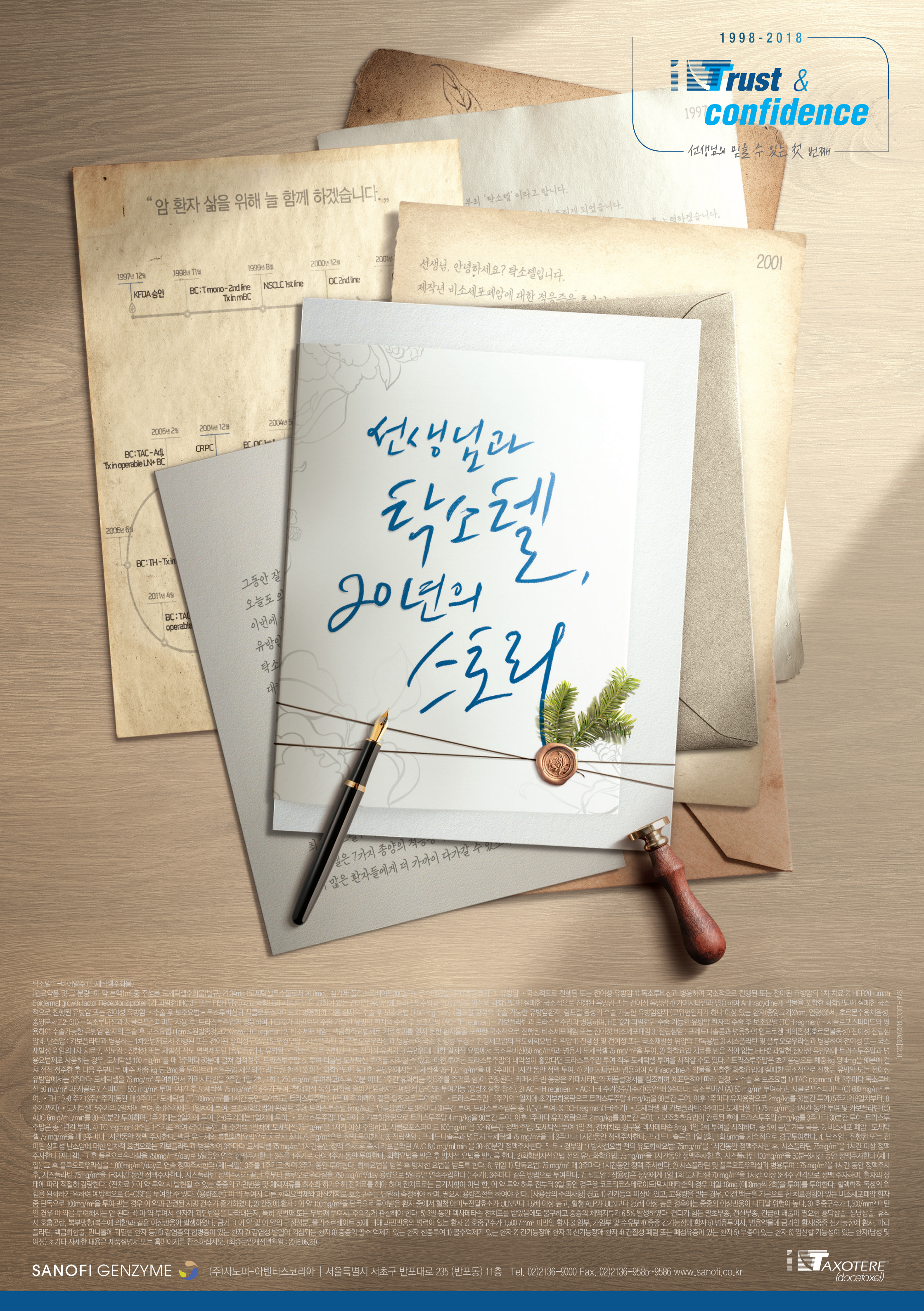

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[제품명] 허쥬마주 150mg, 440mg(트라스투주맙)/(단클론항체, 유전자재조합) **[주성분]** 트라스투주맙 **[효능·효과]** HER2 양성 전이성 유방암, HER2 양성 조기 유방암, 전이성 질환으로 이전에 항암치료를 받은 적이 없는 HER2 양성 전이성 위 선암이나 위식도 접합부 선암 **[용법·용량]** · 전이성 유방암 : 이 약 단독요법 및 파클리탁셀, 도세탁셀, 아로마타제 억제제와의 병용요법 시 이 약의 권장용량은 다음과 같다. ▶ **1주 요법** – 초기부하용량 : 권장 초기부하용량은 4mg/kg이다. / 유지용량 : 권장 유지용량은 매주 2mg/kg이며 초기부하용량 투여 1주일 후부터 투여를 시작한다. ▶ **3주 요법** – 초기부하용량 : 권장 초기부하용량은 8mg/kg이다. / 유지용량 : 권장 유지용량은 6mg/kg이며 초기부하용량 투여 3주 후부터 투여를 시작한다. / 도세탁셀과 파클리탁셀의 병용요법 : 이 약의 최초 투여시에는 이 약 투여 다음날에 파클리탁셀 또는 도세탁셀을 투여한다. 최초 투여에 내약성이 우수한 경우, 이후 투여시에는 이 약 투여후 즉시 파클리탁셀 또는 도세탁셀을 투여할 수 있다. / 아로마타제 억제제와의 병용요법 : 이 약과 아로마타제 억제제는 첫날에 모두 투여한다(투여순서는 상관없음). · 조기 유방암 : 다음의 2가지 투여요법 중 선택하여 투여할 수 있다. ▶ **3주 요법** – 초기 부하용량으로 8mg/kg을 투여하고 이후 매 3주마다 유지용량으로 6mg/kg을 투여한다. / ▶ **1주 요법** – 안트라싸이클린과 싸이클로포스파마이드 병용 화학요법실시후, 초기부하용량으로 4mg/kg을 투여하고 이후 1주마다 2mg/kg을 유지용량으로 투여한다. 이때는 파클리탁셀과 병용투여한다. · 전이성 위암 : ▶ **3주 요법** – 초기 부하용량으로 8mg/kg을 투여하고 이후 매 3주마다 유지용량으로 6mg/kg을 약 90분에 걸쳐 정맥주입 한다. 초기 부하 용량에 내약성이 우수한 경우 유지용량은 30분에 걸쳐 주입할 수 있다. **[사용상의 주의사항]** 1. 경고 1) 심기능 장애 : 트라스투주맙 투여 시 울혈성 심부전뉴욕심장학회(NYHA)등급 2~4등급] 또는 무증상 심기능 장애의 위험이 증가한다. 2) 주입관련 반응, 알러지양 반응 및 과민반응 : 트라스투주맙 주입에 따라 보고된 중대한 이상사례로 흐흡곤란, 저혈압, 천명, 고혈압, 기관지연축, 심실위부정반맥, 산소 포화도 감소, 아나필락시스, 호흡곤란 증후군, 두드러기, 혈관부종이 있다. 3) 폐 이상사례 : 드물게 중증 폐이상사례가 트라스투주맙의 시판후조사에서 보고되었으며 이는 때때로 치명적일 수도 있다. 4) 벤질알코올은 미숙아에게서 치명적인 가쁜 흐흡증상과 연관이 있는 것으로 보고되었다(허쥬마주 440mg에 한함). 2. 다음 환자에는 투여하지 말 것 1)트라스투주맙, 설치류 유래 단백 또는 이 약의 구성성분에 과민반응 병력이 있는 환자. 2)진행성 악성종양에 의한 중증 안정 시 흐흡곤란 또는 산소보충이 필요한 환자. 3)신생아, 미숙아(벤질알코올을 함유하고 있다, 허쥬마주 440mg에 한함) **※ 제품에 대한 자세한 정보는 최신의 제품설명서를 참고하시길 바라며, 홈페이지를 통해 확인하실 수 있습니다.**

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Plenary Lecture

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PL 01

OVERVIEW OF THERAPEUTIC STRATEGIES FOR EARLY BREAST CANCER PATIENTS: PAST, PRESENT AND FUTURE

Eric P. Winer

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The treatment of early stage breast cancer has changed dramatically over the past 20 years. Breast cancer was formerly viewed as a monolithic process, and most patients received nearly identical treatment. The vast majority of women with stage 1-3 breast cancer underwent surgery, chemotherapy, hormonal therapy (if the tumor was estrogen receptor positive), and often radiation. There is no question that treatment reduced the risk of disease recurrence, but many patients needed to receive treatment to benefit a small number.

As a result of both genomic analysis and careful examination of clinical data, it is now clear that breast cancer is heterogeneous disease with several distinct subtypes, if not more. In considering breast cancer treatment, we think separately about triple negative disease, HER2+ disease, and at least two types of ER+ disease, luminal A (generally low grade and highly responsive to hormonal therapy) and luminal B (higher grade and less responsive to hormonal therapy. For patients with triple negative disease, chemotherapy remains the mainstay of adjuvant therapy, and we continue to search for driver mutations and new targets. In contrast, patients with HER2+ disease benefit from highly targeted therapy of HER2, and the availability of HER2 targeting has changed the natural history of the disease. Increasingly, we are trying to back off on chemotherapy in HER2+ disease and rely more on targeted therapy. We are also beginning to understand that there are important subtypes of HER2+ disease. For patients with luminal disease, we are relying on genomic predictors such as Oncotype Dx, the Risk of Recurrence Score, and Mammoprint to assist in decision making, and we are holding back on chemotherapy for an increasing proportion of patients. We have also come to understand that over half of all recurrences of luminal disease arise more than five years after diagnosis, raising questions about how to prevent these late recurrences.

Our molecular understanding of breast cancer will continue to expand and deepen. In the years ahead, and it likely that we will be talking about subtypes of subtypes of breast cancer, with important therapeutic implications for these large groups of patients. It is likely that we will rely more on targeted therapy and less on traditional chemotherapy. It is also likely that we will better understand how to improve the effectiveness of endocrine therapy.

Of course, in parallel with the improvements in adjuvant systemic therapy, there have also

been major advances in both breast surgery and radiation oncology. While these topics are beyond the scope of the lecture, they represent important advances in the field. Our ultimate goal is to eliminate mortality and lower the morbidity of treatment, and these goals appear to be more feasible than ever before, though it will still take many years.

PL 02

APPLICATION OF THE CONCEPT OF INTRINSIC SUBTYPES TO CLINICAL DECISION MAKING

Charles M. Perou

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Gene-expression profiling has had a considerable impact on our understanding of breast cancer biology. During the last 15 years, 5 intrinsic molecular subtypes of breast cancer (Luminal A, Luminal B, HER2-enriched, Basal-like and Claudin-low) and a normal breast-like group have been identified and intensively studied. In this presentation, I will focus on recent data regarding the potential clinical implications of the intrinsic molecular subtypes beyond the current pathological-based classification endorsed by the 2015 St. Gallen's Consensus Recommendations. Within hormone receptor (HR)-positive and HER2-negative breast cancer, the Luminal A and B subtypes represent the vast majority of cases. Compared to Luminal A tumors, Luminal B tumors are characterized by higher expression of proliferation/cell cycle-related genes and lower expression of several luminal-related genes such as the progesterone receptor (PR). Clinically, Luminal B tumors show higher pCR rates following neoadjuvant multi-agent chemotherapy but worse distant recurrence-free survival at 5-years and 10-years regardless of adjuvant systemic therapy compared to Luminal A. This Luminal A vs. B classification, together with tumor size and encompassed with the "ROR Score", also predicts distant recurrence within the 5 to 10-years of follow-up and thus may inform decisions concerning the length of endocrine therapy treatments (i.e. 5 years vs. 10 years).

Interestingly, although we and others have proposed pathology-based surrogate definitions of the Luminal A and B subtypes using semi-quantitative IHC scoring of Ki-67 and PR, the discordance rate versus multi-gene expression assays is still high (~30-40%). Within clinically HER2+ disease, all the 4 main intrinsic subtypes can be identified beyond HR status, albeit with different proportions. Among them, the HER2-enriched subtype represents the majority of HER2+ tumors and shows higher expression of HER2 and lower expression of luminal genes compared to both luminal subtypes. In addition, recent data suggests that patients with HER2-enriched disease benefit the most from neoadjuvant trastuzumab, or dual HER2 blockade with trastuzumab/lapatinib, in combination with chemotherapy.

PL 03

THE ROLE OF BREAST SURGERY: COPING WITH THE PRESENT AND THE FUTURE

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Breast cancer remains a major public health problem around the world. Surgery has been and remains a primary modality for the treatment, staging, and prevention of breast cancer. In order to improve the surgical treatment of breast cancer, we are utilizing ultrasound and fluorescence image guidance to extend the indications for nipple sparing mastectomy, to improve margin determination and to improve sentinel node detection. Wearable Smartgoogles are under development to facilitate image guided breast surgery. To reduce the burden of upper extremity lymphedema following breast cancer surgery, lymphaticovenous bypass is a new approach to restore upper extremity physiologic lymphatic flow and prevent lymphedema. Sentinel node biopsy and axillary node dissection remain important staging tools for selected patients with breast cancer. Recent improvements in selection of patients for neo-adjuvant chemotherapy is reducing the need for complete axillary node dissection in many patients. Molecular diagnostics has become an important component of breast cancer staging and has recently been incorporated in the AJCC breast cancer prognostic staging system. Risk reducing bilateral mastectomy is effective for reducing breast cancer risk in patients with hereditary breast cancer syndromes. Our understanding of breast germline genetics continues to evolve with the introduction of multi-gene panel testing into clinical practice. It is critical that surgeons understand the interpretation of these tests and implications of these tests on proper selection of patients for risk reducing surgery. Sensory preserving mastectomy is also being developed to reduce the morbidity of risk-reducing surgical procedures.

In the future, it is anticipated that surgical interventions will play a less important role in the treatment, staging and prevention of breast cancer. This will occur as a result of advances in systemic treatment and incorporation of emerging technologies into practice. Advances in systemic therapy for breast cancer are resulting in unprecedented tumor response rates. As a result, some patients may be safely spared surgical interventions for breast cancer in the future. In terms of staging, it is anticipated that molecular diagnostics will continue to evolve and enhance the precision of breast cancer staging and decrease the role of surgery in staging breast cancer. Circulating cell-free DNA is also emerging as a powerful tool for early detection and staging of breast cancer. Improvements in understanding of possible new risk factors for breast cancer such at the human microbioime, hold significant promise for preventing breast cancer. Vaccines in development also hold significant promise for preventing breast cancer and for reduc-

ing the need for risk reducing mastectomy in the future.

There remains a great need world-wide for strategies to reduce the burden of breast cancer. There are many new, exciting approaches that are and will continue to improve the surgical management of breast cancer. Ultimately, it is anticipated that continued incorporation of new treatments and technologies into practice will diminish the role of surgery for breast cancer and very importantly, reduce the global burden of breast cancer.

PL 04

MARKER-GUIDED TARGETED THERAPY, PARP INHIBITORS AND IMMUNE CHECKPOINT THERAPY

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Poly (ADP-ribose) polymerase (PARP) inhibitors have emerged as promising therapeutics for many diseases, including cancer, in clinical trials. Three PARP inhibitors have been approved by the FDA to treat ovarian cancer with (olaparib and rucaparib)or without BRCA mutations (niraparib). BRCA1 and BRCA2 play essential roles in repairing DNA double strand breaks, and a deficiency of BRCA proteins sensitizes cancer cells to PARP inhibition. My group recently demonstrated that receptor tyrosine kinase c-Met associates with and phosphorylates PARP1 at Tyr907. Phosphorylation of PARP1 Tyr907 increases PARP1 enzymatic activity and reduces binding to a PARP inhibitor, thereby rendering cancer cells resistant to PARP inhibition. Combining c-Met and PARP1 inhibitors synergized to suppress growth of breast cancer cells in vitro and xenograft tumor models. Similar synergistic effects were observed in a lung cancer xenograft tumor model. These results suggest that PARP1 pTyr907 abundance may predict tumor resistance to PARP inhibitors, and that treatment with a combination of c-Met and PARP inhibitors may benefit patients bearing tumors with high c-Met expression who do not respond to PARP inhibition alone (Nature Medicine 22:194-201, 2016).

Extracellular interaction between programmed death ligand-1 (PD-L1) and programmed cell death protein-1 (PD-1) leads to tumor-associated immune escape. Here, we show that the immunosuppression activity of PD-L1 is stringently modulated by ubiquitination and N-glycosylation. We identified glycogen synthase kinase 3b (GSK3b) as a novel protein that interacts with PD-L1 and can induce phosphorylation-dependent proteasome degradation by b-TrCP. We also demonstrate that epidermal growth factor (EGF) stabilizes PD-L1 via GSK3b inactivation in basal-like breast cancer (BLBC). Inhibition of EGF signaling by gefitinib destabilizes PD-L1, enhances antitumor T cell immunity and therapeutic efficacy of PD-1 blockade in syngeneic mice models. Together, we demonstrated a novel interchange between glycosylation and phosphorylation regulating ubiquitination and degradation of PD-L1. This regulatory event is critical for BLBC cells that escape immune surveillance via PD-L1/PD-1 interaction. Importantly, inhibition of EGF-mediated PD-L1 stabilization enhances a therapeutic efficacy of PD-1 blockade to promote tumor-infiltrating cytotoxic T cell immune response. Thus, targeting PD-L1 stabilization provides a novel strategy to combat BLBC-mediated immunosuppression and may potentially apply to other cancer types (Nature Communications 7:12632, 2016). In a most recent study, we identified TNFα as a major factor triggering cancer cell immunosuppres-

sion against T cell surveillance via stabilization of programmed cell death-ligand 1 (PD-L1) (Cancer Cell, 30:925, 2016). To this end, in collaboration with StCube Pharmaceuticals Inc., we have developed monoclonal antibodies against glycosylation-specific PD-L1. Impressive therapeutic effect was observed through ab-drug-conjugate approach (Cancer Cell 33, 187-201, 2018).

PL 05

RECENT TREATMENT STRATEGIES FOR ADVANCED BREAST CANCER PATIENTS

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Advanced Breast Cancer (ABC) comprises both locally advanced (LABC) and metastatic breast cancer (MBC). Although treatable, MBC remains an incurable disease with a median overall survival of 2–3 years and a 5-year survival of only 25%. Some more recent series seem to indicate an improvement in median overall survival. A recent comprehensive report of the advances in this field in the last decade shows that progress has been slow in terms of improved outcomes, quality of life, awareness and information regarding ABC. The level of evidence used to base many recommendations remains low, and more and better designed trials are needed to address clinically important questions. An improved understanding of the biology of ABC, its heterogeneity, and of the mechanisms of resistance to the different types of therapies is being acquired and it is anticipated that the application of new technologies, such as next generation sequencing, patient xenographs, systems biology, and computer modelling, among others, will accelerate advances.

Symposium

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SP01-1

LIQUID BIOPSY: CTC, CTDNA, EXOSOME ETC.

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Since the advent of targeted agents bringing personalized medicine to reality for breast cancer, there has been further emerging advances in the diagnosis, treatment and monitoring of breast cancer, from personalized medicine to precision medicine over the last decade.

Histopathology with tissue diagnosis has always been the key to better breast cancer care including disease diagnosis, molecular evaluation, prognostic and predictive markers and assessment of treatment response. The challenge of intra-tumour heterogeneity, identifying early recurrence or disease progression and the complexity of performing multiple organ biopsies at the time of recurrence, has led to the demonstration of added value of liquid biopsy.

Over the years, technology has evolved to achieve higher sensitivity and specificity to detect circulating tumour cells (CTCs), cell-free circulating tumour DNA (ctDNA), making early detection of treatment-resistant breast cancer in advanced disease setting, and identification of minimal residual disease in early stage breast cancer possible. The recent CTC molecular profiling techniques have further open a new era of better understanding of the individual pathways of cancer invasion and metastases as well as real-time tumour resistance mechanisms. This presentation will give an overview and latest update of the development of various facets of liquid biopsies facilitating better breast cancer treatment decision making.

SP01-2

CLINICAL UTILITY OF MULTIGENE ASSAYS IN BREAST CANCER

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It has been more than a decade since multigene assay was clinically used for the treatment of breast cancer. With gene expression profiling it was possible not only to identify the intrinsic subtypes of breast cancer in 2000 but also to differentiate the characteristics of clinical breast cancer with subsequent studies. Eventually the first multigene assay based on gene expression profiling, i.e. the 21 gene test (OncotypeDX®) was developed to stratify estrogen receptor (ER)-positive breast cancer based on risk of relapse with treatment in 2004. Thereafter many multigene assays were developed and have been used for prediction of risk of recurrence and of treatment response of breast cancer with chemotherapy. Recently multigene assay as a predictive biomarker in breast cancer was endorsed for decision of adjuvant chemotherapy by ASCO and EGTM. In addition, as a prognostic biomarker multigene assay was incorporated into the new 8th edition of AJCC breast cancer staging manual. However, the role of multigene assay was limited to a small group of breast cancer, i.e. ER-positive, HER2-negative, node-negative breast cancer, because multigene assay was composed of mainly proliferation related gene so that it could not stratify the risk of highly proliferating breast cancer such as HER2-positive or triple negative subtype. Another issue in clinical utility of multigene assay is the prediction of late recurrence in ER-positive breast cancer, because the extended endocrine therapy showed improved survival in some clinical trials. So, it is necessary to identify the high risk group of late recurrence in ER-positive breast cancer for extended endocrine therapy with multigene assay and EndoPredict EPclin, PAM50 ROR, BCI showed better results in prediction of that so far. Finally multigene assays have been used to omit radiation therapy safely in low risk of 10-year loco-regional recurrence in luminal A subtype. Now several prospective randomized clinical trials with multigene assays are ongoing to clarify the clinical utility and to extend its role for the treatment of breast cancer. In conclusion, multigene assay has played an important role as a biomarker for prognosis and benefit from adjuvant therapy in ER-positive, HER2-negative, node-negative breast cancer, and their clinical utility would be clarified and extended with the results of ongoing clinical trials of breast cancer.

SP01-3

ARTIFICIAL INTELLIGENCE IN TREATMENT OF BREAST CANCER PATIENTS: NEED OF THE DAY: ROLE OF AI WATSON FOR ONCOLOGY

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In present day scenario Data Tsunami, overwhelms human cognitive capacity. Just for number facts, 2X medical information is doubling every 5 years, 75 new clinical trials start every day in the US alone, 2.5M peer reviewed articles published in 34,550 scientific journals globally per year (28,000 English languages and 6450 non-English language). If you put that in a gist in research, there are over 700,000 articles published per year. The average researcher reads 200 articles per year. When you factor in all the data sources including clinical and exogenous factors, we believe in one life, an individual generates over 1,100 terabytes of information. It's far beyond human cognition; there's no way for the brain to process it. The corpus of clinical knowledge has expanded beyond capacity of human cognition. With this enormous knowledge explosion and with available limited time to capture and collect details about the patient and to provide personalized care to the patient is a herculean task for the doctors. Doctors and researchers started looking for a friend with super human talent who could analyze so much data with limited time and still give the best of options and a guide toward s personalized care .IBM Watson for Oncology (WFO) developed in collaboration with Memorial Sloan Kettering Cancer Center is a cognitive computing system able to extract structured data from free text documents using natural language processing (NLP) It is a technology platform that uses NLP and machine learning to reveal insights from large amounts of unstructured data. Cognitive computing system creates a new partnership between people and computers that enhances scales and accelerates human expertise. WFO first analyzes unstructured data like news articles, research, social media posts, clinical notes and reports, easily assimilating key patient information written in plain English that may be critical to selecting a treatment pathway by using NLP to understand grammar and context. Next it understands complex questions by evaluating all possible meanings and determines what is being asked. By combining attributes from the patients file with clinical expertise, external research, and data, Watson for Oncology identifies potential treatment plans for a patient. Finally WFO presents answers and solutions based on supporting evidence and quality of information found. WFO is designed to assist oncologists in making treatment decisions driven by cancer types and patient-specific attributes by bringing in together all the available medical information. WFO is a step towards personalized medicine. It could be an essential tool to oncologists by reducing the cognitive burden of physicians in keeping up with medical literature by providing clinically actionable insights to assist them in treating patients.

Our Study:

Background: Breast cancer oncologists are challenged to personalize care with rapidly changing scientific evidence, drug approvals, and treatment guidelines. Cognitive clinical decision-support systems (CDSSs) have the potential to help address this challenge. We report here the results of examining the level of agreement (concordance) between treatment recommendations made by the cognitive CDSS Watson for Oncology (WFO) and a multidisciplinary tumor board for breast cancer.

Methods: Treatment recommendations were provided for 638 breast cancers between 2014-2016 at the Manipal Comprehensive Cancer Center, Bengaluru, India. WFO provided treatment recommendations for the identical cases in 2016. A blinded second review was performed by the center's tumor board in 2016 for all cases in which there was not agreement, to account for treatments and guidelines not available before 2016. Treatment recommendations were considered concordant if the tumor board recommendations were designated "recommended" or "for consideration" by WFO.

Result: Treatment concordance between WFO and the multidisciplinary tumor board occurred in 93% of breast cancer cases. Subgroup analysis found that patients with stage I or IV disease were less likely to be concordant than patients with stage II or III disease. Increasing age was found to have a major impact on concordance. Concordance declined significantly ($p \leq 0.02$; $p < 0.001$) in all age groups compared to patients < 45 years of age, except for the age group 55-64. Receptor status was not found to affect concordance.

Conclusions: Treatment recommendations made by WFO and the tumor board were highly concordant for breast cancer cases examined. Breast cancer stage and patient age had significant influence on concordance, while receptor status alone did not. This study demonstrates that the cognitive clinical decision support system WFO may be a helpful tool for breast cancer treatment decision making, especially at centers where expert breast cancer resources are limited.

SP02-1

HETEROGENEITY OF HER2: MUTATION, AMPLIFICATION, EXPRESSION AND CLINICAL IMPLICATIONS

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Overexpression of human epidermal growth factor receptor-2 (HER2), usually associated with amplification of the HER2 gene, has been identified in 15–20% of breast cancers, and is a target for HER-directed therapy. HER2 status had been considered relatively homogeneous across all cells within a tumor and constant during the progression of breast cancer, suggesting that anti-HER2 therapy would successfully target most of the tumor cells in patients with HER2-positive breast cancer. However, there is increasing recognition of HER2 heterogeneity with regard to amplification, expression and mutation in breast cancers and HER2 alteration during tumor progression. While HER2 heterogeneity may contribute to inaccurate assessment of HER2 status and affect treatment decisions, more importantly it could also attenuate the response to HER2-targeted therapy. In our studies, heterogeneity of HER2 gene amplification was found to an independent predictor of poor prognosis in patients with primary HER2-postive breast cancer. Moreover, low level amplification, heterogeneity of HER2 gene amplification, and heterogeneous HER2 protein overexpression were associated with poor response to trastuzumab in patients with HER2-positive metastatic breast cancer. An obvious clinical implication of these findings is that patients with heterogeneously amplified HER2-positive breast cancer are less likely to benefit from HER-2 targeted therapy. Recently, HER2 somatic mutations are also increasingly detected through genome sequencing in HER2-negative breast cancers, and even in HER2-positive breast cancers. HER2 somatic mutation is an alternative mechanism to activate HER2 in breast cancer, and patients with HER2 mutation-positive breast cancer could benefit from HER2 tyrosine kinase inhibitors, depending on mutation sites.

SP02-2

BIOMARKERS FOR HER2-DIRECTED THERAPIES : PAST FAILURE AND FUTURE PERSPECTIVES

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The development of HER2-directed therapies such as trastuzumab, pertuzumab, trastuzumab emtansine, lapatinib and neratinib, has greatly improved outcomes for patients with HER2-positive breast cancer. However, the identification of clinically useful predictive biomarkers for these agents has been challenging. Because of this lack of biomarkers, it is not possible to determine which patients with HER2-positive cancers are likely to respond to trastuzumab and chemotherapy, which may require a second agent such as pertuzumab, and which tumors are so sensitive to HER2-directed therapy that chemotherapy is not needed at all. This inability to personalize HER2 therapy for each patient leads to overtreatment of some patients and undertreatment of others.

Initial efforts to identify predictive biomarkers for HER2 therapies focused on HER2 itself, and the signaling pathways parallel to, or downstream of HER2. Recent data from the NSABP B-47 trial, and others, make it clear that HER2 gene amplification and/or 3+ protein overexpression are a prerequisite for trastuzumab benefit. However, among HER2-positive cancers, the levels of HER2 amplification, HER2 mRNA, or HER2 protein do not reliably distinguish those patients who will benefit from HER2-directed therapy from those who will not. HER2-positive cancers with activating mutations in PIK3CA, the gene encoding PI3-kinase, a necessary component of the signaling machinery downstream of HER2, have significantly lower rates of pathological complete response (pCR) to neoadjuvant HER2-directed therapies, compared to those with wildtype PIK3CA. However, neither PIK3CA mutations, nor loss of the suppressor of the PI3-kinase pathway PTEN, are associated with decreased benefit of trastuzumab in the adjuvant setting, suggesting that the presence of these PI3-kinase pathway alterations is not a clinically useful biomarker. Overexpression of other transmembrane receptors such as EGFR and IGFR has also been explored as potential biomarkers of decreased sensitivity to HER2-directed therapy. While EGFR overexpression has been associated with decreased pCR in retrospective analyses of some neoadjuvant trials and decreased benefit of trastuzumab in the NCCTG N9831 adjuvant study, this effect has not been uniformly observed and awaits prospective validation.

Estrogen receptor (ER) expression is inversely related to HER2 expression and in preclinical models, ER signaling can promote resistance to HER2 inhibition. In multiple neoadjuvant trials of HER2-directed agents, ER+ cancers have lower pCR rates than ER-negative cancers. In

the HERA and NSABP B31 adjuvant studies of trastuzumab, patients with tumors with lower levels of HER2 and high ER expression derived relatively little benefit from trastuzumab. Despite the limited benefit of trastuzumab seen in this specific small subset of ER+ HER2+ cancers, ER status overall did not predict benefit of trastuzumab in the NSABP B31, NCCTG N9831, and HERA trials. Thus, ER status alone cannot be used as a biomarker to identify patients who will or will not benefit from trastuzumab.

Molecular subtype has also been explored as a potential marker to predict trastuzumab benefit. Indeed, the HER2-enriched subtype is associated with significantly higher rates of pCR compared to other subtypes in multiple neoadjuvant studies of HER2-directed therapy. However, results from adjuvant studies do not support a preferential benefit of trastuzumab in HER2 enriched cancers: in NSABPB31 the benefit of trastuzumab was similar across all subtypes, while in N9831 only the basal like subtype did not appear to benefit from trastuzumab.

Perhaps the most promising predictive biomarkers for HER2-directed therapies are those related to immune activation. Both a high level of tumor infiltrating lymphocytes (TILs) in the tumor bed and the presence of gene signatures reflecting immune activation are associated with higher rates of pCR across multiple neoadjuvant trials. Immune signatures are also associated with benefit of trastuzumab in the NCCTG N9831 and NSABP B-31 adjuvant studies. The association between immune related biomarkers and benefit of trastuzumab likely arises because trastuzumab acts at least in part through immune mechanisms, including the induction of Antibody Dependent Cellular Cytotoxicity (ADCC) and stimulation of cytotoxic T Cell activity.

Other than HER2 itself, at this time, no single gene, protein or gene signature has been validated as a clinically useful biomarker to guide selection of HER2-directed therapy. Immune related markers appear promising, but require further validation. Other approaches, including novel molecular imaging techniques and utilizing early clinical response to anti-HER2 therapy as a biomarker are currently being evaluated and may prove to be clinically useful tools in the future.

SP02-3

EVOLVING STRATEGIES TO OVERCOME RESISTANCE TO HER2 TARGETED AGENTS

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Prognosis for patients with HER2+ metastatic breast cancer has clearly improved following the introduction of anti-HER2 therapies. Dual HER2 receptor blockade or combinatorial approaches with HER2 antibodies and standard therapies has provided additional benefits compared to monotherapy.

Despite the therapeutic success of existing HER2 therapies, individualized treatment and overcoming resistance to these therapies remains a significant challenge.

There are several proposed mechanisms of resistance being studied in the quest to overcome resistance to HER2-targeted therapy in breast cancer.

The strengthening of antibody dependent cell-mediated cytotoxicity (ADCC) shows promise in clinical trials, but there also is potential benefit in exploring other avenues, such as mutations of the PI3-kinase gene and PTEN, parallel pathway activation, antibody-drug conjugates, and the combination of checkpoint inhibitors with HER2 antibodies,

The heterogeneous intra-tumoral HER2 expression and lack of fully predictive and prognostic biomarkers remain significant barriers to improving the use of HER2 antibodies

There are more antibody drug conjugates targeting HER2 in various pipelines (DS-8201, MM-302, SYD-0895, XMT-1522, MEDI 4276).

Conjugating HER2 antibodies with novel toxic payloads or combining HER2 antibodies with cellular immunotherapy provide exciting new opportunities for the management of tumors overexpressing HER2.

Future research on new predictive biomarkers and exploring more suitable synergizing combinations will lead to higher therapeutic responses, lower toxicities and providing insight into the mechanisms of resistance to HER2-targeted treatments.

SP03-1

CURRENT APPROACHES IN TREATMENT OF TNBC

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Significant attention has been focused on the development of novel therapeutics in TNBC, a subset of breast cancer that is typically associated with aggressive biology, short survival, and limited treatment options. In reality, TNBC is a heterogeneous disease that can be further categorized into distinct molecular subtypes with differing prognosis. Unfortunately, current approved treatments for TNBC remain limited to chemotherapy, although a wide range of novel therapeutic agents are being tested actively. Better understanding of the molecular characteristics of TNBC subtypes is key to improving its outcome, as this provides insights on rational development of novel therapeutics and for the refinement of biomarkers to optimize treatment selection. For example, TNBCs characterized by homologous recombination deficiencies are sensitive to platinums, and several assays have been developed to accurately identify these patients. The elevated expression of immune genes, high tumor mutational load, and prominence of tumor-infiltrating lymphocytes in some TNBCs make them potential targets for immunotherapy, and promising activity has been observed with immune checkpoint inhibitors such as pembrolizumab and atezolizumab, in combination with chemotherapy. Another subset of TNBCs, those that are associated with BRCA germline mutations, derived more benefit from a PARP inhibitor than physicians' choice chemotherapy in a randomized trial. Apart from the promise from novel therapeutic agents, the recently published CREATE-X trial also provided proof-of-concept that more chemotherapy (additional adjuvant capecitabine) can be beneficial when sufficiently high risk TNBC patients (those with residual tumor after neoadjuvant combination chemotherapy) are selected, highlighting the fact that deployment of existing agents through rational patient selection remains a valid strategy to improve the outcome of TNBC.

SP03-2

PARP INHIBITORS AND DNA REPAIR

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SP03-3

NOVEL TARGETS AND OVERVIEW OF ONGOING CLINICAL TRIALS

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Although triple negative breast cancer is relatively chemotherapy sensitive for patients who are resistant to standard chemotherapy in the neoadjuvant or adjuvant setting, outcomes remain poor. In spite of increasing understanding of cancer biology, there have been no new treatment options for triple negative breast cancer, especially in the absence of germline BRCA mutations. To date there have been several large scale studies characterizing TNBC, demonstrating that even in chemotherapy resistant disease, there are several potentially actionable genomic alterations. Some of these such as alterations in PTEN, PI3K, Akt are potentially actionable with rationale combinations with PI3K pathway inhibitors. Several other less frequent genomic alterations are actively under investigation. There is also great interest identifying novel targets, and exploring additional targets such as nuclear transport, cell metabolism and epigenetics.

Antibody drug conjugates (ADCs) are also being pursued in TNBC and several ADCs have signal of activity in TNBC with a few already in Phase II and III trials. The next steps will be to look at rational combinations, including immunotherapy to leverage the presumed immunologic effect of ADCs as well as targeted therapies that can modulate cell survival or target expression.

In spite of the excitement surrounding the efficacy of PARP inhibitors for germline BRCA mutations, there is also recognition that even in that scenario, efficacy is limited, with a variety of acquired resistance mechanisms, highlighting the importance of coming up with more effective strategies at the onset. However, preclinical studies also raise possibility that PARP inhibitors may have efficacy beyond BRCA germline mutations. Thus many studies ongoing all identify rational combinations of drugs that generate BRCA-ness in combination with PARP inhibitors or other DNA damage repair agents.

With increasing utilization of molecular profiling and integrated analytics we hope to have increasing treatment options and improved therapy selection.

SP04-1

INDIVIDUALIZED APPLICATION OF ONCOPLASTIC TECHNIQUES

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Breast conserving surgery with adjuvant radiotherapy for breast cancer had been proved as a feasible method in early breast cancer. However, a clear surgical margin is still the most important factor which affect to local recurrence of distant metastasis. These results developed a concept of "oncoplastic breast surgery", which can secure both an adequate resection margins and a natural shape of the breast. Now, the oncoplastic surgery has been a standard treatment for breast cancer.

To obtain proper resection margin, the multicentricity or multifocality of breast cancer should be evaluated before surgery based on imaging modalities. The preoperative imaging assessment is performed by mammography, ultrasonography, magnetic resonance imaging (MRI) or PET/CT scan. And the correlation with multimodality of image findings enables an oncoplastic breast surgery.

To obtain successful results after oncoplastic surgery, it is imperative that patients be risk-stratified based on risk factors associated with positive margins, that relevant imaging studies be reviewed, and that the confirmation of negative margins be confirmed during the initial operation. Patients who had small- to moderate-sized breasts are the most likely to be dissatisfied with the cosmetic outcome of surgery, even if the defect is small; therefore, oncoplastic surgery in this population is warranted. Reconstruction of the remaining breast tissue is divided into volume displacement and volume replacement techniques. The use of the various oncoplastic surgeries is based on tumor location and excised breast volume.

Although the overall cosmetic results seem to be significantly improved with BCS compared with mastectomy, 4% to 20% of all patients with BCS may still be dissatisfied with their final cosmetic outcome. Poor cosmetic results following BCS are not uncommon and occur more frequently with tumors that are large with respect to the size of the breast or unfavorable tumor location . Shape is further compromised when wide resection margins are required to obtain optimal oncologic control and often result in a deformed breast that is different in size compared with the contralateral side. Oncoplastic surgery is a relatively new but increasingly used technique in the treatment of breast cancer. This method combines principles of oncological surgery and plastic surgery to obtain oncologically sound and aesthetically pleasing results in women who require partial mastectomy, as a result of breast cancer. The primary advantage of

this surgical technique is the increased distance of the resection margin and the improved cosmetic outcome. Not all patients with breast cancer may need oncoplastic surgery. Eligible patients usually have an unfavorable breast: tumor size ratio, as well as tumor locations that would result in large visible scars and deep breast defects if BCS were to be performed. The approach used in partial breast reconstruction is to consider different techniques based on tumor location and excised volume. A variety of techniques have been proposed, many of which are specific to the location of the tumor within the breast.

Breast surgeries for the treatment of malignancy can be classified into those involving conventional techniques and those involving oncoplastic techniques. Oncoplastic surgery (OPS) of the breast includes tumour-specific immediate reconstruction, which can be defined as breast cancer surgery with immediate reconstruction in cases of partial and total mastectomy.

Systematic categorisation would help researchers analyse the feasibility and effectiveness of breast cancer surgery. Several oncoplastic surgeons have briefly described classification systems for OPS.

Some doctors classified OPS based on the breast tissue excision volume, tumour location, and glandular density. Other doctors also suggested new classifications for OPS.

We need to analyse various types of surgery, including both conventional and oncoplastic techniques, for the treatment of breast cancer and categorised them based on the surgical techniques and reconstructive methods. The cosmetic and oncological outcomes of each group were also need to be analysed and compared.

SP04-2

EVALUATION OF COSMETIC OUTCOME AND ITS PRACTICAL RELEVANCE TO REAL LIFE

Eisuke Fukuma

Breast Center, Kameda Medical Center, Japan

SP04-3

HOW TO STANDARDIZE TECHNIQUES OF ONCOPLASTIC SURGERY

Maria-Joao Cardoso

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The importance of cosmetic outcomes and quality of life after breast cancer surgery has motivated surgeons to develop the concept of oncoplastic breast conserving surgery around 1980. Training programs are still rare in most countries, and even when they are available, there is little standardization of techniques and even more important of outcome evaluation.

However nowadays, the concept of oncoplastic surgery should be applied to all breast cancer surgeries as a standard of care. The use of an aesthetic approach to breast conservation or mastectomy greatly enhances the number of alternatives that can be chosen by women with breast cancer resulting, hopefully, in a superior outcome.

The major advance towards a better aesthetic outcome has been the widespread use of breast-conserving surgery when indicated. In the last couple of years the evidence from large retrospective population studies showing better DFS and OS when compared to mastectomy specially in early breast cancer stages will be pushing even further the total number of performed breast conserving treatments worldwide.

Offering a wider choice of interventions and expanding the indications for breast conservation as well as improving the outcomes are the key aims of oncoplastic surgery. The pillars of oncoplastic surgery are the optimization of interventions in the diseased breast and the symmetrisation of the contra-lateral side, either immediate or delayed. Oncoplastic breast conserving surgery is usually divided in three main groups: simpler surgery with smaller procedures usually without impact in the contra-lateral breast; larger displacement with bilateral reduction mammaplasty techniques; replacement techniques using outer tissue to cover defects.

However, oncoplastic breast surgery is not just about breast conservation. Applying oncoplastic principles to mastectomy and reconstruction is just as important. All this techniques, in breast conservation and mastectomy must be carefully discussed with patients with a detailed approach of outcomes and possible complications. Surgeons should never forget that patients expectations are a fundamental part of the decision process and also that each situation should always be discussed at the multidisciplinary team meeting.

SP05-1

MULTI-OMICS PROFILING OF YOUNGER ASIAN BREAST CANCERS REVEALS DISTINCTIVE MOLECULAR SIGNATURES

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Breast cancer (BC) in the Asia Pacific regions is enriched in younger patients and rapidly rising in incidence yet its molecular bases remain poorly characterized. We have performed whole exome and transcriptome profiling of primary tumors from 178 Korean breast cancer patients (SMC), of which 88% are pre-menopausal. We then systematically compared multi-omics profiles between SMC and a primarily Caucasian and post-menopausal BC cohort (TCGA). We observed lower estrogen receptor (ER) expression as well as lower proportions of ER+ and Luminal A subtypes but higher proportions of HER2+ and Luminal B subtypes in SMC compared to TCGA. Germline pathogenic mutations affecting BRCA1 or BRCA2 were found in a higher proportion of SMC than in TCGA. TP53 was more frequently mutated in SMC (48.5%) than in TCGA (27.9%) overall and within individual subtypes. Mutation signature analyses revealed significant enrichment of homologous recombination deficiency signature in SMC. Virtual microdissection analyses identified nine factors representative of different tissue compartments and attributed the majority of gene expression differences between two cohorts to the tumor microenvironment. Notably, the factor attributed to tumor infiltrating leukocytes was significantly enriched in SMC, indicating that Asian BC may harbor a more immune-active microenvironment than Western BCs. Hence, younger Asian BCs appeared to harbor significant molecular differences from Western BCs that could hold important implications for patient stratification and therapeutic treatment.

SP05-2

BIOLOGY OF BREAST CANCER IN YOUNG WOMEN AND POTENTIAL CLINICAL IMPLICATIONS

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Breast cancer in young women is highly regarded as a distinct entity. Several studies have shown that young women with breast cancer have poorer outcomes as compared to older patients. Breast cancer arising in young women appears to have somehow unique biological characteristics: it is associated with higher frequency of triple negative and lower incidence of luminal A tumors compared to their older counterparts. Yet, beyond differences in the distribution of breast cancer subtypes, several molecular aberrations were found to be differentially expressed or detected in young breast cancer patients. Better understanding and characterization of these features could open the door for defining tailored therapeutic strategies for these patients. The presentation will be discussing the key biological features of tumors arising in young women, the potential relationship and impact of their reproductive behaviours as well as the possible novel therapeutic venues to be explored.

SP05-3

FERTILITY PRESERVATION AND PREGNANCY OPTIONS FOR YOUNG BREAST CANCER SURVIVORS

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Breast cancer (BC) is the most common female malignancy: overall, about 15% of women are diagnosed during their reproductive years. In Europe, approximately 1 in 200 women under the age of 40 is faced with a diagnosis of BC.

In the last decades women tended to delay childbearing for different (i.e. cultural, educational, professional) reasons: consequently, in an increasing number of patients, BC occurs before the completion of their reproductive plans.

Consequently, fertility and family planning are extraordinarily important issues for this younger patient population and the few surveys conducted in patients facing BC at young age report that infertility concerns often influence treatment decisions.

The best retrospective evidence suggests that pregnancy after BC does not increase a womans risk of recurrence, and it may even confer a protective effect but no definitive data, based on prospective and systematic evaluation, is available. Overall, the number of women who become pregnant after BC is extremely low (less than 10%). Given the amount of uncertainty, patient preferences regarding their future fertility should be part of the discussion as they make their treatment decisions both at diagnosis and in follow-up.

To be able to allow young patients to consider future pregnancy, fertility has to be addressed upfront, according to the planned treatment strategy. Several techniques are nowadays available and should be offered to any young women with potential treatment-related fertility impairment. Specificities in gene mutation carriers should be addressed and fertility needs to be discussed also in advanced breat cancer patients, given the potential long-term survival.

The lecture will summarize all these topics and illustrate the POSITIVE trial which has been designed to answer the still pending questions in this field.

SP06-1

INTRAOPERATIVE RADIATION

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Background: Based on our laboratory work and clinical trials we hypothesised that radiotherapy after lumpectomy for breast cancer could be restricted to the tumour bed. In collaboration with the industry we developed a new radiotherapy device and a new surgical operation for delivering single-dose radiation to the tumour bed – the tissues at highest risk of local recurrence. We named it TARGeted Intraoperative radioTherapy (TARGIT). From 1998 we confirmed its feasibility and safety in pilot studies.

Objective: To compare TARGIT within a risk-adapted approach with whole-breast external beam radiotherapy (EBRT) over several weeks.

Design: The TARGeted Intraoperative radioTherapy Alone (TARGIT-A) trial was a pragmatic, prospective, international, multicentre, non-inferiority, non-blinded, randomised (1:1 ratio) clinical trial. Originally, randomisation occurred before initial lumpectomy (prepathology) and, if allocated TARGIT, the patient received it during the lumpectomy. Subsequently, the postpathology stratum was added in which randomisation occurred after initial lumpectomy, allowing potentially easier logistics and a more stringent case selection, but which needed a reoperation to reopen the wound to give TARGIT as a delayed procedure. The risk-adapted approach meant that, in the experimental arm, if pre-specified unsuspected adverse factors were found postoperatively after receiving TARGIT, EBRT was recommended. Pragmatically, this reflected how TARGIT would be practised in the real world.

Setting: Thirty-three centres in 11 countries.

Participants: Women who were aged ≥ 45 years with unifocal invasive ductal carcinoma preferably ≤ 3.5 cm in size.

Interventions: TARGIT within a risk-adapted approach and whole-breast EBRT.

Main outcome measures: The primary outcome measure was absolute difference in local recurrence, with a non-inferiority margin of 2.5%. Secondary outcome measures included toxicity and breast cancer-specific and non-breast-cancer mortality.

Result: In total, 3451 patients were recruited between March 2000 and June 2012. The following values are 5-year Kaplan–Meier rates for TARGIT compared with EBRT. There was no statistically significant difference in local recurrence between TARGIT and EBRT. TARGIT was non-inferior to EBRT overall [TARGIT 3.3%, 95% confidence interval (CI) 2.1% to 5.1% vs. EBRT 1.3%, 95% CI

0.7% to 2.5%; $p = 0.04$; Pnon-inferiority = 0.00000012] and in the prepathology stratum (n = 2298) when TARGIT was given concurrently with lumpectomy (TARGIT 2.1%, 95% CI 1.1% to 4.2% vs. EBRT 1.1%, 95% CI 0.5% to 2.5%; $p = 0.31$; Pnon-inferiority = 0.0000000013). With delayed TARGIT postpathology (n = 1153), the between-group difference was larger than 2.5% and non-inferiority was not established for this stratum (TARGIT 5.4%, 95% CI 3.0% to 9.7% vs. EBRT 1.7%, 95% CI 0.6% to 4.9%; $p = 0.069$; Pnon-inferiority = 0.06640]. The local recurrence-free survival was 93.9% (95% CI 90.9% to 95.9%) when TARGIT was given with lumpectomy compared with 92.5% (95% CI 89.7% to 94.6%) for EBRT ($p = 0.35$). In a planned subgroup analysis, progesterone receptor (PgR) status was found to be the only predictor of outcome: hormone-responsive patients (PgR positive) had similar 5-year local recurrence with TARGIT during lumpectomy (1.4%, 95% CI 0.5% to 3.9%) as with EBRT (1.2%, 95% CI 0.5% to 2.9%; $p = 0.77$). Grade 3 or 4 radiotherapy toxicity was significantly reduced with TARGIT. Overall, breast cancer mortality was much the same between groups (TARGIT 2.6%, 95% CI 1.5% to 4.3% vs. EBRT 1.9%, 95% CI 1.1% to 3.2%; $p = 0.56$) but there were significantly fewer non-breast-cancer deaths with TARGIT (1.4%, 95% CI 0.8% to 2.5% vs. 3.5%, 95% CI 2.3% to 5.2%; $p = 0.0086$), attributable to fewer deaths from cardiovascular causes and other cancers, leading to a trend in reduced overall mortality in the TARGIT arm (3.9%, 95% CI 2.7% to 5.8% vs. 5.3%, 95% CI 3.9% to 7.3%; $p = 0.099$]. Health economic analyses suggest that TARGIT was statistically significantly less costly than EBRT, produced similar quality-adjusted life-years, had a positive incremental net monetary benefit that was borderline statistically significantly different from zero and had a probability of > 90% of being cost-effective. There appears to be little uncertainty in the point estimates, based on deterministic and probabilistic sensitivity analyses. If TARGIT were given instead of EBRT in suitable patients, it might potentially reduce costs to the health-care providers in the UK by £8–9.1 million each year. This does not include environmental, patient and societal costs.

Limitations: The number of local recurrences is small but the number of events for local recurrence-free survival is not as small (TARGIT 57 vs. EBRT 59); occurrence of so few events (< 3.5%) also implies that both treatments are effective and any difference is unlikely to be large. Not all 3451 patients were followed up for 5 years; however, more than the number of patients required to answer the main trial question (n = 585) were followed up for > 5 years.

Conclusions: For patients with breast cancer (women who are aged ≥ 45 years with hormone-sensitive invasive ductal carcinoma that is up to 3.5 cm in size), TARGIT concurrent with lumpectomy within a risk-adapted approach is as effective as, safer than and less expensive than postoperative EBRT.

Future work: The analyses will be repeated with longer follow-up. Although this may not change the primary result, the larger number of events may confirm the effect on overall mortality and allow more detailed subgroup analyses. The TARGeted Intraoperative radioTherapy Boost (TARGIT-B) trial is testing whether or not a tumour bed boost given intraoperatively (TARGIT) boost is superior to a tumour bed boost given as part of postoperative EBRT.

Trial registration: Current Controlled Trials ISRCTN34086741 and ClinicalTrials.gov NCT00983684.

Funding: University College London Hospitals (UCLH)/University College London (UCL) Comprehensive Biomedical Research Centre, UCLH Charities, Ninewells Cancer Campaign, National Health and Medical Research Council and German Federal Ministry of Education and Research (BMBF). From September 2009 this project was funded by the NIHR Health Technology Assessment programme.

Scientific Summary

Background: Early local recurrence of breast cancer most commonly (>90%) occurs at the site of the primary tumour. Whole-organ analysis of mastectomy specimens, on the other hand, reveals that 63% of breasts harbour occult cancer foci and 80% of these are situated remote from the index quadrant. Therefore, these occult cancer foci may not be clinically relevant and it may not be necessary to treat the whole breast with radiotherapy, which is normally given as a 6-week long course of external beam radiotherapy (EBRT). EBRT is effective but can be inconvenient and costly and may cause many women from geographically remote areas to choose mastectomy. In 1995 we suggested that restriction of radiation therapy to the peritumoural area alone might provide adequate local control for selected patients within a risk-adapted design. In collaboration with the industry we developed a device (INTRABEAM®) and a surgical procedure to enable us to give TARGeted Intraoperative radioTherapy (TARGIT) at a dose of about 20 Gy to the surface of the applicator in 20–30 minutes during surgery in a standard operating theatre environment. We then proceeded to test its feasibility and safety in pilot studies between 1998 and 2000 followed by the TARGeted Intraoperative radioTherapy Alone (TARGIT-A) randomised trial.

Methods: The TARGIT-A trial recruited 3451 patients between 24 March 2000 and June 2012. In this prospective, randomised, non-inferiority trial, women aged ≥45 years with invasive ductal breast carcinoma undergoing breast-conserving surgery were enrolled from 33 centres in 11 countries. Patients were randomly assigned in a 1 : 1 ratio to receive TARGIT or whole-breast EBRT, with blocks stratified by centre and by timing of delivery of TARGIT. Randomisation occurred either before lumpectomy (prepathology stratum – TARGIT concurrent with lumpectomy) or after lumpectomy (postpathology stratum – TARGIT given subsequently by reopening the wound). Such stratification allowed easier operating theatre logistics and more stringent case selection, but needed a re-operation to reopen the wound to give TARGIT as a delayed procedure. Neither patients nor investigators or their teams were masked to treatment assignment. Postoperative discovery of predefined factors (e.g. lobular carcinoma) could trigger the addition of EBRT (excluding tumour bed boost) to TARGIT (in an expected 15% of patients), making the experimental arm a risk-adapted radiotherapy approach vis-à-vis the control arm, which followed a one-size-fits-all policy of giving whole-breast radiotherapy to all patients. The primary outcome was absolute difference in local recurrence in the conserved breast, with a pre-specified non-inferiority margin of 2.5% at 5 years; pre-specified analyses included outcome according to the timing of randomisation in relation to lumpectomy.

Secondary outcomes included complications and mortality. The planned analyses were performed in 2010 after the initial accrual of 2232 patients and again in 2012 after closure of the trial with an accrual of 3451 patients. For the second analysis, standard tests for non-inferiority were performed and at this time for a log-rank test for difference in survival the significance level was set at a *p*-value of 0.01 for local recurrence as this was a second analysis and at a *p*-value of 0.05 for mortality. In 2010 it was calculated that the number of participants needed to prove non-inferiority was 585. For subgroup analysis, before the data were unblinded for the 2012 analysis, we hypothesised that hormone sensitivity might be predictive of response to TARGIT and therefore analysed whether or not the response to radiotherapy in the TARGIT-A trial was dependent on hormone receptor responsiveness using progesterone receptor (PgR) status as a marker. We assessed the effect of hormone sensitivity using PgR status, timing of randomisation/delivery of TARGIT, age, tumour grade, oestrogen receptor status, human epidermal growth factor receptor-2 (HER2) status, presence of ductal carcinoma in situ (DCIS), margin status, whether screen detected or not, lymphovascular invasion and node status, on the outcome in a Cox proportional hazard model. We performed the main analyses on patients in the prepathology stratum who were randomised in the first 8 years of the TARGIT-A trial. We also analysed (1) the effect of omission of EBRT on recurrence of breast cancer in quadrants of the breast other than the index quadrant (the original hypothesis), (2) the effect of omission of EBRT on axillary recurrence, (3) whether or not a beneficial effect of irradiation of the tumour bed on the patient's microenvironment could contribute to the difference in non-breast-cancer mortality, (4) whether or not the higher threshold for margin positivity in the German cohort with regard to adding EBRT improved outcomes and (5) health economics.

Findings

Main findings: In total, 1721 patients were randomised to TARGIT and 1730 to EBRT. Supplemental EBRT after TARGIT was necessary in 15.2% (239/1571) of patients who received TARGIT (21.6% prepathology, 3.6% postpathology). With regard to follow-up, 3451 patients had a median follow-up of 2 years and 5 months (interquartile range 12–52 months), 2020 patients had a median follow-up of 4 years and the first 1222 randomised patients (the earliest cohort) had a median follow-up of 5 years.

First analysis of local recurrence

The first analysis, after completion of the original accrual of 2232 patients (the mature cohort), described the results at 4 years when there were six local recurrences in the intraoperative radiotherapy group and five in the EBRT group. The Kaplan–Meier estimate of local recurrence in the conserved breast at 4 years was 1.20% [95% confidence interval (CI) 0.53% to 2.71%] in the TARGIT group and 0.95% (95% CI 0.39% to 2.31%) in the EBRT group [difference between groups 0.25% (95% CI −1.04% to 1.54%); $p = 0.41$].

Five-year analysis of local recurrence and survival

The test of non-inferiority in terms of control of local recurrence in the conserved breast found that TARGIT was non-inferior to EBRT for the whole trial (Pnon-inferiority = 0.00000012) and for the

prepathology stratum (Pnon-inferiority = 0.0000000013), but not for the postpathology stratum (Pnon-inferiority = 0.06640). For the first 1222 patients randomised in the trial the median follow-up was 5 years and the test for non-inferiority found that TARGIT was non-inferior to EBRT in terms of local recurrence in the conserved breast when both strata were taken together (Pnon-inferiority = 0.040) and for the prepathology stratum (Pnon-inferiority = 0.00914), but not for the postpathology stratum (Pnon-inferiority = 0.35108). The 5-year estimated risk for local recurrence in the conserved breast was 3.3% (95% CI 2.1% to 5.1%) for TARGIT and 1.3% (95% CI 0.7% to 2.5%) for EBRT. TARGIT concurrently with lumpectomy (prepathology, n = 2298) had much the same rate of local recurrence in the conserved breast as EBRT (2.1%, 95% CI 1.1% to 4.2% vs. 1.1%, 95% CI 0.5% to 2.5%; $p = 0.31$). With delayed TARGIT (postpathology, n = 1153) the between-group difference in local recurrence was larger than 2.5% (TARGIT 5.4%, 95% CI 3.0% to 9.7% vs. EBRT 1.7%, 95% CI 0.6% to 4.9%; $p = 0.069$). There was no difference in the 5-year estimated local recurrence-free survival between TARGIT and EBRT [all patients: 93.1% (95% CI 90.8% to 94.9%) vs. 93.8% (95% CI 91.7% to 95.4%); $p = 0.81$; prepathology: 93.9% (95% CI 90.9% to 95.9%) vs. 92.5% (95% CI 89.7% to 94.6%); $p = 0.35$]. Overall, breast cancer mortality was similar between the groups (TARGIT 2.6%, 95% CI 1.5% to 4.3% vs. EBRT 1.9%, 95% CI 1.1% to 3.2%; $p = 0.56$) but there were significantly fewer non-breast-cancer deaths with TARGIT (1.4%, 95% CI 0.8% to 2.5% vs. 3.5%, 95% CI 2.3% to 5.2%; $p = 0.0086$), attributable to fewer deaths from cardiovascular causes and other cancers. Overall mortality was 3.9% (95% CI 2.7% to 5.8%) for TARGIT compared with 5.3% (95% CI 3.9% to 7.3%) for EBRT ($p = 0.099$). For the preferred option of using TARGIT during initial lumpectomy, breast cancer mortality was similar between the groups (TARGIT 17 deaths vs. EBRT 15 deaths; 5-year rates 3.3%, 95% CI 1.9% to 5.8% vs. 2.7%, 95% CI 1.5% to 4.6%; $p = 0.72$). Non-breast-cancer mortality was 12 patients for TARGIT and 27 patients for EBRT (1.3%, 95% CI 0.7% to 2.8% vs. 4.4%, 95% CI 2.8% to 6.9%; $p = 0.016$). Overall mortality was numerically lower by 2.3% in the TARGIT group (4.6%, 95% CI 1.8% to 6.0% vs. 6.9%, 95% CI 4.3% to 9.6%; $p = 0.12$). In total, 817 patients were randomised in the first 8 years of the trial in the prepathology stratum. The median follow-up was 5.01 years. For local recurrence in the conserved breast, TARGIT was non-inferior to EBRT (Pnon-inferiority = 0.00914). The 5-year Kaplan–Meier estimated risk was not statistically different between the groups for local recurrence (TARGIT 1.8%, 95% CI 0.84% to 4.2% vs. EBRT 0.84%, 95% CI 0.3% to 2.6%; $p = 0.32$) and death from breast cancer (TARGIT 3.9%, 95% CI 2.3% to 6.7% vs. EBRT 3.0%, 95% CI 1.7% to 5.4%; $p = 0.34$). There were significantly fewer deaths from causes other than breast cancer with TARGIT (1.9%, 95% CI 0.9% to 3.9% vs. 5.1%, 95% CI 3.2% to 8.0%; $p = 0.04$). It should be noted that the number needed to prove non-inferiority was calculated to be 585 and therefore this earliest cohort of 817 patients had enough power to draw reliable conclusions.

Local toxicity

The frequency of any complications and major toxicity was similar in the two groups [major toxicity: TARGIT 37/1113 (3.3%) vs. EBRT 44/1119 (3.9%); $p = 0.44$]. Radiotherapy toxicity (Radiation Therapy Oncology Group grade 3) was lower in the TARGIT group (six patients, 0.5%) than in the EBRT group (23 patients, 2.1%; $p = 0.002$). In the second analysis in 2012, among complications 6 months after surgery, wound-related complications were much the same between groups but grade

3 or 4 skin complications were significantly reduced with TARGIT (4/1720 vs. 13/1731; $p = 0.029$).

Subgroup analysis

In PgR-positive cases (n = 2462) there was no significant difference between the two arms (TARGIT vs. EBRT) in terms of the 5-year risk of local recurrence (2.3%, 95% CI 1.3% to 4.3% vs. 1.49%, 95% CI 0.75% to 3.0%; $p = 0.51$), whereas in PgR-negative cases local recurrence was higher in the TARGIT arm (7.0%, 95% CI 3.5% to 13.6% vs. 0.5%, 95% CI 0.1% to 3.7%; $p = 0.017$). In the large group of 1625 PgR-positive cases in the prepathology stratum, breast cancer control with TARGIT was similar to that with EBRT (5-year risk of local recurrence 1.4%, 95% CI 0.5% to 3.9% vs. 1.2%, 95% CI 0.5% to 2.9%; $p = 0.77$); this was also the case for breast cancer mortality (1.78%, 95% CI 0.7% to 4.4% vs. 1.98%, 95% CI 0.94% to 4.2%; $p = 0.9$) whereas mortality from other causes was reduced with TARGIT (1.59%, 95% CI 0.7% to 3.4% vs. 4.51%, 95% CI 2.8% to 7.3%; $p = 0.04$), leading to a 3.1% reduction in overall mortality (3.3%, 95% CI 1.83% to 6.04% vs. 6.4%, 95% CI 4.3% to 9.6%; $p = 0.08$). Margin status was a predictive factor only in the EBRT arm. Other factors (such as age, grade, node positivity) did not influence the outcomes: the 5-year rates of local recurrence in the conserved breast were as follows: for 263 patients with age $\leq$ 50 years [events 3/145 vs. 3/118, TARGIT 2.9% (95% CI 0.94% to 8.64%) vs. EBRT 6.2% (95% CI 1.99% to 18.47%); $p = 0.70$]; for 436 grade 3 cancers [events 2/200 vs. 2/216, TARGIT 1.5% (95% CI 0.37% to 5.87%) vs. EBRT 1.7% (95% CI 0.42% to 6.45%); $p = 0.98$]; for the 363 patients with tumour $\geq$ 2 cm [events 1/173 vs. 1/190, TARGIT 0.75% (95% CI 0.1% to 5.2%) vs. EBRT 0.86% (95% CI 0.1% to 6.0%); $p = 0.95$]; for the 472 node positive patients [events 1/245 vs. 2/227, TARGIT 0.72% (95% CI 0.1% to 5.0%) vs. EBRT 1.3% (95% CI 0.3% to 5.2%); $p = 0.56$].

Other analyses

1. Other quadrant recurrences. In total, 94.4% of cases in the TARGIT-A trial did not have a preoperative magnetic resonance imaging (MRI) scan. A total of 793 patients in the prepathology stratum randomised to TARGIT had only TARGIT as their radiotherapy. With 2098 women-years of follow-up, there were nine recurrences in the conserved breast. The 5-year local recurrence rate in those who received TARGIT alone was 2.7% (95% CI 1.3% to 5.5%), which was not different from the rate in the whole prepathology cohort randomised to TARGIT (2.1%, 95% CI 1.1% to 4.2%). In these 793 patients, one would expect 63% of patients (i.e. n = 500) to have additional foci of cancer in their breasts and 80% of these (i.e. n = 400) should be in quadrants other than the index quadrant. In reality, seven patients had recurrence in the scar, six had new contralateral cancers and two had cancers growing in other quadrants, implying that the remaining 398 foci had remained dormant.
Among 935 patients who received whole-breast radiotherapy, the same number of cancers (n = 2) grew in other quadrants and there were five new contralateral cancers. Therefore, cancer foci in the breast that were away from the site of the primary tumour remained dormant and behaved no differently from those in the contralateral breast. They also appeared to be unaffected by whole-breast radiotherapy. This analysis from the randomised TARGIT-A trial provides further evidence supporting partial breast irradiation.

2. Axillary recurrence. We found that omission of EBRT did not increase axillary recurrence when analysed according to treatment received: the number of axillary recurrences was 5 out of 1613 when EBRT was not given compared with 6 out of 1762 when EBRT was given (5-year risk 0.68%, 95% CI 0.28% to 1.6% vs. 0.82%, 95% CI 0.34% to 2.02%; hazard ratio 0.84, 95% CI 0.26 to 2.74; $p = 0.8$).

3. Reduction in non-breast-cancer mortality: could this be a beneficial effect of TARGIT? We found that, among the 1730 patients randomised to receive EBRT, eight cardiac deaths were seen in contrast to the 12 estimated based on age, sex and follow-up period. Most interestingly, there were no deaths from non-breast-cancer causes in the TARGIT+EBRT group compared with 24 in the EBRT group (0/218 vs. 24/892; log-rank $p = 0.012$). Although the numbers are small, these data suggest that EBRT toxicity may not be the only possible explanation for the excess of non-breast-cancer deaths; they lead to the hypothesis that the local effect of TARGIT on the tumour bed by inhibiting cancer-stimulating cytokines may spill over to reduce the systemic inflammatory response to trauma and have significant long-term systemic beneficial effects that might be protective against cardiac and cancer mortality.

4. Adequacy of 1 mm as a threshold for negative margins. Additional EBRT was given in nearly twice the number of patients in the TARGIT arm in the German centres (prompted by the higher limit of a 10-mm tumour-free margin) compared with the TARGIT arm in the rest of the trial population [31.4% (96/306) vs. 17.4% (123/706)]. However, the 5-year local recurrence rate in the German cohort was not lower than in the rest of the sample (German 2.6%, 95% CI 0.87% to 7.8% vs. rest of the sample 1.9%, 95% CI 0.81% to 4.5%). Therefore, a policy of adding EBRT after TARGIT only when the margin is < 1 mm appears appropriate.

5. Health economic analyses. In the base-case analysis TARGIT was less costly than EBRT (mean incremental cost –£685) and produced slightly more quality-adjusted life-years (QALYs) than EBRT (mean QALYs gained 0.034). TARGIT had a positive incremental net monetary benefit that was borderline statistically significantly different from zero and had a probability of $> 90\%$ of being cost-effective. If TARGIT were given instead of EBRT in suitable patients, it might potentially reduce costs to health-care providers by £8–9.1 million each year. This does not include environmental, patient and societal costs.

Interpretation

In cases selected as per the TARGIT-A trial protocol, TARGIT during lumpectomy compared with EBRT was found to have non-inferior local control, similar mortality from breast cancer and significantly lower mortality from non-breast-cancer causes.
Subgroup analysis found that PgR status influenced the outcome of patients overall and those randomised to TARGIT; margin status influenced the outcome of those randomised to EBRT. Other patient or tumour factors had no significant influence on the outcome of patients randomised in the two arms. It appears that hormone receptor positivity identifies a group in whom local control with

TARGIT during lumpectomy is very similar to that with EBRT.
Other analyses provide further evidence supporting limited irradiation and suggest new hypotheses as well as demonstrate the cost-effectiveness of TARGIT.
Several large randomised trials of radiotherapy have found that the effect of radiotherapy on local recurrence is in the first 5 years and that a difference seen at 5 years does not increase with longer follow-up of up to 25 years. Therefore, these results are based on a sufficient number of patients whose follow-up is long enough to enable a change of practice. However, as breast cancer is a chronic illness, we are committed to longer-term follow-up (the protocol aims for a 10-year follow-up of all patients) for ethical, moral, scientific and academic reasons, as a higher number of events, which will accrue with time, could allow for a more in-depth analysis and refinement of our understanding.

Conclusions: For patients with breast cancer selected as per the TARGIT-A trial protocol (women aged ≥ 45 years with unifocal hormone-sensitive invasive ductal carcinoma that is up to 3.5 cm in size), TARGIT concurrent with lumpectomy within a risk-adapted approach is as effective as and safer than postoperative EBRT.

Trial registration: This trial is registered as ISRCTN34086741 and ClinicalTrials.gov NCT00983684.

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SP06-2

EXTENDED RADIATION FIELD FOR ADVANCED BREAST CANCER PATIENTS: WHEN AND HOW?

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As part of multidisciplinary treatment, the strategy of radiotherapy is individual risk-adapted. In patients with low risk of local-regional recurrence, defined by negative axillary nodes and favorable molecular subtypes, efforts has been made to minimize toxicity by reducing the treatment volume (APBI, IORT) and/or reducing the number of fraction (Abbreviated course of WBI). While in patients with increased risk, defined by positive axillary nodes with or without axillary dissection, locally advanced disease undergoing neo-adjuvant systemic therapy, extended radiation field from whole breast/tumor bed and chest wall to regional lymphatic pathway, has become a field of increasing concern. The concerns and controversies in this field can be summarized as follows: 1. In node positive patients after axillary dissection, should regional nodes irradiation be indicated with regard to molecular subtypes and multi-gene prognostic models? 2. In node positive patients undergoing sentinel biopsy without dissection, how should radiation field be extended based on risk factors? 3. In patients with initial stage II-III diseases receiving neo-adjuvant systemic therapy, should the indication of post-surgical radiation, including regional nodes irradiation be varied in patients with different response to systemic therapy? 4. Neo-adjuvant radiotherapy, re-heating the old story or potential state of the art? The latest evidence and review. 5. Potential of radiation therapy to increase the efficacy of immunotherapy in advanced breast cancer. Increasing studies has directed modern radiotherapy to a better precision, not only by physical precision, but also better integration with biological information.

SP06-3

WHOLE BREAST RADIATION: CLASSIC VS. HYPOFRACTIONATION

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Radiation schedule of 50 Gy/25 fractions in 5 weeks used in earlier trials demonstrated the efficacy of breast conserving surgery (BCS) and adjuvant whole breast radiotherapy to be equivalent to that of mastectomy. The support of standard fractionated whole breast irradiation (SF-WBI) for breast cancer is based on the radiobiologic consideration that radiation damage to normal tissue is greater with larger fraction size without additional tumor control. As a result, SF-WBI in the adjuvant treatment after lumpectomy has been the standard for several decades. However, some of the challenges of SF-WBI are cost and inconvenience of the patient involved with daily treatment courses from 5 to 7 weeks. This has led to the suggestion of short fractionation as a new standard following BCS for early stage breast cancer.

Hypofractionated whole breast irradiation (HF-WBI), based on precedent studies over the past two decades, offers an opportunity for improved patient convenience, lower healthcare costs, and greater access to care without sacrificing treatment outcomes. Up until now, 4 randomized trials-the Royal Marsden Hospital/Gloucestershire Oncology Center (RMH/GOC) trial, the UK Standardisation of Breast Radiotherapy (START) trial A and B, and the Canadian trial-have supported the establishment of HF-WBI with recent publication of 10-year outcomes.

Based on these studies, ASTRO published an evidence-based guideline for HF-WBI in 2011. The guideline states that the panel reached a consensus on supporting HF-WBI for patients who meet all of the following criteria: age older than 50 years, stage T1-2N0 disease, no use of chemotherapy, and central axis dose of 93% to 107%. This criteria is based upon the inclusion criteria and outcomes of the key studies stated above, but this recommendation is relatively conservative. This criteria is scheduled to be revised soon. Recommended dose-fractionation scheme is 40-42.5 Gy in 15-16 fraction by NCCN guideline.

HF-WBI has been proved its effectiveness and safety. The 50 Gy in 2528 fractions prescription does not have the advantage of convenience for patients nor the advantage of a reduced biological effectiveness associated with the extended fractionation schedule. HF-WBI shows even better late or acute radiation toxicity for early breast cancer. But in Korea, further investigation to identify the current practice pattern or cost effectiveness is warranted under the national health insurance service system. HF-WBI could be new standard for whole breast radiotherapy in early breast cancer after BCS.

SP07-1

CURRENT OPTIMAL SEQUENCE AND DURATION OF ENDOCRINE TREATMENT

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Hormone receptor-positive (HR+) breast cancer accounts for approximately 75% of all breast cancer patients, and endocrine therapy provide effective treatment options for them with the purpose of decreasing the incidence of recurrence or controlling metastatic disease. In this presentation, current optimal sequence and duration of endocrine treatment would be discussed.

Advanced Breast Cancer

For patients with hormone receptor-positive advanced breast cancer, endocrine therapies, including the selective estrogen receptor modulator tamoxifen, the aromatase inhibitors anastrozole, letrozole, and exemestane, and the selective estrogen receptor degrader fulvestrant, are recommended in clinical guidelines. The addition of targeted agents such as m-TOR inhibitor everolimus or CDK4/6 inhibitors palbociclib, abemaciclib, ribociclib to endocrine therapeutic agents are also recommended as treatment options.

In 90, Dr Hortobagy described the treatment algorism for ER+ ABC (NEJM 339; 974, 1998). For women with limited and nonlife-threatening ER+ disease, hormonal therapy is the initial treatment of choice. Eventually, in most women, metastatic breast cancer becomes refractory to hormonal treatment, at which time the women should receive chemotherapy. But recently, target therapeutic drugs mentioned above have been produced.

Aiming at providing clinically oriented guidelines on how to best manage ABC, the International Consensus Conference for Advanced Breast Cancer have been taken place in Lisbon, every 2 year since 2011. At the 3rd Advanced Breast Cancer Conference, the statements for ER+ and HER2- patients were as follows (Ann Oncol 28:3111, 2017.);

Endocrine therapy is the preferred option for hormone receptor positive disease, even in the presence of visceral disease, unless there is visceral crisis or concern/proof of endocrine resistance. The preferred 1st line endocrine therapy for postmenopausal patients depends on type and duration of adjuvant endocirine therapy as well as time elapsed from the end of adjuvant endocrine therapy; it can be an aromatase inhibitor, tamoxifen or fulvestrant.

The addition of the CDK4/6 inhibitor palbociclib to an aromatase inhibitor, as 1st line therapy, for postmenopausal patients (except patients relapsing < 12 months from the end of adjuvant

AI), provided a significant improvement in PFS (10 months), with an acceptable toxicity profile, and is therefore one of the preferred treatment options, where available. OS results are still awaited.

The optimal sequence of endocrine agents after 1st line endociren therapy is uncertain. It depends on which agents were used in the (neo)adjuvant and 1st line ABC settings. Available options include AI, tamoxifen, fulvestrant+palbociclib, AI+everolimus, tamoxifen+everolimus, fulvestrant, megestrol acetate and estradiol.

At the 4th Advanced Breast Cancer Conference (ABC4) in 2017, topics of endocrine therapy were parts of the most important issues. Despite that most of the clinical trials in estrogen receptor positive (ER+) ABC have not included pre-menopausal women, the panelists considered that pre-menopausal women should have adequate ovarian suppression or ablation (OS/OA) and then be treated in the same way as post-menopausal women with endocrine agents with or without targeted therapies. They announced that future clinical trials should be designed to enroll both of pre- and post-menopausal women.

Early Breast Cancer

In order to decrease the risk of recurrence after surgery for primary invasive breast cancer, systemic adjuvant treatment given for the most of the patients. For women with operable breast cancer, endocrine therapy has been widely used to decrease the incidence of recurrence. The decision on systemic adjuvant treatment should be based on the predicted sensitivity to particular treatment types, the benefit from their use and an individual risk of relapse. ET is indicated in all patients with detectable ER expression (defined as $\geq 1\%$ of invasive cancer cells).

The recently published ATLAS study demonstrated an advantage of 10 years rather than 5 years of tamoxifen. Extended adjuvant therapy should be discussed with all patients, except the ones with a very low risk, although the optimal duration and regimen of adjuvant endocrine therapy is currently unknown. For pre-menopausal women, tamoxifen for 510 years is a standard therapy. The optimal duration of ovarian suppression is not known, although it is usually administered for 25 years. In patients becoming postmenopausal during the first 5 years of tamoxifen, a switch to AI, seems to be particularly beneficial.

In post-menopausal patients, available options include AI, tamoxifen, tamoxifen switched to AI. There is no proven benefit for the routine use of AIs for > 5 years. Endocrine therapy is usually given for 48 months before surgery or until maximum response, and continued postoperatively. AIs are more effective than tamoxifen in decreasing the tumor size and facilitating less extensive surgery.

SP07-2

NOVEL STRATEGIES TO OVERCOME ENDOCRINE RESISTANCE

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Metastatic breast cancer (MBC) is still incurable disease in spite of marked advance of the biologic understanding and targeted therapies. Endocrine therapy is the cornerstone of treatment for hormone receptor positive (HR+) HER2 negative breast cancer. The major limitation of this therapeutic approach is primary or acquired endocrine resistance. A better understanding of endocrine resistance has resulted in newer targeted agents to be added to endocrine therapy. It is believed that the mTOR antagonist everolimus in combination with the AI exemestane and recently, CDK 4/6 inhibitors has evolved to become a valuable addition to the therapeutic options in MBC, based on available data regarding activity and tolerability, combining endocrine therapy with agents targeting putative mechanisms of endocrine resistance is a newer treatment paradigm in HR+ breast cancer. Adding a biologically targeted agent to endocrine therapy results in improved response rate, and clinical benefit rate, and prolonged progression-free survival. A clear advantage in overall survival has not yet been reported. Combination therapy allows delaying chemotherapy but increases toxicities and costs, which are critical factors in decision making in the clinical practice. Today, there are three highly selective CDK4/6 inhibitors in clinical development - palbociclib, ribociclib and abemaciclib. All of three were recently approved by the US FDA in combination with letrozole for the treatment of MBC in a first-line setting, as well as palbociclib in combination with fulvestrant for hormone-receptor (HR)-positive MBC that had progressed while on previous endocrine therapy according to the PALOMA-1, MONALEESA-2, PALOMA-3, and MONARCH-2 trials, respectively. In the recently published randomized phase III MONARCH 2 trial, abemaciclib plus letrozole had longer progression free survival and higher objective response rates with less serious adverse events in advanced HR-positive breast cancer previously treated with hormonal treatment. CDK4/6 inhibition is a new and promising target for patients with hormone-receptor-positive MBC. Both palbociclib and ribociclib showed significant additive benefit for patients receiving firstline treatment for HR-positive, epidermal growth factor receptor-2-negative advanced breast cancer. Palbociclib and abemaciclib also had significant activity in combination with fulvestrant for patients with MBC that progressed on previous endocrine therapy.

The bottom line is that optimal sequencing of these new targeted agents including CDK 4/6 inhibitors or other targeted agent with conventional endocrine therapies including AIs and fulvestrant. Appropriate clinical trial design and patient selection based on prior therapy exposure, together with predictive biomarkers derived through real-time molecular profiling, are needed to enrich future trials and maximize any additional benefit for patients with HR+ MBC.

SP07-3

CLINICAL IMPLICATIONS OF ESR1 MUTATIONS

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Breast cancer is the most common female malignancy in the world. More than 1.3 million new cases of breast cancer are diagnosed annually in the world. Among them, ER (+) breast cancer accounts for about 75%. Medical therapies targeting ER are called endocrine therapy and are the basis of breast cancer treatment. Endocrine therapy can inhibit breast cancer growth by decreasing estrogen level or blocking ER functions. However, due to acquired resistance to treatment, even patients with effective initial endocrine therapy will develop disease progression later. The emergent evidence shows the strong correlation between the abnormality of ER encoding gene ESR1 and endocrine therapy resistance.

The ESR1 gene encodes ER. ESR1 abnormality usually includes gene amplification, rearrangement and mutation. As the new sequencing technologies become more widely available, more and more types of ESR1 mutations have been detected. For example, the striking ESR1 gene mutation is known as the "hot spot" mutation, which is named due to the high frequency mutation sites concentrate on the 537-538 site of ER ligand-binding domain encoded by ESR1. Because the ER LBD plays an important role in the binding of ER to ligands and in the ER proliferation promoting function. So many applications of second-generation sequencing methods to detect ESR1 LBD mutations have explored the location, frequency, function and their association with drug resistance. Based on the recent data, the positive rate of ESR1 LBD is about 20% in patients with metastatic breast cancer who have undergone at least 1-line endocrine therapy. But ESR1 mutation is rare in the nave patients who never undergo endocrine therapy before. It is currently thought that the resistance related to ESR1 gene mutation is mainly acquired drug resistance. Many studies show that the detection rate of ESR1 gene mutation after endocrine therapy is significantly higher than that before the treatment. The mechanism may be as follows: during the endocrine therapy process, ESR1 gene mutation was selected as a survival advantage gene, cells carrying ESR1 gene mutation thus survived, and gradually become the dominant tumor cell line. Therefore, establishing a reasonable screening and monitoring system for patients with ER (+) breast cancer can detect the ESR1 gene mutation as soon as possible so that a better treatment plan can be taken in time. On the other hand, whether ESR1 gene mutation can be used as a reference index for prognosis still needs further large-scale retrospective and prospective studies to confirm.

Based on the mechanism of drug resistance produced by ESR1 gene mutation and drug treatment development in recent years, to overcome the problem of endocrine resistance in breast

cancer, we can consider several aspects, such as AI-resistant patients can be treated with tamoxifen or Fulvestrant; Increase the dose of tamoxifen or Fulvestrant. Apply more powerful SERMs or SERDs; Inhibit the activity of co-regulator; Block downstream pathways that ER exerts its function.

Acquired resistance in breast cancer endocrine therapy may be related to ER encoding gene ESR1 mutation. So, we recommend the monitoring of ESR1 gene mutation should start from the definite diagnosis of breast cancer and run through the whole process of endocrine therapy to further reveal the relationship between the timing and prognosis of ESR1 gene mutation and thus to optimize clinical decision-making.

Panel Discussion

GBCC2018

Global Breast Cancer Conference 2018

PD01-1

CAN WE OMIT SURGERY WITH SUGGESTION OF PCR BY BIOPSY IN THE BREAST?

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Because of the current advances in neoadjuvant systemic therapy (NST), and the development of breast imaging, the non-operative therapy for early breast cancer has emerged as a viable option. Feasibility clinical trials either focusing on the breast or the axilla are being performed around the world. The rate of pathological complete remission (pCR) in the breast cancer following NST is increasing, most of which were the triple-negative breast cancer and HER2 positive tumors. The question thus arises whether or not breast surgery is necessary when there is pCR after NST, and whether it provides any survival benefit when tumor is no longer pathologically detectable. Avoiding surgery with or without even radiotherapy might only be conceivable on the basis of a reliable diagnosis of pCR without operating. We would discuss the recurrence risk if we omit surgery with suggestion of pCR by biopsy in the breast, to find out which subgroup patients may avoid further surgery in the breast.

PD01-2

EVALUATION OF AXILLARY LNS AFTER NEOADJUVANT SYSTEMIC THERAPY

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In patients with breast cancer, the evaluation of axillary lymph node (ALN) status is important in determining optimal treatment and predicting prognosis (1). Traditionally, this has been assessed by sentinel lymph node biopsy (SLNB). After a positive SLNB, subsequent ALN dissection (ALND) was typically pursued. Ultrasound (US)-guided fine-needle aspiration (US-FNA) has been widely accepted for preoperative axillary staging, as it is less invasive than SLNB and involves no radiation hazard. Furthermore, with pre-operative detection of ALN metastasis by US-FNA, patients may have the opportunity to undergo neoadjuvant chemotherapy (NAC).

Recent trials have suggested the feasibility of obviating the ALND in early breast cancer with a few positive SLNBs or performing a SLNB following NAC (2-4). The potential advantage of SLNB in this setting is the avoidance of the morbidity of an axillary dissection in cases where there is an axillary pathologic complete response. However, the overall false-negative rate is still a concern. The selection of suitable patients for this approach remains controversial. The role of imaging evaluation for axillary lymph node after NAC is not well established.

In this talk, several predictive models published for axillary node pathologic complete response after NAC for breast cancer and imaging modalities will be covered (5-8) and the method to improve the accuracy of SLNB after NAC will be discussed (9, 10).

PD01-3

EVALUATION OF PATHOLOGIC RESPONSE IN BREAST CANCER TREATED WITH PRIMARY SYSTEMIC THERAPY

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The increasing use of neoadjuvant treatment for advanced and early stage breast cancer has introduced new challenges in the pathologic evaluation and reporting of breast specimens. Systematic pathologic evaluation of cancer resection specimens plays a vital role in determining the patient's prognosis and facilitating decisions after neoadjuvant chemotherapy. Pathologic complete response in breast cancer after neoadjuvant treatment usually correlates with improved disease-free survival and overall survival for subgroups of breast cancer and is often used as a surrogate marker of outcome. Through monitoring treatment response and tailoring subsequent locoregional and systemic therapy, we can make more individualized patient care. Topics covered in this lecture will include complete pathologic response, different patterns of tumor response in different molecular subtypes, grading of partial response, response in the lymph nodes, evaluation of the axilla before and after treatment, practical approach to sampling of the post- neoadjuvant surgical specimen, detailed method for calculating the residual cancer burden (RCB) score, different pathologic factors after neoadjuvant therapy.

PD01-4

RADIATION THERAPY FOR PATIENTS WITH PCR AFTER NEOADJUVANT CHEMOTHERAPY

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Neoadjuvant chemotherapy (NAC) is an effective treatment modality for locally advanced breast cancer patients. Also, NAC is also a treatment option for early-stage breast cancer patients in terms of breast-conserving surgery (BCS). NAC allows the eradication of micrometastases without waiting for postoperative recovery, the assessment of tumor response to chemotherapy and BCS for patients who would have required a mastectomy. NAC for breast cancer modifies the pathologic extent of disease. NAC achieves a disease response in up to 80%. Also, pathologic complete remission (pCR) is increasing in patients treated with modern systemic chemotherapy and targeted agent in HER-2 overexpression patients before surgery. The potential downstaging by a combination of chemotherapy regimens and target therapy presents a challenge regarding the indications and radiation fields for postoperative radiation.

The benefits of postmastectomy radiation therapy (PMRT) for locally advanced breast cancer were well established from randomized trials. These trials showed PMRT decreased locoregional recurrence and increased cancer survival. However, there are no randomized trials to define the benefits of PMRT after NAC. In 2008, a multidisciplinary expert panel organized by the National Cancer Institute published a statement that PMRT should be considered for patients presenting with clinical stage III disease or with histologically LN (+) after NAC. In patients treated with NAC for locally advanced breast cancer, it is recommended that the RT field encompass whole breast/chest wall and ipsilateral regional LNs.

In a retrospective studies at the University of Texas MD Anderson Cancer Center, breast cancer patients clinical stage II-III breast cancer patients who were treated with NAC and mastectomy but without PMRT were at significant risk for locoregional recurrence, even when there was no LN metastasis or when the patients were in pCR. PMRT was associated with an improvement in locoregional recurrence for patients with clinical stage III disease and pCR after NAC (10-year locoregional recurrence: 7.3% in the 62 stage III patients who received PMRT vs. 33% in the 12 patients who did not).

In contrast to the MDACC findings, results from studies performed in France have shown no increase in the risk for distant metastasis, locoregional recurrence, or death when PMRT was omitted after NAC and mastectomy in clinical stage II-III breast cancer patients with ypN0. A significant association was found between pCR in response to NAC and improved DFS, com-

pared with non-pCR patients. Also, Korean Radiation Oncology Group (KROG) 12-05 study analyzed 151 patients who achieved pN0 at mastectomy after NAC at 9 institutions. The 5-year DFS and OS rates were no difference regardless of PMRT. Pathologic T stage was significant prognostic factor affecting DFS. Recently, KROG 16-16 study which retrospectively analyzed ypN0 breast cancer patients treated with modern systemic NAC regimen and mastectomy also showed no survival difference according to PMRT. According to molecular subtypes, PMRT showed no survival advantages.

Another issue is about radiation field in breast cancer patients with ypN0 who received NAC followed by BCS. French study showed no differences in treatment outcomes whether or not additional elective nodal irradiation (ENI) regardless of clinical status was performed. Also, KROG 12-05 and 16-16 studies analysed ypN0 patients who received NAC followed by BCS and RT. There was no significant difference in survival outcomes according to ENI. ENI did not affect survival outcomes in any of the molecular subgroups.

In conclusion, although PMRT after mastectomy and ENI after BCS in breast cancer patients treated by NAC might not be necessary for ypN0 patients, prospective randomized studies would be needed to confirm the feasibility of whether PMRT or ENI can be safely omitted in ypN0 patients after NAC for breast cancer. A randomized phase III clinical trial (NSABP B-51/RTOG 1304) have been ongoing for evaluating whether the addition of PMRT after mastectomy or ENI after BCS will significantly reduce the rate of events for breast cancer recurrence-free interval in patients who present with histologically positive axillary nodes before NAC but convert to ypN0 after NAC.

PD02-1

HOW TO MAKE A GOOD MASTECTOMY FOR RECONSTRUCTION BASED ON THE ANATOMY

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Mastectomy has been used for the treatment of breast cancer for many years, Breast reconstruction after mastectomy plays an active role in improving the quality-of-life and alleviating the psychological trauma of breast cancer patients, and has become an indispensable part of the comprehensive treatment in breast cancer. Breast reconstruction is the rebuilding of a breast, which involves using autologous tissue or prosthetic material to construct a natural-looking breast. Often this includes the reformation of a natural-looking areola and nipple. This procedure involves the use of implants or tissue taken from other parts of the woman's body. Breast reconstruction after mastectomy is typically staged, taking place over months or even years. A breast can be reconstructed by two methods: prosthetic implants and autologous tissue. The reconstruction can be performed immediately at the time of mastectomy or on a delayed basis.

Retrospective studies found that the flap-based treatment patients usually had higher complication rates of marginal necrosis of incision, but capsular contracture incidence was higher in immediate implant group. There was no difference in blood loss, drainage fluid, and other postoperative complications. Several independent factors were associated with increased postoperative complications included diabetic, obese, and reconstruction with flap. There was no significant difference in the disease-free survival rate and overall survival rate between different surgical groups. Furthermore, patients in the tissue expander group were more likely to get a satisfactory postoperative breast appearance.

Therefore, breast reconstruction following mastectomy could be a feasible surgical treatment option for breast cancer, tissue expander implantation following delayed implant breast reconstruction is a more effective treatment in terms of cosmetic and quality-of-life outcomes, but the appropriate surgical procedures should be chosen according to the patient's actual situation. A larger study population is needed to more accurately determine oncologic outcomes in future.

PD02-2

RECONSTRUCTION WITH AUTOLOGOUS TISSUE

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Options for postmastectomy reconstruction consist of autologous tissues, implants, or both. Factors affecting decisions about the type of reconstruction may include necessary adjuvant therapies, available tissue donor sites, comorbidities, vocation, and acceptability of donor site morbidity. At the time of consultation, the plastic surgeon should address the patients expectations, including those about her ideal breast size, breast shape, and lifestyle. Each patient places her own subjective value upon the presented and perceived risks and benefits of breast reconstruction, and she should feel empowered to make decisions about what is done with her body, provided they are in agreement with sound surgical guidelines.

Free TRAM flaps

Since it was first described in 1979, the free transverse rectus abdominis myocutaneous (TRAM) flap has become one of the most popular and reliable methods of microsurgical breast reconstruction. The free TRAM flap has many features that make it well suited for breast reconstruction. Most patients have adequate lower abdominal skin and subcutaneous tissue available for incorporation into the flap to reconstruct a breast. The robust blood supply of the free TRAM flap reduces the risk of fat necrosis and also enables aggressive folding, trimming, and shaping of the flap to optimize the aesthetic outcome of breast reconstruction. In addition, in most cases the free TRAM flap requires minimal donor site sacrifice. And finally, the flap can be harvested with the patient in a supine position, while mastectomy is being performed.

Over the years, variations on the free TRAM flap, including the free muscle-sparing (MS) TRAM flap, the deep inferior epigastric perforator (DIEP) flap, and the free superficial inferior epigastric artery (SIEA) flap, have been developed to further minimize donor site morbidity by harvesting less muscle and less anterior rectus fascia. Each flap transfers the same lower abdominal skin and subcutaneous tissue and is able to provide an aesthetically pleasing breast reconstruction.

DIEP Flap

If the perforating vessels alone are harvested, thus sparing the entire rectus abdominis muscle, the resulting flap is referred to as a deep inferior epigastric perforator (DIEP) flap. Sparing the entire muscle potentially reduces donor site morbidity, including abdominal bulge and weakness. However, it is controversial whether DIEP flaps reduce these complications significantly more than free MS-TRAM flaps. Because a DIEP flap has fewer perforators than a free TRAM

flap, there is a concern that the reconstructed breast mound might have an insufficient blood supply and cause fat necrosis in the breast mound. Patient selection as well as intraoperative decision-making is crucial to maximize the potential benefit of DIEP flap breast reconstruction.

SIEA Flap

The SIEA flap is based on the superficial inferior epigastric artery, which arises from the femoral artery. The main advantage is that the rectus fascia is not violated, thus resulting in minimal donor site morbidity. However, its use is limited by the variability of the superficial inferior epigastric artery and the reliability of the flap perfusion. Most surgeons limit the use of the SIEA flap to a hemi-flap, discarding the tissue across the midline.

Other flaps

If a patient desires autologous tissue breast reconstruction but is not a candidate for reconstruction with abdominal or back tissues, other donor sites may be available depending on the patients body habitus and her willingness to accept donor site morbidities. Options may include the free superior gluteal artery perforator (S-GAP) flap, the free inferior gluteal artery perforator (I-GAP) flap, the free anterolateral thigh (ALT) flap, and the free transverse gracilis (TG) flap.

CONCLUSION

Many options are available for breast reconstruction. When deciding which option to use, the surgeon should consider the patients disease and treatment as well as her body habitus, comorbidities, lifestyle, and preferences. When applicable, autologous breast reconstruction with free flap can create a breast mound that appears as anatomically and aesthetically normal as possible with minimal morbidity. With the appropriate technique is used, postmastectomy breast reconstruction can be rewarding for both the surgeon and the patient.

PD02-3

RECONSTRUCTION WITH IMPLANT

Hak Chang

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Implant-based reconstruction is the leading form of breast reconstruction. The American Society of Plastic Surgeons reported more than 76,000 implant-based breast reconstruction procedures in 2011 comprising 70–80% of all breast reconstruction. A lot of plastic surgeons use acellular dermal matrix (ADM) for coverage of the inferolateral aspects of breast implant. The use of ADM has many advantages including improved inframammary fold control, better support, reduced malposition, and improved lower pole expansion. However, the most serious complications with ADM use such as seroma, infection, expander/implant loss are also observed. In this study, expander/implant based reconstructed patients with ADM were compared with those without ADM in many clinical aspects and complications.

For the adequate implant-based reconstruction without ADM, the viability of mastectomy skin flap (MSF) is most important. Because mastectomy skin flap necrosis can result in infection, delayed oncologic therapy, and reconstructive failure. The intraoperative approach to evaluate the viability of MSF includes the assessment of skin color, capillary refill, temperature, and marginal bleeding. Recently, intraoperative laser-assisted indocyanine green (ICG) dye angiography (SPY system, Novadaq Technologies, Canada) has been introduced and used for the evaluation of tissue perfusion of MSF. After the skin-sparing or nipple sparing mastectomy, ICG injection and SPY angiography were performed. If there were hypoperfused tissues, debridement was conducted. Then MSF necrosis and wound problem were observed.

The use of postmastectomy radiotherapy (PMRT) has increased with increasing number of patients with breast cancer. PMRT reduces local reoccurrence and improves survival in patients with locally advanced lymph node-positive breast cancer. However, PMRT has an increased risk of various complications including capsular contracture in expander/implant breast reconstruction. Recently, studies have reported that ADM prevent or decrease capsular contracture. By far, research on the effect of ADM on capsule formation has been limited to examining inflammatory response; thus, further study is necessary to investigate any differences due to radiotherapy. This part aimed to examine how ADM reduces capsular formation in expander/implant breast reconstruction and identify cellular and molecular mechanisms of ADM-mediated reduction of capsular contracture in patients treated with radiotherapy.

Each implant-based breast reconstruction patients have different conditions. Therefore, treatment options should be applied adequately according to the patients.

PD03-1

INTERNATIONAL GUIDELINES FOR THE USE OF NGS PANELS

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PD03-2

BIOMARKER DRIVEN CANCER THERAPY BY MULTIPLE NGS PANELS FOR SOMATIC MUTATIONS

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Molecular profiling is a key component of precision medicine for cancer, as it provides actionable information on targetable genes or pathways for personalized treatments. Clinical tests based on panel sequencing platform are accumulating with clinical data of cancer patients. Systematic approaches to integrate clinical and genomic data could uncover the relationship between genomic alterations and clinical outcome. We have established genomic data warehouse with a unique cohort of 5,000 cancer patients with colon, stomach, lung and breast cancer, which is linked to clinical data warehouse in the hospital. Statistical analysis enabled us to extract genomic variants related to patient survival in each cancer type. The prognostic models using both clinical and genomic features outperformed clinical information-only method. The model was capable of predicting patient survival in an independent cohort. Our study provides a valuable resource to realize precision oncology as well as translational research on drug development.

PD03-3

APPLICATION OF MULTIPLE NGS PANELS FOR GERMLINE VARIATION TO REAL PRACTICE

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With the technical advances in genetic tests using next generation sequencing (NGS), it became more feasible to find out germline mutations for hereditary cancer in patients without BRCA1/2 mutations. Indeed, NGS can provide detailed genetic information via multi-gene panel assays. However, the application of NGS multigene panel test in a clinical setting represents a considerable challenge. It is necessary to not only validate this novel technique, but also to select candidates of susceptibility genes. Further, we should establish clinical guidelines for the carriers with germline mutations beyond BRCA1/2.

To understand the clinical and genetic characteristics of multiple susceptibility genes identified by NGS multigene panel test in Korean population, we performed a pilot study using comprehensive multigene panels that included 35 known or suspected cancer susceptibility genes to examine BRCA1/2 mutation-negative Korean women with clinical features indicative of hereditary breast cancer. Among 120 women, 9 patients (7.5%) were found to carry at least one pathogenic or likely pathogenic variants: TP53 in two patients, PALB2 in three patients, BARD1 in two patients, BRIP1 in two patients, and MRE11A in one patient. Other studies also identified cancer susceptibility genetic variants in 2.1–16.8% BRCA1/2 mutation-negative patients using NGS panel tests. Although NGS panels possibly identify cancer susceptibility in some patients without BRCA1/2 mutations, much more still remains to be done. A large number of genes included in a multigene panel can cause an increase in the number of variants of uncertain significance (VUS). In addition, we does not have sufficient information and enough preventive strategies for each genetic variants included in the multigene panels. There is also a need to solve ethical, legal, and social problem about incidental findings in genetic variants.

Considering advances in performance capacity and accuracy, and expected economic benefit, application of NGS panel will continue to expand in real practice. We will have to find more adequate guidelines for selection of the candidates with high risk for hereditary cancer, interpretation of each genetic variants and VUS, and providing of psychosocial support and preventive strategies to the mutation carriers. We are trying to establish a well-organized population-based database, and conduct clinical trials to help to improve knowledge and quality of life of the carriers with germline mutations of cancer susceptibility genes.

PD04-1

ROLE OF PRIMARY RESECTION FOR PATIENTS WITH OLIGOMETASTATIC DISEASE

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There are some important progresses on treatment for Stage IV breast cancer. PET/CT can diagnose small metastatic lesions (Oligometastasis). The order-made treatment according to biomarkers by molecular target drugs are very effective to control the tumor progressions of metastatic disease. Moreover, surgical technique for mastectomy or metastasectomy became less invasive. The surgical approach for Stage IV breast cancer patients are for primary or metastatic lesions. The aim of them are classified 'treatment' to improve the survival and 'examination' to confirm the biology of tumor.

The burst evidence to consider that the surgery can improve the survival (overall or local) significantly are necessary. There is no prospective randomized trials' data analyzing the prognostic effect of metastasectomy. However, oligometastatic disease (single or few detectable metastatic lesions that are usually limited single organ) is defined potentially curable, and surgical procedure (or radiation therapy) can be useful to treat oligometastasis. There are some prospective randomized trials (including JCOG 1017 trial) to evaluate the prognostic effect of primary tumor resection for de novo stage IV breast cancer. We will be able to get the burst evidence from these trials' data. On the other hands, the surgical procedure to examine the tumor biology is considered more important to select the effective drugs.

The surgical approach for stage IV breast cancer should be evaluated the significance to make the most effective (or curable) treatment strategy.

PD04-2

MULTIMODAL APPROACH TO DEAL WITH BONE METASTASIS

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Bone is the most common site of metastases in breast cancer (BC) patients: a recent meta-analysis reported that 12% patients with stage I-III BC developed bone metastasis (BM) during a median follow-up of 5-year comprising 55% of all metastases, and 58% of patients with primary metastatic BC had BM.1 BM in patient with BC most commonly develop in the spine, ribs, pelvis and long bones and the majority of patients who develop BM at first relapse will experience bone complication such as pain, hypercalcemia, and skeletal-related events (SREs). SREs are defined as: a pathologic fracture, spinal cord compression, necessity for radiation to bone or surgery to bone. SREs can lead to severe pain, increased risk of death, increased health care costs and reduced quality of life. The main presenting symptoms comprise pain, hypercalcemia, pathological fracture, spinal instability with cord compression. The main goal of treatment for bone metastasis is as follows: i) pain management; ii) prevent and manage of SREs iii) definite treatment for oligometastasis.

1. Medical treatment

Until recently, to prevent SREs in patients with bone metastasis, zoledronic acid has been the sole standard of care. Denosumab, a receptor activator of nuclear factor kappa-B ligand (RANK-L) inhibitor, has been recently approved for use for this indication, thus presenting another option for these patients. Denosumab was shown to be superior to zoledronic acid in delaying the time to first or subsequent SREs in breast cancer patients with bone metastases, but there is a concern for cost-effectiveness compared with bisphosphonates. Meanwhile, the antitumor effect of bisphosphonates or RANKL inhibitor was suggested in preclinical studies, and the survival advantage of zoledronic acid had been suggested in some clinical trials. However, the following studies failed to prove any survival benefit in patients with breast cancer. In conjunction with systemic anticancer treatments, managements for hypercalcemia and pain with analgesics based on the WHO guidelines and hypercalcemia are also critical for patients with bone metastasis. Furthermore, adjuvant agents such as bisphosphonates, corticosteroids, calcitonin, and radiopharmaceuticals can be added when it is indicated.

2. Radiotherapy

In case of neurologic deficits, particularly motor dysfunction, urgent treatment is required to

avoid progression to plegia. Radiotherapy and decompressive surgery are the most important treatment modalities based on clinical symptoms and sings. For example, Harrington eta al classified bone metastasis from I to V, where IV and V were suggested to need surgical intervention. For the long bone metastasis, Mirels score system is widely use to predict risk of pathologic fracture. External-beam radiotherapy provides excellent palliation for localized metastatic bone pain. Radiotherapy may also be indicated for patients at risk of pathologic fracture and neurologic complications arising from spinal cord compression, nerve root pain, or cranial nerve involvement. Studies have shown that single-fraction regimens (mostly 8 Gy), which can be more convenient for patients and providers, are at least as effective as various fractionated regimens.2 A meta-analysis of eight completed randomized trials of single-fraction radiotherapy (median: 8 Gy) vs. multifraction radiotherapy (median: 20 Gy in five fractions) showed no significant difference in complete overall pain response between the two regimens.3

3. Surgical management

Surgical treatment of bone metastases is generally palliative. All procedures must guarantee stability, early mobilization, and brief hospitalization, in light of what is usually a shortened life expectancy. Surgery is indicated in patients with pathologic fractures of the long bones and those involving the hip joints, in patients with spinal lesions, and in patients with compression of peripheral nerves. In advanced cancer patients in poor overall condition, intramedullary nailing without resection of metastasis is palliative, providing pain relief and partial restoration of function in the involved area.

4. Patient/family education, psychosocial support, and rehabilitation

In the multidisciplinary approach to the treatment of bone metastases, an integral part of the care team's role is the education of patients and their families. By offering diagnosis-and treatment-specific information to patients who have misconceptions and may be hesitant to ask for such information, education aims to reduce the patient's sense of helplessness and inadequacy due to lack of knowledge. Coping-skills training, emotional support, and targeted counseling have also been shown to ease the disruption and distress that accompanies cancer diagnosis. In summary, bone metastasis is one of the most frequent and may cause SREs, causing significant morbidity, low QoL, and poor survival. Therefore, adequate and comprehensive managements are necessary. Furthermore, early measurement to prevent and diagnose the impending SREs is crucial. For these reasons, multidisciplinary team approach for the bone metastasis including rehabilitation and education team is strongly warranted.

PD04-3

RECENT ADVANCES TO TREAT TUMOR RECURRENCE IN CNS

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The incidence of brain metastases (BM) among patients with metastatic breast cancer (MBC) has been reported to range between 10-15%. As such, it represents the second most common source of BM; being only preceded by lung cancer. In recent years, introduction of a wide range of novel agents into the treatment of MBC has significantly improved overall survival, especially in those with HER2 +ve disease. Unfortunately, most of these systemic treatments do not effectively cross the bloodbrain barrier (BBB), which would render the brain as a true sanctuary site for disease relapse. Accordingly, there is a strong concern that the incidence of BM will emerge as a significant clinical problem contributing to morbidity and mortality of MBC patients at a time when many of these patients are showing a good extra-CNS disease control.

Fortunately, the role of surgery and localized conformal radiation therapy in patients with BM has been refined during the last few years, which could provide a better survival outcome in many patients, especially those with a limited number of BM. Hence, many groups- including ours -have underscored the role of clinico-pathological scoring systems, to predict for the occurrence of BM in patients with early breast cancer. This approach aims at establishing a clear indication for regular brain MRI screening, to detect early lesions that are more manageable by local interventions. Although the survival benefits of these methodologies are not yet verified, still they may prove effective in future studies.

Furthermore, better understanding of BBB physiology, and the molecular alterations which arise in the presence BM, has suggested some novel strategies that could be useful in improving drug delivery into the BM lesions. The details of these approaches will be highlighted with special emphasis on current ongoing studies in this direction.

PD05-1

OVERVIEW OF IMMUNE CHECKPOINT INHIBITORS FOR BREAST CANCER TREATMENT: BEYOND PD-1 BLOCKADE

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Activating the immune system for therapeutic benefit in cancer has long been a goal in immunology and oncology. After repetitive failures, the tide has finally changed due to the success of recent proof-of-concept clinical trials using antibodies to blockade immune inhibitory molecules such as CTLA-4 and PD-1. These successes suggest that tolerance raised by tumor microenvironment is a major obstacle for immunotherapy and therefore, blocking the tolerance is the first step to rejuvenate tumor-specific T cell immune responses. However, because the immune conditions are quite different among cancer types and individual patients, appropriate immune-interventions should be used for each person. For instance, the efficacy of PD-1 blockade in clinical trials has been variable in the patients with various types of cancers. In breast cancer including triple negative type, a growing body of evidence suggests that the presence of immune elements within the tumor or in the tumor stroma determines predictive value after PD-1 blockade. Although the presence of PD-L1 expression may enrich for the response, it does not appear to explain completely.

Here, we investigated how various immune checkpoints including PD-1 and TIGIT and their ligands communicate each other to suppress anti-cancer immunity and these interactions are quite different in each individual patient. Especially, the tumor expression of ligands for immune checkpoints, PD-1 and TIGIT, seems to be critical to determine the progression of tumors. Based on our data, we suggest which strategy should be applied to predict and enhance the efficacy of immune checkpoint blockers in each individual patient. Indeed, our data shows that classification of cancers dependent on the expression of immune checkpoint ligands enhance the power of prediction for immune checkpoint blockade therapy. Altogether, a personalized combined immunotherapy based on the evaluation of patients immune status may be exploited for further improvement of current cancer immunotherapies.

PD05-2

EMERGING TISSUE OR SERUM MARKERS FOR IMMUNE CHECKPOINT INHIBITORS

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Breakthrough progress has been made by understanding of immunosuppressive tumor microenvironment; the cytotoxic T lymphocyte antigen-4 (CTLA-4) and programmed death-1/programmed death ligand-1 (PD-1/PD-L1) pathway. Currently, more than handful of monoclonal antibodies targeting either CTLA-4 or PD-1/PD-L1 pathway have been approved based on results from active clinical trials in advanced solid cancers. So far, immune checkpoint inhibitors have generated a significant clinical benefit in cancer patients by showing objective tumor regression of metastatic cancers and increasing survival time. More importantly, those new therapeutics induced durable clinical responses with favorable toxicity profiles in multiple cancer types. Therefore, clinical development and rational application of these promising agents remains an important scientific task. Most of all, challenges should be overcome to identify patients accurately who will benefit from immune checkpoint inhibitors. Next, other biomarkers indicating active tumor-rejecting immune responses, immune tolerance, and time for retreat should be explored. Expression of PD-L1 either on tumor cells and/or immune cells is the most extensively studied and it was approved for companion diagnostics for pembrolizumab in non-small cell lung cancer. However, PD-L1 expression is dynamic and it has low prediction accuracy in other tumor types. Thus, more feasible and clinically applicable surrogate marker should be identified. As the cytotoxic T cells are the final player for tumor cell killing, profiling tumor-infiltrating immune cells in the tumor microenvironment may be important in predicting clinical benefits of immune checkpoint inhibitors. Identification of mutational landscape and mismatch-repair deficiency through genetic analysis is a new approach for judging the potential benefit of immune-oncology drugs. Soluble markers including cytokines and immunosuppressive growth factors have been explored and some of the markers were identified as promising markers in specific therapeutic setting. Continued research to explore reliable markers, and further standardization and validation might increase the value of immunotherapy in oncology clinic.

PD05-3

STRATEGIES FOR THE COMBINATION OF IMMUNE CHECKPOINT INHIBITORS

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Cancer immunotherapy and in particular monoclonal antibodies blocking the inhibitory programed cell death 1 pathway (PD-1/PD-L1) have made a significant impact on the treatment of cancer patients in recent years. However, despite the remarkable clinical efficacy of these agents in a number of malignancies, it has become clear that they are not sufficiently active for many patients. There is emerging evidence that immune checkpoint blockade is effective primarily in tumors that are already recognized by the immune system, as manifest by a pre-existent CD8+ T cell infiltrate. Broadly speaking, the lack of a spontaneous tumor directed immune response may be because of the "invisibility" of the tumor to the immune system due to tumor antigens that are not sufficiently distinct from self-antigens; alternatively, tumor cell intrinsic oncogenic pathways may actively subvert an antitumor immune response as was shown for the β-catenin pathway. Approaches that have the potential to convert a "non-T cell inflamed" tumor into a T cell inflamed tumor such as novel vaccines, oncolytic virus approaches, stimulation of co-stimulatory molecules, targeted therapy, radiation/chemotherapy, and adoptive cell therapy (T cells, CARs) should be prioritized – particularly for tumor types that have shown little response to single agent anti-PD-1/PD-L therapy and for individual patients, ideally biomarker-selected, who have lower predicted response to the PD-1/PD-L1 backbone. Strategies that primarily address additional immunosuppressive mechanisms in the tumor microenvironment, such as indoleamine 2,3-dioxgenase (IDO)-inhibition, TGF-β blockade, regulatory T cell (Treg) depletion, and angiogenesis inhibition may be particularly effective to enhance or rescue tumor responses achieved with anti-PD-1/PD-L1 monotherapy. The goal of combination approaches is to expand the spectrum of patients who respond to cancer immunotherapy (more responding patients in tumors that are sensitive to monotherapy and the identification of new sensitive tumor types that do not respond to monotherapy alone) and to improve the quality of clinical responses (i.e., extension of response duration, PFS, and OS) beyond what can be achieved with monotherapy alone. With research to further elucidate the mechanisms of action behind these agents as well as increased understanding of the resistant counter defense employed by tumors, the development of rational combination approaches is now extending even beyond doublets.

PD06-1

ROLE OF SURGERY FOR THE SUPRACLAVICULAR AND INTERNAL MAMMARY LYMPH NODE(S) METASTASIS

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Locoregional relapse (LRR) occurs in less than 10% of breast cancer patients but associated with high incidence rate of simultaneously or late distant metastasis and eventually died despite optimal local and systemic therapy. A whole genome sequencing study demonstrated that local relapse breast cancer kept the driver mutation and continued to acquire mutation as systemic metastasis. The breast cancer was treated in de-escalating behavior for both primary tumor and axillary node in recent decade. While the approach to LRR should be more aggressive based on our clinical experiences and above mentioned biologic nature.

Between 1990 and 2006, 6,878 consecutive women with primary breast cancer underwent mastectomy. Supraclavicular lymph node metastasis (SLNM) was defined as supraclavicular nodal metastasis with or without concurrent locoregional recurrence. Overall, 88 patients received further treatment were included in analysis. We conducted the inverse probability treatment weights using causal diagrams and marginal structural Cox model analysis.

Of 88 patients with SLNM, 36 patients received selective neck dissection (SND) and chemotherapy, 25 received radiotherapy and chemotherapy, and 27 received chemotherapy alone, respectively. The median follow-up was 43.5 months. After conducting inverse probability weights using variables indicating by the directed acyclic graph, marginal structural Cox model suggested that SND and chemotherapy, and radiotherapy and chemotherapy was significantly improved DMFS compared to that of patients with chemotherapy alone (hazard ratio [HR] 0.36, 95% CI 0.21–0.63, $p < 0.001$, and HR 0.39, 95% CI 0.19–0.83, $p = 0.015$, respectively). In addition, SND and chemotherapy was significantly improved OS compared to chemotherapy (HR 0.57, 95% CI 0.33–0.99, $p = 0.047$), while radiotherapy and chemotherapy was marginally significantly improved OS compared to chemotherapy (HR 0.53, 95% CI 0.26–1.10, $p = 0.088$). Recurrence within 2 years was an effect modifier in both models.The randomized clinical trials including ACOSOG Z0011 reported the low incidence rate of axillary relapse and do not impact the survival. We identified 92 axillary relapse patients from 2000 to 2009, 85 patients were associated with synchronous or metachronous distant metastasis and the 5-year OS of axillary relapse, chest wall and ipsilateral breast recurrence were 29.2%, 36.6% and 61.4%, respectively. Interal mammary (IM) node metastasis was associated with an unfavorable outcome, and IM dissection is not performed routinely now. However, we observed better outcome in those patients IM node(s) positive and been removed while autologous microvasular reconstruction

using the internal mammary vessels as recipient. It indicated the importance of early detection of IM node metastasis by image or sentinel node mapping.

Early detection and multimodality approach, especially aggressive surgical treatment for LRR can improve the survival.

PD06-2

ROLE OF RADIATION THERAPY FOR SKIN, CHEST WALL AND REGIONAL LYMPH NODE(S) METASTASIS

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LRR can be classified according to its anatomic location: skin, mastectomy scar, chest wall, or regional lymph nodes (axillary, internal mammary, infraclavicular or Rotter, and supraclavicular).

From a management perspective, type and extent of prior treatment for the initial cancer is an important factor. In patients who have not received previous radiotherapy, surgical resection and definitive dose of postoperative radiotherapy are therapeutic modalities routinely used to achieve maximal local regional control. For the patients who previously received radiotherapy, since the failure rates of LRR treated with resection alone remain very high, re-irradiation of the recurred site with curative intent has been utilized and seems to improve the outcomes.

Radiation dose for the treatment of a LRR depends on prior radiotherapy administration. Consideration for cumulative tissue toxicity is necessary when determining the dosage and extent of fields in those who have been previously irradiated. To obtain higher cumulative dose safely for better control rate, using chemotherapy or hyperthermia as radiosensitizers has been tried to increase effective dose. A meta-analysis of 16 studies engaging re-irradiation and hyperthermia reported higher complete response rate and improvement of local control.

In cases with inoperable status or medical condition unfit for surgery, radiotherapy may be applied to make the disease resectable or as a palliative treatment modality.

Regional lymph node recurrences generally confer a poor prognosis. For a patient who has an isolated nodal recurrence in a previously radiated field, regional re- irradiation with therapeutic dose is generally not considered safe, but limited field re- irradiation may be considered as a salvage option in patients unresponsive to systemic treatment or those with unresectable disease. In cases with internal mammary node recurrence, for patients who have not previously received radiation, the mainstay of treatment is curative dose of radiotherapy. However, combined utilization of both surgical resection and radiation therapy confer higher disease-free and overall survival than using either modality alone. Therefore, both modalities need to be considered, while the outcome is still unsatisfactory. Isolated supraclavicular recurrences have long term DFS ranging from 15-30% with the utilization of multi-modality therapies.

An LRR confers a poor prognosis because it is associated with high risk of distant metastasis.

To improve the treatment outcome of LRR, systemic therapy also should be considered to manage the risk of distant metastasis, while combination utilization of surgery and radiotherapy is important to gain the local control. Interaction between the treatment modalities must be taken into account, and multidisciplinary individualized approach is essential for the patients with LRR.

PD06-3

MANAGEMENT OF CONTRALATERAL AXILLARY LYMPH NODES METASTASIS

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Contralateral axillary lymph node metastasis (CAM) is quite uncommon. Literature reports the incidence to be anywhere from 1.9% to 6%. CAM has been divided into synchronous CAM (found at time of primary diagnosis) and metachronous CAM (recurrence after primary treatment). Three possible sources of CAM should be considered, i.e. from the original breast tumor, from an occult primary in the contralateral breast; and metastasis from an extra-mammary site. Identification of the source is important as it will influence the management of CAM. Biopsy of the axillary node can exclude the third possibility. Magnetic resonance imaging plays an important role in the differential diagnosis. It can detect tumor within the breast in 62% to 70% of patients with axillary metastasis.

Of the cases of CAM reported in the literature, the overwhelming majority are metachronous CAM, making synchronous CAM even more uncommon. In most literature reports, CAM is associated with aggressive histopathological features of the primary breast tumor, 81% having a tumor grade of 3, 81% having lymphovascular invasion, and larger primary breast tumors with 95% being T3 or T4. And there were increased incidence of hormone receptor negative and Her-2 positive lesions compared to breast cancers without CAM

Although there are no large studies on patient outcomes and treatment option due to the rarity of the disease, there are several small reports which demonstrate treatment modalities Wang et al. reported more than 70% relapse rate, and they found a 25% mortality rate within 23 years due to distant metastasis. They found that radiotherapy and systemic chemotherapy or hormone therapy maybe of most benefit rather than ALND or mastectomy. There was no difference found in recurrence-free survival of patients who underwent ALND, but patients who underwent radiotherapy doubled their median recurrence-free survival. Radiotherapy may be effective because it may treat any occult ipsilateral breast cancer as well as eradicate microscopic disease in the dermal lymphatics that could have spread from the contralateral primary tumor. Based on the metastasis rate, systemic treatment should be an integral part of management of CAM.

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ES01-1

NEW TECHNIQUES AND TECHNOLOGY IN BREAST SCREENING INCLUDING CONTRAST ENHANCED MAMMOGRAPHY

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Mammography is the only imaging modality that has been shown in multiple clinical trials to reduce mortality from breast cancer. However, mammography has a number of limitations. A mammogram is a 2D image of the breast and its sensitivity is reduced in women with dense breasts. Another limitation of mammography is the interval cancer rate; 20% of all breast cancers are interval cancers which are associated with a wore prognosis. Additional limitations of mammography include the recall rate and number of false positives. Approximately 10% of women in the United States are recalled from a screening mammogram for further evaluation of a questionable finding. In the majority of cases, no suspicious abnormality is seen when additional mammographic views and/or ultrasound are performed. Finally, when a biopsy is recommended for a mammographic lesion, approximately 70% of those are found to be benign. These limitations have led to the exploration of alternative modalities for breast cancer screening.

Digital breast tomosynthesis (DBT) is a 3 dimensional mammography technique that attempts to improve the sensitivity and specificity or mammography. DBT obtains a series of low-dose mammograms at varies angles in order to reconstruct 3-dimensional (3D) images of the breast. Multiple studies have demonstrated that DBT detects an additional 0.7 -2.7 cancers per 1,000 women not seen on a routine 2D mammogram. Another benefit of DBT besides increased sensitivity is that the number of women asked to return for additional imaging is reduced by approximately 15%. This is because the tomosynthesis images reduce call backs due to summation of overlapping normal tissue. For these reasons, DBT is slowly replacing conventional 2D full field digital mammogram (FFDM) at many centers throughout the United States. However, DBT still relies on trying to distinguish cancers from the surrounding normal fibroglandular tissue based on a 2D morphological signal.

Vascular based screening is another potential avenue to detect cancers. Breast MRI is a vascular based technique not limited by breast density and has long been known to be the most sensitive imaging modality available to detect breast cancer. However, breast MRI has been restricted to a small subset of women at the highest risk for breast cancer due to its high cost, limited availability, and perceived low PPV. Abbreviated breast MR (AB-MR) and contrast enhanced digital mammography (CEDM) are newer vascular based techniques that have the potential to im-

prove breast cancer screening. CEDM is a FDA approved technique where high and low energy images are almost simultaneously obtained following intravenous iodinated contrast administration. Post imaging processing subtracts the background breast tissue so that areas of enhancement are visualized. Early studies have shown that the sensitivity of CEDM for breast cancer detection is significantly higher than FFDM alone, and approaches that of MRI in patients with newly diagnosed breast cancer. The specificity of CEDM has also been reported to be superior to MRI. Given the high sensitivity of CEDM that is comparable to MRI and a substantially lower false positive rate compared to both MRI and screening breast ultrasound, CEDM may be the best option to supplement FFDM for breast cancer screening.

In conclusion, DBT, due to improved sensitivity and specificity, is already becoming the standard mammography screening technique at many sites in the United States. However, DBT represents a small improvement to 2D mammography. New vascular based techniques such as AB-MR and contrast enhanced mammography will likely be used increasingly in the future to screen women, especially those at intermediate risk and women with dense breasts.

ES01-2

AUTOMATED BREAST US AS SUPPLEMENTAL SCREENING MODALITY IN WOMEN WITH DENSE BREASTS

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A mammography is a basic screening test for breast cancer in women over 40 years of age. However, the sensitivity of mammography is significantly reduced in women with dense breast. In order to overcome this, the proportion of combined screening with mammography and ultrasound is increasing. Automated breast ultrasound system (ABUS) was approved in the USA and Europe to conduct screening studies for breast cancer detection as an adjunct to mammography and for screening symptom-free women with increased density of the breast tissue.

Several studies have shown that breast cancer detection rates have increased with combination of ultrasound and mammography. Screening ultrasound was presented as the solution to detect the mammographically occult cancer. Recently, studies of screening ABUS were reported. However, high false positive rates and biopsy rates are problems. There has been no standardized desirable goal of screening ultrasound.

Benefits and harms of screening ABUS are included in this lesson.

ES01-3

ABBREVIATED BREAST MRI FOR HIGH-RISK BREAST CANCER SCREENING

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Abbreviated breast MRI is a low cost procedure and used to create detailed pictures of the breast in less than 10 minutes (definition by EA1141 trials). Several studies of the use of abbreviated MRI protocols have shown that the shorter protocols have diagnostic accuracy including sensitivity, specificity, and positive predictive value (PPV) of biopsy comparable to that of the conventional full MRI protocol. If abbreviated MRI is effective for demonstration of cancers in the high-risk screening setting, the efficiency and resource savings of an abbreviated protocol would be significant, and would allow for opportunities to provide MRI for additional patients, as well as improved radiologist time management and workflow, with the potential to add real-time MRI interpretation. We hypothesized that the sensitivity of abbreviated breast MRI for second breast cancer detection is significantly higher than mammography or ultrasound whereas specificity is similar to mammography in high-risk women with BRCA testing and treated for primary breast cancer.

ES02-1

ADDRESSING RELATIONSHIPS FOLLOWING A BREAST CANCER DIAGNOSIS: THE IMPACT ON PARTNERS, CHILDREN AND CAREGIVERS

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A breast cancer diagnosis can have a profound impact on the psychosocial health of the patient as well as close family members. Relationships with significant others, children, and parents can be affected and roles may be altered as a consequence of the diagnosis and subsequent treatment. The life stage of a breast cancer patient is also a necessary consideration. Younger women, in particular, may have concerns about how recovery from surgery can affect caring for young children or returning to school or work. As a consequence of treatment, young women may experience premature menopause, which can cause bothersome side effects and adversely impact sexual functioning, which may in turn impact the relationship with one's partner. Recognizing and addressing these potential concerns in this population should be a priority; identifying and implementing effective strategies to help women and their family members cope with these challenges is also essential. Ensuring both material and emotional support for women from the time of diagnosis, through active treatment, and into survivorship, can potentially help all members of the family unit negotiate a new normal. Finally, there is a need focus on the experience of the partners themselves and understand the impact of a breast cancer diagnosis from their own perspective. Attention to the challenges faced by caregivers is critical to better support both the patient and their loved ones following a life-changing illness.

ES02-2

THE EFFECT OF EXERCISE RECOMMENDATION ON THE LEVEL OF PHYSICAL ACTIVITY IN BREAST CANCER

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Physical activity (PA) is associated with prognosis of breast cancer survivors. Recent meta-analysis showed that high level of post-diagnosis PA is associated with significantly reduced all-cause (HR: 0.52, 95% CI 0.43–0.64) and breast cancer mortality (HR: 0.59 95% CI 0.45–0.78). Furthermore, meeting recommended PA guidelines were also associated with significantly reduced all-cause (HR: 0.54, 95% CI 0.38–0.76) breast cancer mortality (HR: 0.67, 95% CI 0.50–0.90). However, we have recently identified that only 35% of Korean breast cancer survivors are meeting PA guideline. One of the most influential factors which influence exercise behavior among cancer survivors is the recommendation from their oncologists. Therefore, we have performed the randomized controlled trial with three arms: 1) control (59 patients); 2) those receiving an oncologist's exercise recommendation (53 patients); and 3) those receiving an oncologist's exercise recommendation with an exercise motivation package (50 patients). Exercise motivation package included pedometer, exercise diary and 15 minutes exercise recommendation. We found that participants who received an oncologist's exercise recommendation with an exercise motivation package significantly increased their level of exercise participation in terms of minutes (47.57 added minutes per week; 95% confidence interval, 9.62-85.52 minutes [$p = 0.022$] vs. control) and in Metabolic Equivalent of Task (MET)-hours per week (4.14 additional MET-hours per week; 95% confidence interval, 1.70–6.58 MET-hours [$p = 0.004$] vs. control) compared with the control group. Participants who received only their oncologist's exercise recommendation did not increase their exercise participation level. Then, we also studied what are factors which influence oncologists exercise recommendation behavior. We found that oncologists' own physical activity levels were associated with their attitudes toward recommending exercise. Belief in the benefits of exercise in the performance of daily tasks, improvement of mental health, and the attenuation of physical decline from treatment were the three most prevalent reasons why oncologists recommend exercise to their patients. Barriers to recommending exercise to patients included lack of time, unclear exercise recommendations, and the safety of patients. Knowing that exercise recommendation from oncologists can influence exercise behavior of cancer survivors, as well as factors influence oncologists exercise recommendation behavior, we have informed oncologists the benefit of exercise to cancer survivors as well as provided exercise counselling service to cancer survivors in the clinic. Based on findings from these studies, we have implemented exercise recommendation from oncologists in conjunction with 15 minute exercise education to over three thousand cancer survivors in our institution. In this presentation, update on these studies will be presented.

ES02-3

HEART DISEASE IN BREAST CANCER SURVIVORS

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Consequences from adjuvant breast cancer treatment can affect to not only quality of life of survivors but also risk of comorbidities that might threat to survival. One of those late effects is cardiac disease that could mitigate the survival gain of adjuvant treatment, especially in some patients who have preexisting risk factors.

Anthracyclines, tyrosine kinase based therapy, and radiation in breast cancer treatment are related to increase risk of cardiac diseases. Factors such as old age, obesity, diabetes, and hypertension increase the risk of chemotherapy-induced cardiotoxicity. Heart diseases such as congestive heart failure (CHF), myocardial infarction (MI), or coronary heart disease showed higher incidence in long-term breast cancer survivors. In a population-based study, old age group showed considerable incidence of cardiovascular death compared to breast cancer related death, while young age group showed low incidence of cardiovascular death.

The use of anthracyclines has been considered as risk factor of developing congestive heart failure. The anthracycline use shows dose-dependent cardiotoxicity, and most of them are seen within 12 months after the chemotherapy has ended. According to NCCN guideline, cardiologic evaluation is recommended within one year after the chemotherapy. In a report using propensity score base methods, MI was more increased in aromatase inhibitor group than the tamoxifen group. From a retrospective cohort evaluation using National Health Insurance Service database in Korea (unpublished data), there were increased incidence of MI and CHF were seen in breast cancer survivor than the non-cancer age matched controls after adjusting comorbidities such as diabetes, hypertension, and dyslipidemia. The use of anthracyclines, trastuzumab, and taxane was associated increased risk of MI and CHF. The population of breast cancer survivor has been grown therefore careful monitoring of developing heart disease in those groups might be required.

ES03-1

APPROPRIATE CONCEPT OF PREVENTION OF LYMPHEDEMA AT THE INITIAL TREATMENT

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Breast cancer associated treatments are one of the most common causes of upper extremity lymphedema. In a systematic review that included 72 studies (29,612 women), the overall incidence of lymphedema in breast cancer survivors was 17% [1]. The main risk factors for lymphedema include axillary lymph node dissection (ALND), radiation therapy (RT), local infection, hematoma/seroma, obesity, and possibly medication effects (taxane).

ALND is the primary cause of breast and upper extremity lymphedema in patients with breast cancer. The incidence of lymphedema increases with increasing number of axillary nodes removed or disrupted. The incidence of lymphedema was approximately four times higher in women who had ALND compared with those who had sentinel node biopsy (SLNB) (19.9% vs. 5.6%).

After treatment for breast cancer, the onset of lymphedema is insidious and is characterized by slowly progressive swelling of the upper extremity ipsilateral to the ALND or RT. The greatest risk for developing lymphedema was within the first two years following diagnosis and treatment. In a study that included 1,713 women who underwent breast-conserving therapy, 40% of those who presented with arm edema had mild lymphedema at initial diagnosis. Freedom from progression to more severe lymphedema was 79% at one year, 66% at three years, and 52% at five years. Women who were morbidly obese, had positive axillary lymph nodes, or received supraclavicular irradiation at the time of breast cancer treatment had a higher risk of progression from mild to more severe arm edema.

The primary prevention of lymphedema mainly involves using SLNB for axillary lymph node staging. The use of axillary staging with SLNB has reduced the number of ALND performed and, consequently, the incidence of lymphedema. Clinically relevant lymphedema occurs in 5–9% of patients who undergo SLNB alone compared with approximately 40% in patients undergoing ALND.

Other measures that may also be effective for prevention of lymphedema include minimizing the extent of lymph node dissection when it is required, advanced RT techniques that limit radiation, and the use of other surgical techniques such as axillary reverse mapping and lymphatic bypass.

Early identification of high-risk patients and appropriate prevention measures may potentially reduce the risk of lymphedema, which is often difficult to treat if it progresses. Given that the highest risk of developing lymphedema is within the first three years of treatment, high-risk patients should be followed closely in this period.

ES03-2

EARLY-STAGE LYMPHEDEMA DETECTION AND CONSERVATIVE TREATMENT

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Breast cancer survivors are at increased risk for the development of breast cancer-related lymphedema (BCRL), a chronic, debilitating, and disfiguring condition that is progressive and requires lifelong self-management of symptoms. Lymphedema (LE) is caused by a disruption of the lymphatic system that, in the initial stages, leads to fluid accumulation in the interstitial tissue spaces, and eventually manifests clinically as swelling of the arm, breast, shoulder, neck, or torso. Early assessment and intervention may be important to correct subtle subclinical LE that, if left untreated, may progress to chronic and severe LE. Previous studies suggested that regular surveillance of upper-body morbidities such as LE should be integrated into the routine postoperative care of women with breast cancer, as early diagnosis potentially contributes to more effective management, and prevention of progression of troublesome conditions.

Detection and management of early-stage LE may prevent progression to chronic disabling disease and may enable cost-effective conservative intervention. Fu et al. found that patient education on the early signs and symptoms of upper-body morbidity, in particular disease progression, was important. Bioimpedance spectroscopy (BIS) assesses changes in extracellular fluid levels and can identify such changes in limbs prior to clinical presentation (thus before the condition becomes non-pitting [fibrotic]). A short trial showed that compression garments effectively treated subclinical LE. A systematic review revealed that compression garments and bandages reduced the volume of cancer-related LE.

A prospective surveillance model may be useful to detect BCRL at an early stage, when the opportunities to reduce risk or slow progression are optimal. A surveillance program would allow healthcare providers to detect BCRL symptoms early, affording better opportunities to prevent progression to the subclinical stage and to institute continuous care plans from the inpatient to the outpatient settings. Few rigorous comparative research studies have been performed on patients with BCRL, compromising the development of evidence-based assessment of, and treatments for, hundreds of thousands of women who have, or are at risk for the development of, BCRL.

In our institute, a surveillance program for LE management (SLYM) program was implemented in May 2011 to identify high-risk LE patients who would benefit from comprehensive surveillance by a transdisciplinary team, with an emphasis on early detection and prevention of

LE. A care plan was initiated immediately after surgery for all patients who underwent ALND to identify patients at high risk of LE.

Our results provide a rationale for the future randomized clinical trials required to validate our program in patients at high risk of LE. We conclude that surveillance reduces the rate of LE developing after surgery. The magnitude of the benefit was modest. Most importantly, the apparent benefit afforded by optimized patient care may be lost unless patients are empowered in terms of self-assessment and self-monitoring. The take-home message is that the LE surveillance program achieved an absolute reduction of ten percentage points in the frequency of advanced LE developing after breast cancer surgery.

ES03-3

SURGICAL TREATMENT OPTIONS FOR ADVANCED LYMPHEDEMA

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Breast cancer related lymphedema (BCRL) is a common complication after axillary lymph node dissection and radiotherapy. The development of microsurgical treatment for lymphedema is an emerging field in recent years. For patients who presented with early staged lymphedema, lymphaticovenous anastomosis (LVA) can be a good surgical option. However, if patients presented with more advanced-staged lymphedema in which lymphatic vessels are fibrotic, LVA can be extremely difficult with variable results.

Vascularized lymph node transfer using different recipient sites have been reported with good results. It presents as a good drainage procedure in treating lymphedema. The real mechanism remains unclear, yet, it is believed that lymph nodes suck the lymphatic fluids and direct the fluid back into venous system via natural lymphatico-venous connection inside the lymph node. Besides lymphatic drainage, the transfer of lymph node can enhance local immunity and reduce infection episodes after surgery. This presentation will cover microsurgical treatments of lymphedema, selection between LVA and lymph node transfer, donor and recipient site selections of vascularized lymph node transfer and a mechanism review of vascularized lymph node transfer in treating BCRL.

ES04-1

OVERVIEW OF AJCC 8TH STAGING IN PATHOLOGIC ASPECTS

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A major change in breast cancer staging is the addition of tumor histologic grade, hormone receptor status (estrogen receptor (ER), progesterone receptor (PR)), humnan epidermal growth factor receptor-2 (HER2), a proliferation marker (Ki-67 or a mittotic count) and genomic assays (such as Oncotype Dx, Mammaprint, Endopredict, PAM50 (Prosigna), Breast Cancer Index, etc) as elements required to assign stage in conjunction with anatomic information on the tumor (T), regional nodes (N), and distant metastases (M) categories. Another major change is that the entity termed lobular carcinoma in situ (LCIS) or lobular neoplasia is no longer included in this staging system as was pTis. The (f) modifier added to N category which indicates diagnosis made by either fine needle aspiration (FNA) or core needle biopsy (CNB). The (sn) and (f) modifiers denoted confirmation of metastasis by sentinel lymph nodes (SLN) or FNA/CNB with no further resection of lymph nodes. The (sn) modifier is not restricted to SLN. All tumors between 1.0 and 2.0 mm are rounded up to 2.0 mm to avoid misclassifying those between 1.0 and 1.5 mm as microinvasive.

Clarifications from AJCC 7th edition Staging is seen. For multiple synchronous tumors, T category is based on a single largest tumor focus, using (m) modifier. When measuring tumor size, the rule does not include satellite foci. In case of multiple foci of microinvasion, report the number of foci and the size of the largest focus. When the tumor is identified in bilateral breast, T staging must be done each side separately. To assign correct pT staging, gross, microscopic and imaging findings must be correlated when necessary. Clear definition that satellite tumor nodules in the skin must be separate from the primary tumor and macroscopically identified to categorize as T4b. Direct extension into skin and skin involvement only identified microscopically are not categorized as pT4b, being categorized based on tumor size. In the absence of clinical findings of inflammatory carcinoma, dermal lymphatic tumor invasions are not categorized as pT4d. ypT is based on the largest single focus of residual invasive carcinomas to assess following neoadjuvant therapy. Treatment-related fibrosis around residual tumor is NOT included in the ypT dimension. Cases with no residual invasive tumor are categorized as ypT0 or ypTis, not ypTx. Pathologic complete response (pCR) is defined as no residual invasive cancer (ypT0 N0 or ypTis N0). Cases categorized as M1 prior to neoadjuvant therapy, the cancer is categorized as M1 even if there is pCR. Metastases to lymph nodes from axillary, intramammary, interpectoral, internal mammary and supraclavicular lymph nodes are regional nodes and

categorized as pN. Metastases to any other lymph nodes, including cervical, contralateral internal mammary or contralateral axillary lymph nodes are categorized as pM1. Invasive tumor nodules in axillary fat without apparent nodal tissue are classified as regional lymph node metastases (pN). When measuring isolated tumor cells (ITCs) in lymph nodes, size of the largest contiguous focus must be reported. Lymph nodes with ITCs only are not included in the overall count of positive nodes.

Prognostic stage grouping is added, being three stage tables. Anatomic Stage Table is based only on T, N and M categories. Clinical Prognostic Stage Table is to be used to assign stage for ALL pateints based on T, N, M, tumor grade, HER2, ER and PR status. Pathological Stage Group Table is based on all clinical information, biomarker data and findings from surgery and resected tissue.

ES04-2

LCIS: CURRENT CONCEPT AND CHALLENGING ISSUES

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Lobular neoplasia (LN) is at present defined as the atypical proliferative epithelial lesions arising from the terminal-duct lobular unit (TDLU) of the mammary gland. The lesion is generally characterized by the proliferation of non-cohesive small epithelial cells and contains atypical lobular hyperplasia (ALH) and lobular carcinoma in situ (LCIS). A number of molecular, pathological and clinical studies on LN has been recently published on LN but the details of LN have not been necessarily well characterized compared to other non-invasive breast disorders. Therefore, in this presentation, the followings will be summarized regarding LN.

1. How clinicians should manage the patients diagnosed as LN in core needle biopsy ?
Most of LN cases have been diagnosed as incidental findings and which parameters of histopathological features of LN could be important in clinical management will be discussed.

2. Clinical course or biological behavior of the patients diagnosed as LN.
LN is at present considered as premalignant or precursor lesion of invasive carcinoma but which lesions, ductal or lobular invasive carcinoma could develop in contralateral or ipsilateral breast and when after the initial diagnosis could develop will be discussed. In addition, the potential risk factors of developing invasive malignancies will be also covered.

3. Histopathological differentiation of LN.
This differentiation includes the following; ALH versus LCIS, LCIS versus DCIS (ductal carcinoma in situ), regular type versus pleomorphic type of LCIS and LCIS versus invasive lobular or ductal carcinoma. In addition, which of those differentiation could be important for clinicians to manage the patients with LN will be discussed in this presentation.

4. Molecular features of LN.
Genetic basis of LN has been recently reported by several groups and those development will be discussed with emphasis upon the potential differences or similarity between regular and pleomorphic subtypes of LCIS and between LCIS and invasive lobular carcinoma.

ES04-3

CLINICAL IMPLICATIONS OF REVISED AJCC 8TH STAGING

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The revised AJCC cancer staging was changed to prognostic staging from anatomic one. Prognostic staging incorporated grade, biomarkers, and multi-gene panel score into tumor, node, and metastasis (TNM).

AJCC 1st edition of TNM system intended to provide a way by which designation for the state of a cancer at various points in time can be readily communicated to others to assist in decisions regarding treatment and to be a factor in judgment as to prognosis. The purpose of staging is to provide a standard nomenclature for prognosis of patients with newly diagnosed breast cancer to select the most effective treatment and to continue evaluation of cancer control measures.

However, breast cancer is heterogeneous and a group of disease with different molecular characteristics. Biologic factors have become more important than the anatomic extent of disease to define prognosis, select the optimal combination of systemic therapies, and influence the selection of locoregional treatments. Several biomarkers including ER, PR, & HER2 should be documented at the time of initial diagnosis.

As a consequence of prognostic staging, more than 40% of patients with stage I-III were reclassified into different stage than AJCC 7th; up-staged (20%) in G3 or triple negative, and down-staged (20.6%) in low grade, ER+ & PR+. Prognostic stage groupings provide a marked improvement in defining prognosis and reflect outcomes with modern-era therapy.

Anatomy- & histology-based TNM staging system is still relevant for breast cancer and provides important insight into a patients prognosis. Addition of various biomarkers refines the prognostic information and leads to better selection of systemic therapies and better outcomes.

What, exactly, is the objective of TNM staging for breast cancer? The 1st answer is to provide continuity to breast cancer investigators, in regards to studying categories of patients that accurately reflect prior groupings over the last six decades. 2nd is to permit current investigators in the field to communicate with one another using a standardized language the reflects disease burden and tumor biology. 3rd is to improve individual patients care.

Clinical and pathological prognostic staging systems reflect the prognosis of patents treated

with current standard multimodality treatment. We should administrate appropriate therapy based on biomarkers and anatomic extent of the cancer.

While the application of prognostic staging in practice, we will feel it is more complicated than anatomic staging, but more accurately predict outcome. Added clinical value outweighs the added complexity. It provides information more relevant to clinical practice.

AJCC 8th edition for cancer staging would be the transition from a Population Based to a More Personalized approach. We need risk assessment models to go the more personalized approach. Only two tools were found to have met all predefined AJCC inclusion and none of exclusion criteria for risk assessment tool; Adjuvant! Online and PREDICT-Plus. AJCC 8th edition for cancer prognostic staging would be a bridge leading to precision medicine.

ES05-1

RECENT BIOLOGY AND TREATMENTS FOR PHYLLODES TUMORS

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Phyllodes tumours are fibroepithelial neoplasms of the breast which exhibit a range of biological behavior as well as a propensity for recurrence. They are generally rare but appears to have an Asian predilection. The distinction between phyllodes tumours and the much commoner fibroadenomas can pose a diagnostic challenge. Furthermore, the range of biological behavior exhibited by such neoplasms makes accurate diagnosis imperative.

While histological features such as stromal overgrowth and cellularity, subepithelial condensation and presence of adipose tissue are indicative of phyllodes tumours, interpretation of such parameters remain highly subjective. The use of immunohistochemical markers such as Ki-67, p16-INK4a, pRB, Collagen I/III, and CD105-positive microvessel density also lack consensus.

Frequent MED12 mutation is seen in all fibroepithelial lesions on a molecular level . However, phyllodes tumours exhibit further mutations in RARA, FLNA, SETD2, KMT2D and PIK3CA. Additional mutations in cancer related genes are seen in borderline and malignant phyllodes tumours. Prevalence of TERT promoter mutations with increasing malignancy in fibroepithelial breast lesions suggests a mechanistic role for TERT alterations in the progression of these tumors.

A RT-PCR assay using a 5 gene (ABCA8, APOD, CCL19, FN1 and PRAME) set to distinguish phyllodes tumours and fibroadnoma on pre-operative core biopsies showed sensitivity and specificity of 82.9% and 94.7% respectively.

The mainstay of treatment for phyllodes tumours remains surgical resection with clear margins of at least 10mm. However, some recent studies suggest that such wide margins may not be necessary. Routine axillary dissection is not recommended. Adjuvant radiotherapy is often recommended for malignant phyllodes when margins are inadequate. While providing superior local control, there is no survival benefit. Adjuvant chemotherapy is not routinely recommended in non-metastatic cases.

Finally, a nomogram based on stromal atypia, mitoses, overgrowth and surgical margins may be used to predict recurrence free survival.

ES05-2

TREATMENT OPTIONS FOR THE PRECANCEROUS ATYPICAL BREAST LESIONS

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Mammographic screening has caused an increased detection of precancerous lesions, making ductal carcinoma in situ (DCIS) accounts for up to 25% of all newly diagnosed breast cancer cases by screening. In addition, mammography has drawn attention to lots of earlier precursor lesions in the close vicinity of invasive breast carcinomas. These include intraductal proliferative lesions with atypia such as flat epithelial atypia (FEA) and atypical ductal hyperplasia (ADH). These lesions found by core needle biopsies has brought about questions regarding their biological role and proper management. They represent a broad spectrum of lesions with various risk of progression. By now, it is not possible to identify absolutely, which of these lesions will progress or not.

Individual tailoring the treatment of precancerous lesions should be a multidisciplinary challenge, which involves radiologists and pathologists as well as breast surgeons and, in case of DCIS, radio-oncologists and medical oncologists. There should be the concerns balancing unnecessary overtreatment or increased risk of recurrence or progression.

Therefore, this issue addresses the topic of precancerous lesions in a multidisciplinary approach. The goal is to improve our understanding and handling of these heterogeneous lesions by bringing together the different perspectives. B3 lesions represent 3~10% of the histologically assessed lesions in mammography screening. They comprise different histopathological entities which provide benign histology, but are either known to show heterogeneity or to have an increased (albeit low) risk of associated malignancy, e.g. FEA, ADH, lobular neoplasia (LN), papillary lesions, radial scar, and phyllodes tumor. However, the biological and clinical significance of some of these lesions should be clarified. The markers with the most promising clinical potential has been reviewed in the articles. Since a number of studies did not find significant differences in genetic alterations or gene expression profiles between the tumor cells of DCIS and invasive carcinomas so far, future findings also focus on the potential role of microenvironment to better understand the transition from DCIS to invasive breast cancer. Further knowledge in this field will hopefully provide improved prognostic and predictive factors and will offer novel therapeutic opportunities to promote individualized treatment in patients with DCIS or other.

ES05-3

MANAGEMENT OF ATYPICAL CELLS ON THE MARGIN AFTER BREAST CONSERVING SURGERY

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ES06-1

RECENT UPDATE IN MEDICAL ONCOLOGY FOR THE MANAGEMENT OF BREAST CANCER

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During the last couple of years, one of the most remarkable advances that have been achieved would be a success with CDK4/6 inhibitors in ER+ metastatic breast cancer. CDK4/6 inhibitors such as palbociclib, ribociclib, and abermaciclib showed a profound effect when they are combined with endocrine therapy as upfront therapy or subsequent therapy following failure to endocrine therapy with similar magnitude of benefit and different profiles of toxicities among them. The other success in metastatic breast cancer is PARP inhibitors including olarparib and talazoparib. This targeted agents provided significant benefit over standard chemotherapy in HER2 negative germline BRCA1/2 mutant metastatic breast cancer patients.

In early breast cancer, adjuvant capecitabine was beneficial in a randomized phase 3 trial performed by Japanese and Korean investigators when it was given in HER2 negative patients with residual tumors after neoadjuvant chemotherapy. In HER2 positive breast cancer, adjuvant pertuzumab provided significant benefit in disease free survival.

In this talk, in additions to representative clinical trials mentioned above, key ongoing and released trials including immunotherapy are also discussed for the future perspective.

ES06-2

RECENT UPDATE IN SURGERY FOR THE MANAGEMENT OF BREAST CANCER

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De-escalation in breast cancer surgery is the most remarkable recent trend. Because of the improvement in multimodality treatment and resultant improved clinical outcome, now focus has moved to enhancing quality of life of the patients. In addition, we now know that advancement in adjuvant systemic therapy has positively impact on the outcome of local treatment. Finally, weve also learned that bigger surgery cannot cure bad biology.

For the treatment of low risk DCIS, there are recent challenges including active surveillance and giving intervention when invasive local recurrence is detected. There are ongoing trials globally that are testing the hypothesis that biopsy alone with active surveillance is not inferior to immediate surgery with or without radiotherapy for DCIS (COMET, LORIS, and LORD trials).

The definition of clear resection margin after breast conserving surgery has become more generous than before. Consensus guidelines support a negative margin, defined as no ink on tumor, for invasive carcinoma treated with breast-conserving therapy. Because of differences in the growth pattern, a margin of 2 mm has been found to minimize the local recurrence risk for DCIS with radiation therapy. Wider negative margins do not improve local control for DCIS or invasive carcinoma and cannot be justified by current evidences.

Also, there have been de-escalation in the surgery of axillary lymph node. The ACOSOG Z0011 trial was a landmark study that was first showed that in clinically node negative women undergoing lumpectomy and breast irradiation who were found to have metastases in limited number of sentinel nodes, a complete axillary dissection or a sentinel node biopsy alone had the same rate of local recurrence and the same disease free and overall survival. Follow-up of this study was updated last year to ten years, and there was still no difference in the risk of nodal recurrence, disease free or overall survival. In a study done at Memorial Sloan Kettering Cancer Center, this result was reproduced in patients with triple negative breast cancer or HER2 overexpressing cancer. With variation in radiation field, such as standard whole breast tangents, prone position, or nodal irradiation, local recurrence in all those groups is exceedingly low and not statistically different. Now we have an evidence that axillary-lymph-node dissection can be replaced by axillary radiotherapy even in patients undergoing mastectomy, reducing morbidity (AMAROS trial).

Another area where we can de-escalate surgery is in women receiving neoadjuvant therapy. From the three trials done for patients with documented axillary lymph node metastasis and underdoing neoadjuvant chemotherapy (SENTINA, ACOSOG Z1071, and SN FNAC), we can conclude that sentinel lymph node biopsy after neoadjuvant therapy is a feasible approach. Appropriate patient selection, dual agent mapping, identification of 3 or more sentinel nodes, use of clip and IHC staining can optimize the accuracy of sentinel node biopsy in this setting. In view of the declining influence of axillary nodal status on adjuvant therapy decision-making, ongoing clinical trials will evaluate whether sentinel node biopsy can be avoided altogether in selected patients (SOUND and INSEMA trials).

The final interesting area of de-escalating surgery is omitting surgery for primary breast lesion in patients who attain a complete clinical response after neoadjuvant chemotherapy. It is suggested that the role of surgical excision may be limited to pathological confirmation, and thus may be omitted when pCR can be correctly predicted. Several trials have just started to address this question worldwide using imaging study like breast MRI or ultrasonography and core needle biopsy with or without vacuum assist.

ES06-3

RECENT UPDATE IN RADIATION ONCOLOGY FOR THE MANAGEMENT OF BREAST CANCER

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Recent advances in radiotherapy (RT) techniques including forward planning using segments, intensity-modulated radiotherapy, image-guided treatment, and respiratory control system as well as a better understanding of tumor biology have enabled change in the field of irradiation and treatment scheme. Hypofractionated (HF) RT has been accepted as a standard option, and it offers increased patient convenience and reduced resource usage. Several studies showed that certain patients could be treated with partial breast irradiation with comparable efficacy. Paradoxically, extended radiation field including regional nodal chain is recommended in node-positive disease, while surgical resection is on a trend of becoming less extensive.

Most human cancer types respond to total dose rather than to the size of daily fractions. However, late responding normal tissues are sensitive to both fraction size and total dose. This biologic difference between cancer and normal tissue was the basis of the historical use of 1.8-2.0 Gy in each fraction for delivering the highest possible tolerated total dose and ensuring the highest rate of tumor control. Such difference in fractionation sensitivity between cancer and late responding normal tissue had been challenged in the last 20 years by high level evidence based on four randomized trials from Canada and the UK.(1-3) These studies showed that breast cancer had comparable sensitivity to fraction size as the normal tissues of the breast and ribcage. The results suggested that there is no disadvantage to HF whole breast RT in terms of safety and efficacy while benefiting patients and health services in terms of convenience and cost. Therefore, a schedule of 40 Gy in 15 fractions was adopted as the UK standard of care in 2009 for adjuvant RT after breast conserving surgery or mastectomy for early breast cancer.(4)

In the 1990s, two studiesthe EORTC 22922/10925 and the NCIC MA.20evaluated the addition of regional nodal irradiation (RNI) to internal mammary nodes and upper axillary nodes including supraclavicular region, in addition to whole breast/chest wall irradiation after breast-conserving surgery/mastectomy.(5, 6) Both trials showed similar results of increase in both disease-free survival and distant disease-free survival. The EORTC 22922/10925 trial showed a trend of improved overall survival and a statistically significant reduction in breast cancer mortality. No increase was observed in other causes of death in both studies. Contemporary RT techniques based on appropriate target volume delineation and treatment planning using predefined dose constraints would provide not only a significant reduction in radiation dose to organs at risk, but also a better coverage of the internal mammary nodes. This may result in a

greater benefit for RNI. According to these evidence, NCCN and ESMO guidelines recommended RNI for patients with N1 disease.(7)

However, generalization of the results of the EORTC 22922/ 10925 and MA.20 trials remains problematic in current developments, including an use of more effective adjuvant systemic therapy, decreasing use of axillary lymph node dissection,, and continuously improving RT techniques. Therefore, RNI should be offered selectively. Consequently, the updated ASTRO guideline for post mastectomy radiotherapy (PMRT) suggested that individual patients should consider factors that may decrease the risk of LRF, attenuate the benefit of reduced breast cancerspecific mortality, and/or increase the risk of complications resulting from PMRT.(8) St Gallen Consensus 2015 described that PMRT should be standard for patients with tumor size 5 cm or greater, a positive macrometastatic sentinel node biopsy but no axillary dissection, and those with N1 and adverse pathology. Conversely, in the absence of adverse pathology, patients with N1 could be treated without PMRT.(9)

There is strong evidence that appropriately dosed HF whole breast RT is both safe and effective for patients with early breast cancer. Further research on accurately estimating the individuals risk of LRF and their potential reductions in LRF and breast cancer mortality with RNI is needed. Until more information is available, RNI and its extent should be determined taking into account the biological characteristics of the tumor, its stage, patients host differences and preferences, and technical resources of the RT facility.

Survivorship Session

GBCC2018
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SU01-1

THE REALITY IN THE FOLLOW-UP OF BREAST CANCER SURVIVORS

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According to the statistics of the National Cancer Registration, the number of Korean cancer survivors is 1.6 million people in 2015 and breast cancer survivors among them are about 179,000 (11.1%), the 4th rank in the total cancer survivors. As the ratio of early breast cancer increased gradually and new therapeutic modalities were developed, survival rates of breast cancer also increased. Through all stages, the 5-year and 10-year overall survival rates of breast cancer were 91.2% and 84.8%, respectively. Like this, in the situation where over 80% of Korean breast cancer patients survive more than 10 years after the primary treatment, the optimal follow-up of breast cancer survivors is very important issue.

The purpose of follow-up of breast cancer patients can be summarized in 4 items: (1) recognition of recurrence or new primary cancer, (2) assessment for complications of therapy, (3) adherence to recommended therapy and screening, and (4) psychosocial and decision-making support. Of these purposes, the early detection of new primary cancer or locoregional recurrence help improve the survival rate, but the diagnosis of distant metastasis is known to have no advantage in survival rate or health-related quality of life. Also, randomized controlled trials and Cochrane review have found that reduced follow-up strategies did not negatively affect patient outcomes or early detection of recurrence, and more intensive follow-up was associated with higher costs without differences in early detection of relapses.

Since the American Society of Clinical Oncology published an evidence-based clinical practice guideline on breast cancer follow-up in 1997, various international guidelines have been published for the surveillance of breast cancer survivors. These guidelines including Korean Breast Cancer Society guideline recommend the minimum follow-up including routine history, physical examination, and regularly scheduled mammography. In actual clinical situation, however, most breast cancer survivors want to receive more examinations because they are afraid of the recurrence when conducting follow-up after the primary treatment. Many physicians also tend to perform more tests more frequently than the extent recommended by the guidelines under the belief that they can increase the survival rate despite lack of evidence.

The follow-up guidelines for the breast cancer survivors published up to now are based on old study which did not contained recent treatments such as target therapy. And follow-up guidelines are not stratified on the basis of stage or tumor biology, and there is no agreement on the

optimal frequency or duration of follow-up modes. Maximizing benefits while minimizing the harms of follow-up for breast cancer survivors requires moving from a "one-size-fits-all" guideline paradigm to more precise strategies. I believe that the time has come to develop optimal follow-up modalities for Korean breast cancer survivors.

SU01-2

COMPREHENSIVE ANALYSIS OF NATIONAL HEALTH INSURANCE DATA FOR BREAST CANCER SURVIVORSHIP

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The National Health Insurance Service (NHIS) is a mandatory social insurance system in South Korea. Because it is the only public insurer in Korea, it covers the entire Korean population. Basically, the Korean people pay insurance contributions to the NHIS and receive medical services from healthcare providers. The NHIS pays costs based on the health care provider's billing records. To manage these processes, the NHIS collects the information on insurance eligibility, insurance contributions, medical history, and medical institutions.

The National Health Information Database (NHID) is a public database constructed by the National Health Insurance Service (NHIS) in 2012. It includes information on health care utilization, health screening, sociodemographic variables and mortality for the whole population of Korea. Initially, the NHID covered data between 2002 and 2014, and then the data from 2014 has been added.

The research using the NHID has been increasing and more than 800 papers have been published until now. Papers published covered various diseases or health conditions like infectious diseases, cancer, cardiovascular diseases, hypertension, diabetes mellitus, and injuries and risk factors such as smoking, alcohol consumption, and obesity. However, we need to be cautious when conducting a study using this database. Information on diagnosis and disease may not be optimal for identifying disease occurrence and prevalence since the data have been collected for medical service claims and reimbursement. Therefore, operational definitions are usually used for identifying diseases.

However, In September 2005, as part of a new NHIS policy, a registration system for serious diseases such as cancer was created and the government started supporting 90-95 percent of medical costs. Korean patients diagnosed with cancer are generally registered with NHIS and receive financial support for cancer-related medical services immediately after being diagnosed with cancer. Under this system, NHIS maintains nationwide medical registration files for cancer patients and original claim data for reimbursement. Therefore it is a very complete and reliable source of information for cancer-related epidemiology research.

Prior to conducting research on breast cancer survivorship using the NHID, we analyzed the

NHID to investigate the annual incidences of breast cancer and changing patterns of breast cancer treatments nationwide. After making a retrospective breast cancer cohort using our operational definition, we obtained the annual incidences and treatment patterns of breast cancer. The annual incidences of breast cancer obtained from NHID were compared to those from the Korea Central Cancer Registry (KCCR) data. The annual treatment patterns analyzed included surgery, chemotherapy, radiation therapy, endocrine therapy, and targeted therapy.

A total of 148,322 women with newly diagnosed invasive breast cancer were identified from 2006 to 2014. The numbers of newly diagnosed invasive breast cancer between NHIS and KCCR data are similar and had a strong correlation ($r = 0.995$; $p < 0.001$). The age distribution of NHIS and KCCR showed strong correlation ($r = 1.000$; $p < 0.001$). About 85% of newly diagnosed breast cancer patients underwent operations. Although the proportions of chemotherapy use have not changed from 2006 to 2014, the total number of chemotherapy prescription of the incident and prevalent cases has sharply increased during the same period. The proportions of radiotherapy and anti-hormonal therapy have increased during the time. Among anti-hormonal agents, tamoxifen has been the most frequently prescribed medication, and letrozole was the most preferred endocrine treatment at age 50 or more. Since 2010, the use of trastuzumab had increased and was reported as 16.8% of incidence cases in 2014.

Now we are conducting a couple of studies on breast cancer survivorship using the same operational definition. Some results of the studies are going to be presented at GBCC in 2019.

SU01-3

BENCHMARKING BREAST CANCER SURVIVAL: INTERNATIONAL COLLABORATIVE RESEARCH PLATFORM TO IMPROVE PATIENTS OUTCOME

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Cancer survival provides a means to assess the effectiveness of early detection strategies and the quality of clinical care and management. At the International Agency for Research on Cancer we coordinate global collaborative projects to pool international data to provide updated report on breast cancer burden and survival. These initiatives provide comprehensive and updated benchmarking of cancer survival between countries taking into account background changes in risk factors, incidence and also mortality, with the aim of increasing our understanding of possible drivers of international differences and informing research, clinical practice and health policy.

In this talk I will utilize results based on the compilations of global series of population-based data with an emphasis on data coming from the Asian region. Key survival measures, including 1- and 5-year breast cancer net survival, will be presented by age, stage, and country using a modelling approach. This will be presented in light of breast cancer burden and changes of breast cancer incidence and mortality over time.

Breast cancer is the most common cancer diagnosis among women in most countries globally. In general we can observe a rising incidence of breast cancer in most countries alongside a global decrease in breast cancer mortality. Mortality decline was most pronounced for the younger age groups and much less so among the oldest age group. This is clearly reflected in survival from breast cancer where cancer-specific survival is worse for the oldest age group, e.g. in the Korea, women age 15-49 had a 94% survival at 5 years after the diagnosis as compared to 83% in women age 65 years and older. Similar differences were seen in other countries with worse survival observed in countries with lower income.

In conclusion, we continue to see international differences in breast cancer burden and also survival. These differences persist even for those with more advanced breast cancer. Possible reasons could be related to differences in detection and treatment but also background risk factors that may contribute to differences in comorbidities and hence survival after the diagnosis. Unveiling the factors contributing to these differences is crucial to reduce the increasing burden from breast cancer, and reduce suffering from breast cancer and eliminate international disparities in breast cancer outcome in the future.

SU02-1

MAMMOGRAPHIC DENSITY AND BREAST CANCER: A SMART APPROACH TO BREAST CANCER CONTROL

John Hopper

School of Population and Global Health, University of Melbourne, Australia

There is more information in a mammogram than just identifying existing tumours. Mammographic density, conventionally defined as the regions on a mammogram that are white or bright, is implicated in both: (a) a womans risk of being diagnosed with breast cancer in the future; and (b) the masking of any existing breast tumours at the time of her current mammogram. Studies of Korean and other Asian women have helped provide new insights into mammography-based measures of risk and masking, which are examples of Screening Measures Associated with Risk and Translation (SMART).

The percentage of a mammogram that is covered by white or bright areas, referred to in the literature as percent mammographic density (PMD), is a strong predictor of masking. The strength of this association does not depend on a womans body mass index (BMI). Therefore, risk of masking can be derived from an assessment of a percentage, such as in the BI-RADS system, without needing to measure or ask about weight. The latter is of practical importance for mammographic screening programs.

When it comes predicting risk, there has been debate about whether the percentage or absolute measure of conventional mammographic density is the best predictor. What has not been well understood is that in all the statistical analyses these risk measures are adjusted for age and BMI. These measures of conventional mammographic density on average decrease with increasing age, and with increasing BMI (in particular for percentage measure), which is the opposite direction of the increasing association of age and BMI with breast cancer risk. Hence the risk factors are not the density measures themselves, but the density measures adjusted for age and BMI.

After adjusting for age and BMI, percentage and absolute mammographic density are very similar (correlation ~ 0.9), so essentially both adjusted density measures are addressing the same issue. The adjustment for BMI is much more severe for percentage mammographic density, so there is greater statistical variation for that measure. This appears to be reflected in the finding that more of the single nucleotide polymorphisms (SNPs) associated with breast cancer risk are associated with absolute, rather than percentage, mammographic density adjusted for age and BMI.

The risk gradient for both these measures of conventional mammographic density are about a 1.4-fold increased risk per standard deviation of the adjusted measure. This compares with about 1.6-fold for genetic risk scores based on genome-wide association studies, and a similar risk gradient for risk measures based on multi-generational family history for Western women (less for Asian women). On a population basis, these are the strongest known risk factors for breast cancer.

It has recently been found that the conventional mammographic density measures might only be surrogates for the causal factors involved in breast cancer susceptibility. Multiple studies of Korean and Australian women have found that risk is better predicted when mammographic density is defined as the bright, as distinct from white, areas on a mammogram. When measures of density defined by in effect different pixel brightness thresholds were considered together, invariably the conventional measure was no longer significant. The risk gradients of these new risk factors are about 1.4-1.8-fold per standard deviation, the higher estimates coming from studies of breast cancer diagnosed at younger ages. The finding that the areas of high pixel brightness better represent the breast tissue with a causal role in breast cancer is important for multiple disciplines, such as: (i) biological research to identify specific tissue markers; (ii) genetic research to try to find pathways implicated in disease risk, and (iii) public health initiatives aimed towards targeted, or tailored screening, by identifying women at increased risk of masking and/or of the disease itself.

Machine learning techniques are being applied to try to find the aspects (not necessarily mammographic density) of a mammographic image that predict breast cancer. We recently found that 11 highly correlated textural features not based on pixel brightness threshold can be combined to predict new and independent risk factors. The risk gradient is about 1.6-fold per standard deviation for measures trained using data for Western women and tested on Asian women, and vice versa.

With digital mammography being rolled out across the world, automating these SMARTSs (mammography-based measures of risk and masking) could revolutionise breast screening across the world. It would enable rapid identification, at the time of mammography, of a substantial subgroup of unaffected women at considerably increased risk of being diagnosed with breast cancer in the future who might benefit from a tailored screening program and consideration of prevention strategies.

SU02-2

FAMILY HISTORY AND BREAST CANCER

Min-Woo Jo

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Family history is an important risk factor for incidence of many diseases including breast cancers. Many studies have been conducted on family history in patients with breast cancers. One meta-analysis reported that odd ratio of family history in first degree on breast cancers is more than 2 which is the highest among breast cancer risk factors. Recent studies on this familial tendency have been focused on genetic factors and they have found many genes or loci such as BRCA1, BRCA2, TP53, PTEN and LKB1 et al. This information could be useful not only to prevent breast cancer primarily but also to encourage detecting it in earlier stages. However, those studies have been still with relatively small-sized participants. Development of methodology in a big data analysis, auto-intelligence and data convergence could be helpful that information will be more precise and certain.

SU02-3

NUTRITION AND DIET BEFORE AND AFTER BREAST CANCER

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The incidence of breast cancer has dramatically increased in recent years in several Asian countries which experienced rapid economic growth along with demographic and environmental changes. Breast cancer rates vary substantially among countries, with incidence in developing countries being less than that in Western countries. Given the upward trend in Asian countries and the large variation in incidence around the world, dietary changes have been thought to contribute to breast cancer development. In particular, nutrients and foods from animal sources have drawn attention as potential causes of breast cancer. However, prospective cohort and intervention studies did not support the hypothesis that adult diet influences breast cancer development. Instead, obesity and energy balance appear to be important factors associated with breast cancer risk. Also, some studies suggest that diet in early life may play a substantial role in breast cancer development, but data and evidence remain limited.

Although etiologic and epidemiologic studies have long studied modifiable risk factors for breast cancer incidence, much remains to be explored in terms of the role of diet after a diagnosis of breast cancer. Several epidemiologic studies have sought to better understand the factors that improve survival rates from breast cancer, including diet, physical activity, and body mass index (BMI). While there is be evidence of the effect of BMI on mortality from breast cancer, the effects of changing ones diet after breast cancer diagnosis on survival or recurrence of cancer are less clear. A report of the World Cancer Research Fund stated that evidences were not sufficient to draw firm conclusions about the effect of diet and nutrition on breast cancer prognosis, but suggested a few indications of links between diet and breast cancer survival.

In Korea, the incidence of breast cancer ranks second to thyroid cancer among women. The age-standardized incidence rate of breast cancer has also steadily increased, reaching 47.7 per 100,000 in 2014. The five-year survival rate for Korean breast cancer patients has also improved remarkably from 78.0% in 1993-1995 to 92.0% in 2010-2014. The improvement in survival emphasizes the importance of supportive care, diet, and quality of life for Korean breast cancer survivors. The incidence of newly diagnosed breast cancer was the highest among women aged 40 to 49 years and the median age at diagnosis was 50 years in Korea, which is younger than Western women. Given that Korean women have different patterns of breast cancer compared to Western women and breast cancer incidence is predicted to continue to increase in Korea, identifying a healthy diet after diagnosis customized to Korean women is of crucial importance.

However, we have very limited studies. We presented what foods and supplements Korean breast cancer patients consumed and the association between diet and quality of life among breast cancer survivors. There is a clear need to examine the role of diet in breast cancer survival in further epidemiologic studies.

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AB01

BREAST AND OVARIAN CANCER RISK ASSESSMENT USING MULTIGENE PANEL TESTS

Antonis Antoniou

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Advances in genomic technologies have enabled more rapid, less expensive genetic sequencing than was possible a few years ago. These technologies allow for the comprehensive genetic profiling for assessing risks to breast and ovarian cancers and include multiplex sequencing panels of several genes and panels of common single nucleotide polymorphisms (SNPs). However, the clinical utility of such multiplex gene and SNP panels depends on having accurate estimates of cancer risks for mutations in the genes included in such panels as well as cancer risk prediction models that consider the multifactorial aetiology to cancer susceptibility. Using results from large international consortia, the presentation will review the key recent advances in characterising the breast and ovarian cancer risks for rare mutations in genes included in multi-gene panels and the cancer risks based on the combined effects of SNPs. The presentation will also describe recent developments to the BOADICEA risk prediction model to incorporate the explicit effects of PALB2, CHEK2, ATM, RAD51C, RAD51D, BRIP1 and Polygenic Risk Scores along with lifestyle/hormonal /reproductive risk factors and mammographic density in order to enable comprehensive breast and ovarian cancer risk prediction. This model is currently being validated in large independent prospective cohorts and is incorporated in the CanRisk tool, a new user-friendly tool that will enable primary, secondary and tertiary health professionals to obtain future cancer risks easily.

AB02

RISK REDUCTION STRATEGY FOR PATIENTS WITH GENETIC SUSCEPTIBILITY TO BREAST CANCER

Ava Kwong

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Women who have inherited mutations in the BRCA1 or BRCA2 genes have substantially elevated risks of breast and ovarian cancer. Mutation carriers have various options, including extensive and regular surveillance, chemoprevention and risk-reducing surgery. Prophylactic surgery (bilateral mastectomy, bilateral salpingo-oophorectomy or a combination of both procedures) has proved to be the most effective risk-reducing strategy for breast cancer and ovarian cancer but there are no randomised controlled trials able to demonstrate the potential benefits or harms of prophylactic surgery and most of the evidence has been derived from retrospective and short follow-up prospective studies, in addition to hypothetical mathematical models. Based on the current knowledge, it is reasonable to recommend prophylactic oophorectomy for BRCA1 or BRCA2 mutation carriers when childbearing is completed in order to reduce the risk of developing breast and ovarian cancer. In addition, women should be offered the options of intensive breast surveillance, chemoprevention or bilateral prophylactic mastectomy. The selection of the most appropriate risk-reducing strategy however is not simple. The impact of risk-reducing strategies on cancer risk, survival, and overall quality of life are the key criteria considered for decision-making. Various other factors should be taken into consideration when evaluating individual mutation carriers' individual situation, namely woman's age, morbidity, type of mutation, and individual preferences and expectations. Moreover in the era of multigene panel testing, such decisions become even more complicated. Various strategies and existing guidelines will be reviewed and discussed.

AB03

RISK REDUCTION FOR OVARIAN CANCER IN WOMEN WITH BRCA1/2 MUTATION

Min Chul Choi

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Although the risk for ovarian cancer is generally considered to be lower than the risk for breast cancer in a BRCA mutation carrier, the absence of reliable methods of early detection, as a result most diagnosis at advanced stage (about 75%) and the poor prognosis associated with advanced ovarian cancer have lent support for the performance of risk-reducing bilateral salpinooophorectomy (RRSO). RRSO recommended typically between 35–40 years and upon completion of child bearing. Because ovarian cancer onset in carriers with BRCA2 mutation is an average of 8–10 years later than in BRCA1 mutation, it is reasonable to delay RRSO until age 40–45 years in carriers with BRCA2 mutation.

The effectiveness of RRSO in reducing the risk for ovarian cancer in carriers of BRCA mutation has been demonstrated. RRSO significantly reduced the risk for BRCA-related gynecologic cancer (ovarian, fallopian tube and peritoneal cancers) by 85% and all-cause mortality by 77%. And RRSO is also reported to reduce the risk for breast cancer in carriers of BRCA mutation. Studies are supported by a meta-analysis that found reductions in breast cancer risk of approximately 50% for BRCA mutation carriers following RRSO.

For those carriers who have not or cannot elected RRSO, transvaginal ultrasound combined with serum CA-125 for ovarian cancer screening may be considered at the clinicians discretion starting at age 30–35 years of age. One study suggest a potential stage shift when a risk of ovarian cancer algorithm (ROCA) based ovarian cancer screening protocol is followed in high-risk women, though it remains unknown whether this screening protocol impact s survival.

Case-control studies have demonstrated that oral contraceptives reduced the risk for ovarian cancer by 45–50% in BRCA1 mutation carriers and by 60% in BRCA2 carriers. However the effect of oral contraceptive use on breast cancer risk among BRCA mutation carriers has reported confliction data. Differences in the study design employed by case-control studies make it difficult to compare outcomes between studies, and likely account for the conflicting results.

RRSO remains the current standard of care for ovarian cancer risk management.

Fertility issues on family planning decisions for individuals of reproductive age who are found to be BRCA mutation carriers. Counseling for reproductive options such as pre-implantation

genetic diagnosis (PGD) with assisted reproduction technique (ART) may be warranted for couples expressing concern over the BRCA mutation carrier status of their future children. Successful births have been reported by the use of PGD and IVF in BRCA mutation carriers; however data in the published literature are still limited. Therefore counseling about PGD should include a comprehensive discussion of the potential risks, benefits, and limitations of reproductive options.

Nursing Session

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NR01-1

CURRENT TRENDS OF BREAST CANCER SURGERY

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Recently, breast cancer surgery has become less invasive, less complicated and more cosmetic. On the other hand, breast surgery in new areas such as prophylactic surgery for patients with BRCA mutations is also increasing.

This is a recent trend of breast cancer surgery (minimizing, cosmetic, risk-reducing)

1) Minimizing of Surgical Area in Breast and Axillary Area

Increasing early breast cancer
Increasing Neoadjuvant systemic therapy
Widening of indication of sentinel lymph node biopsy

2) Oncoplastic Surgery

Increasing needs for cosmesis
Development of surgical technique

3) Risk-reducing Surgery

BRCA carrier (BRCA test)
Decreasing of Economic barrier for reconstruction in Korea

NR01-2

ROLE OF GENETIC COUNSELING NURSE IN BREAST CANCER

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Approximately 7% of all breast cancer cases are associated with hereditary predisposition and BRCA1 and BRCA2 gene account for half of the hereditary breast cancers (HBC). Although majority of breast cancer (BC) occur sporadically, identification of HBC is important in that active adoption of preventive strategies such as surveillance, chemoprevention, and risk-reducing surgery will result in the gain of life expectancy.

Before assessing the role of oncology nurse (ON) in genetic counseling (GC), it is first important for nurses to understand the role the genetic counselor. Genetic counselors who specialize in oncology evaluate family histories of cancer and determine whether patients or their relatives should be tested for gene mutations that can cause hereditary oncologic syndromes, and which tests they should have. After interpreting the results of those blood tests, the counselors help patients make decisions about prevention or management of their cancers, and also offer psychosocial support.

The information the counselors provide can make an enormous difference in quality of life and longevity for patients, including some with cancer and some being followed by oncologists because their family histories make cancer likely. Most commonly, genetic counselors who specialize in oncology investigate the possibility of hereditary breast, colon, ovarian and/or uterine cancers.

Depending on their level of training, oncology nurses will have varying levels of involvement in GC. Many nurses play a facilitator role - recognizing an individuals need for genetic evaluation and then making a referral to a counselor; however some advanced practice nurses participate in the actual counseling: "Advanced practice nurses with specialized training in clinical cancer genetics and genomics and cancer predisposition testing may be involved in the clinical application of cancer genetics, including GC and education."

In Korea, there are several programs for training genetic counselors. The Korean Breast Cancer Society established training program for hereditary breast and ovarian cancer GC program since 2011 for 2 to 3-day course. And since 2014 the Korean Medical Genetic Association started to certify the genetic counselor and in 2018 KMGA certified GC program as a Master's degree course.

The Korean Hereditary Breast Cancer (KOHBRA) study is a prospective multicenter cohort study from 38 major centers identifying cases and their families. Between May 2007 and July 2011, the KOHBRA study enrolled up to 2530 subjects and identified 501 mutation carriers. All participants received GC and BRCA genetic testing; clinical information and blood samples for blood banking were collected. The primary aim of the KOHBRA study I is to estimate the prevalence of BRCA1/2 mutations and ovarian cancer among a high-risk group of patients with hereditary breast cancer (BC) and their families. And the purpose of KOHBRA study II is as follows; first, to develop Korean BRCA mutation prediction model; second, to characterize clinical phenotype and discover novel prognostic factors for BRCA associated BC; third, to identify environmental and genetic modifiers of BRCA1/2 mutation; fourth, to develop nation-wide network of GC.

Asian BRCA Consortium (ABRCA) is organized during Global Breast Cancer Conference that was held in Seoul, Korea on Oct 6 to 8, 2011. Seven countries including Korea, Japan, China, Hong Kong, Malaysia, Singapore, and Indonesia participated ABRCA Consortium. The objectives of ABRCA consortium are 1) to share the knowledge of HBOC in Asian country, 2) to improve the quality of care of HBOC patients in Asia, and 3) to collaborate for researches on HBOC in Asia. Participating countries agreed Korea as headquarter of ABRCA consortium and to have regular meeting every year. Next meeting will be held in Malaysia in September. The examples of research collaboration will be Asian BRCA registry, blood and tissue banking, and Asian HBOC clinical practice guideline and etc. We hope that ABRCA consortium will promote the research collaboration and the management of HBOC syndrome.

NR02-1

SUFFERING IN PATIENTS WITH METASTATIC BREAST CANCER

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Breast cancer is the second most common type of cancer among women in Korea, and the incidence rate has been rising. According to data from the Korean Breast Cancer Society registry, metastatic breast cancer (MBC) approximately 34% of all patients diagnosed with MBC survive for 5 years or more.

Metastatic breast cancer (MBC) is incurable, but patients with MBC can live for many years after diagnosis. The median overall survival (OS) for all patients with MBC is 2–3 years. Patients with only bone metastases, however, have a more favorable prognosis with a median survival of 24-54 months and overall survival of 10 years at 35%.

The experiences of patients with MBC are different from the experiences of women with early breast cancer. Many patients with metastases experience major concerns, including fear of dying, declining quality of life, side effects of treatment, the ability to care for family, and care at the end of life. The goal of care for MBC is prolongation of survival, palliation of symptoms, and improving of quality of life.

Many symptoms depend on the site of metastasis. Common sites of metastasis from breast cancer include bone, liver, lung and brain and commonly occur with fatigue, depression, anxiety, insomnia, and pain.

Patients with MBC are exposed to multiple lines of treatments. Such treatments cause various side effects including nausea, vomiting, neuropathy, alopecia, hand foot syndrome, pain, stomatitis, and menopausal symptoms

Various negative psychological consequences may occur, ranging from depression, anxiety, apprehension related to their cancer, sadness and distress to more existential reactions, such as feelings of loss of identity and independence, hopelessness, uncertainty, and fear of death.

Patients diagnosed with metastatic cancer experience shock, devastation, guilt, and anger at the time of diagnosis. After being diagnosed with MBC, they should live with ongoing symptoms and side effects of treatment. They are also suffering from body image and sexuality dysfunction. Furthermore patients experience repetitive cancer regression and progression, suffering from uncertainty as to how long cancer treatment can prolong their future. Patients with MBC

experience feelings of social isolation and loss of independence and control and suffer from economic difficulties.

Patients cope with physical and psychological distress in a variety of ways. There is a difference in the level of suffering experienced by the patient depending on the psychological coping pattern of stressors of breast cancer. Oncology nurses should sympathize the suffering of the patients and provide guidance based on the most helpful coping style.

NR02-2

NECESSITY OF BREAST CANCER YOGA EXERCISE AND METHOD OF ITS PRACTICE

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Yoga increases quality of life. It can reduce fatigue, pain, sleep disturbances, anxiety and depression, as well as boost the performance of our immune system. Many patients are doing various exercises such as hiking, walking, and muscle stretch training. However, yoga has some special points that is different from other sports. Traditional Yoga can develop calmness and positive feelings, such as charity, joy, and compassion. Nowadays traditional yoga style is expressed as mindfulness yoga. Mindfulness Yoga focuses on breathing and recognizes sensations and feelings in a calm manner.

Breast cancer patients have a long treatment period after surgery. The probability of survival after surgery is more than 95%, But there is a risk of recurrence even after surgery. In the early postoperative period, it is important that reducing the edema and pain of the surgical site, but there is a continuing need to focus on training the body and mind in order to avoid recurring from the past lifestyle.

Chemotherapy, radiation therapy, hormone therapy, etc. can change the mood. It is important to train quietly watching the fluctuating feelings, because of raising your pain from your uncontrollable emotions. Therefore, breast cancer patients need mindfulness yoga for muscle relaxation, lymphatic circulation, muscle strength improvement, and reducing the pain while exercising the mind.

Mindfulness Yoga is divided into posture training, breathing training and meditation training. In the beginner level of learning yoga, it is recommended to focus on posture training. The posture training focuses on breathing, moves slowly, takes a specific yoga posture, stays for 10 seconds to 3 minutes, and observes his or her body sensations. It is good to take several postures for 30 minutes in accordance with your physical ability then gradually increases to one hour.

It should not to compete your yoga with looking at the mirror or other person. It is focus on your senses and feelings with as like as closing eyes. When fear arises, like “It hurts here,” then pause movement and return to breathing. Repeatedly returning to conscious breathing whenever negative feelings occur.

Next about the intermediate level, if you can practice alone without help, you are in there. At the intermediate level, it is good to practice together posture training with breathing training as like

1 hour for posture training, 30 minutes for breathing training. Yoga breathing training is 8 to 10 kinds of artificial changes in the nasal cavity, sinuses, bronchi, lungs and diaphragm to activate parasympathetic nerves, heart, and brain.

Nadi shodhana pranayama (alternate breath), for example, alternates between two nostrils, breathing and exhaling. This can be a refreshing feeling by ventilating the sinuses and reducing the heat of the brain and eyes, and is effective in treating rhinitis by reducing inflammation. Kumbhaka (hold ones breath) technique is also effective in meditating because it is effective in controlling the mind and calming the mind.

Last about the advanced level, if you can practice alone without helping about posture and respiration, you are in there. It is recommended that posture, breathing, and meditation training be performed together as like 1 hour for posture training, 30 minutes for breathing training, 30 minutes for meditation training.

There are several meditation methods, but it is recommended that firstly learn breathing observation meditation in particular. Because when you could not sleep at night, you can do it as lie down with your closing eyes. Breathing observation meditation is concentrate on the nose. At this time, try to stop thinking. Meditation takes about 5–60 minutes. Meditation changes the brain waves into alpha waves, theta waves, and delta waves, stabilizing the nerves and lowering the stress response. It can recognize the emotions and develop the ability of watching quietly, reduce sleep disturbances, and increase positive psychology.

If you continue to practice Mindfulness Yoga, it is reduce to symptoms of physical and psychological, and increase retentivity and self-observation with power of concentration. If swell those of all, you can learn to recover skill, and help to alleviate suffering and develop positive psychology and self-esteem.

In order to change the unbalanced body and mind into balance, you should continue to practice. Breast cancer patients should be self-managed for more than 5 years after surgery. If you keep yoga training for 5 years, you can take care of yourself with calm and serene mind. It can not say that yoga absolutely prevents recurrence or returns to the best physical health. But yoga can change the body and mind of the patient to be strong and healthy.

NR02-3

PHENOMENOLOGICAL APPROACH TO BREAST CANCER

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Mainstream research method for breast cancer has been quantitative study. Quantitative research focuses mostly on measuring of effects of intervention, quality of life or finding risk factors and defining relationships among variables related to specific disease or specific patients. Therefore, it can be said that quantitative study is researcher-oriented because researchers attention is more on the variables or the effects of intervention the researcher is applying to the subjects than on the subjects themselves. However, qualitative study, especially phenomenological approach is seeking to uncover the meaning of experience not in perspective of researcher, but from the perspective of participants who experience the phenomena. The best and basic way to have understanding about some phenomena or experience is to listen carefully what participants say while focusing on the phenomena of interest and being aware of researchers own prejudice on the matter. Steps of phenomenological research are deciding research topic and building research questions, conducting interviews, transcription, and data analysis. The important thing to remember in selecting research topic is to choose what is drawing my attention. During data collection, be sure to be focused on the research topic and research question. The best way to conduct best data analysis and writing is to read and reread raw data. And throughout all the research process, never forget to be aware of researchers own opinion, prejudice, and emotion about the phenomena being searched.

NR02-4

MULTIDISCIPLINARY APPROACH TO YOUNG BREAST CANCER NURSING

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What is breast cancer? Breast cancer is a cancer that develops from breast tissue. Signs of breast cancer may include palpable mass in the breast, a change in breast shape, skin dimpling, skin redness, nipple discharge. In those with distant spread of the disease, there may be bone pain, swollen lymph nodes, shortness of breath.

In recently, the number of young breast cancer patients is increasing.

If you treat young breast cancer patients ; < 40 years because these women have specific issues related to fertility preservation, pregnancy, and lactation that deserve a different approach and management from slightly older pre- and peri-menopausal women, treatment of young breast cancer patients can be considered in many ways such as hormonal status, genetics, pregnancy, and psychotic issues.

Important messages for young breast cancer patients are: All patients, both in the early and advanced setting, should be discussed within a multidisciplinary breast unit team (breast nurses crucial as "navigators").

Personalized psychosocial support, counselling on genetic predisposition, sexuality and fertility should be highly recommended as part of the individual treatment planning.

Satellite Symposium

GBCC2018
Global Breast Cancer Conference 2018

Reference 1. Baselga J, Campone M, Piccart M, et al. Everolimus in postmenopausal hormone-receptor-positive advanced breast cancer. N Engl J Med. 2012;366(6):520-9.

AFINITOR® tablets 2.5mg, 5mg, 10mg (everolimus)

Indications 1. Combination with exemestane in postmenopausal women with refractory to non-steroidal aromatase inhibitor, estrogen receptor-positive, HER-2 negative locally advanced or metastatic breast cancer 2. Advanced neuroendocrine tumors of pancreatic origin (PNET) 3. Progressive, well-differentiated, non-functional neuroendocrine tumors of gastrointestinal or lung origin (GI/Lung NET) that are unresectable, locally advanced or metastatic 4. Advanced renal cell carcinoma after failure of treatment with VEGF-targeted therapy (sunitinib or sorafenib) 5. SEGA associated with tuberous sclerosis (TS) who require therapeutic intervention but are not candidates for curative surgical resection., 6, Renal angiomyolipoma with tuberous sclerosis complex (TSC), not requiring immediate surgery. **Dosage and administration** Afinitor should be administered orally once daily at the same time every day, either consistently with or consistently without food. Afinitor tablets should be swallowed whole with a glass of water. The tablets should not be chewed or crushed. For patients unable to swallow tablets, AFINITOR tablets should be dispersed completely in a glass of water (approximately 30 mL) by gently stirring (approximately 7 minutes), immediately prior to drinking. The glass should be rinsed with the same volume of water and the rinse should be completely swallowed to ensure that the entire dose is administered. Treatment with Afinitor should be initiated by a physician experienced in the use of anticancer therapies. Treatment should continue as long as clinical benefit is observed or until unacceptable toxicity occurs. **1. Breast cancer, Neuroendocrine Tumors, Renal Cell Carcinoma and Renal angiomyolipoma with tuberous sclerosis complex (TSC):** 10 mg, once daily. **2. Tuberous sclerosis complex (TSC) with Subependymal Giant Cell Astrocytoma (SEGA):** Individualize dosing based on body surface area[BSA, in m^2) using the Dubois formula, where seight (W) is in kilograms and height (H) is in centimeters [BSA = (W0.425 x H0.725) x 0.007184]. The recommended starting daily dose for Afinitor for the treatment of patients with TSC who have SEGA is 4.5 mg/m^2, rounded to the nearest strength of Afinitor Tablets. Different strengths of Afinitor Tablets can be combined to attain the desired dose. Dosing should be titrated to attain trough concentrations of 5 to 15 ng/mL. Dosing should be titrated by increasing the dose by increments of 2.5 mg to attain the target trough concentration for optimal clinical response. Efficacy, safety, concomitant therapy, and the current trough concentration should be considered when planning for dose titration. Everolimus whole blood trough concentrations should be assessed approximately 1 to 2 weeks after commencing treatment or any change in dose. Evaluate SEGA volume approximately 3 months after commencing AFINITOR therapy and periodically thereafter, with subsequent dose adjustments taking into consideration changes in SEGA volume, corresponding trough concentration, and tolerability. Once a stable dose is attained, monitor trough concentrations every 3 to 6 months in patients with changing body surface area or every 6 to 12 months in patients with stable body surface area for the duration of treatment. **3.Dose Modifications** (1) Management of severe or intolerable adverse reactions may require temporary dose reduction and/or interruption of AFINITOR therapy. If dose reduction is required the suggested dose is approximately 50% lower than the daily dose previously administered. For dose reductions below the lowest available tablet strength, alternate day dosing should be considered. **Paediatric patients 1. Breast cancer, neuroendocrine tumors, renal cell carcinoma, and renal angiomyolipoma with tuberous sclerosis complex(TSC):** Safety and efficacy of Afinitor is not established for use in paediatric cancer patients. **2. Tuberous sclerosis complex (TSC) with Subependymal Giant Cell Astrocytoma (SEGA):** Dosing recommendations for 1< year of paediatric patients with SEGA are consistent with those for the adult SEGA population. As Afinitor has not been studied in paediatric TSC with SEGA patients < 1 years of age and <18 years of age with TSC who have SEGA and hepatic impairement, using this medicine in this group is currently not recommended. **Patients with hepatic impairment 1. Breast cancer, neuroendocrine tumors, renal cell carcinoma, and renal angiomyolipoma with tuberous sclerosis complex(TSC):** · Mild hepatic impairment (Child-Pugh class A) – The recommended dose is 7.5 mg daily; the dose may be decreased to 5 mg if not well tolerated. · Moderate hepatic impairment (Child-Pugh class B) – The recommended dose is 5 mg daily; the dose may be decreased to 2.5 mg if not well tolerated. · Severe hepatic impairment (Child-Pugh class C) – Not recommended. If the desired benefit outweighs the risk, a dose of 2.5 mg daily may be used but must not be exceeded. Dose adjustments should be made if a patient's hepatic (Child-Pugh) status changes during treatment. **2. Tuberous sclerosis complex (TSC) with Subependymal Giant Cell Astrocytoma (SEGA):** Patients <18 years of age: Afinitor is not recommended for patients <18 years of age with TSC who have SEGA and hepatic impairment. Patients ≥18 years of age · Mild hepatic impairment (Child-Pugh A) – 75% of the dose calculated based on BSA. · Moderate hepatic impairment (Child-Pugh B) – 50% of the dose calculated based on BSA. · Severe hepatic impairment (Child-Pugh C) – not recommended. Everolimus whole blood trough concentrations should be assessed approximately 2 weeks after commencing treatment or after any change in hepatic (Child-Pugh) status. Dosing should be titrated to attain trough concentrations of 5 to 15 ng/mL. Dose adjustments should be made if a patient's hepatic (Child-Pugh) status changes during treatment. **Warnings** 1) Non-infectious pneumonitis 2) Infections 3) Hypersensitivity reactions 4) Oral ulceration 5) Renal failure events 6) Laboratory tests and monitoring (Renal function, Blood glucose, Blood lipids, Haematological parameters) 7) Drug-Drug interactions 8) Hepatic impairment 9) Vaccinations 10) Angioedema with concomitant use of angiotensin-converting enzyme (ACE) **Contraindications** 1) Patients with hypersensitivity to the active substance, to other rapamycin derivatives, or to any of the excipients. 2) Since Afinitor contains lactose, it is not recommended for patients with rare hereditary problems of galactose intolerance, of Lapp lactase deficiency or of glucose-galactose malabsorption. **Before prescribing, consult full prescribing information.**

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SS01

ETHNIC DIFFERENCES IN THE TREATMENT LANDSCAPE OF BREAST CANCER: WESTERN VS. ASIAN

Louis Chow

Organisation for Oncology and Translational Research, Hong Kong

The development of breast cancer treatment is becoming globalised. There is increasing number of Asian patients participating in clinical trials, providing opportunities to analyse differences between Western and Asian patients. End-point analysis on response and survival as well as subsequent clinical experiences have shown that the clinical efficacy and survival benefit did not differ much between ethnic groups. However, differences in adverse events and toxicity profiles have been reported. Asian patients on chemotherapy are more susceptible to hematologic toxicities (especially neutropenia), in terms of both incidence and magnitude, whereas the incidences of non-hematologic toxicities are similar to their western counterparts.

Regarding hormonal therapy, the differences in estrogen levels and rates of drug metabolism as well as the difference in pharmacogenomics among different ethnic groups may account for the differential anti-cancer effects and also toxicities. Asian seems to fare better with tamoxifen than aromatase inhibitors. International studies combining hormonal therapy with MTor inhibitor (Evorolimus) showed that there was a slight disadvantage in efficacy for Asians. Also, Asians tend to have higher incidences of toxicities especially stomatitis and pneumonitis.

Clinical trials on anti-HER-2 therapy with lapatininb in combination with capecitabine reviewed a higher clinical benefit rate for Asians but at the expense of higher incidence of hand-foot syndrome and diarrhea.

Though the exact reasons of these differences remain to be elucidated, awareness and understanding of such differences may help to select a better and more appropriate therapy in the clinics.

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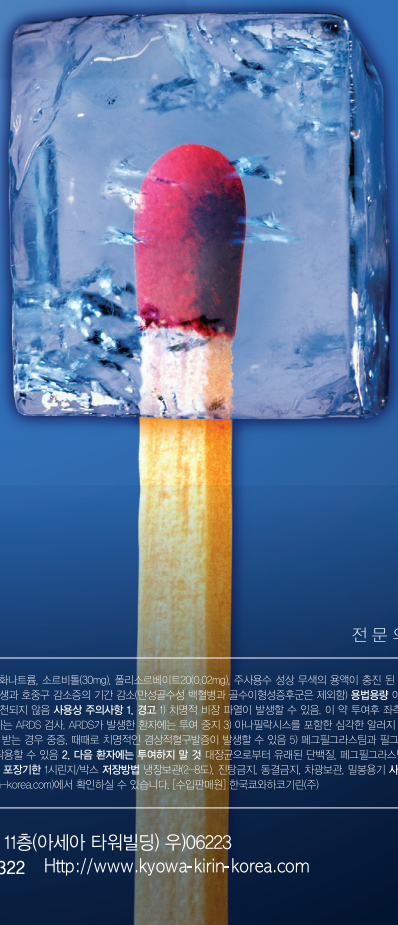

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원료의약품 및 분량 1시린지(0.6밀리리터)중 (주성분) 페그필그라스팀(별규) … 6mg, (첨가제) 빙초산(글라시알아세틱에시드), 수산화나트륨, 소르비톨(30mg), 폴리소르베이트20(0.02mg), 주사용수 성상 무색의 용액이 충진 된 주사침이 달린 투명한 유리프리필드시린지 주사제 효능효과 악성종양에 대한 세포독성 화학요법을 투여 받는 환자의 발열성 호중구 감소증의 발생과 호중구 감소증의 기간 감소(만성골수성 백혈병과 골수이형성증후군은 제외함) **용법용량** 이 약 6mg을 항암화학요법 이후 약 24시간 후에 피하주사 *소아에 대한 사용 제한 *말기 신장애 환자를 포함한 신장애 환자에게 용량 변경은 추천되지 않음 **사용상 주의사항 1. 경고** 1) 치명적 비장 파열이 발생할 수 있음. 이 약 투여후 좌측 상복부, 어깨 통증이 있는 환자는 비장비대, 비장파열 검사 2) 급성 호흡곤란 증후군(ARDS)가 발생할 수 있음. 열, 폐 침윤, 호흡곤란이 있는 환자는 ARDS 검사. ARDS가 발생한 환자에는 투여 중지 3) 아나필락시스를 포함한 심각한 알러지 반응이 발생할 수 있음. 심각한 알러지 반응이 발생한 환자에는 투여를 영구 중지 4) 겸상적혈구질환 환자가 필그라스팀, 페그필그라스팀을 투여 받는 경우 중증, 때때로 치명적인 겸상적혈구발증이 발생할 수 있음 5) 페그필그라스팀과 필그라스팀이 작용하는 G-CSF수용체가 암세포에서 발견됨. 페그필그라스팀이 골수성 암과 골수이형성증을 포함한 암 종류를 증가시키는 요소로 작용할 수 있음 **2. 다음 환자에는 투여하지 말 것** 대장균으로부터 유래된 단백질, 페그필그라스팀, 필그라스팀 등에 과민증이 알려진 환자 **3. 다음 환자에는 신중히 투여할 것** 1) 약물 과민증의 병력이 있는 환자 2) 알레르기 소인이 있는 환자 **포장기한** 1시린지/박스 **저장방법** 냉장보관(2~8℃), 진탕금지, 동결금지, 차광보관, 밀봉용기 **사용기한** 외부포장재에 표시된 사용기한 내에 사용 *제품에 대한 자세한 정보는 제품설명서를 참조해주시기를 바라며, 홈페이지(www.kyowa-kirin-korea.com)에서 확인하실 수 있습니다. [수입판매원] 한국쿄와하코기린(주)

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SS02

MANAGEMENT OF FEBRILE NEUTROPENIA BY PEGFILGRASTIM IN THE UNITED STATES: IMPORTANCE OF RELATIVE DOSE INTENSITY AND CONTROL OF TOXIC EFFECTS OF CHEMOTHERAPY IN EARLY BREAST CANCER

Naoto Ueno

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In patients with early breast cancer, recurrence due to metastasis is the major cause of reduced overall survival. Delays in the conventional chemotherapy cycle (e.g., taxane or anthracycline) may contribute to reductions in the relative dose intensity of administer chemotherapy, which is well known for contributing to recurrence.

In particular, neutropenic fever can be detrimental to timely chemotherapy delivery. Thus, preventing and treating neutropenic fever is essential for optimal management of breast cancer, which leads to improved survival.

Understanding the importance of maintaining relative dose intensity and management of toxic effects including neutropenic fever will improve the quality of care for patients with early breast cancer. The learning objective of this talk is to describe the optimal care for early breast cancer with a focus on febrile neutropenia, an appropriate indication for pegylated granulocyte colony stimulating factor, and other toxicity management.

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- Approved No. 2017-132 by Health Insurance Review & Assessment Service -

From **1 June 2017**, **PERJETA+HERCEPTIN+Docetaxel combination therapy** has been included in reimbursement for patients with HER2-positive metastatic breast cancer (MBC) or inoperable locally recurrent breast cancer as first line treatment.[1-3]

Reimbursement for concomitant drugs in neoadjuvant treatment

(Perjeta should be fully self-paid.)

- Approved No. 2017-132 by Health Insurance Review & Assessment Service -

From **1 June 2017**, Combination therapy with PERJETA has been included in reimbursement for patients with HER2-positive, locally advanced, inflammatory, or early stage breast cancer (greater than 2cm) as **neoadjuvant treatment**.[1,2,4,5]

PERJETA inj. (Pertuzumab) prescription medicine [COMPOSITION] pertuzumab at a concentration of 30 mg/mL [PHARMACEUTICAL FORM] Concentrate for solution for infusion. Clear to slightly opalescent, colourless to pale yellow, liquid. [INDICATIONS] ○Metastatic breast cancer: Perjeta is indicated for use in combination with trastuzumab and docetaxel in adult patients with HER2-positive metastatic or locally recurrent unresectable breast cancer, who have not received previous anti-HER2 therapy or chemotherapy for their metastatic disease. ○Neoadjuvant treatment of breast cancer: Perjeta is indicated for use in combination with trastuzumab and docetaxel for the neoadjuvant treatment of adult patients with HER2-positive, locally advanced, inflammatory, or early stage breast cancer (greater than 2cm) as one of treatment including fluorouracil, epirubicin, and cyclophosphamide/ carboplatin, DOSAGE AND ADMINISTRATION●Perjeta is subject to restricted medical prescription and therapy should only be initiated under the supervision of a physician experienced in the administration of anti-cancer agents. Perjeta should be administered by a healthcare professional prepared to manage anaphylaxis and in an environment where full resuscitation facilities are immediately available. Patients treated with Perjeta must have HER2-positive tumour status, defined as a score of 3+ by immunohistochemistry (IHC) and/or a ratio of ≥ 2.0 by in situ hybridisation (ISH) assessed by a validated test. ● Dosage of combination with trastuzumab and docetaxel: The recommended initial loading dose of pertuzumab is 840 mg administered as a 60 minute intravenous infusion, followed every 3 weeks thereafter by a maintenance dose of 420 mg administered over a period of 30 to 60 minutes. When administered with pertuzumab the recommended initial loading dose of trastuzumab is 8 mg/kg body weight administered as an intravenous infusion followed every 3 weeks thereafter by a maintenance dose of 6 mg/kg body weight. When administered with pertuzumab the recommended initial dose of docetaxel is 75 mg/m2, administered thereafter on a 3 weekly schedule. The dose of docetaxel may be escalated to 100 mg/m2 on subsequent cycles if the initial dose is well tolerated (the docetaxel dose should not be escalated when used in combination with carboplatin, trastuzumab and pertuzumab). The medicinal products should be administered sequentially and not mixed in the same infusion bag. Perjeta and trastuzumab can be given in any order. When the patient is receiving docetaxel, this should be administered after Perjeta and trastuzumab. An observation period of 30 to 60 minutes is recommended after each Perjeta infusion and before commencement of any subsequent infusion of trastuzumab or docetaxel. Patients should be treated with Perjeta and trastuzumab until disease progression or unmanageable toxicity. Neoadjuvant treatment of breast cancer: Perjeta should be administered for 3 to 6 cycles in combination with neoadjuvant trastuzumab and chemotherapy, as part of a treatment regimen for early breast cancer. Four preoperative cycles of Perjeta in combination with trastuzumab and docetaxel followed by 3 postoperative cycles of fluorouracil, epirubicin, and cyclophosphamide [FEC]. Three preoperative cycles of FEC alone followed by 3 preoperative cycles of Perjeta in combination with docetaxel and trastuzumab. Six preoperative cycles of Perjeta in combination with docetaxel, carboplatin, and trastuzumab (TCH) [escalation of docetaxel above 75 mg/m2 is not recommended. Following surgery, patients should continue to receive trastuzumab to complete 1 year of treatment. There is insufficient evidence to recommend continued use of Perjeta for greater than 6 cycles for early breast cancer. There is insufficient evidence to recommend concomitant administration of an anthracycline with Perjeta, and there are no safety data to support sequential use of doxorubicin with Perjeta. ●Delayed or missed doses: If the time between two sequential infusions is less than 6 weeks, the 420 mg dose of pertuzumab should be administered as soon as possible without regard to the next planned dose. If the time between two sequential infusions is 6 weeks or more, the initial loading dose of 840 mg pertuzumab should be re-administered as a 60-minute intravenous infusion followed every 3 weeks thereafter by a maintenance dose of 420 mg administered over a period of 30 to 60 minutes. ● Dose modification: Dose reductions are not recommended for Perjeta. Patients may continue therapy during periods of reversible chemotherapy-induced myelosuppression but they should be monitored carefully for complications of neutropenia during this time. For docetaxel and other chemotherapy dose modifications, see relevant product information. For trastuzumab, dose reductions are not recommended, see trastuzumab product information. If trastuzumab treatment is discontinued, treatment with Perjeta should be discontinued. If docetaxel is discontinued, treatment with Perjeta and trastuzumab may continue until disease progression or unmanageable toxicity in the metastatic setting. ● Hypersensitivity reactions/anaphylaxis: Perjeta must be permanently discontinued in case of severe hypersensitivity. ● Left Ventricular Ejection Fraction (LVEF): Withhold Perjeta and trastuzumab dosing for at least 3 weeks for either: - signs and symptoms suggestive of congestive heart failure (Perjeta should be discontinued if symptomatic heart failure is confirmed) or a drop in LVEF to less than 45% or - LVEF of 40% to 45% with a 10% or greater absolute decrease below pretreatment values. Perjeta may be resumed if the LVEF has recovered to greater than 49% or to 40% to 49% associated with less than a 10% absolute decrease below pretreatment values. If after a repeat assessment within approximately 3 weeks, the LVEF has not improved, or has declined further, Perjeta and trastuzumab should be discontinued, unless the benefits for the individual patient are deemed to outweigh the risks. ● Infusion reactions: The infusion rate may be slowed or interrupted if the patient develops an infusion reaction. The infusion may be resumed when symptoms abate. Treatment including oxygen, beta agonists, antihistamines, rapid iv fluids and antipyretics may also help alleviate symptoms. Perjeta must be permanently discontinued in case of NCI-CTCAE Grade 4 hypersensitivity reactions (anaphylaxes), bronchospasm or acute respiratory distress syndrome. ● Method of administration: Perjeta is administered intravenously by infusion. It should not be administered as an intravenous push or bolus. For the initial dose, the recommended infusion period is 60 minutes. If the first infusion is well tolerated, subsequent infusions may be administered over a period of 30 minutes to 60 minutes. [SPECIAL WARNINGS AND PRECAUTIONS FOR USE] *Contraindications: 1) Perjeta is contraindicated in patients with known hypersensitivity to pertuzumab or to any of its excipients. *Warnings: 1) Left ventricular dysfunction: 2) Decreases in LVEF have been reported with medicinal products that block HER2 activity, including Perjeta. Patients who have received prior anthracyclines or prior radiotherapy to the chest area may be at higher risk of LVEF declines. In the pivotal trial CLEOPATRA in patients with metastatic breast cancer, Perjeta in combination with trastuzumab and docetaxel was not associated with a greater incidence of symptomatic left ventricular systolic dysfunction [LVD] or LVEF declines compared with placebo and trastuzumab and docetaxel. ② In the neoadjuvant period of NEOSPHERE, the incidence of LVD was higher in the Perjeta-treated groups than in those who did not receive Perjeta. An increased incidence of LVEF declines was also observed in patients treated with Perjeta in combination with trastuzumab and docetaxel. LVEF recovered to >50% in all patients. ③ Perjeta has not been studied in patients with: a pre-treatment LVEF value of < 50%, a prior history of congestive heart failure [CHF], LVEF declines to < 50% during prior trastuzumab adjuvant therapy, or conditions that could impair left ventricular function such as uncontrolled hypertension, recent myocardial infarction, serious cardiac arrhythmia requiring treatment or a cumulative prior anthracycline exposure to > 360 mg/m2 of doxorubicin or its equivalent. ④ Assess LVEF prior to initiation of Perjeta and during treatment with Perjeta (every 3 months in the metastatic setting and every 2 cycles in the neoadjuvant setting) to ensure that LVEF is within the institution's normal limits. If LVEF is < 45%, or ≥ 45% to 49% with a 10% or greater absolute decrease below the pretreatment value, withhold Perjeta and trastuzumab and repeat LVEF assessment within approximately 3 weeks. If the LVEF has not improved, or has declined further, discontinuation of Perjeta and trastuzumab should be strongly considered, unless the benefits for the individual patient are deemed to outweigh the risks. ⑤ Infusion reactions: ① Perjeta has been associated with infusion reactions. Close observation of the patient during and for 60 minutes after the first infusion and during and for 30-60 minutes after subsequent infusions of Perjeta is recommended. If a significant infusion reaction occurs, the infusion should be slowed down or interrupted and appropriate medical therapies should be administered. Patients should be evaluated and carefully monitored until complete resolution of signs and symptoms. Permanent discontinuation should be considered in patients with severe infusion reactions. This clinical assessment should be based on the severity of the preceding reaction and response to administered treatment for the adverse reaction. ② Febrile neutropenia: ① In the CLEOPATRA trial in metastatic breast cancer, Patients treated with Perjeta, trastuzumab and docetaxel are at increased risk of febrile neutropenia compared with patients treated with placebo, trastuzumab and docetaxel, especially during the first 3 cycles of treatment. nadir neutrophil counts were similar in Perjeta-treated and placebo-treated patients. The higher incidence of febrile neutropenia in Perjeta-treated patients was associated with the higher incidence of mucositis and diarrhoea in these patients. Symptomatic treatment for mucositis and diarrhoea should be considered. No events of febrile neutropenia were reported after cessation of docetaxel. ④ Hypersensitivity reactions/anaphylaxis: ① Patients should be observed closely for hypersensitivity reactions. Severe hypersensitivity, including anaphylaxes, has been observed in clinical trials with Perjeta. Medicinal products to treat such reactions, as well as emergency equipment, should be available for immediate use. Perjeta is contraindicated in patients with known hypersensitivity to pertuzumab or to any of its excipients. * Precautions for use 1. Fertility, pregnancy and lactation 1) Women of childbearing potential and their partner should use effective contraception while receiving Perjeta and for 6 months following the last dose of pertuzumab. 2) There is limited amount of data from the use of pertuzumab in pregnant women. Studies in animals have shown reproductive toxicity. Administration of pertuzumab to pregnant cynomolgus monkeys during the period of organogenesis resulted in oligohydramnios, delayed fetal kidney development, and embryo-fetal death. 3) Perjeta is not recommended during pregnancy and in women of childbearing potential not using contraception. 4) Because human IgGs is secreted in human milk and the potential for absorption and harm to the infant is unknown, a decision should be made to discontinue breast-feeding or to discontinue treatment, taking into account the benefit of breast-feeding for the child and the benefit of Perjeta therapy for the woman. 5) No specific fertility studies in animals have been performed to evaluate the effect of pertuzumab. Only very limited data are available from repeat-dose toxicity studies with respect to the risk for adverse reactions on the male reproductive system. No adverse reactions were observed in sexually mature female cynomolgus monkeys exposed to pertuzumab. 2. Elderly patients, Renal impairment, Hepatic impairment, Paediatric population 1) Elderly patients: Limited data are available on the safety and efficacy of Perjeta in patients ≥ 65 years of age. No significant differences in safety and efficacy of Perjeta were observed between elderly patients aged ≥ 65 and adult patients aged < 65 years. No dose adjustment is necessary in the elderly population ≥ 65 years of age. 2) Renal impairment: Dose adjustments of pertuzumab are not needed in patients with mild or moderate renal impairment. No dose recommendations can be made for patients with severe renal impairment because of the limited pharmacokinetic data available. 3) Hepatic impairment: The safety and efficacy of Perjeta have not been studied in patients with hepatic impairment. No specific dose recommendations can be made. 5) Paediatric population: The safety and efficacy of Perjeta in children and adolescents below 18 years of age have not been established. There is no relevant use of Perjeta in the paediatric population in the indication of breast cancer. Perjeta-2016-12-20-1.0

References 1. Perjeta® PI 2016-12-20-1.0 2. Announcement of No. 2017-132 in Health Insurance Review & Assessment Service (2017.5.30) 3. Sandra M Swain, Baselga J, Sung-Bae Kim, et al. Pertuzumab, Trastuzumab, and Docetaxel in HER2-Positive Metastatic Breast Cancer. N Engl J Med. 2015;372:724-34. 4. Schneeweiss A, Chia S, Hickish T, et al. Pertuzumab plus trastuzumab in combination with standard neoadjuvant anthracycline-containing and anthracycline-free chemotherapy regimens in patients with HER2-positive early breast cancer: a randomized phase II cardiac safety study (TRYPHAENA). AnnOncol. 2013;24:2278-2284. 5. Gianni L, Pienkowski T, Im Y-H, et al. Efficacy and safety of neoadjuvant pertuzumab and trastuzumab in women with locally advanced, inflammatory, or early HER2-positive breast cancer (NeoSphere): a randomised multicentre, open-label, phase 2 trial. Lancet. 2012;13:25-32

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SS03

CURRENT AND FUTURE PERSPECTIVES IN TREATMENT OF HER2+ BREAST CANCER

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Since the analysis of 4 adjuvant trastuzumab trials (HERA, N9831, BCIRG-006, NSABP B-31), 1 year of adjuvant trastuzumab has become the standard treatment for patients with tumor size larger than 1 cm, and has saved thousands of womens lives. Since then, there have been numerous attempts to increase efficacy and also reduce toxicity of adjuvant treatment for HER2 positive breast cancer.

Increasing duration of adjuvant trastuzumab beyond 1 year failed to show increase in disease free survival (DFS) of HER2+ breast cancer (HERA trial) nor did applying trastuzumab for shorter than 1 year show non-inferiority in DFS (PHARE, SHORT-HER, SOLD trial), consolidating current standard of 1 year of trastuzumab.

Adding new agents to trastuzumab is another strategy. Although greatly anticipated, ALTTO trial failed to show statistically and clinically significant benefit with addition of lapatinib. To the contrary, addition of neratinib after 1 year of trastuzumab improved invasive DFS of HER2 positive breast cancer in the ExteNET trial (5 yr iDFS HR = 0.73, $p = 0.008$), especially in HR positive subgroup (HR = 0.60). Addition of pertuzumab, in APHINITY trial, showed modest gain in 3 year invasive DFS in node positive breast cancer, leading to US FDA approval of adjuvant pertuzumab in patients with HER2 positive breast cancer.

De-escalation strategy was attempted to use less treatment and spare patients from toxicity of adjuvant chemotherapy. In APT trial, weekly paclitaxel + trastuzumab for 12 weeks followed by trastuzumab for a total of 1 year resulted in excellent disease free survival and breast cancer specific survival. In the neaodjvuant KRISTINE and NeoSphere trial, T-DM1-pertuzumab and trastuzumab-pertuzumab combination showed good pathological CR, making biologics only arm an attractive strategy to develop for low risk patients. More studies are ongoing to target crosstalk between ER and HER2, in a subset of HR positive HER2 positive breast cancer patients.

To choose right candidate for escalation and de-escalation strategy, discovery of robust biomarkers of recurrence and also response to anti-HER2 treatment is mandatory. More studies to optimize adjuvant treatment for HER2 positive BC are ongoing and will be discussed at the meeting.

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PRODUCT INFORMATION

FASLODEX (fulvestrant)

[Therapeutic indications] Monotherapy This medicine is indicated for the treatment of hormone receptor positive, HER2 negative, locally advanced or metastatic breast cancer in postmenopausal women. Combination therapy This medicine is indicated in combination with palbociclib for the treatment of hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)- negative locally advanced or metastatic breast cancer in women who have received prior endocrine therapy **[Posology and method of administration]** Adult females (including the elderly) : The recommended dose is 500 mg to be administered intramuscularly into the buttocks (gluteal area) slowly (1 - 2 minutes per injection) as two 5 mL injections, one in each buttock, on days 1, 15, 29 and once monthly thereafter. When FASLODEX is used in combination with palbociclib, the recommended dose is 500 mg to be administered intramuscularly into the buttocks (gluteal area) slowly (1 - 2 minutes per injection) as two 5 mL injections, one in each buttock, on days 1, 15, 29 and once monthly thereafter. The recommended dose of palbociclib is a 125 mg capsule taken orally once daily for 21 consecutive days followed by 7 days off treatment to comprise a complete cycle of 28 days. Palbociclib should be taken with food. Please refer to the full prescribing information of palbociclib. Prior to the start of treatment with the combination of fulvestrant plus palbociclib, and throughout its duration, pre/perimenopausal women should be treated with LHRH agonists according to local clinical practice. Children and adolescents : Not recommended for use in children or adolescents, as safety and efficacy have not been established in this age group. Patients with renal impairment : No dose adjustments are recommended for patients with mild to moderate renal impairment (creatinine clearance ≥30 ml/min). Safety and efficacy have not been evaluated in patients with severe renal impairment (creatinine clearance < 30 ml/min) Patients with hepatic impairment : Use Faslodex with caution in treating patients with mild to moderate hepatic impairment. No dose adjustments are recommended for patients with mild to moderate hepatic impairment. However, as fulvestrant exposure may be increased, Faslodex should be used with caution in these patients. There are no data in patients with severe hepatic impairment. Safety and efficacy have not been evaluated in patients with hepatic impairment **[Warning]** Benzyl alcohol is reported to have relation with fatal gasping respiration symptom in premature. **[Contraindications]** 1. Patients with known hypersensitivity to the active substance or to any of the excipients 2. Pregnancy and in breast-feeding 3. Severe hepatic impairment 4. Neonate, premature(this product includes benzyl alcohol) **[Special warnings and special precautions for use]** 1. Patients with mild to moderate, hepatic impairment.2. Patients with severe renal impairment. 3. Due to the route of administration, use this medicine with caution if treating patients with bleeding diatheses, thrombocytopenia or those taking anticoagulant treatment. 4. Thromboembolic events are commonly observed in women with advanced breast cancer. This should be taken into consideration when prescribing this medicine to patients at risk. 5. There are no long-term data on the effect of fulvestrant on bone. Due to the mode of action of fulvestrant, there is a potential risk of osteoporosis. **[Undesirable effects]** 1) This section provides information based on all adverse reactions from the clinical trials, PMS and spontaneous reports. The most commonly reported adverse reactions are injection site reactions, asthenia, nausea, and increased hepatic enzymes (ALT, AST, ALP).The following frequency categories for adverse drug reactions (ADRs) were calculated based on the Faslodex 500 mg treatment group in pooled safety analyses of the studies that compared FASLODEX 500mg with FASLODEX 250mg [CONFIRM (Study D6997C00002), FINDER 1 (Study D6997C00004), FINDER 2 (Study D6997C00006), and NEWEST (Study D6997C00003) studies], or from FALCON (Study D6998C00001) alone that compared FASLODEX 500 mg with anastrozole 1 mg. Where frequencies differ between the pooled safety analysis and FALCON, the highest frequency is presented. The frequencies in the following table were based on all reported adverse drug reactions, regardless of the investigator assessment of causality. The adverse reactions are summarised as follows:

SOC	Very common ≥ 10%	Common ≥ 1 - < 10%	Incommon ≥ 0.1 — < 1%
Nervous system disorders		Headache	
Gastrointestinal disorders	Nausea	Vomiting, diarrhoea	
Infections and infestations		Urinary tract infections	
Skin and subcutaneous tissue disorders	Rash[a]		
Musculoskeletal and connective tissue disorders	Joint and musculoskeletal pain[a]	Back pain[a]	
Metabolism and nutrition disorders		Anorexia[a]	
Vascular disorders	Hot flushes[a]	Venous thromboembolism[a]	
General disorders and administration site conditions	Asthenia, Injection site reactions[b]		Injection site haemorrhage, Injection site haematoma
Immune system disorders	Hypersensitivity reactions[c]		
Hepatobiliary disorders	Increased Hepatic enzymes (ALT, AST, ALP)[f]	Elevated bilirubin[e]	Hepatic failure[f] hepatitis[f] elevated gamma-GT[f]
Reproductive system and breast disorders		Vaginal haemorrhage[d]	Vaginal moniliasis Leukorrhea
Blood and lymphatic system		Reduced platelet count[e]	

a: Includes adverse drug reactions for which the exact extent of the contribution of Faslodex cannot be assessed due to the underlying disease. **b:** The term injection site reactions does include sciatica, neuralgia, neuropathic pain and neuropathy peripheral and does not include the terms injection site haemorrhage and injection site haematoma. **c :** The event was not observed in major clinical studies (CONFIRM, FINDER 1, FINDER 2, NEWEST). The frequency has been calculated using the upper limit of the 95% confidence interval for the point estimate. This is calculated as 3/560 (where 560 is the number of patients in the major clinical studies), which equates to a frequency category of 'uncommon'. **d:** Includes: arthralgia, and less frequently musculoskeletal pain, myalgia and pain in extremity. **e:** Frequency category differs between pooled safety dataset and FALCON. **f:** ADR was not observed in FALCON

2) Results of local post-marketing study As a result of local post-marketing study for 7 years with 121 patients, 233 AEs were reported in 70 subjects (57.9%) during this period regardless of causal relationship with study drug. Of these, serious adverse events and serious adverse drug reactions which cannot be excluded of causality with the drug are listed in the table below by frequency. (Refer to the latest Product Information to see the table.) Additionally, unexpected adverse events and unexpected adverse drug reactions which cannot be excluded of causality with the drug are listed in the table below by frequency. (Refer to the latest Product Information to see the table.) **[General Precautions]** 1. Injection site related events including sciatica, neuralgia, neuropathic pain, and peripheral neuropathy have been reported with Faslodex injection. Caution should be taken while administering Faslodex at the dorsogluteal injection site due to the proximity of the underlying sciatic nerve. 2. Interference with estradiol antibody assays Due to the structural similarity of fulvestrant and estradiol, fulvestrant may interfere with antibody based-estradiol assays and may result in falsely increased levels of estradiol. **[Interaction with other medicinal products and other forms of interaction]** 1. A clinical interaction study with midazolam demonstrated that fulvestrant does not inhibit CYP 3A4. 2. Clinical interaction studies with rifampicin (inducer of CYP 3A4) and ketoconazole (inhibitor of CYP 3A4) showed no clinically relevant change in fulvestrant clearance. Dosage adjustment is therefore not necessary in patients who are coprescribed fulvestrant and CYP 3A4 inhibitors or inducers. **[Fertility, Pregnancy and lactation]** 1. Pregnancy : This medicine is contraindicated in pregnancy. Fulvestrant has been shown to cross the placenta after single intramuscular doses in rat and rabbit. Studies in animals have shown reproductive toxicity including an increased incidence of foetal abnormalities and deaths. If pregnancy occurs while taking this medicine the patient must be informed of the potential hazard to the foetus and potential risk for loss of pregnancy. 2. Breastfeeding : Breast-feeding must be discontinued during treatment with this medicine. Fulvestrant is excreted in milk in lactating rats. It is not known whether fulvestrant is excreted in human milk. Considering the potential for serious adverse reactions due to fulvestrant in breast-fed infants, use during breast-feeding is contraindicated. 3. Woman of childbearing potential : Patients of child-bearing potential should be advised to use effective contraception while on treatment. 4. Fertility : The effects of this medicine on fertility in humans has not been studied **[Overdose]** There are isolated reports of overdose with FASLODEX in humans. If overdose occurs, manage symptomatically. There is no human experience of overdosage. Animal studies suggest that no effects other than those related directly or indirectly to anti-oestrogenic activity were evident with higher doses of fulvestrant. **[Instructions for use and handling and disposal]** Administer the injection according to the local guidelines for performing large volume intramuscular injections. NOTE: Due to the proximity of the underlying sciatic nerve, caution should be taken if administering Faslodex at the dorsogluteal injection site (see Special Warnings and Precautions for Use). Warning - Do not autoclave safety needle (BD SafetyGlide Shielding Hypodermic Needle) before use. Hands must remain behind the needle at all times during use and disposal. For each of the two syringes: 1. Remove glass syringe barrel from tray and check that it is not damaged. 2. Peel open the safety needle (SafetyGlide™) outer packaging. 3. Parenteral solutions must be inspected visually for particulate matter and discolouration prior to administration. 4. Hold the syringe upright on the ribbed part (C). With the other hand, take hold of the cap (A) and carefully tilt back and forth until the cap disconnects and can be pulled off, do not twist (see Figure 1). 5. Remove the cap (A) in a straight upward direction. To maintain sterility do not touch the syringe tip (B) (see Figure 2). 6. Attach the safety needle to the Luer-Lok and Twist until firmly seated (see Figure 3). 7. Check that the needle is locked to the Luer connector before moving out of the vertical plane. 8. Pull shield straight off needle to avoid damaging needle point. 9. Transport filled syringe to point of administration. 10. Remove needle sheath. 11. Expel excess gas from the syringe. 12. Administer intramuscularly slowly(1-2 minutes/injection) into the buttock (gluteal area). For user convenience, the needle bevel-up position is oriented to the lever arm (see Figure 4). 13. After injection, immediately apply a single-finger stroke to the activation assisted lever arm to activate the shielding mechanism (see Figure 5). NOTE: Activate away from self and others. Listen for click and visually confirm needle tip is fully covered. Disposal - Pre filled syringes are for single use only. - Any unused medicinal product or waste material should be disposed of in accordance with local requirements **[Special precautions for storage]** 1. Store at 2°C-8°C (in a refrigerator) Store the pre-filled syringe in the original package in order to protectfrom light. 2. Be cautious since placing in wrong box would be the cause of accident or not be desirable in quality maintenance. **[Others]** 1. This medicine has no or negligible influence on the ability to drive or use machines. However, during treatment with this medicine , asthenia has been reported very commonly. Therefore caution must be observed by those patients who experience this symptom when driving or operating machinery. 2. In the absence of incompatibility studies, this medicinal product must not be mixed with other medicinal products. 3. Combination therapy with palbociclib : See palbociclib prescribing information. **[Shelf life]** : 48 months

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SS04

OPTIMAL TREATMENT STRATEGY FOR ER-POSITIVE, HER2-NEGATIVE MBC - IMPLICATIONS FROM THE CLINICAL TRIAL AND EXPERIENCE

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Endocrine therapy is the mainstay of treatment for patients with estrogen receptor-positive (ER+)/HER2-negative (HER2-) metastatic breast cancer (MBC). Sequential endocrine therapy enables a better treatment life and the maintenance of a better quality of life (QOL) for MBC patients. However there are some primary resistance cases and almost cases developed acquired resistance during long endocrine treatment. Due to overcome resistance, combination therapies with targeting agents as mTOR inhibitor and CDK inhibitors have been developed. In real world, there are different medical environment as approval condition, cover of cost by insurance and government and standard follow up system after primary treatment. I would like to review the optimal treatment strategy for ER-positive, HER2-negative MBC base on clinical trials and Japanese experience in real world.

THE FIRST IN CLASS CDK4/6 INHIBITOR[1]

STRONGER TOGETHER

IBRANCE® is indicated for the treatment of HR-positive, HER2-negative advanced or metastatic breast cancer in combination with[2]

- Letrozole as initial endocrine based therapy in postmenopausal women or
- Fulvestrant in women with disease progression following endocrine therapy

Pre/perimenopausal women treated with the combination IBRANCE® plus endocrine therapy should be treated with luteinizing hormone-releasing hormone (LHRH) agonists according to local clinical practice standards.

IBRANCE® (palbociclib) + Letrozole[3]

mPFS 24.8 months

IBRANCE® (palbociclib) + Fulvestrant[4]

mPFS 9.5 months

Safety Information: Neutropenia was the most frequently reported adverse event in the clinical study and monitoring complete blood count is needed. Please refer to the Product Information for the dose modification related to neutropenia.

Study Design

• PALOMA2 : In double-blind, phase 3 study, patients were randomly assigned, in a 2:1 ratio, 666 postmenopausal women with ER-positive, HER2-negative breast cancer, who had not had prior treatment for advanced disease, to receive palbociclib plus letrozole (n=444) or placebo plus letrozole (n=222). The primary endpoint was progression-free survival, as assessed by the investigators. Secondary endpoints were overall survival, objective response, clinical benefit response, patient-reported outcomes, pharmacokinetic effects, and safety. Adapted from Finn RS, et al. N Engl J Med 2016;375:1925-36.

• PALOMA3 : In multicentre, double-blind, randomised phase 3 study, 521 women with HR-positive, HER2-negative metastatic breast cancer that had progressed on previous endocrine therapy were stratified by sensitivity to previous hormonal therapy, menopausal status, and presence of visceral metastasis. The primary endpoint was investigator-assessed progression-free survival. Secondary endpoints were confirmed objective response, clinical benefit, safety including type, incidence, and severity of adverse events. Adapted from Cristofanilli M, et al. Lancet Oncol 2016;17:425-39.

References 1. Dhillon S. Palbociclib: first global approval. Drugs 2015;75:543-51. **2.** IBRANCE® PRESCRIBING INFORMATION, 2016.08.29. **3.** Finn RS, et al. Palbociclib and letrozole in advanced breast cancer. N Engl J Med 2016;375:1925-36. **4.** Turner NC, et al. Palbociclib + fulvestrant versus placebo + fulvestrant for treatment of hormone-receptor-positive, HER2-negative metastatic breast cancer that progressed on previous endocrine therapy (PALOMA-3): final analysis of the multicentre, double-blind, phase 3 randomised controlled trial. Lancet Oncol 2016;17:425-39.

IBRANCE® Capsules [COMPOSITION] Palbociclib 75 mg, 100 mg, 125 mg **[INDICATIONS]** IBRANCE® is indicated for the treatment of hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer in combination with: • letrozole as initial endocrine based therapy in postmenopausal women, or • fulvestrant in women with disease progression following endocrine therapy **[DOSAGE AND ADMINISTRATION]** The recommended dose of IBRANCE® is a 125 mg capsule taken orally once daily for 21 consecutive days followed by 7 days off treatment to comprise a complete cycle of 28 days. IBRANCE® should be taken with food. When co-administered with palbociclib, the recommended dose of letrozole is 2.5 mg taken once daily continuously throughout the 28-day cycle (Please refer to the registered information of letrozole). When co-administered with palbociclib, the recommended dose of fulvestrant is 500 mg administered on Days 1, 15, 29, and once monthly thereafter (Please refer to the registered information of fulvestrant). Patients should be encouraged to take their dose of IBRANCE® at approximately the same time each day. If the patient vomits or misses a dose, an additional dose should not be taken. The next prescribed dose should be taken at the usual time. IBRANCE® capsules should be swallowed whole (do not chew, crush or open them prior to swallowing). Capsules should not be ingested if they are broken, cracked, or otherwise not intact. Pre/perimenopausal women treated with the combination IBRANCE® plus endocrine therapy should be treated with luteinizing hormone-releasing hormone (LHRH) agonists according to local clinical practice standards. **[PRECAUTIONS FOR USE]** 1. Warnings 1) Neutropenia: Neutropenia was the most frequently reported adverse event in clinical studies. Monitor complete blood counts prior to starting IBRANCE® therapy and at the beginning of each cycle, as well as on Day 14 of the first 2 cycles, and as clinically indicated. Dose interruption, dose reduction or delay in starting treatment cycles is recommended for patients who develop Grade 3 or 4 neutropenia. Febrile neutropenia has been reported in about 1% of patients exposed to IBRANCE®. Physicians should inform patients to promptly report any episodes of fever. 2) Pulmonary Embolism: Monitor patients for signs and symptoms of pulmonary embolism and treat as medically appropriate. 3) Embryo-fetal Toxicity: Based on findings from animal studies and its mechanism of action, IBRANCE® can cause fetal harm when administered to a pregnant woman. In animal reproduction studies, administration of palbociclib to pregnant rats and rabbits during organogenesis resulted in embryo-fetal toxicity at maternal exposures that were ≥4 times the human clinical exposure based on area under the curve (AUC). Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with IBRANCE® and for at least 3 weeks after the last dose. 2. Contraindications 1) Because of lactose contained in this drug, it should not be administered to the patients with hereditary problems of galactose intolerance, Lapp-lactase deficiency or glucose-galactose malabsorption.
[LATEST APPROVED DATE] 2016.08.29. ※For the lately revised product information, please visit www.pfizer.co.kr. For further information about the product, please refer to your local product labeling for full prescribing information.

Pfizer Oncology

IBRANCE™ palbociclib

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SS05

PARADIGM SHIFT IN THE TREATMENT OF ER+/ HER2- MBC: PALBOCILIB IN THE REAL WORLD PRACTICE

Giuseppe Curigliano

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Invited Oral Presentation

GBCC2018
Global Breast Cancer Conference 2018

IOP01

INVASIVE MICROPAPILLARY CARCINOMA OF THE BREAST

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Background: Invasive micropapillary carcinoma (IMPC) of the breast is a histologic subtype of breast cancer associated with high incidence of lymphovascular invasion (LVI), lymph node metastasis (LNM) and poor prognosis. This prospective study was undertook to investigate the impact of precise pathologic diagnosis and individualized treatment on the outcomes of IMPC patients.

Methods: The study group included 2,299 women with IMPC (SgIMPC) out of 39,714 women with invasive breast cancer diagnosed at Tianjin Medical University Cancer Institute and Hospital between January 2004 and December 2015. SgIMPC were prospectively examined with whole serial sections and orientation method (WSSOM), and received precise pathological diagnosis and individualized treatment. The control group IMPC (CgIMPC) consisted of 163 cases, which were selected from 9,056 cases of invasive breast cancer through a retrospectively review of IMPC diagnosed at our institution between January 1989 and December 2003 by routine pathology evaluation (non WSSOM). The clinicopathological features, treatments and outcomes were compared between the two groups.

Result: The incidence of IMPC in SgIMPC group was 5.79% (2,299/39,714), significantly higher than that of CgIMPC group (1.80%; 163/9,056 cases). The 5-year disease free survival (DFS) of SgIMPC wassignificantly higher than that of CgIMPC (83.8% vs.45.4%; $p < 0.05$). The 5-years overall survival (OS) was significantly increased from 57.4% in CgIMPC to 90.9% in SgIMPC ($p < 0.05$). Multivariate analysis proved LVI, estrogen receptor (ER) and LNM to be the independent prognostic indicators for the patients with IMPC.

Conclusions: Although IMPC of breast is associated with poor prognosis, precise pathological diagnosis and individualized treatment improve DFS and OS of patients. Precise pathological diagnosis is the premises for individualized treatments and for improving the outcomes of patients with breast IMPC.

IOP02

NO ASSOCIATION OF POSITIVE SUPERFICIAL AND/OR DEEP MARGINS WITH LOCAL RECURRENCE IN INVASIVE BREAST CANCER TREATED WITH BREAST-CONSERVING SURGERY

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Purpose: We evaluated the effect of positive superficial and/or deep margin status on local recurrence (LR) in invasive breast cancer treated with breast-conserving surgery (BCS) followed by radiotherapy.

Methods: In total, 3,403 stage 1 and 2 invasive breast cancer patients treated with BCS followed by radiotherapy from January 2000 to December 2008 were included in this study. These patients were divided into 3 groups according to margin status: clear resection margin status for all sections (group 1, n = 3,195); positive margin status in superficial and/or deep sections (group 2, n = 121); and positive peripheral parenchymal margin regardless of superficial and/or deep margin involvement (group 3, n = 87). The LR-free survival between these 3 groups was compared and the prognostic role of margin status was analyzed.

Result: Across all groups, age, tumor size, nodal status, and human epidermal growth factor receptor 2 status did not significantly differ. High grade, positive extensive intraductal component, hormone receptor positivity, hormone therapy received, and chemotherapy not received were more prevalent in groups 2 and 3 than in group 1. Five-year LR rates in groups 1, 2, and 3 were 1.9%, 1.7%, and 7.7%, respectively. Multivariate analysis revealed that group 3 was a significant predictor for LR (hazard ratio (HR) = 4.78, $p < 0.001$), but that positive superficial and/or deep margin was not (HR = 0.66, $p = 0.57$).

Conclusions: Superficial and/or deep margin involvement following BCS is not an important predictor for LR.

IOP03

IMAGING BIOMARKER FOR MOLECULAR ONCOLOGY: FOCUSING ON HER2 EVALUATION

Ilhan Lim

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The need for the imaging agents that verify the presence and levels of molecular biomarkers in malignant tumors is increasing in the field of oncology. This new imaging technology, referred to as molecular imaging, may supply crucial data for the selection of appropriate targeted therapies, play a role in reassessing disease status, and be used to monitor treatment response. The imaging biomarker has many advantages in terms of non invasiveness, global assessment, the assessment of protein expression, the evaluation of drug accessibility.

There are 2 types of imaging biomarker. One is a marker for evaluating the protein expression, another is a marker for analyzing tumor characteristics.

When it comes to the evaluation of the protein expression, clinicians hope to utilize the imaging biomarker for estimating HER2 expression and the hormone expression in case of breast cancer. Cu-64 DOTA-trastuzumab, Zr-89-trastuzumab has been developed for evaluating the HER2 status. These radiolabelled monoclonal antibodies can visualize the HER2 expression in each site of lesions. Moreover, this technology might predict the success probability of antibody based treatment such as T-DM1, pertuzumab, radioimmunotherapy because they can provide the information of body distribution.

Recently we started to perform clinical trial of evaluating HER2 expression using Cu-64 DOTA-trastuzumab. During this trial, we found out that imaging HER2 expression can be applied for patients as non-invasive tool. For example, a patient with rising serum HER2 underwent F-18 FDG PET/CT and this scan showed multiple FDG uptakes in retroperitoneal lymph nodes. She also had the history of nontuberculous mycobacteria. From the Cu-64 DOTA-trastuzumab, there are multiple uptakes in retroperitoneal lymph nodes and we made a decision of treating the patient with trastuzumab without further invasive procedure such as laparoscopic biopsy. Another patient revealed multiple mediastinal lymph nodes from FDG PET/CT during the trastuzumab treatment. The Cu-64 DOTA-trastuzumab displayed slight or minimal uptakes in mediastinal lymph node and we decided to change the treatment although biopsy demonstrated HER2 strong positivity. In spite of the limited number of cases, we realized that imaging biomarker can be employed in practice for the assessment of HER2 expression.

F-18 fluoroestradiol (F-18 FES), an estradiol analogue, has been applied to evaluate the expression and the binding capacity of estrogen receptor in breast cancer. This technique might decrease the number of biopsies during the evaluation of breast cancer recurrence. Similarly, it will be helpful for practice to develop the imaging assessment of HER2 status.

Regarding analysis of tumor characteristics, PET/CT and MRI are widely employed using diverse functional parameters. In one study performed in HER2 positive patients with neoadjuvant treatment, early (2 weeks) PET/CT metabolic response distinguished pathologic complete response after surgery. Another study revealed the potential to predict prognosis using functional parameters. In this study, functional parameters of both FDG PET and MRI after the first cycle of neoadjuvant chemotherapy are useful for predicting disease free survival (DFS) in patients with advanced breast cancer. The researchers found out that combination of PET parameter and MRI parameters showed a significantly higher recurrence rate (77.8%) than the remaining of patients (13.3%, $p < 0.0001$) (hazard ratio 9.91, 95% confidence interval (CI). 1.68 – 58.3, $p < 0.0001$).

This presentation will summarize studies which have showed the usefulness of imaging biomarker with respect toanalyzing tumor characteristics and evaluating the protein expressionin breast cancer. These results strongly indicate that imaging biomarker may play an important role for personalized and precision medicine in the near future.

IOP04

A PHASE II TRIAL OF PAN-HER INHIBITOR POZIOTINIB, IN PATIENTS WITH HER2-POSITIVE METASTATIC BREAST CANCER WHO HAVE RECEIVED AT LEAST TWO PRIOR HER2

Yeon Hee Park[1], Kyung-Hun Lee[2], Joohyuk Sohn[3], Keun Seok Lee[4], Kyung Hae Jung[5], Jee Hyun Kim[6], Ki Hyeong Lee[7], Jin Seok Ahn[1], Tae-Yong Kim[2], Gun Min Kim[3], In Hae Park[4], Sung-Bae Kim[5], Se Hyun Kim[6], Hye Sook Han[7], Young-Hyuck Im[1], Jin-Hee Ahn[5], Jung-Yong Kim[8], Jahoon Kang[9], Seock-Ah Im[2]

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Background: Although the introduction of HER2 directed therapy including trastuzumab, pertuzumab, lapatinib, and TDM-1 in the treatment of HER2-positive metastatic breast cancer (mBC) patients favorably changed the natural history of this disease, HER2-positive mBC will eventually progress i n most patients. Poziotinib is a novel, oral pan-HER kinase inhibitor which showed potent anti-tumor activities through irreversible inhibition of HER family tyrosine kinases.

Methods: This open-label, multicenter phase 2 study was designed to evaluate the efficacy and safety of poziotinib monotherapy in patients with HER2-positive mBC who have progressed from more than 2 HER2-directed therapies. Patients received poziotinib 12 mg once daily on a 14-day on/7-day off schedule. Dose escalation up to 16 mg was allowed at appropriate time point and dose reduction to 8-10 mg were performed according to toxicities. Progression-free survival (PFS) as the primary endpoint and objective response rate (ORR), overall survival (OS), and safety were evaluated.

Result: From Apr 2015 to Feb 2016, 106 patients were enrolled in the trial from 7 institutes in Korea. The patients were median age of 50 (range: 30–76) who had received median 4 prior anti-cancer therapies including median 2 HER2-directed therapies in the advanced or metastatic setting. Median follow up duration was 12 months. The median PFS was 4.04 months (95% CI,

2.94–4.40 months), and median overall survival has not been reached. The disease control rate was 75.49% (77/102) including 20 patients with confirmed partial response. The most common treatment-related AEs were (total/grade ≥ 3) diarrhea (96.23%/14.15%), stomatitis (92.45%/12.26%), and rash (63.21%/3.77%).

Conclusions: Poziotinib showed meaningful clinical activity in heavily-treated HER2-positive mBCs. Diarrhea and stomatitis were the major toxicities leading to dose modification. Biomarker study being analyzed from pre- and on-treatment biopsies is warranted to support further on the meaningful clinical outcomes of poziotinib in HER2-positive mBC.

IOP05

RIBOCICLIB PLUS GOSERELIN AND TAMOXIFEN OR A NON-STEROIDAL AROMATASE INHIBITOR (NSAI) FOR PREMENOPAUSAL WOMEN WITH HORMONE RECEPTOR-POSITIVE (HR+), HUMAN EPIDERMAL GROWTH FACTOR RECEPTOR 2-NEGATIVE (HER2−) ADVANCED BREAST CANCER (ABC) IN THE RANDOMIZED PHASE III MONALEESA-7 TRIAL

Seock-Ah Im[1], Joohyuk Sohn[2], Debu Tripathy[3], Louis Chow[4], Marco Colleoni[5], Fabio Franke[6], Aditya Bardia[7], Nadia Harbeck[8], Sara Hurvitz[9], Keun Seok Lee[10], Kyung Hae Jung[11], Young-Hyuck Im[12], Nagi El Saghir[13], Mei-Ching Liu[14], Melissa Tripodi[15], Rahul Tyagi[15], Gareth Hughes[16], Michelle Miller[15], Yen-Shen Lu[17]

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Background: In the MONALEESA-2 study, ribociclib (cyclin-dependent kinase inhibitor) + letrozole significantly prolonged progression-free survival (PFS) vs. letrozole alone in postmenopausal women with HR+, HER2– ABC. Here we report results from MONALEESA-7 (NCT02278120), the first Phase III trial evaluating ribociclib + tamoxifen/NSAI and goserelin specifically in premenopausal patients.

Methods: Pre- or peri-menopausal women (N = 672) with HR+, HER2– ABC with no prior endocrine therapy (ET) and ≤ 1 line of prior chemotherapy for ABC were randomized 1:1 to ribociclib (600 mg/day, 3-weeks-on/1-week-off) or placebo + tamoxifen (20 mg/day) or an

NSAI (letrozole [2.5 mg/day] or anastrozole [1 mg/day]) and goserelin (3.6 mg every 28 days). The primary endpoint was locally assessed PFS.

Result: At the primary analysis, PFS was significantly improved in the ribociclib arm (median PFS: 23.8 months) vs. the placebo arm (median PFS: 13.0 months), with a hazard ratio of 0.553 (95% CI: 0.441–0.694; $p = 9.83 \times 10^{-8}$). Subgroup analyses demonstrated consistent PFS benefits for ribociclib vs. placebo, including patients treated in Asia (hazard ratio: 0.419; 95% CI: 0.266–0.659). All-grade adverse events (≥ 25% patients; ribociclib vs. placebo) were: neutropenia (76% vs. 8%), hot flush (34% vs. 34%), nausea (32% vs. 20%), leukopenia (31% vs. 6%), arthralgia (30% vs. 27%). Of these, neutropenia (61% vs. 4%) and leukopenia (14% vs. 1%) were the only Grade 3/4 events reported in ≥ 5% of patients (ribociclib vs. placebo).

Conclusions: Addition of ribociclib to first-line ET (tamoxifen/NSAI + goserelin) significantly prolonged PFS and had a manageable safety profile in premenopausal women with HR+, HER2– ABC.

IOP06

DIFFERENT PROGNOSIS OF YOUNG BREAST CANCER PATIENTS IN THEIR 20S AND 30S DEPENDING ON SUBTYPE: A NATIONWIDE STUDY FROM THE KOREAN BREAST CANCER SOCIETY

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Purpose: Numerous studies have demonstrated that breast cancer in young women (BCY) has unfavorable prognostic features and more unfavorable subtypes. However, few studies have evaluated the effect of subtype disparities on breast cancer prognosis by age, especially for BCY. We analyzed breast cancer mortality stratified by tumor subtype according to age among patients younger than 50 years.

Methods: Data from the Korean Breast Cancer Society Registry for patients diagnosed with invasive breast cancer when aged less than 50 years between 2003 and 2010 were reviewed retrospectively.

Result: We identified 30,793 patients with breast cancer who were eligible for analysis. Of these, 793 (2.6%) were aged 20-29 and 8926 (28.8%) were aged 30-39. Median follow-up duration was 84 months. Mean age was 42.4 years. Patients in their 20s were more likely to have cancer of advanced stage and higher nuclear grade, present with lymphovascular invasion, and have unfavorable subtypes. Patients in the 20s group showed worse prognosis. In multivariate analysis for overall survival (OS), the hazard ratio (HR) for patients in the 20s group was higher than that for the 30s and 40s groups, and patients with triple-negative breast cancer (TNBC) showed higher HR than patients with HER-2 or luminal subtype (all $p < 0.0001$). When stratified by subtype, luminal subtype showed significantly worse prognosis in the 20s group than the 30s and 40s groups, whereas HER-2 and TNBC subtypes showed no significant difference.

Conclusions: Patients in their 20s with breast cancer had unfavorable characteristics and worse prognosis than patients in their 30s and 40s. When stratified by tumor subtype, patients in their 20s with luminal subtype of breast cancer showed worse prognosis than older patients, whereas HER-2 and TNBC subtypes showed no significant differences.

Oral Presentation

GBCC2018

Global Breast Cancer Conference 2018

OP01-1

DEAD-BOX RNA HELICASE DP103 ENHANCES YAP SUMOYLATION FOR YAP-TEAD DEPENDENCE AND STATIN SENSITIVITY IN TRIPLE NEGATIVE BREAST CANCER

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Background: Simvastatin, a lipophilic statin used for lowering cholesterol, inhibits 3-hydroxy-3-methylglutaryl-CoA reductase (HMGCR), the key enzyme of the mevalonate pathway. Studies have shown that cancer cells express deregulated level of HMGCR and statins exert anti-tumoral activities.

Methods: We first assessed correlation between mevalonate pathway genes and DDX20 (DP103, Gemin-3) in 1325 breast cancer patients and observed a positive correlation between DDX20 and the mevalonate pathway genes. Having this data, we then proceeded to explore the effect of statins on DDX20 expression. We used various in vitro cell lines and in vivo statin clinical trial patients specimens, mouse xenograft, mouse intravenous tail injection and Drosophila (wild-type vs. Gemin-3 knockdown vs. Gemin-3 overexpression flies) models.

Result: We show exposure to statin decreases the expression of DDX20. Through a series of add-back experiments, we show that the decrease in DDX20 expression by statins is via the mevalonate pathway and downstream of RhoA. In clinical specimens, we observed breast cancer patients with high baseline DDX20 positively correlates with high baseline YAP-TEAD expression. Having known that SUMOylation of YAP maintains its activity and that DDX20 is a critical enhancer of the SUMOlyation machinery, we showed through a series of experiments that a physical interaction between DDX20 and YAP is crucial for maintaining SUMOylation of YAP; thereby decreasing its ubiquitination and degradation.

Conclusions: Interestingly, we also identified for the first time that DDX20 is a direct target of YAP-TEAD complex and that maintenance of DDX20 expression is needed as a positive feedback forming an Achilles heel for sustained YAP-TEAD activity.

OP01-2

RESVERATROL SUPPRESSES BREAST CANCER PROLIFERATION THROUGH INHIBITION OF STAT3 ACTIVATION AND M2-MACROPHAGE POLARIZATION

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Background: Tumor-associated macrophages (TAM), M1 and M2 macrophages, are the most abundant leukocyte population that play critical role in breast cancer progression. M1 macrophages inhibit tumor growth while M2 macrophages enhance tumor progression. Resveratrol, a naturally occurring polyphenolic compound, is well known for its antitumor effect by targeting several cancer-related inflammatory pathways. This study aimed to investigate the effect of resveratrol on TAM polarization in breast cancer progression.

Methods: The antitumor effect of resveratrol was examined in MDA-MB-231(MB231) and cisplatin resistance MDA-MB-231 (cisR) cells by cell proliferation assay using MTT. Gene expressions of M1 and M2 markers in macrophages derived from THP-1 cells, treated with tumor-conditioned medium (TCM) with or without resveratrol, were examined by qPCR and immunofluorescence (IF) staining. Cytokine profile of TCM was examined by Qiagen Multi-Analyte ELISArray and expression of cytokines in TCM was validated by qPCR. Expression of potential downstream targets of resveratrol were examined by western blot analysis.

Result: Resveratrol significantly reduced cell proliferation and enhanced chemosensitivity in MB231 and cisR cells. Resveratrol inhibited CD163 (M2 marker) and increased CXCL10 and iNOS (M1 marker) expression. Downregulation of ARG1 (M2 marker) was also observed by IF staining. In addition, resveratrol decreased exogenous IL-1A and IL-6 levels in TCM. Moreover, resveratrol significantly decreased phosphorylation of STAT3 in cells.

Conclusions: Our data demonstrated that resveratrol suppressed breast cancer cell proliferation by inhibiting M2-macrophage polarization and STAT3 activation through reducing the secretion of IL-1A and IL-6. This study revealed a novel mechanism on resveratrol-mediated macrophage polarization on breast cancer progression.

Oral Presentation

OP01-3

ESTROGEN RECEPTOR POSITIVE IS NOT ENOUGH TO PREDICT THE PROGNOSIS OF BREAST CANCER

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Background: Since 2018, ER status incorporated in the 8th AJCC staging. ER positive breast cancer is expected to be down-staged. We analyzed characteristics and prognosis, and examined a molecular prognostic signature according to ER status.

Methods: A retrospective review was conducted women with invasive breast cancer between 2003 and 2012. ER negative (group I), ER weakly positive (group II), and ER strong positive (group III) is defined as Allred score 0-2, 3-5, and 6-8. We examined a BCT score which is a new developed prognostic model for predicting the risk of distant metastasis in patients with pN0-N1, HR+/HER2-, in an independent cohort.

Result: Overall, 4,949 patients were enrolled; 1,310 (26.5%), 361 (7.3%), and 3,277 (66.2%) patients were categorized group I, II and III. Median F/U duration was 57.8 mo. Compare to patients in group I, less patients underwent CTx (84% vs. 78%, $p < 0.0001$) and RTx (74% vs. 69%, $p < 0.0001$) in group II. OS, BCSS, DFS, and DMFS are significant difference among three groups (all $p < 0.001$). In the univariate analysis, patients in group II are significantly worse OS than group III (HR, 2.051; 95% CI, 1.202–3.500). Additional adjust factors, HR for OS showed worse in group II/I than group III. The baseline median BCT score showed lower risk score and more likely to have lower risk group according to ER status.

Conclusions: The level of ER status could affect the prognosis of breast cancer. We should not underestimate especially, ER weakly positive breast cancer.

OP01-4

CLINICOPATHOLOGICAL FACTORS AFFECTING DISTANT METASTASIS IN LOCOREGIONAL RECURRENCE OF BREAST CANCER

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ASAN Medical Center, Korea

Background: The purpose of this study is to investigate which clinicopathological factors affect the distant metastasis (DM) in patients with locoregional recurrence (LRR) of breast cancer.

Methods: We reviewed the medical data of 495 patients with locoregional recurrence after curative surgery for breast cancer in Asan medical center between 1990 and 2008. Kaplan-Meier curves and the Cox regression method were used to analyze the correlation between clinical factors and survival.

Result: DM occured in 44.4% (220/495) of all LRR patients and in 38.0% (93/245) of patients with local recurrence and in 50.8% (127/250) of patients in regional recurrence each other. Some clinical factors were associated with DM in univariate analysis, including the type of primary surgery ($p = 0.005$), tumor size ($p = 0.001$), nodal status ($p < 0.001$), administration of initial adjuvant chemotherapy ($p = 0.002$) and disease free interval ≤ 24 months ($p < 0.001$). In multivariate analysis of DM-free survival, both shorter DFI ($p = 0.007$) and higher pathologic node stage ($p = 0.002$) showed poor outcome.

Conclusions: Disease free interval and pathologic node stage is the most important prognostic factors associated with distant metastasis in locoregional recurrence in breast cancer patients.

OP01-5

ULTRASOUND-GUIDED RESTAGING AND LOCALIZATION OF AXILLARY LYMPH NODES AFTER NEOADJUVANT CHEMOTHERAPY FOR GUIDANCE OF AXILLARY SURGERY IN BREAST CANCER PATIENTS: EXPERIENCE WITH ACTIVATED CHARCOAL

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Background: To review our experience with ultrasound (US)-guided localization of axillary lymph nodes using activated charcoal for the guidance of axillary surgery after neoadjuvant chemotherapy (NAC) in clinically node-positive breast cancer patients.

Methods: Between April 2016 and April 2017, US-guided localization of the most suspicious axillary lymph nodes at restaging US with activated charcoal (Charcotrace™) was performed in 45 consecutive, clinically node-positive breast cancer patients who had less than two suspicious nodes after NAC and axillary surgery with sentinel node biopsy. Sentinel nodes were defined as radioactive node or nodes containing blue dye. The concordance between and final pathological results for the tattooed nodes and sentinel nodes were analyzed.

Result: The sentinel node biopsy failed in five patients (11%), in whom axillary surgery was performed under the guidance of the tattooed node. The tattooed nodes were identified in the surgical field in 44 patients (98%). Of the 44 tattooed nodes, 25 nodes (57%) were concordant with the sentinel nodes and 19 nodes (43%) were non-sentinel nodes, including the five nodes with failed sentinel node biopsy. In the final pathological results, 18 patients (40%) had metastatic nodes. The sensitivities for detecting axillary metastasis of the sentinel node biopsy, tattooed node biopsy, and the sentinel and/or tattooed node biopsy were 61% (11/18), 67% (12/18), and 78% (14/18), respectively.

Conclusions: US-guided localization of axillary lymph nodes with activated charcoal at restaging after NAC in clinically node-positive breast cancer patients is a useful technique to guide axillary surgery, with a high identification rate.

OP01-6

APPLICATION OF ROBOTIC SURGERY (DA VINCI) IN THE MANAGEMENT OF BREAST CANCER- PRELIMINARY RESULTS AND EXPERIENCE SHARING

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Background: The experience and preliminary results of robotic surgery in the management of breast cancer was reported in current study.

Methods: The medical records of patients who underwent robotic surgery for breast cancer during the period March 2017 to December 2017 were collected from single institution. Data on clinicopathologic characteristics, type of surgery, method of breast reconstruction, complications and recurrence were analyzed to determine the effectiveness and oncologic safety of robotic breast surgery.

Result: Twenty-five robotic breast surgery procedures were performed in 23 female patients with breast cancer, including 2 patients with bilateral disease. Among these 25 robotic breast procedures, 23 was robotic nipple sparing mastectomy (R-NSM) related. One patient with bilateral breast cancer received bilateral R-NSM without breast reconstruction. The other 21 R-NSM were associated with immediate breast reconstruction (IBR). Two patients received R-NSM and IBR with robotic assisted harvested of latissimus dorsi flap, and 19 patients received R-NSM and IBR with Gel implant. The mean operation time for R-NSM with IBR was 324.5 ± 93.2 mins (225-505). No major peri-operative complication was found. Two (8%) patients suffered from transient partial nipple ischemia change, which was received after conservative treatment. No (0%) total nipple areolar complex necrosis case was observed. No local recurrence, distant metastasis or case mortality was found during mean 6 ± 2 months follow-up.

Conclusions: From our preliminary experience, R-NSM alone or combined with IBR is a safe procedure, with good cosmetic results, and cloud be a promising new technique for breast cancer patients indicated for mastectomy.

OP01-7

CHARACTERIZATION OF THE MICROBIOME OF BREAST TISSUE AND GUT IN KOREAN BREAST CANCER PATIENTS

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Background: The important roles of human microbiome in human health have been reported. Furthermore, recent studies have been reported the presence of microbiome within the mammary tissue as well as within the gut. However, the precise roles of microbiome in breast tissue and gut on human diseases including breast cancer is still unknown. Furthermore there are no studies that investigate the microbiome of breast tissue in Asian woman. Therefore, we investigated the microbial community in breast tissue and gut in 15 breast cancer patients.

Methods: We analyzed the breast tissue from 15 breast cancer patients and analyzed the stool from 15 breast cancer patients and 15 age and BMI-matched healthy control women in Korea. Bacterial community analysis was performed by using 16s rRNA sequencing method.

Result: The most abundant phylum was Proteobacteria in breast tissue and Firmicutes in stool samples of cancer patients. Higher prevalence of Firmicutes and Lactobacillus levels and lower prevalence of Bacteroidetes in breast tissue were related with higher stage of breast cancer. When compared with healthy control, Firmicutes and Lactobacillus levels were higher and Bacteroidetes and Provotella levels were lower in breast cancer group. Additionally, bacterial groups of control group showed higher diversity.

Conclusions: This study showed the characteristics of microbiome in breast tissue and gut of Korean female breast cancer patients. Further large-scaled studies should be performed to elucidate the precise roles of microbiome in breast cancer. This work was supported by Korea Breast Cancer Foundation.

OP01-8

PREDICTING THE RISK OF PERIPHERAL NEUROPATHY BY THE COMBINATION OF FOUR SERUM MICRORNAS

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Background: MicroRNA (miRNAs) has been recently reported that it is useful in diagnosis of cancer. However, the relation with peripheral neuropathy as adverse events of chemotherapy has not yet been reported.

Methods: Serum samples of patients with breast cancer who have received paclitaxel as neoadjuvant or adjuvant chemotherapy (n = 84) between January 2011 and September 2013 in National Cancer Center Hospital were obtained. A comprehensive quantitative expression analysis of miRNA was performed using DNA chip 3D-Gene (Toray Industries Inc.) Clinical data was retrieved from medical records. Grading of peripheral neuropathy was assessed by the investigator and confirmed by the other medical oncologists according to CTCAE version 4.0.

Result: Of 84 patients who received paclitaxel, 25 received neoadjuvant, and 59 received adjuvant chemotherapy. Median age of the patients was 50 years (range 27–74). Thirty eight of the patients had peripheral neuropathy over grade 2, and 46 of them had under grade 1. The serum samples before treatment were randomly divided to training set and test set (2:1). Three formulas with combination of four miRNAs were found to be able to predict peripheral neuropathy (PNmiR sets). PNmiR sets had a sensitivity, specificity and accuracy over 75% in the test cohort. It should be noted that one of the four miRNAs, which constructs two of the three formulas, represents the drug-transporter protein P-glycoprotein, potentially promoting paclitaxel resistance.

Conclusions: The combination of four miRNAs (PNmiR set) measured from serum can be used to predict peripheral neuropathy by paclitaxel-contained chemotherapy. One of the potential miRNAs suggests the relation with metabolism of paclitaxel.

OP02-1

EFFICACY AND SAFETY OF ACUPUNCTURE FOR THE HOT FLASHES IN BREAST CANCER PATIENTS TAKING ADJUVANT TAMOXIFEN: A MULTICENTER STUDY IN KOREAN WOMEN

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Background: Tamoxifen is widely used in premenopausal patients with estrogen receptor positive breast cancer. Among the side-effects of tamoxifen, hot flashes is a challenging one. Previous pilot study suggested the effectiveness of acupuncture for relief of symptoms. This study was performed to evaluate the efficacy and safety of acupuncture for treatment of hot flashes in Korean women breast cancer patients taking tamoxifen as adjuvant endocrine therapy.

Methods: Thirty breast cancer patients taking adjuvant tamoxifen and reported moderate to severe hot flashes were enrolled from two institutes. Patients were randomly assigned into acupuncture group (n = 15) and control group (n = 15). The acupuncture group received acupuncture 3 times a week for 4 consecutive weeks, at 5 predefined points. Control group received no treatment. The score of hot flash visual analogue scale (VAS) and total hot flash score, EORTC QLQ-C30 and QLQ-BR 23 questionnaire were recorded before treatment, once every treatment week and 4 weeks after treatment for both groups.

Result: Acupuncture group showed significantly reduced severity of hot flashes during treatment assessed with either VAS and total hot flash score ($p < 0.001$ and $p = 0.008$, respectively). Also, acupuncture group showed improvement of global health status and physical functioning score assessed with EORTC QLQ-C30 ($p = 0.004$ and $p = 0.027$, respectively). Four weeks after the treatment, these trends were retained. No adverse events were notified

Conclusions: Acupuncture may have feasibility and safety for alleviate hot flashes of Korean women breast cancer patients taking tamoxifen as adjuvant endocrine therapy. Long-term follow up results and further study with a larger sample size is required.

OP02-2

CANASSIST-BREAST: A COST-EFFECTIVE MORPHOMETRIC IMMUNOHISTOCHEMISTRY TEST FOR PROGNOSTIC RISK STRATIFICATION OF EARLY STAGE ESTROGEN RECEPTOR POSITIVE BREAST CANCER PATIENTS

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Background: Assessment of risk of recurrence in ER+ breast cancer patients based on clinical parameters and existing biomarkers is insufficient, and majority of patients in Asia are treated with chemotherapy.We focused our efforts on developing a cost-effective predictive test which will: i) accurately estimate the risk of recurrence for ii) a broader (node - & +) set of patients.

Methods: Using a retrospective training cohort of 300 node and node+ patients, we developed CanAssist-Breast(CAB)- a Morphometric Immunohistochemistry based test comprising 5 biomarkers plus three clinical parameters (Tumor size, node status and grade) to arrive at a CAB Score. The risk stratification model was developed using SVM based machine learning technology and classifies patients into low- or high-risk for recurrence.

Result: Using a retrospective training cohort of 300 node and node+ patients, we developed CanAssist-Breast(CAB)- a Morphometric Immunohistochemistry based test comprising 5 biomarkers plus three clinical parameters (Tumor size, node status and grade) to arrive at a CAB Score. The risk stratification model was developed using SVM based machine learning technology and classifies patients into low- or high-risk for recurrence.

Conclusions: We have developed and validated CAB- a cost-effective IHC based risk stratifier for ER+ breast cancer.

OP02-3

FEASIBILITY OF PREOPERATIVE AXILLARY LYMPH NODE MARKING WITH A CLIP IN BREAST CANCER PATIENTS BEFORE NEOADJUVANT CHEMOTHERAPY: A PRELIMINARY STUDY

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Background: The aim of this study was to determine the feasibility of image-guided marker-clip placement in axillary lymph nodes (ALNs) for breast cancer upon initial presentation and to assess the reliability of this method with sentinel lymph node biopsy (SLNB) for axillary re-staging after neoadjuvant chemotherapy (NAC).

Methods: Between June 2015 and August 2016, a marker clip was placed at a clinically positive ALN under ultrasonography (US) guidance before initiation of NAC in 20 patients. Preoperative localization of marker-clipped LNs was performed, and the localized LNs were removed by SLNB. We compared the postoperative results of the marker-clipped LNs, SLNs and ALNs.

Result: Image-guided marker-clip placements and localization of marker-clipped LNs were performed successfully in 20 patients. A total of 24 marker clips were inserted, and 23 marker-clipped LNs were successfully retrieved during surgery (identification rate, 23/24, 95.8%). In the 11 patients with pathologically confirmed metastatic marker-clipped LNs, 4 became negative after NAC, and 7 maintained metastatic residues on the marker-clipped LNs. Three of the 7 patients had metastatic residues on the ALNs, and 2 of the 7 had negative SLNs. Marker-clipped nodes accurately predicted the axillary nodal status in these 2 patients compared with SLNs alone.

Conclusions: Image-guided marker-clip placement on positive ALNs before NAC and removal with SLNB is technically feasible. This technique can improve the accuracy of the residual disease evaluation on the axilla, especially in patients with negative SLNB results, and can identify candidates for limited axillary surgery after NAC.

OP02-4

EVOLVING INDICATIONS AND LONG TERM ONCOLOGIC OUTCOMES OF RISK REDUCING BILATERAL NIPPLE SPARING MASTECTOMY

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Background: Bilateral nipple sparing mastectomy (BNSM) is a technically feasible operation and is associated with excellent cosmetic outcomes. We evaluated the trends, indications, and long term outcomes of BNSM for breast cancer (BC) risk reduction.

Methods: We performed a retrospective review of our experience with BNSM for BC risk reduction in patients without BC (2001-2017). Trends were evaluated for 4 time periods: (1) 2001-2005; (2) 2006-2009; (3) 2010-2013; (4) 2014-2017. Statistical analysis performed using Kruskal Wallis and Chi-Square. $p < 0.05$ was significant.

Result: Two hundred seventy two NSMs were performed; mean age = 40 years. The number of BNSM increased time (1, n = 24; 2, n = 34; 3, n = 82; 4, n = 132). The most common indication was a mutation in a BC associated gene (n = 104, 76%) which included (BRCA1 [n = 62], BRCA2 [n = 35], PTEN [n = 2], TP53 [n = 3], ATM [n = 2]). Other indications were family history of BC (n = 19, 14%); LCIS (n = 10, 7%); and history of mantle radiation (n = 3, 3%). The % of patients having BNSM for a mutation in a BC associated gene increased over time (1, 17%; 2, 53%; 3, 83%; 4, 92%) ($p < 0.01$). Mean f/u for the patients was 53 months. No BCs have developed among these patients.

Conclusions: Use of BNSM for BC risk reduction is increasing and the indications of BNSM for BC risk reduction have evolved over the last 16 years. Most patients now have risk reducing BNSM for a mutation in a BC associated gene. These excellent long term oncologic results suggest that risk reducing BNSM should be the gold-standard for surgical BC risk reduction.

OP02-5

ADDED VALUE OF DOPPLER US AND ELASTOGRAPHY PRIOR TO PERCUTANEOUS BIOPSY TO IDENTIFY CANDIDATES FOR AVOIDANCE OF SURGERY IN BREAST CANCER PATIENTS FOLLOWING NEOADJUVANT SYSTEMIC THERAPY

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Background: We prospectively evaluated added value of Doppler US and elastography prior to percutaneous biopsy to identify candidates for avoidance of surgery in breast cancer patients following neoadjuvant systemic chemotherapy (NST).

Methods: Between September 2016 and December 2017, 32 breast cancer patients (median age, 50 years; range, 32–67 years) who showed high possibility of pathologic complete response (pCR), defined as lesion size ≤0.5 cm or lesion-to-background parenchymal signal enhancement ratio ≤1.6 on preoperative MRI, and underwent Doppler US and elastography examinations were prospectively enrolled. On the morning of surgery, all women underwent US-guided percutaneous needle biopsy for tumor bed. In the prediction of pCR, the negative predictive value (NPV) of MR images, that of percutaneous biopsy, and added value of Doppler US and elastography were evaluated.

Result: After surgery, nine women showed residual invasive cancers (1 ILC, 2 DCIS, 6 IDC) and 23 women showed pCR. Addition of percutaneous biopsy improved NPV from 72% (23/32) to 92% (23/25) ($p=0.06$). Two women with false-negative biopsy results had 0.3 cm and 0.2 cm residual DCIS, respectively. One showed positive vascularity and soft elastography and the other showed no vascularity but positive elasticity for tumor bed. If the candidates showing positive Doppler US or elastography prior to biopsy were more thoroughly sampled during biopsy procedure, the false negative results might have been reduced.

Conclusions: Addition of Doppler US and elastography prior to percutaneous biopsy have the potential to reduce false negative results to identify candidates for avoidance of surgery in breast cancer patients following NST.

OP02-6

A PILOT STUDY OF SENTIMAG/SIENNA XP AND THE STANDARD MODALITY FOR SENTINEL LYMPH NODE IDENTIFICATION IN PATIENTS WITH BREAST CANCER

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Background: Sentinel lymph node biopsy (SLNB) is the standard surgical procedure for the axilla in early node-negative breast cancer. The current standard of care for SLNB is the technique of using radiotracer 99m Tc with or without blue dye. The aim of the study is to evaluate Sienna XP, the new magnetic technique for SLNB against the standard use of radiotracer and/or blue dye.

Methods: A total of 20 women with clinically and radiologically node negative early unilateral breast cancer were recruited from a single centre. SLNB was undertaken after administration of both the magnetic and standard tracer (radioisotope or blue dye).

Result: The sentinel node identification rate was 95% (19 of 20) for the standard technique versus 100% (20 of 20) for the magnetic technique. We detected 56 SLNs in 20 patients using both Sienna XP and standard techniques. 55 SLNs were identified by the SentiMag technique, and 40 SLNs were identified by standard technique. SentiMag identified an average of 2.8 nodes per patient while the standard technique identified 2 nodes per patient. Of 30% (6 of 20) of patients with lymph node involvement, 25% (5 of 20) had at least 1 macrometastases-of these 5 patients, 3 were identified with both the magnetic and standard techniques, while 2 patients were identified by only the SentiMag technique.

Conclusions: This prospective clinical study from our centre is the first study done in Asia, which provides convincing results that magnetic SLNB can be performed easily, safely and equivalently well in comparison to the standard technique .

OP02-7

EXPERIENCE OF USING HIGH-INTENSITY FOCUSED ULTRASOUND ABLATION (HIFU) IN THE TREATMENT OF BENIGN TUMORS OF THE MAMMARY GLANDS

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Background: Fibroadenoma is one of the most common breast conditions representing the largest part of all benign tumors. Traditional invasive surgeries have disadvantages, such as skin damage and related recurrences and complications. Therefore, it is important to develop new non-invasive techniques and compare them with conventional surgical technique in order to propose effective fibroadenoma treatment

Methods: The study involved 80 patients with breast fibroadenomas, 40 patients of which were treated with HIFU (main group) and others were treated surgically (control). All patients underwent core and aspiration biopsy, breast sonography and mammography to diagnose localized breast fibroadenomas. Next, we carried out morphocytological study to categorize fibroadenoma as intracanalicular, pericanalicular or mixed. We used Model-JC Focused Ultrasound Tumor Therapeutic System (Chongqing Haifu Medical Technology Co. Ltd., China) equipment with 1 MHz frequency, 21.5 cm lens diameter and 16.2 focused distance for HIFU treatment. For comparison analysis, the results of morphological investigation (cytological analysis, aspiration biopsy and electronical microscopy) and breast ultrasonography were subject to statistical analysis with software STATISTICA 6.1 and IBMSPSS v.18. To study the power effect of ablation, we conducted in vitro investigations with 3 circular cross-sections of breast fibroadenomas ablated by HIFU with 100 W, 200 W, 300 W. One cross-section was used as a reference and was not ablated. All of them were analyzed during morphocytological study. For comparison purposes, both main and control groups were surveyed by Questionnaire SF-36 checking physical functioning, level of pain, overall well-being, livability, social functioning, emotional state and mental health

Result: No postoperative complications were observed in the main group, whereas 8 cases (20%) of postoperative complications (hematoma, infiltration, suppuration) were recorded in the control group. In addition, recurrences after 12–18 months were revealed in 5 patients (13%) of the control group with zero recurrence in the main group. Also, the duration of inpatient stay was decreased by 52% in the HIFU treated patients, at 3.90 days, as opposed to 7.47 days for the surgically treated group. Power ablation investigations show that 100 W ablation

created initial changes related to coagulation necrosis in fibroadenoma, while full coagulation necrosis was observed at 200 W and 300 W were we observed complete destruction of tissue. SF-36 Questionnaire results showed that HIFU treatment reduced intensity of pain by 44.7% and stimulated early resumption of functional activeness in women by 66.7%.

Conclusions: HIFU therapy is an effective method of treatment for breast fibroadenoma, that has less post-treatment complications and recurrences than surgical method, and may be used as an independent treatment of breast fibroadenoma.

OP02-8

PREDICTION OF PATHOLOGIC COMPLETE RESPONSE TO NEOADJUVANT CHEMOTHERAPY IN BREAST CANCER USING IMAGE-GUIDED BIOPSY: A PROSPECTIVE CLINICAL TRIAL

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Background: Patients who attain a pathologic complete response (pCR) after neoadjuvant chemotherapy (NAC) have a favorable long-term outcome. The role of surgery in these patients may be limited to pathological confirmation of pCR and thus may be omitted. We investigated whether image-guided biopsy can accurately predict pCR.

Methods: We prospectively enrolled 40 patients who were suggested to have pCR on preoperative MRI, defined by size ≤ 0.5 cm or lesion-to-background parenchymal signal enhancement ratio (SER) ≤ 1.6. Core needle biopsy (CNB, 14G) or vacuum-assisted biopsy (VAB, 10G) was alternatively performed for patients, obtaining tissue around a clip marker placed during the course of NAC. Standard surgery was performed after biopsy. Matched biopsy and surgical specimen were compared for pCR assessment.

Result: A pCR was confirmed in 27 (67.5%) surgical specimens, including 14/19 (73.7%) in HR-/HER2- and 6/8 (75%) in HR-/HER2+ patients. Biopsy had an accuracy of 90% (95% CI: 76–97%), negative predictive value of 87.1% (95% CI: 75-94%), and a false-negative rate of 30.8% (95% CI: 14-70%). Among four patients with false biopsy results, three had > 0.5 cm lesion on MRI and two had < 5 cores biopsied. Obtaining at least five cores in patients with ≤ 0.5 cm lesion on MRI resulted in a 100% accuracy. There was no difference in accuracy between CNB and VAB cases. In breast pCR did not correlate with nodal status in 11.1% (3/27).

Conclusions: Image-guided CNB or VAB can accurately identify patients with breast pCR. Results from this trial will be used in a trial for omitting breast surgery for patients predicted to have pCR on biopsy.

OP03-1

LONG TERM SURVIVAL STUDY OF DE-NOVO METASTATIC BREAST CANCERS WITH OR WITHOUT PRIMARY TUMOUR RESECTION

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Background: Treatment of de novo metastatic breast cancer is usually palliative with systemic treatment; surgical excision of the primary tumour is reserved in patients with significant symptoms from the primary tumour. Survival benefit of primary tumour surgery remains controversial.

Methods: This study was registered in the research registry (researchregistry.com). All patients treated with de novo metasatatic invasive ductal breast cancer (MBC) between January 2007 - December 2016 were retrieved from a prospectively-maintained database. Patient baseline demographic and tumour characteristics were compared. Overall survival (OS) was analysed using Kaplan Meier Method and log-rank test. Multivariate analysis was performed to evaluate the survival prognosticators.

Result: Median age of diagnosis was 53 year-old (Range 24–91 years old). 91 patients received resection of the primary tumour, including 86 mastectomies and 5 breast conserving surgeries (surgical group). 81 patients were never treated surgically (non-surgical group). Baseline patient and tumour characteristics were comparable (apart from being younger age in the surgical group). 5-year OS in surgical group was significantly better than non-surgical group (43.9% vs. 33.9%, $p = 0.026$). Multivariate analysis found that advanced age (Hazard ratio: 1.034, $p = 0.005$, 95% CI 1.010–1.058) and presence of visceral metastasis (Hazard ratio: 1.672, $p = 0.038$, 95% CI 1.028–2.719) remained statistically significant through multivariate analysis with stepwise Cox regression; while positive oestrogen receptor (ER) status was the only positive prognosticator in the analysis (Hazard ratio: 0.42, $p = 0.001$, 95% CI 0.256–0.688).

Conclusions: Surgical excision of primary breast tumour may confer survival benefit in de novo MBC, in carefully selected patients.

OP03-2

EARLY EXPERIENCE OF ACCELERATED PARTIAL BREAST IRRADIATION USING ROBOTIC STEREOTACTIC OR INTENSITY MODULATED RADIATION THERAPY IN SELECTED EARLY STAGE BREAST CANCER

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Background: Here we report the early outcome with the dosimetric assessment from patients underwent accelerated partial breast irradiation (PBI) using intensity-modulated radiation therapy (IMRT) or robotic stereotactic RT.

Methods: We identified 114 consecutive women (117 breasts) who received external beam ABPI after breast-conserving surgery from 2015 to 2017. Per NSABP B-39 protocol, 34 Gy in 10 fractions (n = 69) was delivered using arc-based IMRT-PBI or stereotactic-PBI. Since March 2017, 30 Gy in 5 fractions was used (n = 48).

Result: By the 2017 update ASTRO guidelines, 65.8%, 34.2%, and 0% of patients was the suitable, cautionary, and unsuitable group, respectively. The BCCT.core software scored the cosmesis as excellent/good in 67% of the patients at baseline without worsening cases after PBI. After PBI, 82.6% of patients had no skin change and remained 17.4% had a minimal skin reaction. One patient experienced chest wall pain due to fractured rib but resolved spontaneously. With a median follow-up of 13 months (range, 2–25), all 114 patients remain locally controlled with no evidence of disease. In the dosimetric analysis, target coverage and dose-volume constraints were excellent in all regimens. Doses of contralateral and ipsilateral breast were significantly reduced in stereotactic-PBI than IMRT-PBI (Ps < 0.05).

Conclusions: Although longer follow-up and larger scale research is warranted, our results show feasibility, minimal toxicity and excellent cosmesis of PBI with a cutting-edge technology. Stereotactic robotic PBI has the advantage of minimizing low-dose radiation exposure to the remnant breast over arc-based IMRT PBI.

OP03-3

UTILITY OF A VOLUME REPLACEMENT TECHNIQUE WITH A LATERAL INTERCOSTAL ARTERY PERFORATOR FLAP AFTER BREAST-CONSERVING SURGERY

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Background: Immediate partial breast reconstruction after breast-conserving surgery (BCS) has become a new paradigm in treating breast cancer. Among the volume replacement techniques used for small to moderate-sized breasts, the perforator flap method has many advantages. We present anatomic studies and two surgical techniques using lateral intercostal artery perforator (LICAP) flaps.

Methods: We selected 40 patients who underwent breast reconstruction using the LICAP flap, between January 2011 and June 2016. We conducted comparative analyses of the propeller flap and the turnover flap. We used 3D-CT in LICAP anatomical studies, analyzing the distribution probability of the dominant perforator, the vertical distance from the axillary fold, and the horizontal distance from the anterior border of the latissimus dorsi.

Result: The most dominant perforator flaps used were the 6th LICAP, utilized in 43.75% of cases, followed by the 7th LICAP, utilized in 39.06% of cases, and their mean distances from the latissimus dorsi and the axillary folds were determined and reported. With respect to complications, a total of 3 cases required additional treatment for fat necrosis (propeller method - 2 cases, turnover method - 1 case), and venous congestion was found in only 2 cases that used the propeller method. Cosmetic satisfaction was ≥ 90% for both techniques, indicating results that were rated as either excellent or good.

Conclusions: We believe that our study results can broaden the application of partial breast reconstruction by using the LICAP flap after BCS, with 3D-CT for anatomic studies, and using one of our two described surgical techniques.

OP03-4

IDENTIFICATION OF EXOSOMAL MICRORNA TARGETING BRCA-DEFICIENT BREAST CANCER

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Background: Several studies reported that BRCA mutation carriers had a higher recurrence rate and less favorable tumors than non-carriers. Exosomes are small membrane-derived vesicles that function to mediate cell-cell communication by transferring cancer promoting microRNAs (miRs). However, the selectivity of miRNA released from tumor-derived exosomes and its relevance in cancer treatment has not been studied.

Methods: Exosomes were isolated from plasma of breast cancer patients and healthy individuals. Breast cancer-derived exosomal-miRNAs (exo-miRs) were profiled by RNA-sequencing and microarray. Real-time RT-PCR was used for validation in pre- and post-operative plasma, as well as primary tumor tissues. Characterization of exo-miR on cell proliferation was performed in exo-miR transfected cells.

Result: BRCA-associated exo-miRNAs (miR-106a, miR-20a, miR-23a, miR-451 and miR-486) were identified from array data and further validated in BRCA-positive, BRCA-negative and healthy controls by real-time RT-PCR. In addition, the expression levels of miR-106a, miR-451 and miR-486 were lowered in post-operative plasma of BRCA-carriers than non-carriers High expression of exo-miR-106a, miR-20a, miR-23a, miR-451 and miR-486 were also seen in breast cancer cell lines (MB-231 and MB-468) relative to normal breast cells (MCF-10A). Importantly, expression of miR-451 was reduced after tumor resection in BRCA mutation carriers. Cells transfected with miR-451 inhibitor significantly reduced cell proliferation in breast cancer cells, suggesting that exosomes carrying miR-451 retard cancer cell growth.

Conclusions: These findings suggest that exo-miR plays a critical role in breast cancer progression, and yet reduce its expression significantly suppressed tumor growth. This study provides a rationale for targeting exo-miR as an alternate therapeutic option for BRCA-associated tumors.

OP03-5

A PHASE II STUDY INVESTIGATING ACUTE TOXICITY OF TARGETED INTRAOPERATIVE RADIOTHERAPY AS TUMOR-BED BOOST PLUS WHOLE BREAST IRRADIATION AFTER BREAST-CONSERVATIVE SURGERY IN KOREAN PATIENTS

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Background: We evaluated acute toxicity after intraoperative radiotherapy (IORT) with low-energy X-ray plus whole breast irradiation (WBI) in Asian breast cancer patients who have smaller breast volumes compared to Western women.

Methods: A single-arm, single-institute, phase II trial aimed to investigate acute toxicity after completion of radiotherapy (targeted IORT followed by WBI) in Korean patients treated with breast-conservative surgery (BCS). In the conventional WBI arm from TARGIT-A trial, the incidence of acute toxicity within 6 months is 15%. To prove a non-inferiority of an acute-toxicity rate, this trial would need to enroll 215 patients in total. This trial is registered with ClinicalTrials.gov, number NCT02213991.

Result: Two-hundred and thirty-three women were screened, and 215 undergoing IORT were enrolled. In 35 patients, clinically significant complications during acute period are noted. The rate of patients experiencing acute toxicity was 16.3% (95% CI, 11.3–21.2%). The actual non-inferiority margin of our trial was 21.7% under the pre-specified margin as 23.0%. There were 29 patients with seroma collection (more than 3 times when aspiration volume is over 10 cc), 4 with wound infection, and 2 with skin break down. There was no difference according to the tumor volume or the tumor-breast volume ratio in the rate of complications. Old age and high BMI were risk factors for acute complications.

Conclusions: Targeted intraoperative radiotherapy is a safe procedure for Korean breast cancer patients with acceptable toxicity profile in acute period.

OP03-6

CHOLESTEROL MEDICATION USE AND MAMMOGRAPHIC DENSITY IN PREMENOPAUSAL WOMEN

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Background: Having dense breasts on mammograms is associated with a 4-6-fold increased risk of breast cancer. Studies suggest that mammographic breast density is modifiable, hence reducing breast density could be a path to reducing breast cancer development. We therefore investigated the associations of cholesterol medication use and mammographic density in premenopausal women scheduled for an annual screening mammogram at Washington University School of Medicine, St. Louis, Missouri in 2016.

Methods: Cholesterol medication use in the preceeding 12 months was assessed using a questionnaire. We used Volpara software to determine volumetric percent density (VPD), and dense volume (DV). Multiple linear regression models, adjusted for confounders were used to evaluate the associations of medication use with mammographic density. Means were generated within each category of medication use, and back-transformed for easier interpretation.

Result: Thirty seven women used cholesterol medications in the preceeding 12 months compared to 317 who did not. Comparing users to non-users, the least square means were 6.5% vs. 7.7%, p-value = 0.05 for VPD; and 1,051.6 cm^3 vs. 864.1 cm^3 for dense volume, p-value = 0.02. There was evidence suggestive of dose response. VPD was 6.8% for women who used cholesterol medications 1-3 days/week and 6.4% for women who used ≥ 4 days/week. Dense volume was 1,017.4 cm^3 for women who used cholesterol medications 1-3 days/week and 1,069.8 cm^3 for women who used ≥ 4 days/week.

Conclusions: Cholesterol medication is associated with lower mammographic density in premenopausal women. If confirmed in prospective studies, cholesterol medication could have utility in reducing breast density, and potentially, breast cancer development in premenopausal women.

OP03-7

COMPARISON OF THE 5-YEAR OVERALL SURVIVAL RATES BETWEEN THE 7TH AND UPDATED 8TH EDITIONS OF THE AJCC TNM STAGING SYSTEM FOR BREAST CANCER : A SINGLE-INSTITUTION STUDY OF 3,563 PATIENTS IN KOREA

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Background: The aim of this study was to evaluate whether updated 8th edition of the American Joint Committee on Cancer (AJCC) on tumor-node-metastasis (TNM) staging systems represents a better refinement of the 7th edition for breast cancer.

Methods: We retrieved the data of 3,563 patients who were newly diagnosed with malignant breast cancer between 2005 and 2015. We restaged invasive breast cancer according to updated 8th edition of the AJCC TNM staging system, distributed in 15 December 2017, and compared the 5-year overall survival rates between the 7th and updated 8th editions.

Result: Stage migration was observed in 39.6% (n = 909) of the patients. Of these, 8.3% (n = 190) and 31.3% (n = 719) showed an upgraded stage and downgraded stage, respectively. According to the 7th edition the 5-year overall survival rates was lower for patients with stage IB than stage IIA according to the 7th edition (92.1% vs. 94.7%, $p < 0.001$). The 5-year overall survival did not differ significantly between stage IIB and IIIA (90.7% vs. 90.3%, $p = 0.204$). However when using updated 8th edition, there was a significant negative correlation between increased stage and the 5-year overall survival rate, and the 5-year overall survival rates among the stages differed significantly (97.9% for stage IA, 94.7% for stage IB, 93.6% for stage IIA, 91.9% for stage IIB, 78.4% for stage IIIA, 73.3% for stage IIIB, and 71.3% for stage IIIC, $p < 0.001$).

Conclusions: Updated 8th edition of the AJCC TNM staging system allows for finer stratification of breast cancer. It is especially useful when trying to predict prognosis for stage IB and IIA, and stage IIB and IIIA.

OP03-8

AXILLARY LYMPH NODE DISSECTION IS NOT MANDATORY IN BREAST CANCER PATIENTS WITH PREOPERATIVE BIOPSY-PROVEN AXILLARY LYMPH NODE METASTASIS

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Background: The ACOSOG Z0011 trial demonstrated that axillary lymph node dissection (ALND) is unnecessary in patients with 1-2 positive sentinel lymph nodes (SLNs). ALN biopsy accurately predicts ALN metastasis but it does not identify patients with more than 2 positive ALNs. The aim of this study is to identify patients who can be considered of SLN biopsy (SLNB) when preoperative ALN biopsy results are positive.

Methods: A total of 603 breast cancer patients who underwent preoperative ALN biopsy between January 2009 and December 2016 were retrospectively reviewed. Among them, patients who had no palpable ALN, no neoadjuvant therapy and had positive biopsy results were included for analysis. Clinicopathologic characteristics and imaging results were compared between patients with 1-2 positive LNs and > 2 positive LNs.

Result: A total of 198 patients were included for analysis. Almost half of these patients (n = 90, 45.4%) had 1-2 positive LNs. Clinicopathologic factors that were significantly associated with 1-2 positive LNs were clinical tumor size ≤ 2 cm, no lymphovascular invasion and 0-1 suspicious LNs on axillary ultrasonography, breast MRI images or PET-CT images. The correlation between PET-CT images and LN disease burden was notable on logistic regression analysis (HR 9.809; 95% CI 5.077, 18.951; p-value < 0.001). Only 25% patients with 0-1 suspicious LNs on PET-CT images had > 2 positive LNs.

Conclusions: Almost half of breast cancer patients with preoperative biopsy-proven ALN metastasis had 1-2 positive LNs. Patients with biopsy-proven ALN metastasis but have only 0-1 suspicious LNs on PET-CT images can be considered as candidates for SLNB.

Poster Presentation

GBCC2018

Global Breast Cancer Conference 2018

PO001

CAN THE BRCA GENE MUTATION BE USED AS A PROGNOSTIC FACTOR FOR BREAST CANCER?

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Background: BRCA mutations occur frequently in breast cancer (BC), but their prognostic impact on outcomes of BC has not been determined. BRCA1, 2+ and UV patients were identified. According to BRCA mutation, we investigate the differences in pathologic features, overall survival and disease free survival.

Methods: We analyzed 93 patients who underwent BRCA gene testing among 1,000 patients treated for breast cancer. The survival rate was measured using the Kaplan-Meier method. The association of each other was measured using linear by linear association test.

Result: The mean age of BRCA gene tested breast cancer patients was 39.7 ± 4.2 years. 52 patients (55.9%) had BRCA non-carrier patients. 25 patients (26.9%) had BRCA UV (Unverified Variation). 16 patients (17.2%) had BRCA gene mutation. BRCA 1 positive was 10 patients (10.5%) and BRCA 2 positive was 6 patients (6.5%). 12 patients (12.9%) had family history of breast cancer or ovarian cancer. 3 patients (3.2%) were UV group and 3 patients were BRCA positive group. OS and DFS do not showed statistically significant difference with BRCA gene mutation. Also, there was no significant difference in BRCA and T stage, but N stage was statistically significant. ($p = 0.01$) Of the 93 patients, 23 (24.7%) had triple negative breast cancer. Six patients (60%) of BRCA 1 positive 10 patients were found to TNBC. But not in BRCA 2 group.

Conclusions: There was no significant difference in OS and DFS associated with BRCA gene mutation. The pathologic features showed only statically significant correlation with N stage. It is considered that the treatment should be maintained in accordance with pathological differences of BRCA 1, 2.

PO002

LONG-READ NEXT GENERATION SEQUENCING APPROACH TO CLOSE THE GAPS OF SHORT-READ SEQUENCING IN HEREDITARY BREAST AND/OR OVARIAN CANCER

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Background: Advances in next generation sequencing (NGS) have revolutionized genetic profiling in hereditary breast cancer. The development of molecular barcode NGS enables simultaneous detection of DNA-copy number variation (CNV) and nucleotide variation, therefore replacing the use of multiplex ligation-dependent probe amplification (MLPA). The breakpoints can further be resolved by long-read sequencing with/without coupling of long range PCR (≤ 10 kb).

Methods: Germline DNA from high-risk breast cancer patients were subjected to a 6 genes (BRCA1, BRCA2, TP53, PTEN, PALB2 and CDH1) human BRCA Plus QIAseq DNA panel (Qiagen) for NGS using MiSeq (Illumina). Sequencing data were analyzed by in-house developed bioinformatic pipeline. Cases identified with CNV were further characterized by MinION (Oxford Nanopore) long-read sequencing.

Result: Eleven retrospective controls with unique BRCA1 or BRCA2 CNV identified by MLPA were tested positive using molecular barcode NGS. Eight new CNV cases, including BRCA1, BRCA2 and PALB2, were found from > 200 prospective samples tested. The breakpoints of 10 cases were characterized using long-range PCR coupled with long-read sequencing and 1 case solely with long-read whole-genome sequencing (N50 = 19 kb). The rest are under investigation.

Conclusions: Incorporating molecular barcodes in NGS enables de-duplication of reads from amplicon sequencing, thus allowing CNV to be accurately identified. The capability of extremely long-read sequencing has proven to be useful in solving genomic breakpoint in the base-pair level. Here we showed the prototype of coupling short- and long-read sequencing, which could be the standard workflow for germline mutation detection. It is potentially applicable in somatic breast and ovarian cancers for targeted therapy.

Poster Presentation

PO003

COST EFFECTIVENESS OF ONCOTYPE DX FOR EARLY STAGE BREAST CANCER UNDER NATIONAL HEALTH INSURANCE

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Background: In Korea, all citizens are covered by national health insurance (NHI), besides patients just pay 5% of hospital bill, if who diagnosed with cancer. NHI can help solve the financial burden for cancer patients. This study was conducted for existing cost-effectiveness analyses of Oncotype DX (ODx) in Korea.

Methods: We analyzed the hospital expenses of patients who diagnosis early-stage breast cancer from October 2010 to October 2016 in Seoul National University Hospital. All patients are possible candidates for adjuvant chemotherapy. Among them 273 patients were tested ODx. A cost-utility analysis (CUA) was performed. We analyzed the hospital expenses of chemotherapy by regimens who underwent adjuvant chemotherapy (CTx) patients, and costs of accompanying adverse event.

Result: Of 273 patients, 39 (14.3%) were underwent adjuvant chemotherapy. Each patients hospital expense are roughly 3,000 USD (2,200–4,000 USD), it including all costs of blood test, CT, chest x-ray, chemoagents and other medications. Of these costs, patients should pay only 5% so it could be around 150 USD (110–200 USD).

Conclusions: The economic benefits ODx of are modelled by an overall reduction in CTx usage, thus avoiding associated costs and disutility, and an increase in CTx usage in the high RS group, reducing the risk of recurrence and improving health outcomes. Under the special environment of Korea that most costs who diagnosed with cancer covered by NHI, it relatively expensive than other countries. So it deserve much consideration that necessity of further studies and researches to develop new tools that could be more reasonable in cost in Korea.

PO004

DETERMINING THE FACTORS PREDICTING THE RESPONSE TO ANTI-HER2 THERAPY IN HER2-POSITIVE BREAST CANCER PATIENTS

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Background: We aimed to identify the overexpressed genes or related pathways associated with good responses to anti-HER2 therapy and to suggest a model for predicting drug response in neoadjuvant systemic therapy with trastuzumab in HER2-positive breast cancer patients.

Methods: We recruited 64 women with breast cancer and categorized them into 3 groups: complete response (CR), partial response (PR), and drug resistance (DR). The final number of patients in the study was 20. RNA from 20 core needle biopsy paraffin-embedded tissues and 4 cultured cell lines (SKBR3 and BT474 breast cancer parent cells and cultured resistant cells) was extracted, reverse transcribed, and subjected to GeneChip array analysis. The obtained GeneChip data were analyzed using Gene Ontology (GO), Kyoto Encyclopedia of Genes and Genomes (KEGG), and datab]ase for annotation, visualization, and integrated discovery (DAVID).

Result: In total, 6,656 genes differentially expressed between trastuzumab-susceptible and trastuzumab-resistant cell lines were identified. Among these, 3,224 were upregulated and 3,432 were downregulated. Expression changes in 34 genes in several pathways were found to be related to the response to trastuzumab-containing treatment in HER2-type breast cancer, interfering with adhesion to other cells or tissues (focal adhesion) and regulating extracellular matrix interactions and phagosome action. Thus, decreased tumor invasiveness and enhanced drug effects might be the mechanisms explaining the better drug response in the CR group.

Conclusions: This multigene assay-based study provides insights into breast cancer signal transduction and the possible prediction of treatment response to targeted therapies such as trastuzumab.

PO005

PREVALENCE AND ONCOLOGIC OUTCOMES OF BRCA1 AND BRCA2 GERMLINE MUTATIONS IN UNSELECTED PATIENTS WITH TRIPLE NEGATIVE BREAST CANCER

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Background: Triple negative breast cancer (TNBC) account for 15–20% of all breast cancer, and TNBC is enriched for germline mutation of BRCA. NCCN guidelines suggest that BRCA 1/2 test is needed patients with TNBC less than 60 years, while as many Asian countries do not suggest because of lack of evidence in Asian ethnic population. We examined BRCA 1/2 mutation in patients with unselected TNBC and analyzed the prognosis.

Methods: Among 1,051 women with TNBC operated at Samsung Medical Center (SMC) between 2008 to 2016, 999 samples were available from SMC biobank for testing germline BRCA 1/2 mutation by next generation sequencing method. All patients were Korean.

Result: Mean follow-up duration was 60.0 months. Overall, 125 patients (12.5%) had BRCA mutations; 92 (9.2%) in BRCA 1, and 33 (3.3%) in BRCA 2. Median age was 49.7. The mean age of diagnoses of BRCA1/2 mutation carriers was significantly younger than that of non-carriers (45.4 vs. 50.3, $p < 0.0001$). In patients with TNBC less than 50 years old, the prevalence of BRCA mutation was 16.0%. There is no significant difference in OS and DFS between BRCA 1/2 and sporadic breast cancer (Log rank $p = 0.138$ and $p = 0.993$). There is significantly more contralateral breast cancer in BRCA 1/2 mutation patient ($p < 0.001$).

Conclusions: We found a 12.5% incidence of BRCA mutations in unselected TNBC. TNBC patient with less than 50 years old should be added as criteria to genetic screening guidelines in Korea.

Poster Presentation

PO006

SURVIVAL ANALYSIS OF YOUNG AGE BREAST CANCER PATIENTS AND RELATED CLINICOPATHOLOGIC FACTORS IN CIPTO MANGUNKUSUMO HOSPITAL 2008-2015

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Background: Various cancer registrations had confirmed the higher proportion of young women with breast cancer in Asian countries. This mandates special attention for clinician since this group of patients need different management approach. We conducted a study to describe the clinicopathological characteristics of young age breast cancer in Indonesia and its relation with overall survival.

Methods: This is a survival analysis study using samples all young age women (n = 390) with histologically-proven cancer diagnosis that underwent treatment (surgery and/or chemotherapy and/or radiation therapy) since January 2008–August 2015 in Cipto Mangunkusumo Hospital, the national referral hospital in Indonesia. Kaplan-Meier and Cox Regression analysis were performed.

Result: Young age women comprises 35% of total breast cancer patients in Cipto Mangunkusumo Hospital, with majority of cases were in the locally advanced stage (35%), histologic type NST (82%), grade 2, no lymphovascular invasion, positive hormone receptors (55%), negative HER2 status (60%), high Ki-67 (58%) and Luminal B subtype (50%). The 5-year overall survival rates were 64%; variables with statistically significant corelation was tumor size, lymph node involvement, metastatic status and clinical stage. Histologic type NST, grade 2, positive lymphovascular invasion, high Ki-67 and positive HER2 were related to survival, but this correlation was not statistically significant.

Conclusions: The 5-year overall survival rates of young age breast cancer at RSCM was 64%, lower than figures from other countries. Clinical stage was the only variable with statistically significant correlation. Luminal B subtype was observed the most, but the worst survival was found in the HER2 group.

PO007

MUS81 NUCLEASE ACTIVITY IS ESSENTIAL FOR REPLICATION STRESS TOLERANCE AND CHROMOSOME SEGREGATION IN BRCA2-DEFICIENT CELLS

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Background: Failure to restart replication forks stalled at genomic regions that are difficult to replicate or contain endogenous DNA lesions is a hallmark of BRCA2 deficiency. The nucleolytic activity of MUS81 endonuclease is required for replication fork restart under replication stress elicited by exogenous treatments. Here we investigate whether MUS81 could similarly facilitate DNA replication in the context of BRCA2 abrogation.

Methods: We performed DNA fibre assays to measure the effect of MUS81 depletion on replication in BRCA2-deficient cells. We assessed the mitotic consequences of under-replication by immunofluorescence assays. We measured the impact of severe under-replication on cell viability by proliferation assays and clonogenics. We demonstrated that the MUS81 nuclease activity is essential in BRCA2-deficient cells through complementation assays.

Result: Our results demonstrate that replication fork progression in BRCA2-deficient cells requires MUS81. Failure to complete genome replication and defective checkpoint surveillance enables BRCA2-deficient cells to progress through mitosis with under-replicated DNA, which elicits severe chromosome interlinking in anaphase. MUS81 nucleolytic activity is required to activate compensatory DNA synthesis during mitosis and to resolve mitotic interlinks, thus facilitating chromosome segregation.

Conclusions: In summary, MUS81 provides a mechanism of replication stress tolerance, which sustains survival of BRCA2-deficient cells and can be exploited therapeutically through development of specific inhibitors of MUS81 nuclease activity.

PO008

TARGETING MITOCHONDRIAL STAT3: DEVELOPMENT OF A NOVEL MITOTAM FOR TARGETED THERAPY IN TRIPLE NEGATIVE BREAST CANCER

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Background: MitoTam, a modified parental drug of Tamoxifen, used for the treatment of Triple Negative Breast Cancers, is regulated by inhibiting Signal Transducers and Activators of Transcription family 3 (STAT3) signaling pathway, which is highly unregulated in breast tumors. Signal Transducers and Activators of Transcription family 3 (STAT3) plays a crucial role in normal development, acute phase response, metabolism, and cancer progression. While it was generally believed that STAT3 was just a transcription factor, several studies have paved the way for revolutionary findings that some STAT3 localizes in mitochondria. Therefore, mitochondrial STAT3 functions challenge the current design of therapies that solely target STAT3 as a transcription factor and suggest the need for design thinking, to intervene the STAT3 pathway.

Methods: In this presentation, we will discuss development of a novel in-house mitochondrial target MitoTam. Inhibition of mitochondrial STAT3 by MitoTam is required for its anticancer effect in vitro cell-based and in vivo subcutaneous xenograft and patient-derived xenograft (PDX) models of triple negative breast cancer. Furthermore, inhibition of the constitutively active mitochondrial STAT3, phosphorylated at Ser727, abrogated mitochondrial metabolism inhibiting complex-1 driven respiration.

Result: Our results showed down-regulation of STAT3 mediated phosphorylation of receptor tyrosine kinases.In addition, we also found PKCs decrease associated with decreased phosphorylation of STAT3 at Ser727 which are required for the maximal STAT3 transcriptional activity involved in several cellular functions including cell differentiation, proliferation, survival, and oncogenesis.

Conclusions: Our results indicate that MitoTam is a promising candidate drug against triple negative breast cancer and establish mitochondrial STAT3 as its key molecular target.

PO009

CHAGA MUSHROOM INHIBITS METASTASIS AND INDUCES APOPTOSIS IN 4T1 MOUSE BREAST CANCER CELLS

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Background: Chaga mushroom (Inonotus obliquus) is popular traditional remedy in Eastern Europe, and it is widely known as anti-tumor and immunologic effect. Many cancer patients are taking the chaga mushroom, even during chemotherapy or radiotherapy, but verification studies are rare. So, we tried to confirm the effect of chaga mushroom on 4T1 mouse breast cancer cells, which is known as triple negative breast cancer cells.

Methods: After extracting chaga mushroom with 70% ethanol, its cytotic effect was analyzed by MTT assay. And metastatic potential was evaluated by wound healing assay and invasion assay. The phosphorylation of H2AX was measured to assess DNA damage, and expressions of Bcl-xL, caspase-3, and PARP were analyzed to study its effect on apoptotic pathway.

Result: Chaga mushroom extraction (CME) efficiently inhibited cell proliferation of 4T1 cells, and it was a concentration-dependent manner. CME treatment significantly inhibits metastatic potential of 4T1 cells both in a wound healing assay and an invasion assay. We found that CME increased H2AX phospholyation and apoptotic signals in 4T1 cells, indicating by cleavage of caspase 3 and PARP, and the decreased expression of Bcl-XL.

Conclusions: CME increased DNA damage and apoptosis, and decreased metastatic potency in 4T1 mouse breast cancer cells. Further study about the interactions with standard treatment, such as, chemotherapy and radiotherapy, is required.

PO010

FUNCTIONAL CHARACTERIZATION OF HAPTOGLOBIN (HP) IN BREAST CANCER

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Background: Altered energy metabolism is one of the hallmarks in cancer which is characterized by preferential dependence on glycolysis. HP is a secreted glycoprotein which binds to free hemoglobin and prevent the loss of iron. Elevated HP was detected in patients with inflammatory diseases and a variety of cancers. In this study, we aim to investigate the functional roles of HP in breast cancer especially the relationship with glycolysis pathway.

Methods: MTT, cell cycle, apoptosis, aldehyde dehydrogenase (ALDH) activity and glucose uptake assay were performed in triple negative breast cancer cells (MDA-MB-231 and MDA-MB-468). Gene expression was analyzed by qRT-PCR and serum HP concentration was evaluated by enzyme-linked immunosorbent assay (ELISA). Lactate dehydrogenase (LDH) activity kit was used for enzyme activity quantification.

Result: HP was overexpressed in cancer tissues and serum of breast cancer patients. Knockdown by siRNA led to decreased cell proliferation which was associated with G1 phase cell cycle arrest and increased early apoptotic cells. ALDH activity was inhibited upon HP knockdown. Glucose uptake and LDH activity was significantly impeded in breast cancer cells and cell culture supernatant, respectively. Also, qRT-PCR analysis revealed that glycolysis-related genes were altered upon HP silencing.

Conclusions: Our data suggested that HP is overexpressed in breast cancer with oncogenic role and it is involved in glycolysis. These findings may provide novel diagnostic and therapeutic strategies towards this malignant disease.

PO011

THE PROGNOSTIC VALUE OF TUMOR-INFILTRATING LYMPHOCYTES AND HEMATOLOGIC PARAMETERS IN PATIENTS WITH BREAST CANCER

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Background: Carcinogenesis and tumor growth are associated with chronic inflammation and the host immune system. Here, we investigated the clinical significance of tumor-infiltrating lymphocytes (TILs) and hematologic parameters, and their relationship to evaluate the association between local and systemic immune responses in patients with breast cancer.

Methods: Invasive ductal breast cancer patients (N = 145) who underwent surgery were retrospectively evaluated. Samples were obtained using a core needle biopsy for CD8+, FOXP3+ TIL assessment. Blood lymphocytes, neutrophils, monocytes, and platelets were obtained by peripheral venous punctures.

Result: Lymphocyte-monocyte ratio (LMR) (cut-off - 5.3, range = 0.73–12.31) was independent predictor of DFS (HR 0.43 [0.20–0.90]) and OS (HR 0.17 [0.04–0.80]). However, in subgroup analysis, LMR did not have any value as a prognostic factor in HER+ breast cancers. TILs had different prognostic impacts across breast cancer subtypes, although they were not statistically significant. CD8+TILs were significantly associated with absolute lymphocyte count (ALC), the absolute monocyte count (AMC) and LMR (AMC $r = 0.22$, $p = 0.010$; ALC $r = -0.24$, $p = 0.004$; LMR $r = 0.20$, $p = 0.019$).

Conclusions: A relevance between TILs and hematologic parameters in breast cancer was demonstrated. LMR has important value to predict outcome, but the influence of the immune system on breast cancer progression may differ by subtype.

Poster Presentation

PO012

PROGNOSTIC ROLE OF CHANGES IN NEUTROPHIL-LYMPHOCYTE RATIO, TUMOR-INFILTRATING LYMPHOCYTE WITH PROGRAMMED DEATH LIGAND-1 IN TRIPLE-NEGATIVE BREAST CANCER

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Background: Neutrophil-to-lymphocyte ratio (NLR), tumor-infiltrating lymphocyte (TIL) and programmed death-ligand 1 (PD-L1) expression is known to be associated with immunogenicity and prognosis of breast cancer. We analyzed baseline NLR and its clinical association in triple-negative breast cancer (TNBC). The changes of NLR, TIL and PD-L1 during neoadjuvant chemotherapy (NAC) and their association to recurrence was analyzed.

Methods: Between Jan 2008 to Dec 2015, 358 TNBC patients were analyzed. NLR was based on initial complete blood count (CBC). Fifty paired NLR (initial diagnosis, after completion of NAC) and 34 paired tissues (initial diagnosis, surgical specimen) were collected. Changes of TIL, CD4, CD8, forkhead box P3 (FOXP3) and PD-L1 expression were assessed with immunohistochemical stain. The relationship of prior markers and tumor recurrence was analyzed.

Result: Low NLR (NLR ≤ 3.16) was associated to superior survival (overall survival; 41.83 vs. 36.5 months, $p = 0.002$; disease-free survival (DFS) 37.85 vs. 32.14 months, $p = 0.032$). After NAC, patients with radical NLR changes (NLR change $< -30\%$ or $> 100\%$) showed inferior DFS (38.37 vs. 22.37 months, $p = 0.015$). Same or increased TIL after NAC showed trends for superior DFS (80.0 vs. 46.0 months, $p = 0.366$). Positive PD-L1 ($\geq 1\%$) in tumor cells at baseline was associated to superior DFS (97.45 vs. 33.02 months, $p = 0.031$), and positive tumor PD-L1 at post-NAC tissues showed trends for superior DFS (86.43 vs. 38.76 months, $p = 0.056$).

Conclusions: In TNBC, low NLR might be associated with superior survival. Modest changes of NLR or increased TIL after NAC may reflect good prognosis. Positive tumor PD-L1 was associated with superior DFS in our study.

PO013

THE EFFECTS OF BACTERIAL EXTRACELLULAR VESICLES FROM STAPHYLOCOCCUS AUREUS AND KLEBSIELLA PNEUMONIAE FOR GROWTH ON BREAST CANCER CELL LINES

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Background: Bacterial extracellular vesicles (EVs), which are typically 20-100 nm in diameter and have been known to play various roles in cancers. However, to date, there is little elucidation on the effects of bacterial EVs in breast cancer. Herein, the effects of two bacterial EVs were evaluated based on cell growth and drug efficacy.

Methods: Breast cancer cellsMCF7, BT474, and MDA-MB-231were cultured and treated with EVs derived from S. aureus and K. pneumoniae. Cell cycles, as well as cyclins and TNF-a were observed by FACS, immunoblotting, and qRT-PCR.

Result: Cell growth was decreased in MDA-MB-231 cells by co-treatment of S. aureus and K. pneumonia EVs. Its action mechanism was AKT-down regulation of S.aureus EV, and TNF-a upregulation of K.pneumoniae EV. Response to tamoxifen was enhanced in MCF7 cells after treatment of S. aureus or K. pneumonia EVs. When estrogen receptor-positive breast cancer cells were co-treated with tamoxifen, each EVs were effective. S.aureus EV up-regulated the TNF-a expression and K.pneumoniae EV reduced the cyclin E2 expression. These results enhanced tamoxifen efficacy.

Conclusions: Co-treatment of S.aureus and K.pneumoniae EVs decreased cell growth of MDA-MB-232 cells via AKT and p-AKT down regulation. Co-treatment of S.aureus and K. pneumoniae EVs enhanced the response to tamoxifen via increasing TNF-a and down regulation of cyclin E2. The major limitation of this study is the uncertainty of which molecules in EVs were responsible for the results observed. In a future study, molecules responsible for inducing changes in cell signaling should be investigated.

PO014

NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY-BASED URINARY METABOLOMICS ANALYSIS IN KOREAN PATIENTS WITH BREAST CANCER

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Background: Investigations for early detection for breast cancer are essential for successful treatment and favorable outcome. In this study, we investigated nuclear magnetic resonance spectroscopy (NMR)-based urinary metabolomics in breast cancer patients. Metabolic fingerprints from NMR analysis were compared between invasive breast cancer, ductal carcinoma in situ (DCIS) and benign breast disease with urine specimens

Methods: Urine samples (n = 55) and clinicopathologic data were obtained from the Inje Biobank at the Inje University Busan Paik Hospital, Republic of Korea. These samples were collected from the all patients who underwent surgery for benign and malignant breast disease from March 2016 to July 2016. Case populations were consisted of 10 cases of benign disease, 10 cases of DCIS and 35 cases of invasive cancer. We measured NMR profiles of the urine samples with a NMR analyzer. Spectral data acquired by NMR were expressed as relative metabolite concentrations.

Result: Trimethylamine N-oxide (TMAO) was significantly decreased in both invasive breast cancer patients group and DCIS group, comparing with benign breast disease group ($p = 0.003$). Area under the ROC curve is 0.731 ($p = 0.0203$). Moreover, TMAO levels showed the decreasing trend in the order of control, DCIS and invasive cancer groups ($p = 0.0121$).

Conclusions: This study revealed that TMAO levels were significantly decreased in breast cancer patients. We carefully suggest that decreased urinary TMAO can be an attractive potential biomarker for breast cancer screening which needs a noninvasive and patient-friendly methods. In the future, further investigations are required to elucidate the exact mechanism of changes in TMAO metabolism in breast cancer.

PO015

SYNERGISTIC ANTICANCER EFFECTS OF RUXOLITINIB AND CALCITRIOL IN ESTROGEN RECEPTOR-POSITIVE, HUMAN EPIDERMAL GROWTH FACTOR RECEPTOR 2-POSITIVE BREAST CANCER CELLS

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Background: The JAK1 and JAK2 inhibitor, ruxolitinib, and the calcitriol were previously reported to possess anticancer effects in breast cancer. The present study investigated the combined effects of ruxolitinib and calcitriol on an ER-positive, HER2-positive breast cancer cell line. The ER and HER2-positive MCF7-HER18 breast cancer cell line was used to investigate the combination effect of ruxolitinib and calcitriol.

Methods: A bromodeoxyuridine (BrdU) assay was used to investigate cell growth inhibition. The synergism of this combination therapy was examined using the Chou-Talalay method. Cell cycle analysis was performed by flow cytometry, and apoptosis was evaluated by flow cytometry following annexin V-FITC and PI staining. Alterations in protein expression levels were analyzed by western blotting.

Result: The BrdU assay indicated that combination treatment using ruxolitinib and calcitriol produced a synergistic anti-proliferative effect in MCF7-HER18 breast cancer cells. Annexin V-FITC/PI staining and cell cycle analysis identified a synergistic increase in apoptosis and sub-G1 arrest in the presence of ruxolitinib and calcitriol. Western blot analysis revealed that these synergistic effects of ruxolitinib and calcitriol were associated with reduced protein levels of JAK2, phosphorylated JAK2, c-Myc proto oncogene protein, cyclin-D1, apoptosis regulator Bcl-2 and Bcl-2-like protein 1, and with increased levels of caspase 3 and Bcl-2-associated agonist of cell death proteins.

Conclusions: The results of the present study demonstrated the synergistic anticancer effects of ruxolitinib and calcitriol in ER and HER2-positive MCF7-HER18 breast cancer cells. Based on these findings, ruxolitinib and calcitriol may have potential as a combination therapy for patients with ER and HER2-positive breast cancer.

PO016

THE ROLE OF BREAST CANCER STEM CELLS IN RADIORESISTANCE AND THE MOLECULAR SUBTYPE CONVERSION OF HER2-NEGATIVE BREAST CANCER

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Background: Although it has been proposed that the beneficial effect of HER2-targeted therapy in HER2-negative breast cancer is associated with the molecular subtype conversion, the underlying mechanism and the clinical biomarkers are unclear.

Methods: We utilized MCF7 cells sorted with CD44+/CD24- to mimic breast cancer stem cells (BCSCs), which implies molecular subtype conversion of HER2-negative breast cancer cells. The data of 1,846 patients with invasive ductal carcinoma or invasive lobular carcinoma were analyzed to evaluate the relationship between the changes in serum HER2 and tumor burden in patients.

Result: Our study showed that BCSCs mediated HER2 subtype conversion and radioresistance in HER2-negative breast cancer cells and evaluated serum HER2 as a clinical biomarker for HER2 subtype conversion. We found that the CD44+/CD24- BCSCs from HER2-negative breast cancer MCF7 cells overexpressed HER2 and EGFR and showed the radioresistant phenotype. In addition, we showed that trastuzumab treatment sensitized the radioresistant phenotype of the CD44+/CD24- cells with decreased levels of HER2 and EGFR, which suggested that HER2-targeted therapy in HER2-negative breast cancer could be useful for targeting BCSCs that overexpress HER2/EGFR. Importantly, our clinical data showed that serial serum HER2 measurement synchronously reflected the disease relapse and the change in tumor burden in some patients who were initially diagnosed as HER2-negative breast cancer, which indicated that serum HER2 could be a clinical biomarker for the evaluation of HER2 subtype conversion in patients with recurrent HER2-negative breast cancer.

Conclusions: Therefore, our data have provided in vitro and in vivo evidence for the molecular subtype conversion of HER2-negative breast cancer.

PO017

NAD(P) DEPENDENT STEROID DEHYDROGENASE-LIKE, INVOLVED IN CHOLESTEROL BIOSYNTHESIS, REGULATES PROLIFERATION AND METASTASIS IN BREAST CANCER

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Background: Breast cancer is the most common cancer for women. Target genes are extracted based on NGS data for breast cancer patients to regulate their emergence and to study their function and mechanism in the formation and progression of cancer. In this study, we studied NSDHL (NAD(P) Dependent Steroid Dehydrogenase-Like), involved in cholesterol biosynthesis.

Methods: In patients diagnosed with breast cancer, breast cancer tissues and normal tissues or blood samples were analyzed by whole exome sequencing using HiSeq 2000 (Illumina, California, USA). Among them, we evaluated NSDHL expression in breast cancer cells and cell proliferation, metastasis after transfected with siRNA of NSDHL. In addition, we identified which drug is more efficient for treatment, as a target drug for NSDHL.

Result: In whole exome sequencing data of 120 breast cancer patients, we selected 198 somatic mutations with expression volume > 0.3, 3 or more mutations per gene, and the targets of anticancer drug. NSDHL mRNA and protein levels are more presented in ER+positive breast cancer cell (MCF-7) than ER-negative breast cancer cell (MDA-MB-231). To investigate the mechanism of cholesterol pathway mediated proliferation and metastasis, we inhibited NSDHL. Silencing of NSDHL by siRNA decreased proliferation ($p < 0.01$), migration and cholesterol levels in breast cancer cells. In addition, after inhibition of NSDHL, EGFR inhibitor (Erlotinib) and cholesterol synthesis inhibitor (Statin) are effectively inhibit cell growth. Now, were studying the NSDHL functions in breast cancer cells related to cholesterol pathway in in vitro studies.

Conclusions: In conclusion, we found that the NSDHL could be therapeutic targets in breast cancer progression and metastasis.

PO018

PPM1H AND RNF150 AS PREDICTIVE MARKERS FOR TRIPLE NEGATIVE BREAST CANCER CHEMOTHERAPY

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Background: Recently, there has been an increasing interest in patient-derived tumor xenograft (PDX) models for cancer research. Since these models mostly retain histological and genetic characteristics of patients, they are also useful for studies that elucidates the cancer cell survival during cytotoxic chemotherapy. Paclitaxel is one of the well-known chemotherapeutic agents for breast cancer patients but most advanced cases often develop resistance to the paclitaxel during the treatment.

Methods: We performed in vivo paclitaxel treatment experiment using a patient-derived xenograft model. We established two TNBC PDX models separately derived from single patients primary and recurrent tumor. For each TNBC PDX model, control (n = 5) and paclitaxel (n = 5) mice were intraperitoneally (IP) injected with either PBS or paclitaxel (15 mg/kg) for 4 weeks. Transcriptome and exome sequencing data were obtained by selecting three of five tumors for control and paclitaxel group.

Result: Both PDX models were sensitive to paclitaxel treatment. Transcriptome data showed 13 genes upregulated in paclitaxel group ($p \leq 0.05$, 2-fold ≥ 0.5). Among these genes, we selected four genes CXCL10, FMO2, PPM1H and RNF150 (adjusted $p \leq 0.1$). PPM1H and RNF150 gene expression was not affected by short-term in vitro paclitaxel treatment using breast cancer cell lines suggesting potential biologic implications of the genes in paclitaxel resistance. PPM1H and RNF150 overexpression and siRNA based gene silencing had substantial effects on cell proliferation, migration, and invasion.

Conclusions: Paclitaxel treatment may increase PPM1H gene expression levels in both TNBC PDX tumors and breast cancer cells. Increased PPM1H expression levels also elevated tumor suppressor p27 protein levels.

Poster Presentation

PO019

TARGETING SHP-1/STAT3/VEGF-A AXIS AS ANTI-TNBC METASTASIS STRATEGY

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Background: Patients with triple-negative breast cancer (TNBC) had an increased likelihood of distant recurrence and death, as compared with those with non-TNBC subtype. Regorafenib is a multi-receptor tyrosine kinase (RTK) inhibitor targeting oncogenesis and has been approved for metastatic colorectal cancer and advanced gastrointestinal stromal tumor. Recently, several reports showed that regorafenib also acts as a SHP-1 phosphatase agonist. Here, we investigated the potential of regorafenib and regorafenib derivative to suppress metastasis of TNBC cells by mitigating autocrine and paracrine feed-forward loops of p-STAT3-mediated VEGF-A signaling through targeting the SHP-1 phosphatase.

Methods: Cell migration ability was demonstrated by Transwell migration assay. Cell protein expressions were determined by Western blot. The levels of VEGF-A in clinical TNBC and animal tumor tissues were analyzed by immunohistochemistry.

Result: We observed a significant correlation between migration ability and SHP-1/p-STAT3/VEGF-A expression in several human TNBC cell lines. In addition, we demonstrated that VEGF-A expression is correlated with worse disease-free and distant metastasis-free survival in clinical TNBC patients. Furthermore, we showed that regorafenib could inhibit the migration of human TNBC cells, which was related to downregulation of p-STAT3 and VEGF-A. To exclude the role of RTK inhibition in regorafenib-induced anti-metastasis, we synthesized a regorafenib derivative, SC-78, that had minimal effect on VEGFR2 and PDGFR kinase inhibition, while having more potent effects on SHP-1 activation. SC-78 demonstrated superior in vitro and in vivo anti-migration ability to regorafenib. Furthermore, VEGF-A dependent autocrine/paracrine loops were disrupted by regorafenib and SC-78.

Conclusions: This study implies that the more potent SC-78 may be a promising lead for suppressing metastasis of TNBC, and the SHP-1/p-STAT3/VEGF axis is a potential therapeutic target for metastatic TNBC.

PO020

SYNERGISTIC GROWTH INHIBITORY ACTIVITY OF BLACK COHOSH EXTRACT AND HERCEPTIN IN HUMAN BREAST CANCER CELLS: AN IN VITRO STUDY

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Background: The purpose of this study was to determine whether black cohosh contains constituents that inhibit the growth of human breast cancer cells, and therefore might eventually be useful in the prevention or treatment of breast cancer.

Methods: Breast cancer cell cultures; MDA-MB-453, MCF7 and MDA-MB-231, were exposed to different concentrations of black cohosh, estradiol (E2), tamoxifen, and herceptin to examine the effect on cell proliferation.

Result: E2 markedly stimulated the proliferation of MCF-7 cells ($p < 0.01$). Tamoxifen inhibited in a dose-dependent fashion the proliferative effect of E2 ($p < 0.001$). Black cohosh alone did not show any stimulatory effect and exhibited a cytotoxic effect, which was significant ($p < 0.001$). Interestingly, the combination of black cohosh with tamoxifen further inhibited MCF-7 cell growth. On MDA-MB-231 cells, neither E2 nor tamoxifen displayed any detectable effect. However, black cohosh inhibited MDA-MB-231 cell proliferation ($p < 0.05$), and this inhibitory effect was enhanced by increasing tamoxifen concentrations. On MDA-MB-453 cells, black cohosh also inhibited cell proliferation, and this inhibitory effect was enhanced by adding herceptin to MDA-MB-453 cells ($p < 0.05$).

Conclusions: This study reveals a cytotoxic effect of black cohosh on both estrogen-sensitive and estrogen-insensitive breast cancer cells and a synergism with herceptin for inhibition of her-2-positive cancerous cell growth.

PO021

EXPRESSION OF RHOA AND CXCRY IN PRIMARY TUMOUR OF OPRABLE BREAST CANCER AS THE RISK FACTORS FOR INFILTRATION TO NIPPLE AREOLA COMPLEX

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Background: The nipple areola complex (NAC) infiltration in operable breast carcinoma (OBC) is very important for breast cancer reconstruction and associated with local reccurence. Studies about molecular pathogenesis of NAC infiltration in OBC suggest that there are some risk factors that influence to migration and infiltration of OBC cells to NAC, such as expression of RHOA and CXCR4 protein in primary tumour. The aim of this studi is to analyze the role of RHOA and CXCR4 protein expression as the risk factors of NAC infiltration in OBC.

Methods: This is an analytic observational, coupled categorical comparative, with cross sectional study. This study include 40 subjects diagnosed as OBC with NAC infiltration and 40 subjects as OBC without NAC infiltration which were selected by matching process. The expression of ROA and CXCR4 protein within each group were identified by immunohistochemistry staining and hitosscore based on McCarty criteria (1995), with cutoff point based on the result of Reciever Operating Characteristic (ROC). Chi quadrat bivariate analysis test was conducted to determine the correlation of protein and NAC infiltration.

Result: Our data shows with bivariate analysis; RHOA and CXCR have correlation with Nipple Areola Complex Infiltration, $p = < 0.001$ with POR 7.00; 95% CI: 2.28–21.53; CXCR4, $p = 0.001$ with POR 6.33; 95% CI: 2.06–19.49.

Conclusions: RHOA and CXCR4 protein in primary tumour have a role as the risk factors of NAC infiltration.

PO022

LNCRNA-CTD-2108O9.1 REPRESSES BREAST CANCER METASTASIS BY INFLUENCING LIFR

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Background: Breast cancer (BC) is an aggressive malignant disease in women worldwide with a high tendency to metastasize. However, impactful biomarkers for BC metastasis remain largely undefined. Thus, finding metastasis-related markers is a pressing need in both clinical and basic research. LncRNA-CTD-2108O9.1 is an lncRNA molecule that locates at less than 50 kbp upstream of LIFR, a reported metastatic suppressor in BC.

Methods: Real-time PCR was performed to quantify expression levels of lncRNA-CTD-2108O9.1 in BC cell and tissue samples. Transwell migration and Matrigel invasion assays, scratch wound healing assays and CCK-8 assays in vitro were used to explore biological function of BC cells, while mice xenografts and lung colonization assays in vivo were performed. MS2-TRAP assay and LC-MS were additionally used to explore potential mechanism.

Result: LncRNA-CTD-2108O9.1 was significantly down-regulated in BC tissues and associated with lymph node metastasis. Overexpression of lncRNA-CTD-2108O9.1 inhibits BC cells migration and invasion in vitro and metastasis in vivo, while knockdown lncRNA-CTD-2108O9.1 led to an increase of metastasis capacity of BC cells. Further investigation found that lncRNA-CTD-2108O9.1 may influence BC metastasis induced by LIFR, EMT-related markers and MMP family.

Conclusions: Low expression of lncRNA-CTD-2108O9.1 in BC and its correlation with high lymph node metastasis indicated that lncRNA-CTD-2108O9.1 is involved in BC progression. And both in vitro and in vivo assays intimated that lncRNA-CTD-2108O9.1 can inhibit the metastatic ability of BC through important metastasis-related genes, serving as a metastasis suppressive gene. All above may provide clues for potential future clinical applications of lncRNA-CTD-2108O9.1.

Poster Presentation

PO023

BREAST CONSERVATION THERAPY VS. MASTECTOMY IN PATIENTS WITH T1-2N1 TRIPLE-NEGATIVE BREAST CANCER: A POOLED ANALYSIS OF KROG 14-18 AND 14-23

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Background: Triple-negative breast cancer (TNBC) has a higher risk for locoregional recurrence than other molecular subtypes. Without specific guidelines on post-mastectomy radiotherapy (RT) in pT1-2N1 breast cancer, it is questionable whether mastectomy alone is a sufficient local treatment for pT1-2N1 TNBC. The purpose of this study was to compare the outcomes of breast conserving surgery (BCS) plus RT vs. mastectomy for patients with pT1-2N1 TNBC.

Methods: Using two multicenter retrospective studies on breast cancer, a pooled analysis was performed among 320 patients with pT1-2N1 TNBC. All patients who underwent BCS (n = 212) received whole breast RT with or without regional nodal RT, while none who underwent mastectomy (n = 108) received it. All patients received taxane-based adjuvant chemotherapy. The median follow-up periods were 65 months in the BCS+RT group, and 74 months in the mastectomy group.

Result: The median age of all patients was 48 years (range, 24-70). Mastectomy group had more patients with multiple tumors ($p < 0.001$), lymphovascular invasion ($p = 0.001$), higher number of involved lymph node ($p = 0.028$), and higher nodal ratio ≥ 0.2 ($p = 0.037$). Other characteristics were not significantly different between the two groups. The 5-year locoregional failure-free, disease-free, and overall survival rates of BCS+RT group vs. mastectomy group were 94.6% vs. 87.7%, 89.5% vs. 80.4%, and 95.0% vs. 87.8%. respectively, and the differences were statistically significant after adjusting for covariates ($p = 0.010$, 0.006, and 0.005, respectively).

Conclusions: In pT1-2N1 TNBC, breast conservation therapy achieved a better locoregional failure-free, disease-free, and overall survival rates compared with mastectomy.

Poster Presentation

PO024

A TECHNIQUE TO LOCALIZE OCCULT BREAST LESIONS DETECTED MAMMOGRAPHICALLY - THE HYBRID OF WIRE LOCALIZATION AND SONOGRAPHY GUIDED PATENT BLUE MARKING

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Background: The use of mammography has increased the number of patients with non-palpable radiographic findings needing surgical biopsy. Wire localization excisional biopsy is the most common procedure. The disadvantages of this include wire displacement, incision via puncture site, unacceptable scarring, etc.. The wound may also interfere with subsequent oncoplastic surgery. We have developed a new technique that easily and efficiently deals with these challenges.

Methods: Between July and October 2017, we treated seven patients with mammography-detected microcalcification, needing surgical biopsy. They underwent wire localization under mammography prior to operation. Each patient was injected with 0.5 mL of Patent blue dye around the tip of the wire hook under sonography guidance before the procedure. The breast tissue, including the wire tip with Patent blue marking, was excised via peri-areolar incision. If the lesions were far away from the nipple-areola complex, a Hopkin's telescope was used.

Result: The average age of the patients was 50.4. Single biopsy procedures were performed on each patient. No complications were recorded. Post-procedural specimen mammography showed that the microcalcification was adequately probed and no re-excision was necessary. All the patients experienced minimal wound discomfort and were satisfied with the wound appearance. The pathological report will be shown in the presentation.

Conclusions: Our preliminary data demonstrates many advantages of the hybrid technique. A peri-areolar incisional wound results in a better cosmetic result and doesn't interfere with subsequent procedures for cancer patients. It is less traumatic and results in less post-operative pain. Lastly, a more accurate result is achieved.

PO025

INTRAOPERATIVE RADIOTHERAPY BOOST VERSUS EXTERNAL BEAM RADIOTHERAPY BOOST IN BREAST CANCER PATIENTS : A RETROSPECTIVE COMPARISON STUDY OF CLINICAL OUTCOMES AND TOXICITY

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Background: Currently, breast conservative treatment followed by whole-breast irradiation with external beam radiotherapy (EBRT) boost could achieve the best local control. Intraoperative radiotherapy (IORT) boost could take place in term of accurate tumor bed, shortening time to radiation and concising the radiation period. This review is to compare oncologic results and complications between IORT boost and EBRT boost in our institute.

Methods: The data was reviewed retrospectively from January 2008 to December 2016 at Queen Sirikit Centre for Breast Cancer and King Chulalongkorn Memorial Hospital. There were 116 patients with IORT boost and 139 patients with EBRT boost. The IORT boost was 50-kV low energy X-ray 20 Gy. 3-year local recurrence and overall survival were calculated.

Result: Median follow up time was 49 months in IORT group and 55 months in EBRT boost group. Mean age was 54.3 years and 52 years respectively. Neoadjuvant chemotherapy was more used in EBRT boost group. Half of the tumours were below 2 cm. The post-operative grade 2 complications were 24.1% in IORT group and 15.8% in EBRT group. Meanwhile, post-radiation grade 2 complications were 1.7% and 2.9% respectively. Local recurrence occurred 2 patients in each group. Calculated 3-year local recurrence and survival in IORT boost group and EBRT boost group were 2% vs. 1.9% and 97.8% vs. 96.3% respectively (p-value 0.69 and 0.66).

Conclusions: The IORT boost showed non-inferior oncologic outcome comparing to EBRT boost. The complications were not different. Therefore, IORT boost was the tumor bed boost option for early breast cancer patients.

PO026

CHANGI GOLDILOCKS MASTECTOMY: OUR INITIAL EXPERIENCE

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Background: Goldilocks Mastectomy was first introduced in 2012 as a viable reconstructive option for patients with breast cancer in which a breast mound is reconstructed from cutaneous mastectomy flap without the need for additional flap or implant

Methods: 'Changi Goldilocks Mastectomy' is a modification of conventional Goldilocks mastectomy whereby the lateral thoracic tissue is raised independently as a lateral intercostal artery perforator (LICAP) flap to allow better mobilization of the mastectomy skin flap along the inframammary fold (IMF) to shape the medial breast mound whilst the LICAP flap can be positioned to provide a better definition to the lateral breast mound.

Result: In this series, 13 cases of Changi Goldilocks Mastectomy was successfully performed in 10 patients. Flap necrosis was reported in one patient and wound dehiscence in another. Poorly controlled diabetes mellitus and wound infection had been shown to be common contributing factors for these two cases on detailed review of patients perioperative notes. Hence, it would be prudent to achieve good glycemic control and prevent wound infection for patients undergoing this procedure.

Conclusions: Incorporating lateral thoracic tissue as a LICAP flap to Goldilocks mastectomy offers additional volume and improved versatility to shape the breast mound. This technique is promising as it offers patients reconstruction without the added costs of implant prosthesis as well as risks of free flap reconstruction.

PO027

POTENTIAL SKELETAL SIDE EFFECTS ASSOCIATED WITH ADJUVANT CHEMOTHERAPY FOR PREMENOPAUSAL BREAST CANCER PATIENTS

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Background: Outcomes of breast cancer (BC) patients have improved with adjuvant chemotherapy. Among premenopausal Chinese with BC, there is scanty literature on bone health after adjuvant chemotherapy.

Methods: Eligibility included premenopausal Chinese patients aged < 45 years at diagnosis, early stage BC 3-10 years prior to study entry, and having received adjuvant chemotherapy. BC characteristics and adjuvant treatment were collected. At study entry, dual energy X-ray absorptiometry (DXA) scans were performed.

Result: Two hundred seventy one eligible patients had DXA. The median time from BC diagnosis to study entry was 5.0 years. One hundred seventy seven pts (65.3%) received anthracyclines, 72 underwent anthracyclines and taxanes. Two hundred five (75.7%) received adjuvant tamoxifen. At study entry, 32 were aged < 40, 74 were aged 41-45, 165 were aged > 45. Twenty eight patients (10.3%) became peri-menopausal and 134 (49.5%) were postmenopausal. The median T-score for hip was -0.30 (IQR: -1.0 to +0.5); that for spine was -0.80 (IQR: -1.5 to +0.2). One hundred thirty six patients (50.2%) had T-score ≤ -1 for either hip or spine; T-score for hip was ≤ -1 in 67 pts (24.7%); T-score for spine was ≤ -1 in 122 patients (45.0%); 53 patients (19.6%) had T-score ≤ -1 for both hip and spine.

Conclusions: At a median of 5 years after adjuvant chemotherapy, over 50% of premenopausal breast cancer patients were detected to have osteopenia/osteoporosis in hip or spine. Further research is needed to assess possible associated factors for changes in their bone health. Acknowledgement: This study was supported in part by Hong Kong Cancer Fund and Madam Diana Hon Fun Kong Donation for Cancer Research.

PO028

ONCOLOGY EFFICACY OF GONADOTROPIN-RELEASING HORMONE AGONIST ADMINISTRATION IN HORMONE RECEPTOR STRONG POSITIVE YOUNG BREAST CANCER PATIENTS TREATED WITH NEOADJUVANT CHEMOTHERAPY

Hee Jun Choi, Jae Myung Kim, Jai Min Ryu, Isaac Kim, Emad Alsharif, Seok Jin Nam, Seok Won Kim, Jong Han Yu, Se Kyung Lee, Jeong Eon Lee

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Background: Breast cancer in young women has been shown to have an aggressive behavior and worse prognosis. This study aimed to evaluate the outcomes of young patients treated with neoadjuvant chemotherapy (NAC) and the oncologic efficacy of gonadotropin-releasing hormone (GnRH) agonist treatment in young breast cancer patients.

Methods: This study was medial record review based on prospectively collected database. We included 995 patients who were diagnosed with invasive breast cancer and treated with NAC followed by curative surgery at Samsung Medical Center between January 2006 and December 2015. Among strong hormone receptor (HR) positive breast cancer (n = 177), we surveyed characteristics and oncology outcome between younger than 35 years old group and older group.

Result: Among 177 patients with NAC and strong HR-positive breast cancer, 27 patients were 35 years old and 150 patients were over 35 years old. Median follow up is 64 months. The pathological complete response (pCR) rate of two groups is both low (3.7% vs. 4.0%). There is no significant difference in disease free survival (DFS) and overall survival (OS) between patients younger than 35 years and patients older than 35 years. GnRH agonist was significant used in patients younger than 35 years old (59.3% vs. 12.0%, $p < 0.001$). At DFS according to GnRH agonist among younger than 35 years group, Patients with GnRH agonist are better DFS ($p = 0.045$).

Conclusions: More recent use of ovarian suppression like GnRH agonist might improve oncology outcome in these patients. Therefore, HR-positive young breast cancer patients with NCA should be treated GnRH agonist and tamoxifen.

PO029

ONCOLOGY OUTCOME OF SENTINEL LYMPH NODE BIOPSY AFTER NEOADJUVANT CHEMOTHERAPY IN CYTOLOGY-PROVEN AXILLARY NODE POSITIVE BREAST CANCER

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Background: To evaluate the prognostic effects of sentinel lymph node biopsy (SLNB) on recurrence and survival after neoadjuvant chemotherapy (NAC) in patients with cytology-proven, node-positive breast cancer.

Methods: This study was a registered medical record review based on a prospectively collected database. We included 506 patients who were diagnosed with invasive breast cancer and axillary lymph nodes metastasis and treated with NAC followed by curative surgery at Samsung Medical Center between January 2007 and December 2014. We analyzed and compared outcomes including prognoses and survival among all groups.

Result: The median age at the time of surgery was 44.4 years. The median follow-up time was 47.0 months. The median number of retrieved sentinel lymph nodes (SLNs) was 5.0. One hundred thirty-four patients had negative SNLs, 85 of whom had no further dissection (Group 1), and 49 of whom had further axillary lymph node dissection (ALND) (Group 2). One hundred four patients with positive or undetected SLNs had further ALND. Of the patients who did not undergo SLNB, 79 had ALND with no residual axillary metastasis (Group 3), and 189 with pathological nodal-positive disease underwent ALND. The SLN identification rate was 98.3%, and the false negative rate (FNR) of SLNB after NAC was 7.5%. There was no significant difference in disease-free survival (DFS, $p = 0.578$) or overall survival (OS, $p = 0.149$) among Groups 1, 2, and 3.

Conclusions: SLNB might be feasible after NAC for node-positive breast cancer and could help reduce morbidity by avoiding standard axillary lymph node dissection in negative SLN patients.

PO030

PREDICTIVE FACTORS INDICATING REOPERATION AMONG BREAST CONSERVING SURGERY IN DUCTAL CARCINOMA IN SITU: SINGLE INSTITUTION REVIEW

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Background: The detection of ductal carcinoma in situ(DCIS) was increased markedly in breast cancer screening era. The manifestations included microcalcifications, non-palpable mass and soft tissue opacity. Breast conserving surgery would be initially proposed, however, the rate of reoperation was high in some literatures. This study aims to review 11-year DCIS in single institution and identify the predictive factors indicating risk of reoperation.

Methods: A single centre retrospective review was performed in patients who underwent breast conserving surgery of pure DCIS from May 2006-May 2017. The hospital database had been reviewed. Clinical history, radiologic findings and pathologic results were included. Univariate analysis and multivariate analysis were carried out using logistic regression method.

Result: The study included 74 patients with DCIS underwent breast conserving surgery. There were 12 patients (16.2%) underwent reoperation with 5 mastectomies. Median radiological size was 1.3 cm (0.38–4.6 cm). Median follow up time was 44 months. Ipsilateral breast DCIS recurrence was found in 1 patient. The baseline characteristics of both groups were not different statistically. Radiological size, presence of microcalcifications, pre-operative MRI and pre-operative tissue sampling were not related to multiple operation. Meanwhile, Ki67 level was associated with reoperation in univariate and multivariate analysis models ($p = 0.042$).

Conclusions: BCS in DCIS remained high reoperation rate. Surgical decision should be performed with multidisciplinary team approach. Pre-operative tissue sampling did not predict multiple operation. DCIS with high ki67 index should be excised with wider margin.

PO031

POST MASTECTOMY ADJUVANT RADIOTHERAPY IN BREAST CANCER: A COMPARISON OF CARDIAC TOXICITY IN HYPOFRACTIONATED AND NORMAL FRACTIONATION PROTOCOLS

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Background: RT reduces the risk of local recurrence by 50%. Hypo-fractionated radiotherapy (HFR) is increasingly being used as they involve fewer treatment sessions. In our study we evaluated cardiac toxicity of two radiotherapy fractionation techniques.

Methods: This is a prospective randomized clinical trial conducted at clinical oncology department – Menoufia University to assess cardiac toxicity of two fractionation techniques. Between August 2009 and June 2010, 120 patients were randomizes into two groups each group 60 patient. Group A: conventional radiation (50 Gy/25 fractions/5 weeks, at 2 Gy/fraction). Group B: (HFR) was 40 Gy in 15 fractions over 3 weeks, at 2.67 Gy/fraction. (ECHO), (ECG) were performed at base line before chemotherapy, at start of radiotherapy, after 6 months, then annually.

Result: Median follow up time 60 months. Median age is 47 ranges (23-70), (25-68) in group A & B respectively. Patients with left sided breast cancer and/or hypertension showed significant decline in ejection fraction in both groups $p < 0.05$. In (group A) hypertensive patients had a median base line EF 63% which declined to 54% at last follow up in comparison to non-hypertensive patients who had baseline EF of 65% and declined to 60%. (group B) hypertensive patients had a median baseline EF 62% which declined to 54% at last follow up in comparison to normotensive patients who had baseline EF 64% which declined to 59%.

Conclusions: HFR as adjuvant treatment of breast cancer has no additional cardiac toxicity in comparison to normal fractionation.

PO032

FEMALE-TO-MALE GENDER AFFIRMING TOP SURGERY

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Background: Mastectomy, referred to here as Top Surgery is an important surgical step for female-to-male (FTM) transgender patients. I would like to introduce some cases I have experienced.

Methods: Seven patients who have been treated with FTM at the Spring day clinic were analyzed for clinical factors retrospectively. According to redundant type and skin elasticity, subcutaneous mastectomies with nipple-areolar complex sparing or free nipple graft after liposuction were performed on all cases by single surgeon (Dr. Hwang).

Result: The mean age was 28.4 years old, the body mass index (BMI) was 28.4 kg/m^2 in FTM patients. The subcutaneous mastectomies with nipple-areolar complex sparing was performed on five FTM patients. The subcutaneous mastectomies with free nipple graft (SM c FNG) was performed on rest two FTM patients. The chest binding, poor skin elasticity, long distance from nipple to inframammary fold were more observed in SM c FNG group.

Conclusions: For safe and aesthetically pleasing results, experiences with FTM techniques and definite algorithm how to select the most appropriate surgical technique will be need in FTM patients.

PO033

THE CHANGING LANDSCAPE OF BREAST CANCER PATIENTS IN ONCOLOGY EARLY PHASE I TRIALS FOR ADVANCED SOLID TUMORS

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Background: Number of oncology early phase I clinical trials for advanced solid tumor is growing. This study was conducted to investigate the characteristics of breast cancer patients participated in phase I trials.

Methods: Breast cancer patients participating in phase I clinical trials at our institute between December 1996 and December 2016 were monitored. Clinicopathological characteristics were retrieved from database and medical records.

Result: Fifty-five breast cancer patients of 1,225 phase I trial participants were included to the analysis. These patients were enrolled to 71 trials. Median age was 55 y.o. (range 32–82). Thirty (54.5%) were hormone receptor (HR)-positive. Fifteen (27.3%) were HER2-positive. Median number of previous chemotherapy was 3 (range 0–10). Median number of endocrine therapy in HR-positive patients was 2 (range 0–6). Median number of participated phase I trials was 1 and maximum number was 4. Three (5.5%) patients participated to the trials from 1996 to 2005. Forty (72.7%) patients participated from 2006 to 2015. Twelve (21.8%) patients participated in 2016. Median survival time was 608 days with 306 days of median follow up time.

Conclusions: Number of breast cancer patients in oncology early phase I trials is increasing. Median survival time is longer than previous report with all types of cancer (J Clin Oncol. 2015;30:2051). Phase I trials are one of the treatment option for advanced breast cancer patients.

PO034

RISK OF CENTRAL NERVOUS SYSTEM FAILURES IN PATIENTS WITH HER2-ENRICHED BREAST CANCER UNDERGOING POSTOPERATIVE RADIOTHERAPY: A MULTICENTER, RETROSPECTIVE STUDY (KROG 16-15)

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Background: The aim of this study is to evaluate the risk of central nervous system (CNS) failures in patients with human epidermal growth factor receptor 2 (HER2)-enriched breast cancer treated with surgery followed by postoperative radiotherapy (RT).

Methods: A total of 749 patients from 8 institutions were enrolled in this study. All patients underwent surgery followed by postoperative RT from 2003 to 2011. 246 patients (32.8%) received neoadjuvant chemotherapy, and 649 patients (81.7%) received adjuvant chemotherapy. Adjuvant trastuzumab was administered to 386 patients (48.6%).

Result: The median duration of follow-up was 84 months (range, 8–171). There were 40 CNS failures (5.3%) including 30 brain metastases, 2 leptomeningeal metastases, and 8 brain and leptomeningeal metastases. On univariate analysis, neoadjuvant chemotherapy, mastectomy, higher T and N categories, lymphatic invasion, absence of adjuvant chemotherapy, and adjuvant trastuzumab were adverse prognosticators for CNS failures. On multivariate analysis, the receipt of adjuvant trastuzumab was the only prognostic factor predicting a higher CNS failure rate (hazard ratio 2.176; 95% confidence interval 1.038-4.561; $p = 0.040$). However, it was not associated with loco-regional recurrence-free, distant metastasis-free, and overall survival on both univariate and multivariate analyses.

Conclusions: HER2-enriched breast cancer is a well-known risk factor for CNS failures. Adjuvant trastuzumab was associated with a higher CNS failure rate in these patients treated with surgery followed by postoperative RT.

PO035

PROGNOSTIC FACTORS AFFECTING SURVIVAL IN BREAST CANCER PATIENTS WITH BRAIN METASTASES AND BENEFIT WITH REGARD TO DIFFERENT BREAST GRADED PROGNOSTIC ASSESSMENT SUBGROUPS

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Background: To examine the efficacy of WBRT in breast cancer (BC) patients with brain metastases (BM) presented with different clinical characteristics, based on the breast cancer-specific Graded Prognostic Assessment (Breast-GPA).

Methods: Medical records of 79 BC consecutive patients treated with WBRT between Jan 2010 and Mar 2016 in our Department were retrospectively reviewed. Enhanced MRI confirmed the diagnosis of BM. Thirty-eight patients received 30Gy in 10 fractions, while in 41 patients 40Gy in 20 fractions was delivered.

Result: The median age at BM was 49 years, and the median KPS was 80. Median overall-survival (OS) after BM was significantly associated with Breast-GPA, as following: 4.3, 11.5, 14.8 and17.9 months in 0–1.0, 1.5–2.0, 2.5–3.0 and 3.5–4.0 sub-groups, respectively ($p = 0.001$). Multivariate analysis showed that infra-tentorial localization, dose/fraction and systemic treatment were independent prognostic factors for OS. In the Breast-GPA 2.54.0 subgroup, the median OS was significantly better in 40Gy/20F cohort (20.9 vs. 10.7 months, $p = 0.03$). In the Breast-GPA 0–2.0 group, those who received upfront WBRT had longer OS than WBRT subsequent to stereotactic radiosurgery (SRS) or systemic treatment (11.6 vs. 4.3 months, $p = 0.03$).

Conclusions: Individual therapeutic strategy based on integrated prognostic factors and anatomical location of BM is important. Unfavorable prognostic patients, such as Breast-GPA subgroup 0–2.0 might benefit from upfront WBRT. Patients with more favorable prognosis with Breast-GPA subgroup 2.5–4.0 might benefit from the higher total dose and small fraction of WBRT. Continuing systemic therapy after WBRT without infra-tentorial involvement is associated with better local control and OS.

PO036

SAFE DELAYED PROCEDURE OF NIPPLE RECONSTRUCTION IN POORLY CIRCULATED NIPPLE

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Background: Nipple-areolar complex (NAC) reconstruction represents the final step in breast reconstruction. There are ongoing studies on nipple reconstruction techniques while minimizing complications and improving the final outcome and patient satisfaction. However, there is no gold standard nipple reconstruction technique that addresses the issue of blood circulation in the flap, which is the most basic complication.

Methods: In the present study, nipple reconstruction was performed in 21 patients who had their NAC sacrificed during breast reconstruction following mastectomy for breast cancer. A delayed procedure was performed when a poor outcome was expected due to marginal pinpoint bleeding in the distal tip after flap elevation during nipple reconstruction. Risk factors that could affect poor circulation were categorized into 4 types (previous radiation therapy, previous scar, smoker, and diabetes mellitus).

Result: The mean patient age was 44.2 (range 32–50) years. Regarding nipple reconstruction methods, 16 patients used the C-V flap and 5 used the Hammond flap. Patients with 2 more than 4 risk factors and with a history of preoperative radiation therapy showed higher probability regarding the occurrence of necrosis/ischemia ($p < 0.045$/$p < 0.012$, respectively). The mean projection of the reconstructed nipple at the immediate postoperative period and postoperative 6 and 12 months was 8.9 ± 1.1, 5.6 ± 0.9, and 5.1 ± 0.9 mm, respectively. The overall patient satisfaction for 17 patients was excellent or good.

Conclusions: The delayed nipple reconstruction applied in the present study can be viewed as a safe and reliable method for improving nipple blood circulation, reducing complications, and enabling long-term nipple projection maintenance in high-risk patients.

PO037

EFFECT OF TRASTUZUMAB ON LOCOREGIONAL RECURRENCE IN HUMAN EPIDERMAL GROWTH FACTOR RECEPTOR 2-POSITIVE BREAST CANCER TREATED WITH CHEMOTHERAPY AND RADIOTHERAPY

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Background: To examine whether adjuvant trastuzumab reduces locoregional recurrence in human epidermal growth factor-2 (HER-2) overexpressed breast cancer receiving adjuvant chemotherapy and radiotherapy.

Methods: We retrospectively included 520 patients with HER-2 overexpressed breast cancer who received radical surgery followed by adjuvant radiotherapy and cytotoxic chemotherapy from 2003 to 2011. Adjuvant trastuzumab was administered in 286 patients. Propensity score matching was conducted to compare trastuzumab-treated and -non-treated cohorts.

Result: Median follow-up duration was 7.1 (range, 0.7–14.1) years. Propensity score matching yielded 171 matched pairs of patients with no significantly different clinical factors (all $p > 0.10$). Improved 7-year locoregional control rate (LRC) was observed in trastuzumab-treated cohort (96.2% vs. 88.3%, $p = 0.005$). On multivariate analysis, negative hormone receptor ($p = 0.003$), positive lymph node ratio ≥ 0.25 ($p = 0.047$), and omission of adjuvant trastuzumab ($p = 0.012$) were identified as significant risk factors of poor LRC. Adjuvant trastuzumab significantly reduced locoregional recurrence in patients with 1 or 2 risk factors (7-year LRC = 94.1% vs. 83.2%, $p = 0.007$); however, the benefit of adjuvant trastuzumab was not significant in patients with no risk factors (7-year LRC = 100% vs. 95.7%, $p = 0.24$).

Conclusions: Adjuvant trastuzumab seems to improve LRC in HER-2 overexpressed breast cancer receiving adjuvant radiotherapy and cytotoxic chemotherapy, especially in HER-2 enriched subtype and high positive lymph node ratio (≥ 0.25).

PO038

THE EFFECT OF STROMAL VASCULAR FRACTION ON BREAST CANCER GROWTH AND FAT RETENTION IN NOD/SCID MOUSE

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Background: Autologous fat grafting is a useful technique for contour improvement in the reconstructed breast. To overcome unpredictable resorption of fat graft, cell-assisted lipotransferusing (SVF) has been introduced. However, there is debate about effect of SVF on the stimulation of cancer growth and its oncological safety. We investigated the effect of SVF on adjacent breast cancer and transplanted fat in an animal model.

Methods: A breast cancer xenograft model was constructed by injecting 2×10^6 MDA-MB-231-luc breast cancer cell line on right lower back of 40 SCID mice. Two weeks later, the cancer size was sorted according to signal density using IVIS and 38 mice were included. Human fat was extracted from abdomen, and SVFs were isolated using the SmartX kit (Dongkoo bio&Pharma Co., Korea). Control Group A, group B injected with SVF, group C injected with 0.5ml fat, 30ul saline, and group D injected with 0.5mL fat, 30 uL SVF. MRI, micro CT volumetric analysis were performed at 4, 8 weeks.

Result: Tumor volume was calculated to be Group A 6,775 mm^3, Group B 5,943 mm^3, Group C 6,085 mm^3, Group D 5,569 mm^3 after 8 weeks of initial Group A 47 mm^3, Group B 42 mm^3, Group C 49 mm^3 and Group D 42 mm^3. Fat retention volumes after 8 weeks were 72% in group C and 79% in group D.

Conclusions: Two months follow up after fat graft in the xenograft model, SVFs injection shows increased fat survival rate, and does not seem to increase the adjacent tumor growth significantly.

PO039

REAL-WORLD EXPERIENCE WITH ERIBULIN AS TREATMENT FOR METASTATIC BREAST CANCER IN THAILAND

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Background: Patients with metastatic breast cancer (MBC) often have several lines of treatment. Many remain fit and functional despite multiple treatment. Evidence from EMBRACE showed that eribulin provided surivial benefits in this setting.

Methods: We retrospectively assessed the efficacy and safety of eribulin in MBC who had failed prior chemotherapy regimens. Seventy-three cases were collected from 3 major university hospitals in Bangkok (Ramathibodi (60 cases), Siriraj (6 cases), and King Chulalongkorn Memorial Hospital (7 cases) from 2014–2017.

Result: Median age was 57 (39–77), ECOG 0-1 in 86.5%. Sixteen patients (22%) were HER2 positive, 19% triple negative, and 70% HR positive. Nearly all (93%) had visceral metastasis, 80% having >3 metastatic sites, most commonly lung (81%), liver (73%) and nodes (66%). Fourteen patients (19%) had brain metastasis. Prior adjuvant chemotherapy was given in 73%, 40% had >3 pallitative chemotherapy. Prior exposure to taxane and anthracycline were 93% and 88%, respectively with 80% and 30% being taxane and anthracycline refractory. Two-thirds (67%) had capecitabine. Median cycles of eribulin was 4 (1–23). PR observed in 11% and SD 41%. Dose delayed and reduction were 51% and 45%; G-CSF used in 27%. Median OS was 12.8 months (6.5–19.1). grade ¾ neutropenia was common (40%) and 13% had febrile neutropenia. Other common AE were anemia, neuropathy and fatigue.

Conclusions: Despite higher number of metastatic organs in this study, eribulin in Thai patients with pretreated MBC demonstrated similar benefit to that reported in EMBRACE. Higher rate of febrile neutropenia was seen in Thai population.

PO040

COMPARISON OF TRADITIONAL ELECTROSURGERY SYSTEM VERSUS LOW THERMAL TISSUE DISSECTION SYSTEM FOR TOTAL MASTECTOMY: A PROSPECTIVE RANDOMIZED CONTROLLED TRIAL

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Background: Various novel surgical equipments has been used in breast surgery to reduce post-operative seroma. However, real benefit from previous studies were controversial. This study was conducted to compare the benefit of low thermal dissection system (PEAK Plasmablade®; PB) and traditional electrosurgery system (TE) in terms of seroma volume after mastectomy.

Methods: A prospective randomized controlled trial was designed. Patients who underwent mastectomy at a tertiary hospital in Bangkok from March 2017 to December 2017 were randomized into two arms; PB vs. TE (n = 25 each). Post-operative seroma, duration of tube drain insertion, hospital stay, pain score, blood loss and number of aspiration attempts were recorded and analysed using two-tail independent t-test.

Result: All patients received mastectomy with or without axillary surgery. Both groups showed similar characteristics; in terms of age, breast weight. There were no statistical significance of drainage volume (mean PB = 862 cc and mean TE = 759.8 cc; $p = 0.53$). The hospital stay, estimated blood loss, pain score, duration of tube drain insertion also demonstrated no statistical significance in both groups. However, in PB group duration of tube drain insertion was lower than in TE group without statistical significance (4.2 and 5.6 days; $p = 0.11$).

Conclusions: From this study, the low thermal dissection system is a precise surgical equipment that is not inferior to the traditional electrosurgery system. Conflict of interest : PEAK Plasmablade® used in this study was supported by Medtronic co., Ltd.

PO041

A NOMOGRAM FOR PREDICTING THE METASTASIS OF SENTINEL LYMPH NODES BY EX VIVO SHEAR WAVE ELASTOGRAPHY

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Background: Because of the disadvantages of intraoperative frozen examination, there is unmet need to evaluate the sentinel lymph node (LN) easily during the breast cancer surgery. In our previous prospective analysis, the ex vivo shear wave elastography (SWE) showed that the metastatic axillary LN was correlated with larger size and high elasticity values, so it could be a feasible method to predict axillary LN metastasis intraoperatively. We hypothesized that the nomogram constructed with ultrasound feature and elasticity values could predict accurately the sentinel LN metastasis during the surgery.

Methods: A nomogram was developed from our previous analysis cohort using nodal size, mean stiffness, and ratio. The nomogram was validated with independent cohort to evaluate the prediction accuracy of sentinel LN metastasis. A total 223 sentinel LNs excised from prospectively enrolled 84 patients in Gangnam Severance Hospital from August 2015 to April 2016 were included in the validation cohort.

Result: The area under curve (AUC) of nomogram was 0.8559 (95% confidence interval [CI], 0.783–0.9288) in the development cohort. The mean stiffness (23.54 and 10.74 kPa, $p < 0.0059$) and the elasticity ratio (3.24 and 1.54, $p = 0.0316$) were significantly higher in validation cohort. The nomogram well predicted the sentinel LN metastasis with an AUC of 0.783 (95% confidence interval [CI], 0.6582–0.9072) in the validation cohort.

Conclusions: Our constructed nomogram showed high performance of predictability for sentinel LN metastasis. Therefore, this model will allow surgeons to easily identify the sentinel LN metastasis using intraoperative ex vivo SWE.

PO042

THE ROLE OF PRIMARY TUMOR SURGERY IN METASTATIC BREAST CANCER

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Background: The aim of the study was to investigate the impact of primary tumor surgery on overall survival and distant free survival in patients with primary metastatic breast cancer

Methods: This retrospective study included 59 women with primary metastatic breast cancer. 45.1% had surgery for the primary tumor. Overall survival was evaluated using Kaplan-Meier estimates. Predictive factors for overall survival were determined.

Result: Median follow-up was 61.5 months for all patients. In univariate analysis, patients with surgery of the primary tumor had significantly prolonged overall survival (29.4 vs. 22.5 months). Within the surgery group, patients with one metastatic organ system had a better outcome (37.9 vs. 22.8 months). Independent risk factors for shorter overall survival were hormone receptor negativity and involvement of multiple organ system.

Conclusions: The results of this study showed a favorable effect of locoregional treatment in patients with primary metastatic breast cancer. However, larger patient numbers are needed to prove these findings in the multivariate model.

PO043

COMPARATIVE STUDY BETWEEN THE CONGNITIVE COMPUTING SYSTEM AND TUMOR BOARDS FOR TREATMENT IN BREAST CANCER

Dohoon Kim, Yun Yeong Kim, Hee Kyung Ahn, Ki Hoon Sung, Min Ji Hong, Eun Young Yoo, Sang Yu Nam, Kyu Chan Lee, Eun Kyung Cho, Hye Young Choi, Heung Kyu Park, Yong Soon Chun

Gachon University Gill Medical Center, Korea

Background: IBM Watson For Oncology (WFO) is a Memorial Sloan Kettering Cancer Center-trained cognitive computing system that provides oncologists with ranked, evidence based treatment options for cancers. WFO treatment options are presented in three categories: Recommend, For Consideration and Not Recommend. The aim of this study is to examine the concordance of treatment options for breast cancer between WFO and the multidisciplinary tumor board from Gachon University Gil Medical Center in Korea.

Methods: We enrolled 143 patients with breast cancer between December 2016 and December 2017. The patients were composed of 137 patients who needed additional treatment after surgery and 6 patients who were thought to need preoperative treatment. Cases were processed using WFO and outputs were compared with actual treatment patients received using retrospective clinical data. Definition of concordance is that GMC oncologist's recommendation is correspond to "Recommend" or "For consideration" in WFO treatment options.

Result: Overall, treatment recommendations were concordant in 125 (87%) of 143 evaluated breast cancer cases. Main reason attributed to discordance were age and reimbursement plan. In adjuvant chemotherapy, concordance is 120 (88%) of 137 and in neoadjuvant chemotherapy, concordance is 5 (83%) of 6.

Conclusions: Treatment options suggested by WFO were concordant with the GMC tumor board in large majority of breast cancer patients.

PO044

DOES ERIBULIN HAVE AN EFFECT ON ANTI-TUMOR ACTIVITIES OF THE SUBSEQUENT REGIMEN IN BREAST CANCER PATIENTS?

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Background: Eribulin improved overall survival (OS) in metastatic breast cancer patients. However, the beneficial effect on progression free survival (PFS) did not reach a statistically significant point in a phase 3 study. To explain this phenomenon, preclinical studies have suggested that eribulin may promote antitumor activities of the next anticancer regimen. We aimed to investigate eribulin-induced effect on the next line regimen in real world.

Methods: Eribulin improved OS in metastatic breast cancer patients. However, the beneficial effect on PFS did not reach a statistically significant point in a phase 3 study. To explain this phenomenon, preclinical studies have suggested that eribulin may promote antitumor activities of the next anticancer regimen. We aimed to investigate eribulin-induced effect on the next line regimen in real world.

Result: Median follow up period was 70.5 months. Eribulin was administered in 3rd to 11th line regimens, therefore matched controls had received 4 to 12 lines of treatment. Eribulin did not bring significant changes on the PFS of the next line regimen (4.1 vs. 5.4 mo; $p = 0.64$). However, OS of the next line regimen was improved (8.6 vs. 5.4 mo; $p < 0.001$, HR 0.27; 95% CI 0.16–0.638, $p < 0.001$). Earlier treatment with eribulin improved OS of the next line regimen (4th regimen compared to 3rd: HR 2.53; 95% CI 1.19–5.35, 5th or over: HR 3.18; 95% CI: 1.49–6.8 $p = 0.03$) .

Conclusions: Eribulin had no beneficial effect on the PFS of the next line regimen in our study. However OS of the next line regimen was significantly improved compared to those without eribulin treatment.

PO045

CHARACTERISTICS AND TREATMENT PROGNOSIS OF 23 CASES OF MALE BREAST CANCER

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Background: To investigate the characteristics, treatment and prognosis of male breast cancer (MBC).

Methods: A total of 23 cases of male breast cancer in our hospital from August 2006 to July 2015 were analyzed retrospectively, 113 cases of female breast cancer (FBC) treated in the same period were selected as control. We evaluated the patient's clinical data and treatment, and followed up the patient. The Kaplan-Meier method was employed to estimate the survival rate, the log-rank test was adopted to compare the survivals between two groups.

Result: In this study, for MBC, the median age is 60 years (36–84), the tumor size ranged 2–5 cm accounted for 60.9%, patients with lymph node metastasis accounted for 34.7%, clinical stage was mainly in phase II, hormone receptor positive proportion 95.7%, Her-2 positive rate is 13%, most patients were type of luminal, the histological classification are mainly invasive ductal carcinoma which accounted for 78.3%, 52.2% of the patients had other systemic diseases, such as high blood pressure, heart disease, diabetes. These clinical features of MBC are different from that of FBC. In the treatment about MBC, 91.3% underwent modified radical mastectomy, 73.9% received adjuvant chemotherapy, 26.1% received radiotherapy, 54.5% received endocrine therapy. The 5 year survival rate and the 5 year disease-free survival rate in MBC were 86% and 75.3% respectively. These values were not significantly different from the FBC. Univariate analysis indicated that the axillary lymph nod estatus, clinical stage and endocrine therapy significantly affected the prognosis of the patients ($p < 0.05$). Age, comorbidities, chemotherapy and radiotherapy did not significantly affect prognosis.

Conclusions: Compared with FBC, MBC were usually associated with advanced age, more complications and late stage. Histological classification are mainly invasive ductal carcinoma. Modified radical mastectomy is a widely accepted procedure. Chemotherapy and radiotherapy do not significantly improve the prognosis. Most of MBC patients are hormone receptor positive and benefit from adjuvant endocrine therapy. Tamoxifen is the first choice for endocrine therapy.

PO046

HIF-1A EXPRESSION CORRELATES WITH RESPONSE TO NEOADJUVANT CHEMOTHERAPY IN WOMEN WITH BREAST CANCER

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Background: HIF-1a has been shown to contribute to resistance to chemotherapy in breast cancer. The purpose of this study was to investigate whether HIF-1a is predictive for pathological response and the prognostic value of HIF-1a in local advanced breast undergoing neoadjuvant chemotherapy.

Methods: Pre-treatment formalin-fixed paraffin-embedded tissue biopsies from 220 local advanced breast cancer patients that subsequently received neoadjuvant chemotherapy were assessed for HIF-1a protein expression by immunohistochemistry. Associations between HIF-1a expression and pathological complete response (pCR) were analyzed using univariate and multivariate analysis. Independent prognostic factors for RFS was identified by multivariate Cox's proportional hazard analysis.

Result: A total of 41 patients (18.6%) achieved a pCR after neoadjuvant chemotherapy in the present study. HIF-1α negative patients had a significantly higher pCR rate than HIF-1α positive patients ($p = 0.027$). Multivariate analysis demonstrated that HIF-1α negative expression is an independent favorable predictor of pCR. Multivariate Cox regression analysis demonstrated that the HIF-1a expression before NCT showed an independent prognostic value for RFS (HR = 4.168, 95% CI: 1.012–17.170, $p = 0.048$).

Conclusions: HIF-1a expression correlates with pCR in breast cancer undergoing neoadjuvant chemotherapy. Absent expression of HIF-1a was associated with a better pathological response and could indicate a favorable prognosis in non-pCR breast cancer patients.

PO047

CARBOPLATIN INCREASED PATHOLOGICAL COMPLETE REMISSION RATE AND HEMATOTOXICITY INCIDENCE IN NEOADJUVANT TREATMENT OF TRIPLE NEGATIVE BREAST CANCER: A META-ANALYSIS

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Background: To evaluate the efficacy and safety of carboplatin-based neoadjuvant chemotherapy in triple-negative breast cancer patients (TNBC).

Methods: PubMed, EMBASE, the Web of Science, the Cochrane Library, major clinical trial registries, and abstract collections from major international meetings were systematically searched for relevant randomized controlled trials. Endpoints included rates of pathologic complete response (pCR) and hematotoxicity. Relative risk (RR) was calculated for each endpoint using a fixed- or random-effect model depending on the heterogeneity among included studies.

Result: A total of 6 randomized controlled trials involving 1007 patients were included in the meta-analysis. Carboplatin-based chemotherapy was associated with a pooled pCR rate of 53.3%, which was significantly higher than the rate associated with non-carboplatin therapy (37.8%, RR: 1.43, 95% CI: 1.24–1.64, $p < 0.00001$). Carboplatin-based chemotherapy was associated with higher incidence of grade 3 or 4 anemia (RR = 16.67, 95% CI 7.65–50.56, $p < 0.00001$), neutropenia (RR = 2.40, 95% CI 1.42–4.06, $p = 0.001$), and thrombocytopenia (RR = 11.15, 95% CI 5.89–21.10, $p < 0.00001$) than non-carboplatin therapy.

Conclusions: The available evidence suggests that carboplatin-based preoperative chemotherapy is associated with significantly better pCR and higher hematotoxicity rates than non-carboplatin-based therapy in TNBC patients.

PO048

NEOADJUVANT CHEMOTHERAPY AND TIMING OF SENTINEL LYMPH NODE BIOPSY IN DIFFERENT MOLECULAR SUBTYPES BREAST CANCER WITH CLINICALLY NEGATIVE AXILLA

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Background: This study aims to determine the optimal time to perform sentinel lymph node biopsy (SLNB) for cN0 patients following neoadjuvant chemotherapeutic (NAC).

Methods: From October 2010 to November2017, 206 patients with breast cancer underwent operation after NAC were included in this study in our breast cancer center. Patients with cN0 before and ycN0 after NAC received SLNB and axillary lymph node dissection (ALND) in case of positive sentinel lymph node (SLN). Patients with cN+ before and ycN0 after NAC received SLNB and ALND. Patients with ycN+ after NAC received ALND without SLNB.

Result: Among the 183 cN+ patients, the overall axillary nodal pathologic complete response (apCR) rate was 33.3%, and the apCR rates were significantly higher in patients with HER2+ (62.1% with and 34.5% without targeted therapy respectively) and triple-negative (TN) disease (41.0%) than that in patients with hormone receptor positive/HER2 negative (HR+/HER2-) (19.8%, $p < 0.001$). Among the 23 cN0 patients, the positive rate of SLN was 26.1% (6/23).

Conclusions: The pCR rates were significantly related to tumor subtype. Combining the pCR rates in different tumor subtypes of cN+ patients and excellent locoregional control of AOSOG Z0011 and AMAROS trials in cN0 patients, it would be preferable to perform SLNB prior to NAC for cN0 patients with HR+/HER2- subtype, and SLNB after NAC for those with TN and HER2+ subtype to increase the chance of avoiding ALND. As for patients with initial cN+ converting to ycN0, TN and HER2+ subtypes would benefit more from axillary downstaging surgery with NAC than HR+/HER2- subtype.

PO049

PATHOLOGICAL SHRINKAGE MODES OF THE PRIMARY TUMOR AFTER NEOADJUVANT CHEMOTHERAPY IN DIFFERENT MOLECULAR SUBTYPES OF BREAST CANCER

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Background: The objective of this study was to investigate the differences of shrinkage mode of the primary tumor in different molecular subtypes of breast cancer after neoadjuvant chemotherapy (NAC).

Methods: Ninety-one women with pathologically proven solitary invasive ductal carcinoma (IIA-IIIC) were recruited. All patients received whole cycles of NAC. Breast specimen was prepared with part-mount sub-serial section (PMSS), and residual tumors were microscopically outline, scanned and registered by Photoshop software. The three-dimensional (3D) model of residual tumors was reconstructed with 3D-Doctor software to evaluate the shrinkage model. We defined the shrinkage modes as 5 categories: I. Surgical pCR: no residual tumors, II. solitary lesion without surrounding lesions, III. multinodular lesions, IV. solitary lesion with adjacent spotty lesions, and V. diffuse lesions. Further, the clinic-pathologic shrinkage modes were divided into 2 categories: concentric shrinkage mode (CSM, the longest diameter of the pathological residual tumors was less than 50% and ≤ 2 cm in comparison with the primary tumor before NAC) and non-concentric shrinkage mode (NCSM, the longest diameter of the pathological residual tumors was more than 50% and/or > 2 cm in comparison with the primary tumor before NAC).

Result: Of the 18 case Luminal A, 24 case Luminal B (HER2-), 17 case Luminal B (HER2+) , 8 case HER2+, and 24 case triple negative subtype breast cancer, the CSM rate was 50.0%, 58.3%, 82.4%, 75.0%, and 79.2%, respectively ($p < 0.05$).

Conclusions: Luminal B (HER2+), HER2+ and triple negative subtypes were more likely to have concentric shrinkage mode than Luminal A and Luminal B (HER2-) subtypes after neoadjuvant chemotherapy. Molecular subtype might be helpful to predict the regression mode of the primary tumor and select the appropriate candidates and negative margin widths for breast conserving therapy after neoadjuvant chemotherapy.

PO050

INTRAOPERATIVE SENTINEL LYMPH NODE DETECTION USING FLUORESCEIN IN BREAST CANCER

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Background: Technetium-99m (99mTc) is widely utilized as a sentinel lymph node (SLN) mapping agent in breast cancer patients, but it raises concern of radiation exposure. Fluorescein, visible light fluorescence, has no radiation exposure and can be detected easily using a curing light. This study aims to investigate the feasibility and safety of fluorescein imaging for SLN detection in axillary lymph node staging.

Methods: This is a prospective study from a single institute. Sixty-one patients with breast cancer, for whom SLN biopsy had been planned, were enrolled in this study. All the patients received periareolar injection of 99mTc-phytate and 10% fluorescein (1:5 diluted) solution. The SLNs emitting green light under a curing light were retrieved first and detected using a gamma detection probe. The detection rate and lymph node status were analyzed in the enrolled patients.

Result: SLNs were detected in 57 of 61 enrolled patients (93.4%) using 10% fluorescein and the detection rate was similar to 99mTc-phytate ($p = 0.25$). Sensitivity and specificity of 10% fluorescein were also not different with 99mTc-phytate significantly ($p = 0.22$). The false-negative of 10% fluorescein rate was 5 percent and concordance rate between SLN emitting the most fluorescent and having the highest radioactivity was 98.2 percent. There was no complications among the enrolled patients.

Conclusions: Intraoperative SLN detection using fluorescein in breast cancer was feasible and safe.

PO051

DIAGNOSING MALIGNANT MASS ON BREAST ULTRASOUND BY DEEP LEARNING ALGORITHMS USING KERAS LIBRARIES

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Background: Prediction of malignant mass on ultrasound is important on breast cancer screening study. Deep learning algorithms is non-invasive procedures using specific variables associated with malignant imaging.

Methods: Data from 2011 to 2016 are included in our study. input variables were shape, direction , boundary, echogenicity, shadowing and peritumoral feeding vessels. Deep learning algorithms was constructed from factors important for predicting on malignant mass. The deep learning algorithms was composed of two subunits: training set and testing set. The process of deep learning algorithms is composed of two steps: forward and back. The endpoint of this study is accuracy of deep learning algorithms

Result: Two hundred cases were included in this study. Individual sensitivity of training set and test set for predicting on malignant mass were 90.5% and 92.8% respectively. So the accuracy of our study was 84.5%.

Conclusions: Prediction model based on deep learning algorithms appears to be effective in predicting on predicting on malignant mass and, in particular, is expected to be reduced to unnecessary invasive biopsy.

PO052

EFFECTIVENESS OF PREOPERATIVE CORE NEEDLE BIOPSY AND SURGICAL SPECIMENS(DUAL METHOD) TO DETERMINE ADJUVANT TREATMENT PLAN IN BREAST CANCER PATIENTS

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Background: Core needle biopsy (CNB) is a widely used procedure for breast cancer diagnosis and analyzing results of immunohistochemistry (IHC). IHC is an important determinant of adjuvant treatment. Several studies have concordance or difference of IHC result between preoperative CNB and specimens(SS). This study will evaluate the effectiveness of the dual method than the single method (CNB, SS only) through comparison of each determined subtypes and adjuvant treatment plans

Methods: We analyzed the medical records of patients who underwent breast cancer surgery from 2009 to 2017. We collected data of ER, PR, HER2 and Ki-67. Based on the results of IHC, St Gallen molecular subtypes were classified. And adjuvant treatment was established in according to the current NCCN guideline. The treatment based on the results of the single method was compared with the dual method

Result: We found that 118 (20.0%) of 591 subtypes were differently classified as the results of CNB and SS. When adjuvant treatment was based on the results of the dual method, 27 (4.5%) treatment were changed from SS only. There were 22 (3.7%), 5 (0.8%) cases that hormone, anti-HER2 treatment were added. Additionally, 14 (2.4%) treatment were changed from CNB only. There were 3 (0.5%), 11 (1.8%) cases that hormone, anti-HER2 treatment were added

Conclusions: More treatments, not performed according to the results of the single method, were added by the results of the dual method. As a result, 41 (6.9%) patients benefit in treatment. It is important to use the dual method rather than the single method because of the benefits of the additional treatment

PO053

PREDICTING INTERVAL AND SCREEN-DETECTED BREAST CANCERS FROM MAMMOGRAPHIC DENSITY DEFINED BY DIFFERENT BRIGHTNESS THRESHOLDS

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Background: Case-control studies show that mammographic density is a stronger risk factor when defined at higher than conventional pixel brightness thresholds. We asked if this applied to interval and/or screen-detected cancers.

Methods: We conducted a nested case-control study with in the prospective Melbourne Collaborative Cohort Study including 168 interval and 422 screen-detected breast cancers, and 498 and 1,197 matched controls, respectively. We measured absolute and percent mammographic density using the CUMULUS software at the conventional threshold (Cumulus) and two increasingly higher thresholds (Altocumulus and Cirrocumulus, respectively). Mammographic density measures were transformed and adjusted for age and body mass index (BMI). Using conditional logistic regression and adjusting for BMI by age at mammogram, we estimated risk discrimination by the odds per adjusted standard deviation (OPERA) and the area under the receiver operating characteristic curve (AUC).

Result: For interval cancer, the association was strongest for Cumulus as a percentage (OPERA = 2.33 (95% confidence interval (CI): 1.85–2.92); AUC = 0.75), and the BMI association was independent of age at mammogram. After adjusting for Cumulus, no other measure was associated with risk. For screen-detected cancer, associations increased with pixel intensity threshold and were strongest for absolute Cirrocumulus (OPERA = 1.32 (95% CI: 1.18–1.48; AUC = 0.63). More importantly, after adjusting for Cirrocumulus, no other measure was associated with risk.

Conclusions: The amount of brighter areas is the best mammogram-based measure of screen-detected breast cancer risk. The percentage of the breast covered by white or bright areas is the best mammogram-based measure of interval breast cancer risk, irrespective of BMI.

Poster Presentation

PO054

A RETROSPECTIVE COMPARATIVE STUDY OF ONCOLOGICAL OUTCOMES OF SCREEN-DETECTED AND SYMPTOMATIC BREAST CANCER

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Background: After primary surgical resection, breast cancer survivors regularly undergo surveillance using multiple modalities to detect recurrences. However, post-treatment surveillance programs for patients with breast cancer have not been firmly established. The aim of this study was to analyze the clinicopathological and long-term follow-up data of symptomatic and screened breast cancer patients.

Methods: This was a retrospective observational study evaluating breast cancer patient with recurrence between 2006 and 2008. Patients were analyzed by initial detection modality (symptomatic vs. screened). Clinical, radiological, and pathological findings including immunohistochemistry findings of primary and recurrent cancers were reviewed.

Result: Four hundred sixty nine patients were identified with a recurrence (mean age 45.7 years). One hundred sixty two (34.5%) recurrences were symptomatic-detected, 307 (65.5%) were screen-detected. The 5-year survival after recurrence rates for symptomatic detected, and screen-detected recurrences were 46.1%, and 43.9%, respectively. Also, the overall 5-year survival rates for symptomatic detected, and screen-detected recurrences were 69.4%, and 73.2%, respectively. There were no significant differences in these observational group.

Conclusions: A number of different guidelines regarding post-treatment surveillance of patients with breast cancer have been produced worldwide. Our results showed screening modality did not bring any significant improvement in patient survival after recurrence or overall survival for the breast cancer patients compared to the symptomatic group.

PO055

PREDICTION OF NON-SENTINEL LYMPH NODE METASTASIS IN BREAST CANCER; EXTERNAL VALIDATION OF MEMORIAL SLOAN KETTERING CANCER CENTER MODEL AND SUGGESTION OF NEW NOMOGRAM

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Background: With sentinel lymph node (SLN) metastasis in breast cancer patients, tangential radiotherapy without additional axillary LN dissection (ALND) is the standard treatment. However, many surgeons are performing ALND to identify additional axillary LN metastasis. The purpose of this study is to validate the nomogram of Memorial Sloan Kettering Cancer Center (MSKCC, New York, NY) and to propose a new model predicting non SLN metastasis to avoid unnecessary axillary dissection in low risk patients.

Methods: From 2003 to 2012, 591 patients with SLN metastasis and who underwent complete ALND were recruited from Yonsei Cancer Center (YCC). We used receiver operating characteristic (ROC) curve to externally validate MSKCC nomogram. New YCC nomogram was made with new variables collected from logistic regression and internally validated using sample split technique.

Result: MSKCC nomogram underestimated the probability of non SLN metastasis of YCC data. Area under curve (AUC) of MSKCC nomogram induced from our population was 0.69 (less predictive). Therefore, we made new nomogram using different variables which are breast tumor size, the number of positive/negative sentinel LNs, LVI, perinodal extension of SLN metastasis, and human epidermal growth factor receptor 2 (HER2) status. AUC of the new nomogram was 0.75 which is comparable to source nomogram of MSKCC.

Conclusions: The nomogram of MSKCC underestimated the probability of additional non SLN metastasis in our data. We made new nomogram to predict the probability of non SLN metastasis including the variables of PNE of SLN metastasis and HER2 status. External validation is expected to confirm the validity of the new model.

PO056

CLINICOPATHOLOGIC ANALYSIS OF ULTRASOUND-GUIDED VACUUM-ASSISTED BREAST BIOPSY FOR THE DIAGNOSIS AND TREATMENT OF BREAST DISEASE: EXPERIENCE WITH 11,221 CASES IN A SINGLE INSTITUTE

Hai Lin Park, Ka Young Kim, Jong Seob Park, Ji-Eun Shin, Hye-Rin Kim, Bora Yang, Jiyoung Kim, Jeong Yun Shim, Eun-Ah Shin, Song-Mi Noh

CHA Medical Center, Korea

Background: Vacuum-assisted breast biopsy (VABB),performed using a mammotome system, is an effective and safe procedure for performing excisional breast biopsies and removing benign lesions with curative intent; it minimizes post-procedural scarring and complications. This study aimed to assess the clinical and histopathologic data of patients who underwent VABB and to evaluate the usefulness and safety of VABB performed for diagnostic and treatment purposes.

Methods: From January 2003 to December 2015, 11,221 VABB procedures were performed for 8,748 patients at the Department of Surgery, Kangnam CHA Hospital, Korea. Complete excisional VABB was performed for Breast Imaging Reporting and Data System(BI-RADS)ultrasound category 3 or 4a lesions; incisional VABB was performed for category 4b–5 lesions

Result: The patients' mean age was 37.8 years; 58.2% were aged < 40 years. Most lesions (n = 4,443 [39.6%]) were 0.6–1.0 cm in diameter, 355 (3.2%) were ≥ 3.0 cm, and the largest lesion was 7.9 cm. Histologically, fibroadenomas were most common (n = 5,226 [46.6%]), while 414 (3.7%) lesions were malignant and required further surgical management. Eight (14%) of the 57 cases of atypical ductal hyperplasia(ADH) were misclassified—their histologic findings were underestimated based on additional excisional biopsy and follow-up observations. There were 6,791 (60.5%) category 3 lesions, 42 of which were malignant (positive predictive value [PPV] = 0.6%). The PPVs for category 4a (n = 4,019), 4b, 4c, and 5 lesions were 3.4%, 34.8%, 66.2%, and 93.8%, respectively. The mean ± standard deviation number of core specimens removed with an 8-gauge probe was 9.5 ± 8.8 and the mean procedure time was 3.4 ± 2.7 min. Hence, an average of 11 and 18 core specimens for lesions ≤ 2.0 cm and ≤ 3 cm, respectively, is required for complete excision. One patient developed intra-procedural hemorrhage requiring blood transfusion and conversion to open surgery; no other serious complications occurred. Follow-up ultrasonography was performed to detect residual lesions after excisional VABB. No residual lesion was confirmed in 94.4% of the 7,480 cases where follow-up was possible 3–6 months later, while four patients required re-excisional VABB due to residual lesions; all four lesions were benign.

Conclusions: The study suggests that VABB can replace ultrasound-guided core biopsy and excisional biopsy procedures for diagnosis and therapeutic management of benign breast lesions, which account for the majority of breast diseases.

Poster Presentation

PO057

DIFFUSIONAL KURTOSIS IMAGING FOR DIFFERENTIATION OF ADDITIONAL SUSPICIOUS LESIONS ON PREOPERATIVE BREAST MRI OF PATIENTS WITH KNOWN BREAST CANCER

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Background: To investigate the potential of diffusional kurtosis imaging (DKI) and conventional diffusion weighted imaging (DWI) for evaluation of additional suspicious lesions on preoperative breast MRI patients with known breast cancer.

Methods: Fifty-three pathologically confirmed additional suspicious breast lesions >10 mm were included. Diffusion MRI was performed using b-values of 0, 50, 600, 1,000, and 3,000 sec/mm^2. Apparent diffusion coefficient (ADC) and for DKI, diffusivity (D, diffusion coefficient with correction of non-Gaussian bias) and kurtosis (K, deviation of tissue diffusion from a Gaussian pattern) were calculated. Histogram measures of D, K and ADC were compared between benign vs. malignant lesions, and between benign vs. ductal carcinoma in situ (DCIS) vs. invasive breast lesions.

Result: Twenty-three lesions were benign and 30 were malignant (DCIS, n = 14; invasive carcinoma, n = 16). Between benign and malignant lesions, D-25th percentile, D entropy and ADC skewness differed significantly. Between benign vs. invasive lesions, histogram parameters of D (mean, 50th percentile, 75th percentile, 90th percentile, and entropy) and ADC-75th percentile differed significanly. Between DCIS vs. invasive lesions, D-50th percentile and ADC-50th percentile differed significantly. Between benign vs. DCIS lesions, only K-10th percentile showed a significant difference. ROC curve analysis showed high specificity of multiple D parameters and ADC-75th percentile for distinguishing invasive vs. benign lesions, and high specificity of D-50th percentile for distinguishing DCIS vs. invasive lesions.

Conclusions: DKI can help evaluate additional suspicious lesions detected on breast MRI in patients with known breast cancer, but may have lower potential in differentiating benign vs. DCIS breast lesions.

PO058

USEFULNESS OF MULTIFUNCTIONAL MAGNETIC NANOWIRES FOR DETECTING CIRCULATING TUMOR CELLS FROM BREAST CANCER

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Background: Circulating tumor cells (CTCs) are recognized as promising biomarkers for diagnosis and indication of the prognosis in breast cancer. A non-invasive biomarker has been recognized. However, previous studies showed CTCs detection rates as about 20% was low. The aim of this study is to identify the development of multifunctional magnetic nanowires for the efficient isolation and detection of CTCs in breast cancer and a more sensitive and specific method to be applied to a clinical biomarker.

Methods: The study group consisted of all consecutive 50 breast cancer patients who diagnosed at National Cancer Center, Korea from 2015 to 2017. CTCs isolated from 1 mL to 3 mL of the peripheral blood of patients using multifunctional magnetic nanowires. The relation of clinicopathological factors and CTCs was analyzed.

Result: Of the 50 breast cancer patients, 43 (86%) found CTCs. From stage 0 to stage IV, CTCs were isolated. Of them, six patients had received neoadjuvant chemotherapy. The mean number of detected CTCs was 3.6. The number range of isolated CTCs was at least 1 to maximal 9. Univariate analysis showed age, tumor grade, stage, tumor type, venous or lymphatic invasion were not significantly associated with CTCs detection ($p = 0.514$).

Conclusions: This study found high rate of detection and isolation of CTCs using multifunctional magnetic nanowires through small volumes of blood. The result might be clinical availability of CTCs as biomarker to various stages of breast cancer.

PO059

DIAGNOSTIC ACCURACY OF NON-MASS ENHANCEMENT WHICH EXTENDS TO THE NIPPLE ON BREAST MRI

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Background: Although nipple sparing mastectomy (NSM) is increasingly performed for cosmetic purpose, the presence of non-mass enhancement (NME) in the base of nipple on preoperative MRI frequently leads to sacrifice the nipple. However, the relationship between pathologic involvement of nipple and NME is unknown. In this prospective study, we evaluated the diagnostic accuracy of NME toward the nipple on MRI compared with pathologic findings.

Methods: From December 2016 to November 2017, we prospectively enrolled the breast cancer patients underwent mastectomy with NME in the subareolar region on MRI. NME positive group is defined as the presence of NME up to the base of nipple on MRI. Histopathologic mapping to measure the distance from the base of nipple to cancer cell was performed by microscopic examination of vertically cutting slices with 2-3mm thickness from nipple to the breast cancer lesion. The positive result is the presence of cancer cells at the base of nipple.

Result: Of 49 patients, 35 (71%) were NME-positive group and 14 (29%) were NME-negative group. The distance from the base of nipple to cancer cell measured by pathologic examination was significantly different between the NME positive and negative group (-1.3 ± 8.2 mm vs. 6.5 ± 4.3, $p = 0.002$). The PPV and NPV of the NME was 71.4% and 92.9%.

Conclusions: Our results showed that the diagnostic accuracy of NME extending nipple base identified by MRI is high in terms of PPV and NPV. Therefore, NSM is considered to be difficult to perform when NME extents to the nipple base on MRI.

PO060

DIAGNOSTIC SIGNIFICANCE OF BREAST CANCER SUBTYPES VIA BACTERIAL EXTRACELLULAR VESICLES IN URINE

Jeongshin An[1], Jinho Yang[2], Won-Hee Lee[2], Jong-Kyu Kim[1], Hyungoo Kim[1], Sehyun Paek[1], Jun Woo Lee[1], Joohyun Woo[1], Jong Bin Kim[1], Hyungju Kwon[1], Woosung Lim[1], Yoon-Keun Kim[2], Byung-In Moon[1], Nam Sun Paik[1]

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Background: The microbiome has a symbiotic relationship with a human, and when the symbiosis is broken, these bacteria can cause diseases such as cancers. Many cancers are associated with microbiome and have an unusual distribution of microbiome compared to normal group. The distribution of microbiome can be found through 16s rDNA sequencing using bacterial extracellular vesicles (EVs) in urine samples. We distinguished between breast cancer and normal group and differentiated subtypes of breast cancer through urine samples.

Methods: Urine samples in female (127 breast cancer patients and 220 normal individuals) were collected from September 2014 and to August 2015 at Ewha Womans University Mokdong Hospital and Haeundae Paik Hospital. The mean age was 51.8 in patients and 59.2 years in controls. The samples were analyzed by metagenomic sequencing (NGS) using a universal bacterial primer of 16S rDNA, A T-test was performed to discover the significantly different between breast cancer patients and controls

Result: Bacterial extracellular vesicles from thirty genera were elevated, and forty-seven were decreased in urine samples of breast cancer patients compared to the normal group. Methylophilaceae family only existed in luminal A type. Odoribacter was most prevalent in luminal B type, and Schwartzia was only discovered in luminal B type at genus-level. Butyricimonas was most prevalent in HER2 type. Beijerinckiaceae family was predominant in TNBC type.

Conclusions: We found bacterial-EV has a difference of distribution according to breast cancer subtypes. These results might be used as a basic research for developing a biomarker to distinguish the breast cancer subtype using urine samples.

PO061

IS DIGITAL BREAST TOMOSYNTHESIS FAVORABLE FOR THE EVALUATION OF BREAST MICROCALCIFICATIONS AND FOR PRE-PROCEDURAL STUDY OF STEREOTACTIC BIOPSY?

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Background: To investigate the diagnostic power of digital breast tomosynthesis (DBT) in evaluation of breast microcalcifications and usefulness as a pre-procedural study for stereotactic biopsy in comparison with full-field digital mammogram (FFDM) and FFDM plus magnification image (FFDM+MAG).

Methods: An IRB approved retrospective observer performance study on DBT, FFDM, and FFDM+MAG was done. Image quality was rated in 5-point scoring system for lesion clarity (1, very indistinct; 2, indistinct; 3, fair; 4, clear; 5, very clear) and compared by Wilcoxon test. Diagnostic power was compared by diagnostic values and AUC with 95% confidence interval. Additionally, procedural report of biopsy was analysed for patient positioning and adequacy of instruments.

Result: DBT showed higher lesion clarity (median 5, interquartile range 4-5) than FFDM (3, 2-4, p-value < 0.0001), and no statistically significant difference to FFDM+MAG (4, 4-5, p-value = 0.3345). Diagnostic sensitivity and specificity of DBT were 86.4% and 92.5%; FFDM 70.4% and 66.7%; FFDM+MAG 93.8% and 89.6%. The AUCs of DBT (0.88) and FFDM+MAG (0.89) were larger than FFDM (0.59, p-values < 0.0001) but there was no statistically significant difference between DBT and FFDM+MAG (p-value = 0.878). In 2 cases with DBT, petit needle could be appropriately prepared; and other 3 without DBT, patient repositioning was needed.

Conclusions: DBT showed better image quality and diagnostic values than FFDM and equivalent to FFDM+MAG in evaluation of breast microcalcifications. Evaluation with DBT as a pre-procedural study for breast stereotactic biopsy can lead to more accurate localization and successful biopsy and also waive the need for additional magnification images.

PO062

IMAGING OF BREAST CANCER USING RADIOLABLED-TRASTUZUMAB PET FOR EVALUATING HER2 EXPRESSION

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Background: Assessment of HER2 status requires tissue biopsy. However, it is not feasible in some circumstances. Theoretically, imaging using radiolabeled trastuzumab (trastuzumab-PET) could represent the HER2 status and the binding ability to HER2 protein without biopsy. The purpose of this study is to evaluate the ability of trastuzumab-PET in predicting tissue HER2 status and tratuzumab susceptibility.

Methods: 64Cu-DOTA-trastuzumab and conventional FDG-PET were performed on breast cancer patients who had measurable lesions regardless of being primary or metastatic. We compared the tumor-to-liver ratio (TLR) of trastuzumab-PET with that of FDG-PET, to tissue HER2 expression status of primary breast cancer. TLR was defined as SUVmax of the tumor normalized to SUVmean of the liver in the same patient.

Result: The first patient had multiple distant metastasis, and her primary breast cancer had been a HER2(+) disease. The lesions were well-visualized in FDG-PET (TLR 6.0) as well as in trastuzumab-PET (TLR 2.7). The imaging results were concordant with the HER2 status of the primary lesion. The second patient had multiple metastasis, and the primary breast cancer had been a HER2(-) disease. The lesion was well-visualized in FDG-PET (TLR 4.6) but not in trastuzumab-PET (TLR 1.0). The third patient had distant metastasis developed at 5 months after the completion of adjuvant trastuzumab. The lesion was well-visualized in FDG-PET (TLR 3.6) but not in trastuzumab-PET (TLR 0.7), implicating problems in the binding ability of tratuzumab. This might reflect the trastuzumab-resistant characteristics of the primary cancer.

Conclusions: Trastuzumab PET was effective in evaluating HER2 status and trastuzumab susceptibility in breast cancer patient.

PO063

WHAT TO CONSIDER IN A CULTURALLY TAILORED TECHNOLOGY-BASED CANCER PAIN MANAGEMENT PROGRAM

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Background: Technology-based interventions are easily accepted by marginalized populations including racial/ethnic minorities, and the marginalized populations frequently prefer Internet resources to traditional resources due to their difficulties in establishing equal and trustworthy relationships with their physicians in face-to-face settings. Despite the high potential of technology-based interventions, little is still known about what to consider in a technology-based cancer pain management program for racial/ethnic minorities. The purpose of this presentation is to identify the issues encountered in implementing a technology-based cancer pain management program among Asian American breast cancer survivors.

Methods: The parent study was a pilot study to determine the preliminary efficacy of a technology-based cancer pain management support program for Asian American breast cancer survivors [CAPAA] on the women's cancer pain experience. The pilot study was a randomized controlled intervention study among 94 Asian American breast cancer survivors. Throughout the research process, the research team wrote research diaries and kept the minutes of weekly research team meetings. Then, the data consisting of research diaries and minutes were analyzed using content analysis to extract the themes reflecting the practical issues.

Result: The identified issues included those related to: (a) diversities within Asian American breast cancer survivors; (b) survivors treatment and healing process; (c) Internet resources from the participants countries of origin; (d) building trust between researchers and participants/gatekeepers; (e) fidelity of the intervention; and (f) cultural sensitivity in word selection.

Conclusions: Future design and implementation of technology-based cancer pain management programs for racial/ethnic minorities need to consider these practical issues.

PO064

DEVELOPMENT OF COMPUTER SOFTWARE FOR UPDATED EIGHTH AJCC BREAST CANCER STAGING

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Background: The eighth American Joint Committee for Cancer (AJCC) staging system of breast cancer was published recently for more accurate prediction of prognosis adding biomarkers such as ER, PR, and HER2. But it is very complicated and difficult to use for clinicians. The authors developed a software to aid in setting up the staging system and confirmed its usefulness by applying it to theoretical combinations and actual clinical data.

Methods: The software was developed by Microsoft Excel Macro. We used the software for the anatomic, clinical and pathological prognostic stages in the 588 theoretical combinations. We also calculated the stages using the 840 breast cancer patients without preoperative chemotherapy, carcinoma in situ or distant metastasis.

Result: The anatomic, clinical and pathological prognostic stages were identical in 240 out of 588 theoretical combinations. In the actual patients' data, stage IB and IIIB were more frequent in clinical and pathological prognostic stage then anatomic stage. The anatomic stage was same with clinical prognostic stage in 58.2% of patients and was same with pathological prognostic stage in 61.9%. Oncotype DX could change the pathological prognostic stage in the 2.1% of patients.

Conclusions: The developed software was useful for new staging system. Additional studies using survival data would be needed in the future.

PO065

MOLECULAR SUBTYPE AS A PROGNOSTIC MARKER FOR BRAIN METASTASIS IN BREAST CANCER: A POPULATION-BASED ANALYSIS USING THE SEER DATABASE

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Background: To evaluate the impact of molecular subtype on incidence and prognosis of brain metastasis from breast cancer.

Methods: The Surveillance, Epidemiology, and End Results (SEER) 18 registry was used to select breast cancer patients from 2010 to 2014. Molecular subtypes were classified as luminal A (hormone receptor [HR]+/human epidermal growth factor receptor 2 [HER2]-), luminal B (HR+/HER2+), HER2 (HR-/HER2+), or triple negative breast cancer (TNBC) (HR-/HER2-). The incidence and prognosis of brain metastasis was evaluated according to molecular subtype.

Result: Among the 206,913 breast cancer patients selected, the HER2 subtype showed the highest incidence of brain metastasis (1.0%) followed by TNBC (0.7%). HER2 and TNBC patients with multiple extracranial metastases (bone, liver, and lung) showed a high incidence of brain metastasis (28.0% and 30.8%, respectively). Incidence of brain metastasis in the TNBC subtype was sporadic irrespective of T and N stages. For brain metastasis patients, combined visceral metastasis significantly decreased overall survival (OS) whereas bone metastasis did not. On multivariate analysis, the order of molecular subtype by favorable prognosis was luminal B, luminal A, HER2, and TNBC in all brain metastasis, while for brain metastasis patients without visceral metastasis, the order was luminal B, HER2, luminal A, and TNBC.

Conclusions: Molecular subtype and visceral metastasis should be considered when evaluating prognosis for patients with brain metastasis. In patients with HER2 and TNBC cancer subtypes, particularly those with visceral metastasis, close surveillance could contribute to early detection of brain metastasis and improve survival and quality of life for these patients.

PO066

CLINICOPATHOLOGIC CHARACTERISTICS AND PROGNOSTIC FACTORS OF PURE MUCINOUS BREAST CANCER

Sung-Chan Gwark, Jisun Kim, Seung Wook Yang, Sung Ui Jung, Cheol Min Kang, Sae Byul Lee, Guiyun Sohn, Il Yong Chung, Beom Seok Ko, Hee Jeong Kim, Jong Won Lee, Byung Ho Son, Sei Hyun Ahn

ASAN Medical Center, Korea

Background: Mucinous carcinoma of the breast is an uncommon particular type of breast cancer presents a more favorable prognosis than IDC-NOS. Pathologically, mucinous carcinoma is divided into two subtypes: pure and mixed. In this study, we reviewed the clinicopathologic characteristics and prognostic factors of pure mucinous carcinoma.

Methods: We reviewed the 23 years cumulative data of pure mucinous breast cancer patients from the database of the Breast Cancer Center at ASAN Medical Center, Korea, between 1989-2011, retrospectively. Total 386 pure mucinous carcinoma cases were reviewed to analyze clinicopathologic characteristics and prognosis.

Result: Mean age was 46.7. 149 patients underwent modified radical mastectomy and 236 underwent breast-conserving therapy. The T-stage was T1 in 187 patients, T2 in 178 patients, T3 in 17 patients and T4 in 4 patients. Node negative was 325 and node positive was 61. ER+ in 342 and ER- in 29. PR+ in 276 and PR- in 95. HER2+ in 47 and HER2- in 273 patients. The 5-year disease free survival(DFS) rate was 93.3%, 5-year cancer specific survival rate was 98.2% and the 5-year overall survival rate was 96.6%. Univariate analysis showed that ER, lymph node and Her2 status appeared to be a prognostic factor of DFS rate. In multivariate analysis, only nodal status is the most significant prognostic factor for DFS rate.

Conclusions: Pure mucinous carcinoma of the breast is a rare subtype with a favorable prognosis. Nodal status rather than ER status, Her2 status is considered to be the most significant prognostic factor for pure mucinous breast cancer.

PO067

ANALYSIS OF SERIAL CIRCULATING TUMOR CELL COUNT DURING NEOADJUVANT SYSTEMIC THERAPY IN BREAST CANCER PATIENTS

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Background: We aimed to evaluate the clinical implication of circulating tumor cell (CTC) counts in correlation with prognosis and radiologic/pathologic response to therapy in locally advanced breast cancer patients undergoing preoperative systemic therapy.

Methods: From Feb 2014 to May 2017, 207 patients without distant metastasis were prospectively enrolled from AMC. CTC counts were analyzed before-during-after the therapy. CTC isolation was performed using a SMART BIOPSY™ SYSTEM Isolation kit (Cytogen, Inc., Seoul, Korea). Recurrence-free and overall survival was analyzed according to CTC counts.

Result: The mean follow-up period was 22.46 months and mean age was 46.48 years. One or more CTC was identified in 132 of 203 patients (65.0%) before NST, in 135 of 186 patients (72.0%) during NST and 103 of 171 patients (60.2%) after NST. Initial tumor burden at diagnosis -tumor size, lymph node metastasis- was not correlated with CTC positivity. Overall, CTC count (≥ 1 CTC, ≥ 2 CTCs, and ≥ 5 CTCs) was not correlated with response to therapy. Using RECIST criteria, 86.5% (179/204) were responders (complete, partial response, CR/PR) and 12.1% (25/204) were non-responders (stable, progressive disease, SD/PD). 14.5% (30/207) showed a pathologic complete response (pCR), yet no association was found between CTC count/changes and radiologic/pathologic response to therapy. Also, CTC count was not correlated with prognosis among the whole population. However, HR+ tumors, CTC detection before NST was significantly associated with treatment response by RECIST criteria (responder vs. non-responder) ($p = 0.003$, $p = 0.017$ and $p = 0.023$, respectively).

Conclusions: Our findings support limited value of CTC count for locally advanced breast cancers undergoing neoadjuvant systemic therapy.

Poster Presentation

PO068

ENDOCRINE THERAPY ONLY IN N1 STAGE BREAST CANCER PATIENTS WITH HORMONE RECEPTOR POSITIVE AND HER-2 NEGATIVE

Sung Ui Jung, Sei Hyun Ahn, Byung Ho Son, Jung Won Lee, Il Yong Chung, Beom Seok Ko, Hee Jeong Kim, Jisun Kim, Guiyun Sohn, Sae Byul Lee, Sung-Chan Gwark, Cheol Min Kang, Seung Wook Yang

ASAN Medical Center, Korea

Background: The purpose of this study was to compare treatment outcomes between endocrine therapy only and chemotherapy with endocrine therapy in hormone-receptor-positive, HER2-negative and lymph-node-positive breast cancer.

Methods: This was a retrospective study if 18,549 patients who were surgically treated for invasive breast cancer at Asan Medical Center between January 1993 and December 2012. 1:1 case control matching was performed with endocrine therapy only group (N = 104) and chemotherapy with endocrine therapy group (N = 110). Lymph-node-positive, Hormone-receptor-positive and HER2-nevative breast cancer patiehts was compared between endocrine therapy group and chemotherapy group.

Result: The median follow up time was 85.15 months (range, 2–221 months). In survival analysis, 5 years recurrence free survival of endocrine therapy only group and chemotherapy with endocrine therapy group were 96.9% and 90.2%, respectively. Ten years RFS were 88.9% and 87.9%, respectively. 5 years Overall Survival rate of two groups were 99.0% and 95.6%, respectively. Ten years OS were 95.6% and 97.2% respectively. There were no differences in RFS ($p = 0.48$) and OS ($p = 1.0$) between the 2 groups.

Conclusions: Some populations with clinicopathologic features such as hormone receptor positive and HER2 negative can avoid chemotherapy even with lymph node metastasis. Future studies with a large number of patients and longer follow-up time are necessary to determine.

PO069

A RETROSPECTIVE PROGNOSTIC EVALUATION ANALYSIS USING THE 8TH EDITION OF AMERICAN JOINT COMMITTEE ON CANCER (AJCC) CANCER STAGING SYSTEM FOR BREAST CANCER

Sae Byul Lee, Guiyun Sohn, Jisun Kim, Il Yong Chung, Hee Jeong Kim, Beom Seok Ko, Jong Won Lee, Byung Ho Son, Sei Hyun Ahn

ASAN Medical Center, Korea

Background: The present study aimed to analyze the prognostic value of AJCC 8th edition Cancer Staging System in breast cancer, on a retrospective cohort.

Methods: This study was a retrospective single-center study of breast cancer cases diagnosed from January 1999 to December 2008. We restaged patients based on the 8th edition of the AJCC cancer staging system and analyzed prognostic value of the Anatomic Stage Group and the Prognostic Stage Group.

Result: The study enrolled 9,075 breast cancer patients with 98.7 months median follow-up period. Prognostic stages of 5,388 cases (77.4%) changed compared with anatomic stages, with 5,017 (72.1%) upstaged cases and 371 (5.3%) down staged case. Both 5 year DFS and 5 year OS were significantly different in the different anatomic and prognostic stage groups. Survival rates by subtype are shown in the order of HR(+)/HER2(-)(5-year OS, 90.9%), HR(+)/HER2(+) (84.7%), HR(-)/HER2(+)(81.1%) and HR(-)/HER2(-)(80.9%). In the anatomic stage, the survival rate of patients with HR(+)/HER2(-) of stage III (5-year OS, 88.3%) is better than that of HR(-)/HER2(-) of stage II (86.5%). On the other hand, in the prognostic stage, both 5-year and 10-year survival rates of patients with HR(-)/HER2(-) of stage II (5-year DFS, 90.1%; 5-year OS 79.1%) are higher than those of patients with HR(+)/HER2(-) of stage III (5-year DFS, 94.3%; 5-year OS, 88.9%) in DFS and OS.

Conclusions: The prognostic staging system proposed in the AJCC 8th edition refines the anatomic stage group in breast cancer and will lead to a more personalized approach to breast cancer treatment.

PO070

A PREDICTION OF OVERALL SURVIVAL STATUS BY DEEP LEARNING USING PYTHON PACKAGE IN BREAST CANCER: A NATIONWIDE STUDY FROM THE KOREAN BREAST CANCER SOCIETY

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Background: Prediction of overall survival status is important into decided in adjuvant treatment. Deep belief network is a kind of artificial intelligence (AI). We intended to construct prediction model by deep belief network using associated clinicopathologic factors.

Methods: Data from 2007 to 2014 in Korean Breast Cancer Registry are included in our study. Deep belief network was constructed from factors statistically important for predicting on overall survival status. The DBN was composed of two subunits: training set and testing set. The process of DBN is composed of two steps: forward and back. The endpoint of this study is accuracy of Deep belief network

Result: One hundred three thousand Eight hundred eighty one cases were found in the Korean Breast Cancer Registry. After preprocessing of data, a total of 15,733 cases were enrolled in this study. In univariate analysis for overall survival (OS), the patients with advanced AJCC stage showed relatively high HR (HR = 1.216 95% CI: 0.011-289.331, $p = 0.001$). Based on results of univariate and multivariate analysis, input variables for learning model included 17 variables associated with overall survival rate. Output was presented in one of two states : event or censored. Individual sensitivity of training set and test set for predicting overall survival status were 89.6% and 91.2% respectively. And specificity of that were 49.4% and 48.9% respectively. So the accuracy of our study for predicting overall survival status was 82.78%.

Conclusions: Prediction model based on Deep belief network appears to be effective in predicting overall survival status and, in particular, is expected to be applicable to decide on adjuvant treatment after surgical treatment.

PO071

TREATMENT PATTERNS AND CLINICAL OUTCOMES IN ELDERLY BREAST CANCER PATIENTS

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Background: The proportion of Korean elderly population (≥ 65-year old) is expected to be about 30% in 2035. Therefore, elderly breast cancer patients have been increasing. However, establishment of standard treatment and prognosis for elderly patients is difficult due to multimorbidity. In this study, we evaluated the prognostic factors associated with survival in elderly breast cancer patients and also assessed the impact of comorbidity on prognosis.

Methods: This retrospective study included 362 patients (≥ 65 years old) who underwent breast cancer surgery between 2003 and 2014. For characterization, the patients were divided with two groups by age: aged group ($65 \leq Age < 75$, n = 277) and super-aged group ($Age \geq 75$, n = 85). Comorbidity was parametrized using American Society of Anesthesiologists (ASA). The Kaplan Meier analysis was used for overall survival(OS) and distant metastasis free survival (DMFS).

Result: Super-aged group had higher ASA score than aged group (90.6% vs. 75.8%, $p = 0.004$). The proportion of patients who did not have chemotherapy (87.1% vs. 54.5%, $p < 0.001$) and radiotherapy (56.5% vs. 36.1%, $p < 0.001$) was higher in the super-aged group. In multivariate analysis, poor OS was observed in patients with higher histologic grade (HR 3.6, $p = 0.013$), T stage (HR 6.9, $p = 0.001$), and N stage (HR 3.4, $p = 0.009$) and patients without radiotherapy (HR 1.4, $p = 0.021$). The prognostic factors associated with DMFS were super-aged group (HR 4.1, $p = 0.023$), higher T stage (HR 18.4, $p < 0.001$), and no-chemotherapy (HR 7.4, $p = 0.002$). Comorbidity did not affect DMFS and OS statistically in univariate and multivariate analysis.

Conclusions: Comorbidity and important prognostic factors of general breast cancer such as systemic therapy and subtype did not affect overall survival, but radiotherapy was an important prognostic factor in elderly patients.

PO072

MICRORNA-137 INHIBIT CELL MIGRATION AND INVASION BY TARGETING DEL-1 IN TRIPLE NEGATIVE BREAST CANCER CELLS

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Background: This study aimed to investigate the function of microRNA-137 in Del-1 expression in breast cancer cells and tissues.

Methods: The Del-1 mRNA and microRNA levels were measured using a qRT-PCR in breast cancer cells (MDA-MB-231, MCF7, SK-BR3 and T-47D) and tissues from 15 patients with triple-negative breast cancer (TNBC). The effects of the two microRNAs on cell proliferation, migration, and invasion were determined using MTT, wound healing, and Matrigel Transwell assays.

Result: Results showed that, compared to the other breast cancer cell lines, miR-137 levels were remarkably low, while Del-1 mRNA expression was higher in MDA-MB-231. The luciferase reporter assay revealed that both miRNAs bind directly at the 3-UTR of Del-1 and the Del-1 expression was down-regulated by mimics and rescued by inhibitors of both miR-137. Among 15 TNBC specimens, miR-137 were down-regulated in 11 specimens.

Conclusions: In conclusion, miR-137 regulates Del-1 expression in TNBC via directly binding with Del-1 gene, and thereby affect cancer progression, which suggests that this miRNAs can be new biomarkers for TNBC.

PO073

LONG-TERM FOLLOW UP OF 433 PURE DUCTAL CARCINOMA IN SITU CASES; A SINGLE CENTER STUDY

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Background: Ductal carcinoma in situ (DCIS) is a high risk disease of developing invasive tumor. Although with excellant prognosis, many are treated heavily with surgery, radiation, endocrine therapy. We aimed to evaluate clinical and pathologic factors associated with invasive recurrence focusing on locoregional, distant disease after breast conserving surgery (BCS).

Methods: Four hundred thirty three patients from single institute were analyzed. All were diagnosed pure DCIS with no invasive component after BCS between January 2000 to December 2008. Clinico-pathological characteristics, margin status and adjuvant therapy were analyzed. Duration of endocrine therapy in hormone receptor positive DCIS patients were assessed from both drug prescription and/or patients report from EMR.

Result: During median follow-up duration of 123 months, 8.5% (37/433) cases of recurrence with 12 (32.4%) in situ and 25 (67.6%) invasive recurrence were observed. While all initial in situ recurred cases developed no subsequent recurrence, 24.0% (6/25) developed distant metastasis after invasive recurrence. Adjuvant radiotherapy (RT) was performed in 403 of 433 patients (93.1%) and permanent resection margin involvement was observed in 38 cases (8.8%). Invasive recurrence were independently associated with young age (≤ 40), and hormone receptor (HR) negativity (95% CI 1.83–8.49 and 95% CI 1.49–8.61 respectively) while radiotherapy and margin positivity were not. Notably, among hormone receptor positive patients, duration of endocrine treatment was not associated with recurrence.

Conclusions: Young age, negative HR status were independently associated with increased risk of invasive recurrence. Analysis with in larger cohort of pure DCIS would be crucial to confirm the optimal strategy for adjuvant therapy in this group.

PO074

SYSTEMATIC ANALYSIS OF GENETIC ALTERATIONS AND CLINICAL OUTCOMES OF CYCLOOXYGENASE 2(PTGS2) IN BREAST CANCER USING GENOMIC DATA ANALYTIC PLATFORMS

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Background: The expression of Cyclooxygenase 2 (PTGS2) is altered in many cancers. The present study aims to determine whether PTGS2 can serve as a prognostic marker in breast cancer patients.

Methods: The PTGS2 expression was evaluated using Oncomine database to determine the gene alteration during cancer progresseion.The copy number alteration, or mutations of PTGS2 were analyzed and visualized using cBioPortal. The clinical impact of PTGS2 expression related to the survival of cancer patient was assessed using Oncolnc, Kaplan-Meier plotter, and PrognoScan database.

Result: The PTGS2 expression was down-regulated in 13/13 studies among Oncomine database. TCGA dataset in Cbioportal for cancer genomics have genetic alterations of PTGS2 in 142 (13%) of 1098 sequenced cases. Interestingly, PTGS2 up-regulation has a good prognosis in breast cancer patients at Oncolnc, Kaplan-Meier plotter, and PrognoScan database.

Conclusions: PTGS2 might serve as a prognostic marker or therapeutic target for breast cancer patients.

PO075

EXPRESSION OF VITAMIN D RECEPTOR MRNA IN MALIGNANT BREAST TISSUE USING VARIOUS BIOINFORMATICS ANALYSES

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Background: Breast cancer is the second most frequent malignancy in Korean women, with a continuously increasing incidence. The importance of vitamin D in many cancers, including breast cancer, has been demonstrated. The actions of the vitamin D hormone 1,25-dihydroxyvitamin D3 (1,25(OH)2D3) are mediated by the vitamin D receptor (VDR), a ligand-activated transcription factor that functions to control gene expression. To determine the correlation between vitamin D expression and breast cancer using different types of genomic data.

Methods: The VDR expression was accessed using Oncomine database to determine the gene alteration during carcinogenesis, copy number alteration using cBioPortal and gene set analysis using Genemania. Prognostic survival was analyzed by PrognoScan database. Further subgroup analyses separating the cancer patients based on receptor status using programming with TCGA data in R language.

Result: The expression of VDR was analyzed between breast tumor and normal breast tissues using the Oncomine database. The VDR was over-expressed in Finak breast study with *p*-value 3.18E-20, fold change 2, and top gene ranks 10%. There was statistically significant difference according to the degree of expression in 3 data in Prognoscan database (204255_s_at, 213692_s_at and 1410_at). Two out of three data shows better DFS in underexpression of VDR. Subgroup divided according to the type of receptors revealed differences in VDR expression. There was statistically significant differences in Her2 group that VDR was overexpressed.

Conclusions: VDR expression was significantly upregulated in different receptor status using various tools of bioinformatics analyses. Further validation study should be performed to clarify the correlation of expression with prognosis.

PO076

PROGNOSTIC FACTORS IN EARLY LUMINAL BREAST CANCER: MULTI-INSTITUTIONAL STUDY

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Background: Luminal A and a fraction of luminal B breast cancer are hormone-receptor positive and HER2 negative. These are more common and associated with better prognosis. However, most studies have focused on non-luminal breast cancers or advanced luminal breast cancers because their prognosis is poor. The aim of this study was to evaluate the clinicopathological factors affecting the prognosis of early luminal breast cancers.

Methods: We collected data on 716 female patients with luminal breast cancer at three institutions from 2005 to 2012. Early breast cancer was defined as T1/N0, T1/N1, T2/N0, and T2/N1 according to the 7th edition AJCC TNM staging system. We collected standard demographic and clinicopathologic data, including age, tumor size, histologic grade, status of lymphovascular invasion, number of LNs harvested, number of metastatic LNs identified, Ki-67 labeling index (LI), and operation methods.

Result: The median follow-up time was 82 months. We found a higher proportion of locoregional recurrence in patients with luminal B than in patients with luminal A. In multivariate analysis, younger age (≤ 40) and Grade 2/3 were statistically significantly associated with poor breast cancer disease-free survival in the overall population. We divided the patients into 4 groups according to age and histological grade; group A: age (> 40) and G1; group B: age (> 40) and G2/3; group C: age (≤ 40) and G1; group D: age (≤ 40) and G2/3. Group D had higher percentage of breast cancer recurrence.

Conclusions: In early luminal breast cancer, breast cancer recurrence was associated with age and histologic grade, not other clinicopathologic factors, especially, tumor size, nodal involvement, or adjuvant therapy.

Poster Presentation

PO077

THE IMPACT OF TIME INTERVAL BETWEEN DIAGNOSIS AND SURGERY IN EACH TYPE AND STAGE OF BREAST CANCER

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Background: There are many factors that might contribute to the delay of surgery in patients with breast cancer. Previous studies investigate the influence of delay of surgery, but they reported inconsistent results. The aim of this study was to evaluate the impact of time of surgery on prognosis of breast cancer.

Methods: We performed a retrospective review of the patients with breast cancer, who received surgery between 1992 and 2014, by using data from Korea Breast Cancer Society Registry. Kaplan-Meier survival analysis and Cox regression model were used to evaluate the impact of time to surgery in breast cancer and subgroup analysis including each molecular subtypes and stages.

Result: A total 51,164 patients were included for analysis. Delay of surgery more than 30 days was associated with worse survival for breast cancer (hazard ratio (HR) = 1.29; 95% confidence internal (CI), 1.27–1.31, $p < 0.001$). Subgroup analysis for hormone receptor positive and HER2 negative ($p < 0.001$), hormone receptor positive and HER2 positive ($p < 0.001$), hormone receptor negative and HER2 positive ($p < 0.001$), triple negative ($p < 0.001$), stage I ($p < 0.001$), II ($p < 0.001$), III ($p < 0.001$), even in DCIS ($p < 0.001$) showed that over 30 days of surgical delay were associated with worse survival.

Conclusions: Surgical delay of more than 30 days were significant risk factor for worse outcome of breast cancer in each molecular subtype and stages. Although preoperative evaluation is required, surgical delay should be shortened to enhance survival of breast cancer patients.

PO078

EXTERNAL VALIDATION OF IBTR! 2.0 NOMOGRAM FOR PREDICTION OF IPSILATERAL BREAST TUMOR RECURRENCE

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Background: IBTR! 2.0 nomogram is web-based nomogram predicting ipsilateral breast tumor recurrence (IBTR) after breast conserving treatment. In this study, we aimed to validate the IBTR! 2.0 using an external data set.

Methods: The cohort consisted of 2,206 patients, who received breast conserving surgery and radiation therapy from 1992 to 2012 at Yonsei cancer center where wider surgical excision is institutional policy. Discrimination and calibration were used for assessing model performance. Discrimination was quantified by receiver operating characteristic curve and the area under the curve. For calibration, Kaplan-Meier curves for actual IBTR rate were delineated based on four risk groups. We also plotted calibration plot to observe the actual IBTR rate against the nomogram-derived 10-year IBTR probabilities.

Result: Median follow up period was 73 months (0–277 month). The area under ROC curve was 0.607, showing modest accordance between estimated and observed recurrence rate. Calibration plot confirmed that IBTR! 2.0 nomogram predicted the 10-year risk of IBTR higher than the observed IBTR rates in all risk groups. High discrepancies between nomogram IBTR predictions and observed IBTR rates were observed in overall risk groups. Compared with original development dataset, our patient cohort had characteristics of less high grade tumor, margin positivity, and lymphovascular invasion and more use of modern systemic therapies.

Conclusions: This study demonstrates IBTR! 2.0 nomogram seems to have moderate discriminative ability with tendency of over-estimating risk rate. It is clinically of value to be aware of own clinical setting before adopting the IBTR 2.0 in the real practice

PO079

DEEP SURVIVAL MODEL IDENTIFIED THE PROGNOSTIC SUBGROUPS IN TRIPLE-NEGATIVE BREAST CANCER PATIENTS

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Background: Triple-negative breast cancers (TNBC) are known for poor outcome and prognosis of patients with TNBC was unpredictable. Therefore, new prediction model was needed.

Methods: We enrolled 7,915 patients above pathologic stage 2 who went surgery (May 1996–January 2015) and then sorted patients randomly into training group (80%, n = 6,288) and test group (20%, n = 1,627). The survival recurrent neural network (SRN) model was constructed based on logistic regression and long short-term memory recurrent neural network.

Result: The mean area under the receiver operating characteristics curve (AUC) of the five-fold validation sets was 0.780 at 1st year, 0.840 at the 2nd year, 0.857 at 3rd year, 0.869 at 4th year, and 0.834 at 5th year. The mean AUC of test set was 0.945 at 1st year, 0.861 at 2nd year, 0.834 at 3rd year, 0.825 at 4th year, and 0.805 at 5th year. The c-index of the final model was 0.810 in the test group. TNBC patients were classified into subgroups by SRN-suggested survival probability. In stage 2 patients, Kaplan Meier survival curves were statistically meaningful not only in conventional stage of IIA and IIB but also in SRN guided subgroup. In stage 3 patients, the difference of cumulative survival rate was significant among SRN guided subgroup A, B and C (p value < 0.0001) but not among conventional stage IIIA, IIIB and IIIC (p value = 0.292).

Conclusions: Our SRN model provides a useful tool for survival prediction of TNBC patients above 2 stage. Besides, SRN model divides subgroup according to survival more precisely than conventional stage.

PO080

AN ANALYTICAL VALIDATION OF THE GENESWELL™ BCT MULTIGENE PROGNOSTIC TEST IN PATIENTS WITH EARLY BREAST CANCER

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Background: GenesWell™ BCT is a 9-gene test suggesting the prognostic risk score (BCT Score) for distant metastasis within the first 10 years in early breast cancer patients with hormone receptor-positive, HER2-negative, and pN0~1 tumors. In this study, we validated the analytical performance of GenesWell™ BCT.

Methods: We performed the experiments for identification of LOD, precision and specificity of GenesWell™ BCT using each group pooled RNAs extracted from FFPE specimens of Korean early breast cancer patients categorized into low risk group, high risk group and near-cut off by the BCT Scores.

Result: GenesWell™ BCT could detect gene expression of each of the 9 genes from less than 1 ng/μL of RNA. Repeatability and reproducibility across multiple testing sites resulted in 100% and 98.3% consistencies of risk classification, respectively. Moreover, it was confirmed that the potential interference substances does not affect the risk classification of the test.

Conclusions: The findings demonstrate that GenesWell™ BCT have high analytical performance with over 95% consistency for risk classification.

PO081

COMPARISON AND EVALUATION OF REFERENCE GENES BETWEEN GENE EXPRESSION-BASED PROGNOSTIC ASSAYS FOR BREAST CANCER

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Background: The selection of reliable reference genes is essential to precise quantification of qRT-PCR data. However, some reference genes have excessive expression level or are not verified its stability in tumor. Here we compared and evaluated expression values of the reference genes from three qRT-PCR based breast cancer prognostic assays including GenesWell™ BCT (BCT Score), 21-gene assay (Recurrence Score), and 12-gene assay (EPclin Score).

Methods: To assess expression levels and its heterogeneity of the reference genes used in each assay, we analyzed the RNA-seq expression profiles in various types of human normal tissue by The Genotype-Tissue Expression (GTEx) project and thousands of breast invasive carcinoma by The Cancer Genome Atlas (TCGA) data.

Result: We showed that the expression of reference genes (CTBP1, CUL1 and UBQLN1) of GenesWell™ BCT display lower heterogeneity and similar with prognostic genes expression rather than those of the other assays.

Conclusions: When qRT-PCR is designed, use of reference genes with stable and similar expression levels to target genes is recommended for calculating accurate expression value. In this regard, our results suggest that the reference genes of the GenesWell™ BCT are more suitable for normalization and quantification of prognostic genes in breast cancer when compared with other reference genes.

PO082

PREDICTIVE VALUE OF THE GENESWELL™ BCT FOR CHEMOTHERAPY BENEFIT IN PATIENTS WITH LYMPH NODE-NEGATIVE, HORMONE RECEPTOR POSITIVE AND HER2 NEGATIVE BREAST CANCER

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Background: GenesWell™ BCT has been validated to predict the risk of distant metastasis in hormone receptor-positive and human epidermal growth factor 2-negative (HR+/HER2-) early breast cancer in previous study. In addition to its prognostic value, we investigated the predictive value of the GenesWell™ BCT for adjuvant chemotherapy benefit in lymph node-negative (LN-), HR+/HER2- breast cancer.

Methods: The risk score (BCT score) of GenesWell™ BCT was measured in each tumor sample and the patients were categorized as the BCT high-risk and BCT low-risk group according to the BCT score criteria. The probability of survival was estimated using the Kaplan-Meier method, and the log-rank test was used to assess statistical differences in survival between groups.

Result: A total of 346 patients who treated with hormone therapy alone (n = 203) or hormone therapy plus chemotherapy (n = 143) were included and there was no significant difference in 10-year distant metastasis-free survival (DMFS) between two treatment groups. However, when they were classified as low-risk and high-risk group according to the BCT score, there was a significant improvement in 10-year DMFS by the addition of adjuvant chemotherapy to hormone therapy in patients classified as BCT high-risk group, whereas no benefit of chemotherapy was observed in BCT low-risk group.

Conclusions: Our study suggests that GenesWell™ BCT not only provides prognostic information, but also predicts the benefit of adjuvant chemotherapy in patients with LN-, HR+/HER2- breast cancer.

PO083

COMPARISON OF GENESWELL™ BCT SCORE WITH ONCOTYPE DX RECURRENCE SCORE IN HORMONE RECEPTOR POSITIVE AND HER2 NEGATIVE INVASIVE BREAST CANCER

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Background: Several genomic tests are commonly used for making therapeutic decisions of early breast cancer. GenesWell™ BCT as the prognostic diagnostics test of breast cancer obtained the first manufacturing and product approval from MFDS (Class III) by validating the clinical efficacy in Korea. This study aimed to investigate the concordance of BCT Score (BS) and recurrence Score (RS) in same patients.

Methods: Breast cancer specimens with HR+/Her2-, pN0 or pN1, which were evaluated by Oncotype DX, were collected from 5 medical centers in Korea (Asan Medical Center, Gangnam Severance Hospital, Korea University Guro Hospital, National Cancer Center, Samsung Medical Center). The specimens were classified into low (< 4) and high risk group by BS, while RS categorized as three risk groups; low, intermediate, and high risk group. Comparison analysis was conducted under blind conditions.

Result: Total 784 specimens were involved in comparison analysis. RS results were analyzed in two ways: conventional classification and trial classification based on TAILORx trial. Overall Percent Agreement (OPA) were 62.8% (conventional classification) and 76.3% (trial classification) at node negative breast cancer patients. OPA were 54.7% (conventional classification) and 51.3% (trial classification) at node positive patients

Conclusions: The results demonstrate that significant but moderate concordances were indicated between BS and RS at node negative breast cancer patients, while the concordances were relatively poor at node positive patients. Differences in results can be explained by weighting of nodal status in BS. Further studies are required to elucidate the clinical relevance of discrepant test results with respect of distant metastasis.

PO084

EXPLORE ALTERNATIVE WAY TO REPLACE ONCOTYPE DX USING BIOMARK ASSAY

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Background: Currently the 21-gene recurrence score (RS) assay called Oncotype DX is recommended in NCCN guideline for defining chemotherapy benefit. To overcome the disadvantages in the cost and the turnaround time, a multigene assay designed from Korean breast cancer patients was explored to compare the correlation of the RS and our predicted score.

Methods: Paraffin-embedded tissues of 50 cases with early-stage ER-positive breast cancer who underwent Oncotype DX after surgery were used. From the other project, 149 candidate genes with high correlation with RS were identified. BioMark RT-qPCR assays using integrated fluidic circuit were conducted and the correlation analysis was performed with BRB ArrayTools.

Result: We used a least angle regression (LAR) algorithm to make a predictive model by the coefficient and gene expression and finally found 49 genes. If the cut-off is 18 or more, predicted model is 18 out of 50 cases and RS is 19, indicating the difference rate of predicted against RS is 2%. If the cut-off is 10 or more, we have 39.5 and RS is 38, showing a difference of 3%. Genes common to Oncotype DX and BioMark are MKI67, AURKA, MYBL2, ERBB2, GSTM1, ESR1, PGR, BCL2, SCUBE2 and 5 reference genes. The remaining 35 genes are involved in various pathway and function.

Conclusions: BioMark array is expected to evaluate the prognosis of breast cancer by predicting the risk of disease recurrence and judging the necessity of chemotherapy or otherwise preventing chemotherapy. It would be meaningful to be able to replace expensive foreign tests such as Oncotype DX.

PO085

CLINICOPATHOLOGICAL MARKERS ASSOCIATED WITH PROGNOSIS IN DCIS BY AGE GROUP

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Background: DCIS is non-invasive cancer of breast but its significance of biological marker and predict for recurrence remain unclear. This study was conducted to evaluate the effect of the immunohistochemical markers to the recurrence in DCIS by age.

Methods: Data from 226 patients diagnosed as DCIS at Gachon University Gil Medical Center between 2007 and 2015 were reviewed. ER, PgR, HER2, Ki67 values and patient age at diagnosis were used as factors for recurrence of subsequent tumor including IBTR or IDC. Univariate and multivariate analysis was conducted to examine associations between time to recurrence and biological markers according to age < 40, < 50, < 60 and ≥ 60 years.

Result: Median age at diagnosis was 50.61 ± 9.3 (29–83) and median follow up was 51.4 months. The recurrence rate was 4.9% (11/226 cases). On univariate analysis, ER- and high Ki67 values (20–50%) were markers increasing risk for recurrence ($p = 0.014$, $p = 0.008$). The hazard ratio for recurrence for ER- and Ki67 in DCIS was 4.450 ([CI] = 1.357–14.590) and 5.333 ([CI] = 1.544–18.427) respectively. ER- was associated with recurrence at the age of 40s ($p = 0.031$, HR 4.583, [CI] = 1.145–18.349) and Ki67 was associated with recurrence at the age of 50s ($p < 0.001$). On multivariate analysis, ER- was the only marker increasing risk for recurrence ($p = 0.016$, HR 22.493, [CI] = 1.780–284.268).

Conclusions: This data indicate that ER and Ki67 status may become a significant parameter for the management and treatment of DCIS. At the age of 40s and 50s, the ER and Ki67 biologic markers are associated with the rate of recurrence of any tumor respectively.

PO086

DEL-1 PROMOTES THE PROLIFERATION AND MIGRATION OF TAMOXIFEN-RESISTANT BREAST CANCER

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Background: We previously demonstrated a prognostic role of exosomal Del-1 with breast cancer patients. However, the mechanisms of Del-1 expression are barely understood. Development of resistance to tamoxifen is an important clinical issue in the treatment of breast cancer. Accordingly, we investigated the function of Del-1 in tamoxifen-resistant (TAMR) breast cancer cell line.

Methods: Del-1 expression in MCF7 and TAMR MCF7 cells was performed by quantitative RT-PCR, western blot, and ELISA. The effects of Del-1 with RNA interference on proliferation, migration and invasion of TAMR MCF7 cells were observed by MTT, wound healing and Matrigel transwell assay.

Result: Del-1 was highly expressed in TAMR MCF7 cells compared to MCF7 cells. Moreover, down-regulation of Del-1 inhibited the proliferation and migration of TAMR MCF7 cells. There was no difference in the invasion of TAMR MCF7 cells.

Conclusions: Prominent expression of Del-1 in TAMR MCF7 cells was associated with the proliferation and migration of TAMR MCF7 cells. Therefore, our findings suggest that the expression of Del-1 promote tamoxifen resistance in breast cancer cells and could be a novel target for anti-breast cancer treatment.

PO087

INTERLEUKIN ENHANCER BINDING FACTOR 2 AS A PROGNOSTIC BIOMARKER AND PREDICTOR OF THE RESPONSE TO NEOADJUVANT CHEMOTHERAPY IN BREAST CANCER

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Background: Interleukin enhancer binding factor 2 (ILF2) participates in several aspects of DNA and RNA metabolism and regulates gene expression at multiple levels. The precise role of ILF2 in breast cancer remains undefined.

Methods: The variant statuses of ILF2 in human cancer were evaluated using the COSMIC database. The alterations of ILF2 mRNA expression in normal breast tissue relative to cancer tissue and in breast cancer patients with different clinical-pathological characteristics, molecular subtypes, clinical outcomes and responses to chemotherapy were examined using Oncomine, GOBO, Kaplan-Meier plotter and GEO datasets. To explore the possible biological networks of ILF2 in breast cancer, we performed ingenuity pathway analysis on ILF2-related differentially expressed genes.

Result: We found that breast cancers were likely to display ILF2 gene copy number variation and increase ILF2 gene expression. We also observed that elevated ILF2 expression was correlated with selected aggressive features, such as high histological grade and BRCA1 mutation TNBC/basal-like subtype, which resulted in short survival in breast cancer. Moreover, ILF2 expression predicted the response to anthracycline/taxane-based treatment. IPA revealed selected ILF2-related biological functions involved in the promotion of cell survival, viability, and proliferation, as well as cell cycle progression and DNA repair. Certain well-known oncogenes (such as MYC and HGF), cytokines (such as CSF2, IFNG and IL5) and microRNAs (miR-21, miR-155-5p and let-7) may participate in the ILF2-related expression network in breast cancer.

Conclusions: ILF2 is involved in the development and progression of breast cancer and maybe a predictive biomarker for better response to anthracycline/taxane-based treatment.

PO088

A COMPARATIVE ANALYSIS OF OUTCOMES AND CLINICOPATHOLOGICAL CHARACTERISTICS OF SYNCHRONOUS AND METACHRONOUS CONTRALATERAL BREAST CANCER

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Background: Numerous studies have described the amount of controversial issues between synchronous contralateral breast cancer (sCBC) and metachronous contralateral breast cancer (mCBC).Therefore, the aim of this study was to compare the clinical characteristics and outcomes of sCBC and mCBC, and detect the predictive factors for survival of sCBC and mCBC.

Methods: Using Surveillance, Epidemiology, and End Results Program database, we identified patients with sCBC or mCBC from 2000 to 2010. Kaplan–Meier method and Cox proportional hazards regression analysis were used to analyze overall survival (OS) and breast cancer-specific survival (BCSS) of sCBCs and mCBCs.

Result: We selected a total of 14,057 patients in our study, 8,139 (57.9%) and 5,918 (42.1%) patients developed sCBC and mCBC, respectively. The first tumors of mCBC were more likely infiltrating ductal carcinoma (IDC), III or IV grade, localized stage, estrogen receptor (ER) negativity, progesterone receptor (PR) negativity and less axillary nodal involvement. The second tumors of mCBC were more often IDC, III or IV grade, adverse stage, ER-negativity, PR-negativity and more axillary nodal involvement. Patients with mCBC had a significantly favorable BCSS compared to sCBC within 5 years, but a worse BCSS in long-term years. Moreover, subgroup analysis showed that there was no significant difference of BCSS between sCBC and mCBC among 18–60 years old cases. A multivariate analysis suggested that age at diagnosis, grade and stage of two tumors, surgery for second tumor and ER status of second tumor were independent prognostic factors for BCSS of CBC.

Conclusions: There were significant differences in characteristics and outcome of sCBCs and mCBCs. The sCBC and mCBC patients of different age may have different prognosis, and the prognosis of CBC was determined by both the first and the second tumor.

PO089

A RETROSPECTIVE STUDY OF BREAST MALIGNANT PHYLLODES TUMORS: THE MALIGNANCY GRADING SYSTEM AND THE RELATIONS WITH PROGNOSIS

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Background: Malignant phyllodes tumors (PTs) of the breast, as opposed to its benign counterpart, can be characterized by an unusually aggressive course and have been reported to have the local regional recurrence (LRR) and distant metastasis (DM) capacity. The aim of this study was to analyze the malignancy grading system of malignant PTs and to investigate the prognostic significant of the malignancy grading system.

Methods: We consult the grading system of soft tissue sarcomas and the experience in diagnosis of PTs to conclude the malignancy grading system of malignant PTs. The relationship between disease free survival (DFS), distant metastasis-free survival (DMFS) and overall survival (OS) and clinicopathologic parameters were investigated.

Result: A total of 188 cases malignant PTs were classified according to the malignancy grading system: 88 (46.8%) low grade, 77 (41%) intermediate grade, and 23 (12.2%) high grade. In our study population, the features of distant metastasis and death associated with the malignancy grade of malignant PT ($p < 0.001$). In the DFS curves, tumor with heterologous elements ($p = 0.003$) and younger age ($p = 0.012$) retained independent prognostic significance. The malignancy grade retained independent prognostic significance merely in the DMFS and OS ($p < 0.001$, $p = 0.009$).

Conclusions: Our study showed that the higher grade of breast malignant PTs were associated with poor prognosis. The malignancy grading system may be generalized in the future.

PO090

EXPRESSION OF LAPTM4B AND LOSS OF P27KIP1 ARE CORRELATED AND PREDICT POOR PROGNOSIS IN TRIPLE NEGATIVE BREAST CANCER

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Background: Triple-negative breast cancer is strongly associated with an aggressive phenotype and poor prognosis, and the lack of druggable markers leads to the unavailability of targeted therapies. Thus, there is an urgent need to identify potential targets for triple-negative breast cancer. In the current study, we aim to assess the expression of LAPTM4B and p27kip1 in triple-negative breast cancer and its clinical significance.

Methods: The expression and association of LAPTM4B and p27kip1 in human breast cancer databases were analyzed. The expression of LAPTM4B was knocked down to analyze the role of LAPTM4B in the aggressiveness of the human triple-negative breast cancer cell line MDA-MB-231 and HCC1187. Cell proliferation, migration and apoptosis were assessed in vitro. The immunohistochemistry examination of LAPTM4B and p27kip1 expression was performed using specimens from 188 primary triple-negative breast cancer patients.

Result: Through analyses of several independent breast cancer cohorts, we found a strong association of the expression of LAPTM4B and p27kip1. Remarkably, the knockdown of LAPTM4B restored p27kip1 expression and inhibited the aggressiveness of breast cancer cells. Meanwhile, the knockdown of p27kip1 released the suppression of cell migration. Consistent with the analysis of breast cancer cohorts, the immunohistochemistry results showed that the expression levels of LAPTM4B and p27kip1 were significantly correlated in 188 breast cancer samples ($p = 0.019$). We also validated that the LAPTM4B+/p27kip1- subgroup predicted the worst prognosis ($p < 0.001$).

Conclusions: The overexpression of LAPTM4B together with the loss of p27kip1 is potentially novel prognostic markers of triple-negative breast cancer and candidate targets for therapeutic intervention.

PO091

THE MANAGEMENT OF SMALL BREAST CANCER

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Background: Recurrences and mortality occur in small breast cancer though as a low rate and the clinical decision making process can sometimes be contentious. In this study, we will discuss the recent progress in diagnosis, management, outcomes of the small breast cancer (≤ 1.0 cm).

Methods: The English language articles on small breast cancer accessible on PubMed database and the relevant conference presentations on American Society of Clinical Oncology (ASCO) Annual Meetings, San Antonio Breast Cancer Symposium, and the International St. Gallen Breast Cancer Conference were reviewed.

Result: The incidence of small breast cancer has been increasing due to the widely use of screening techniques. It is clear that age, histology subtypes and axillary lymph node status are the most important prognostic factors associated with the patient survival. Patients younger than 35 years old are associated with a high risk of breast cancer recurrence. The HER2-positive cases have poorer prognosis than HER2-negative. Triple-negative breast cancer and lymph node status are independent prognostic factors for the recurrence and metastasis of T1a and T1b tumors.

Conclusions: The clinicopathological characteristics of the small breast cancer are highly variable, resulting in the controversies over the treatment options. Patients with subcentimetric node-negative breast cancer usually have good prognosis, with more than 90% surviving longer than 10 years with no relapse, and are mostly excluded from adjuvant chemotherapy.

PO092

A NOMOGRAM FOR PREDICTING AXILLARY LYMPH NODE STATUS AFTER NEOADJUVANT CHEMOTHERAPY FOR BREAST CANCER

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Background: Parts of breast cancer patients benefit from neoadjuvant chemotherapy (NAC), especially for the group achieving pathological complete response (pCR), the longtime survival outcome will be improved. So lymph node (ALN) status is crucial to determine axilla surgical methods for breast cancer patients after receiving NAC.

Methods: Patients with cT1-4N0-1M0 breast cancer who received NAC and followed by axillary lymph node dissection from 2013 to 2017 were identified (n = 475). After eliminating ineligible individual, 320 patients were enrolled finally. Univariate and multivariate logistic regression analyses were used to filtrate related factors predicting axillary lymph node status. The model performance was measured internally by the receiver operating characteristic curve (ROC) and calibration curve.

Result: After univariate and multivariate logistic regression analyses, we found that estrogen receptor (ER) Ki67 tumor regression degree clinical tumor stage after NAC (ycT) node stage after NAC under ultrasound (ycN are related to the status of axillary lymph node(ALN). The nomogram constructed by these factors had an AUC of 0.802 (95% CI: 0.7485–0.8554), and the calibration plot revealed a well agreement among the actual and predicted outcomes of ALN status after NAC.

Conclusions: This nomogram will help to predict the status of ALN after receiving NAC regardless of the initial condition of ALN of breast cancer patients, and it will be helpful for choosing an appropriate surgical method.

PO093

CHALLENGES IN A CULTURALLY TAILORED TECHNOLOGY-BASED INTERVENTION FOR ASIAN AMERICAN BREAST CANCER SURVIVORS

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Background: Despite an increasing number of culturally tailored technology-based interventions for racial/ethnic minorities, little is still known about challenges in implementing a culturally tailored technology-based intervention among breast cancer survivors. The purpose of this presentation is to identify practical challenges in implementing a culturally tailored technology-based intervention among Asian American breast cancer survivors.

Methods: The parent study aimed to examine the efficacy of a culturally tailored technology-based intervention on improving survivorship experience of 330 Asian American breast cancer patients. Throughout the research process, research team members kept the minutes of research team meetings and wrote memos on challenges in implementing the intervention. Then, a content analysis was used to analyze the minutes and written memos.

Result: Six themes of challenges were identified. First, most of the participants did not have a computer, and those who were using smart phones did not want to use the project website. Second, the four languages used in the study could not sometimes cover the diversities within languages. Third, due to cultural stigma attached to breast cancer, the participants were reluctant to discuss their personal experience and issues. Fourth, the qualifications of the interventionists needed to be changed at several times. Fifth, the participants were afraid of losing their privacy when they participated in the study. Finally, time zone differences between the participants and interventionists often interfered the intervention implementation process.

Conclusions: Future researchers need to consider several practical issues in designing and implementing culturally-tailored technology-based interventions.

PO094

AN INTERNET CANCER SUPPORT GROUP AND ILLNESS UNCERTAINTY: ASIAN AMERICAN BREAST CANCER SURVIVORS

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Background: In the current era of the so-called Fourth Revolution, there has been an emphasis on technology-based programs for disease management. With an increasing number of people from different racial/ethnic groups residing in same countries, the necessity of culturally-relevant programs have increased. The purpose of this study was to explore the effects of a technology-based cancer pain management program (CAPAA) on illness uncertainty among Asian American breast cancer survivors.

Methods: The study used a randomized repeated measures pretest/posttest control group design among 94 Asian American breast cancer survivors (64 for an intervention and 30 for a control group). Before and after one month of using the program, illness uncertainty of the participants was measured and compared using the Mishel Uncertainty in Illness Scale-Community. The covariates included: degree of cancer pain, perceived isolation, personal resources, support care need, and self-efficacy. The data were analyzed using descriptive and inferential statistics, including repeated measures analysis of variance.

Result: The intervention group showed significant improvements in illness uncertainty from the pre-test ($M = 2.70$, $SD = 0.74$) to the 1-month post-test ($M = 2.24$, $SD = 0.79$) ($p < 0.01$). Moreover, three covariates significantly improved in this group: perceived isolation ($p < 0.01$), personal resources ($p < 0.05$), and support care need ($p < 0.01$). However, the control group did not show any significant changes in the study outcomes across the time points.

Conclusions: The study supported the beneficial effects of the CAPAA on illness uncertainty and other factors associated with Asian American breast cancer survivors disease experience.

Poster Presentation

PO095

IS A SOCIAL CAPITAL-BASED EXERCISE ADHERENCE INTERVENTION HELPFUL FOR BREAST CANCER SURVIVORS WITH MODERATE CANCER RELATED FATIGUE?

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Background: Cancer related fatigue (CRF) is the most common symptom in breast cancer survivors (BCS), with severe impact on quality of life. CRF can be reduced through exercise, but conversely, is also a barrier to exercising. This study examines the effectiveness of BLESS, a 12 week social capital-based exercise adherence program for BCS, on psychosocial and physical health.

Methods: Forty-seven BCS with moderate (≥ 4) or higher CRF, participated in this quasi-experimental study (experimental group: 23, control group: 24). The intervention group participated in group sessions based on strategies to activate social capital while targeting CRF, and supervised exercise sessions, supplemented by home-based exercise. The control group received a workbook on exercise. SNS messages were sent to both groups. Pre and post measurements were done for psychosocial health and level of physical activity.

Result: The majority of participants were < 2 years since surgery and many had high levels of depression, anxiety, and sleep disturbance. The experimental group had a significant decrease in the behavioral domain of CRF ($t = 2.484$, $p = 0.017$), and an increase in physical activity (Mann-Whitney U test, $p = 0.003$) compared to the control group. However, there were no significant differences in sleep quality, depression, anxiety, and quality of life between the two groups.

Conclusions: The BLESS program improved behavioral fatigue domain and physical activity level after 12 weeks in this group of early survivors. The BLESS study is still underway and its effectiveness will be followed to confirm the persistence of these effects among BCS as well as examine potential changes.

Poster Presentation

PO096

EFFECT OF COMBINED EXERCISE AND WEIGHT CONTROL PROGRAM ON LYMPHEDEMA CONTROL

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Background: To evaluate the effects of home-based exercise program and dietary modification on lymphedema control and quality of life (QOL) of lymphedema patients. We hypothesized that a structured home-based program consists of resistance exercises of limbs, aerobic and stretching exercises, dietary modification. It would help relieving the symptoms of lymphedema, enhancing upper limb function and improving the QOL of breast cancer patients.

Methods: Inclusion criteria: Lymphedema cases with BMI < 17 > 25 The patient received a one-year structured program consists of 3 components: a conventional treatment program with lymphedema group exercise and physiotherapy intervention, home-based program with progressive resistance on therband exercise, aerobic and stretching exercise prescribed by physiotherapist, dietary education conducted by nurse. Outcome measures were captured upon each visit as follows: -Subjective improvement: Numeric global rating of change scale (NGRCS) -Physical assessment on shoulder movement and upper limb heaviness score (VAS) -Upper limb function: Disability of the Arm, Hand and Shoulder questionnaire (quick DASH) -Measurement of bio impedance on upper limb body water difference, body mass index (BMI) and percentage body fat (PBF) -Quality of life: FACT- B questionnaire

Result: There were 9 cases recruited. There were improvement in heaviness score (38.1%) and NGRCS (4.3). There were also decrease in upper limb body water difference (19.9%), BMI (8.7%) and PBF (19.4%) in some cases. Combined exercise program and dietary modification lead to improvement in upper limb volume, heaviness score, BMI and QOL. Individuals with lymphedema can safely participate in regular exercise without experiencing a worsening of lymphedema or related symptoms.

Conclusions: One-year structured program was composed of conventional treatment program, home based exercise program and dietary modification. It promoted active life style and quality of life, decreased the avoidance of arm function and enhanced dietary modification. It improved the lymphedma symptoms and ceased the disease progression.

PO097

BREAST CANCER SURVIVORS EXPERIENCE OF A SOCIAL CAPITAL-BASED EXERCISE ADHERENCE PROGRAM - A QUALITATIVE APPROACH

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Background: The role of social capital in promoting physical activity (PA) among breast cancer survivors (BCS) has not been investigated. Therefore, the purpose of this study was to conduct an in-depth examination of the experience of participating in a social capital-based exercise program for BCS.

Methods: Participants from a larger study, BLESS, were invited to participate in this exploratory research. BLESS is a 12 week exercise adherence program for BCS, focusing on strengthening core muscles and lymphedema prevention. The data were collected through focus-group interviews (n = 21) at 8-10 weeks, and in-depth interviews (n = 7) during the home-based exercise phase. Interviews were audiotaped and transcribed and content analysis was done.

Result: The exercise program was found to be feasible for BCS with adequate intensity and the type of exercise involving specialized movements for BCS. In addition, the social capital-based exercise component involving exercise plans and check-ups, provided motivation as it provided BCS with a sense of camaraderie, support, and mutual strength. Furthermore, exercise was shown to be effective in enhancing positive changes in BCS as it led to improved health perception and change in attitude seeking to implement exercise in their daily lives. Finally, the study shows that interaction among BCS was a source of motivation for each other to continue exercise.

Conclusions: These results provide supportive evidence for exercise programs that are tailored to the needs of BCS, in terms of specific exercise components as well as activities that can potentially mobilize social capital among survivors.

PO098

THE CHANGES OF QUALITY OF LIFE AND THE ASSOCIATED FACTORS AMONG BREAST CANCER WOMEN FROM BREAST CANCER SURGERY TO POST-TREATMENT SURVIVORSHIP

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Background: Women's quality of life has been found to be predictive of the survival rates and the risk of breast cancer recurrence. Up to date, there is a lack of study examining the changes of the quality of life from the post-surgery to the post-treatment survivorship stages.

Methods: This 14-month study with prospective longitudinal design examined the changes of the general and breast specific quality of life and the associated factors. Breast cancer women were recruited when they completed breast cancer surgery with in one week. They were asked to complete the questionnaires: European Organization for Research and Treatment of Cancer Core Cancer Quality of Life Questionnaire (EORTC QLQ-C30) and its breast cancer specific complementary measure (EORTC QLQ-BR23), BDI-II depression scale, State-Trait Anxiety Inventory (STAI), Experiences in Close Relationships-Revised (ECR-R) scale.

Result: The scores of QOL-30, and QLQ-BR23 have changed toward recovery from breast cancer surgery during the 14-month follow ups. The lower scores of QOL-30 occurred in breast cancer women who received neo-adjuvant chemotherapy and those with cancer stage 3. BDI depression is the main predictor of the changes of both QOL-30 and QOL-BR23. The insecure patterns of Close relationship ECR-R are associated with the changes of QOL-BR23 function and symptoms.

Conclusions: The general and breast specific quality of life have been changes toward recovery from the post-breast cancer surgery to the post-treatment survivorship stages. The psychosocial programs aiming to reduce depression and enhance secure close relationship need to develop to improve quality of life for breast cancer women.

PO099

COLLAGENOUS SPHERULOSIS ASSOCIATED WITH LOBULAR CARCINOMA IN SITU OF THE BREAST: TWO CASE REPORTS

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Background: Collagenous spherulosis (CS) of the breast is rare, but frequently occurs in association with other benign proliferative lesions of the breast. CS can be also associated with lobular carcinoma in situ (LCIS), on which we are reporting two cases.

Methods: Two patients came to our attention for the presence of nodules on ultrasound imaging.

Result: Case 1 was an asymptomatic 51-year-old woman with multiple small nodules in the right breast. Case 2 was a 47-year-old woman with an incidentally detected lesion in the left breast. Both patients underwent ultrasound-guided vacuum-assisted biopsy. Microscopically, the lesions had enlarged lobular glands filled with neoplastic cells. The neoplastic cells in both cases showed discohesive growth and negative E-cadherin immunoreactivity. Case 1 and case 2 were LCIS, a classic type and pleomorphic type, respectively. In both cases, the multiple spherules showing cribriform architecture lined by flattened epithelial cells were seen adjacent to the LCIS area. The space of the spherules contained a faintly basophilic fibrillary substance. Two types of cells, myoepithelial and luminal, were found in the spherules, which were outlined by myoepithelial cells stained with p63 and calponin. The cells of the spherules were negative for c-kit. The basophilic fibrillary materials were positive for laminin. Overall, the spherules displayed the usual microscopic characteristics typical of CS. E-cadherin-negative LCIS cells had colonized the several spherules of CS and replaced the luminal epithelial cells.

Conclusions: This is the first report of cases of CS associated with LCIS of the breast in Korea.

PO100

PTEN MUTATION IDENTIFIED IN YOUNG WOMAN WITH BREAST CANCER

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Background: PTEN hamartoma tumor syndrome is a spectrum of disorders characterized by unique phenotypic features including multiple hamartomas caused by mutations of the tumor suppressor gene PTEN. Cowden syndrome and Bannayan-Riley-Ruvalcaba syndrome are representative diseases, and both have several common clinical features and differences. Because PTEN mutations are associated with an increased risk of malignancy including breast, thyroid, endometrial, and renal cancers, cancer surveillance is an important element of disease management.

Methods: We report the case of a young woman diagnosed with breast cancer, dermatofibrosarcoma protuberans, and follicular neoplasm who had the pathogenic PTEN mutation.

Result: A 29-year-old woman visited our hospital with a palpable left breast mass and right chest wall mass. Multiple pulmonary nodules and right thyroid nodule were detected on 18F-fluorodeoxyglucose (FDG) positron emission tomography (PET)-computed tomography. She underwent a modified radical double mastectomy. Histopathological examination revealed an invasive ductal carcinoma in the left and dermatofibrosarcoma protuberans in the right. In addition, she had more phenotypic features of importance. She had mucosal papillomatous lesions on the upper gingiva and hard palate and gastrointestinal polyps distributed throughout the entire intestine. A core needle biopsy of thyroid nodule was perfomed and revealed a follicular neoplasm. Pulmonary nodules also revealed colloid-filled thyroid follicles with various size. We performed a PTEN gene test and identified a frameshift PTEN mutation: c.723dupT (p.Glu242Terfs) in exon 7.

Conclusions: This case suggests that it is critical for clinicians to recognize the phenotypic features associated with these syndromes to accurately diagnose them and provide preventive care.

PO101

CASE REPORT: SUCCESSFUL SENTINEL LYMPH NODE BIOPSY IN SIMULTANEOUS PRIMARY BREAST CANCER AND ECTOPIC BREAST CANCER IN AXILLA

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Background: The simultaneous development of ectopic breast cancer (BC) in the axilla and ipsilateral primary cancer in the breast is extremely rare and no standard method for sentinel lymph node biopsy (SLNB) is available.

Methods: We report an extremely rare case of axillary ectopic BC and primary BC who underwent SLNB.

Result: A 52-year-old woman presented with a right axillary tumor and a speculated mass in the breast on mammography. Sonography demonstrated an ipsilateral geographic hypoechoic area in the outer upper breast apart from the axillary tumor. Both tumors were histopathologically diagnosed as ductal carcinoma. MRI revealed an axillary irregular lesion apart from the speculated mass in the breast. Computed tomography presented no evidence of metastases. Partial resection of the primary BC (1.5 cm in diameter, histologically classified as scirrhous carcinoma) and wide resection of the ectopic BC in the axilla (2.6 cm, microinvasive carcinoma) with SLNB were performed. We used two types of tracer: a radioisotope injected around the primary BC and the nipple, and indigo carmine dye injected near the ectopic tumor and the primary BC. We detected one hot (isotope-labeled) and blue sentinel lymph node that histologically showed invasive ductal carcinoma. Ten lymph nodes in the axilla were dissected and metastasis was detected in only the sentinel lymph node.

Conclusions: SLNB could be performed using a dual technique of radioactive tracer and dye in cases with concurrent primary BC and ectopic BC in the axilla.

PO102

BREAST CALCIFICATIONS IN PATIENTS WITH END-STAGE RENAL DISEASE

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Background: Patients with end-stage renal disease (ESRD) on dialysis are more prone to soft tissue calcifications due to secondary hyperparathyroidism. Breast calcifications seen on mammography are therefore, not uncommon. These calcifications may show features mimicking ductal carcinoma in-situ (DCIS) and the patients may have to undergo breast biopsies to exclude malignancy.

Methods: We followed the clinical course of a single patient, 43 years old female with ESRD, who presented to the breast clinic for evaluation of bilateral breasts calcifications picked up on screening mammogram. Mammogram showed dystrophic calcifications in areas of both breasts, some of which were linear branching-type pattern, suggestive of intraductal calcifications associated with high grade DCIS. Recommendation was made for biopsy to exclude malignancy.

Result: Patient underwent breast core biopsies, results of which revealed benign breast tissue with stromal fibrosis and calcifications. However, it was deemed that the samples were inadequate and patient subsequently underwent stereotactic guided hookwire-localisation and excision biopsy of bilateral breasts calcifications. Final histological analysis showed similar stromal sclerosis and calcifications in both breast specimens. No malignancy was found.

Conclusions: Increased breast calcifications in ESRD patients on dialysis are common and most of these calcifications are benign, as shown in various past studies and in our case report. Being aware of the patients background renal disease and the mammographic morphological features of the breast calcifications from secondary hyperparathyroidism can help reduce unnecessary breast biopsies.

PO103

THE PATIENT UNDERWENT AXILLARY LYMPH NODE DISSECTION WAS TREATED WITH A MIXTURE OF POLOXAMER AND ALGINATE (GUARDIX-SG) IMPACT ON RANGE OF ACTION

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Background: Restricted shoulder mobility is a major upper limb dysfunction related to lower quality of life and disability after breast cancer surgery. We hypothesized that mixture of Poloxamer and Alginate (Guardix-SG) applied after axillary lymph node dissection (ALND) would significantly reduce pain and improve range of motion (ROM) of the shoulder in breast cancer patients.

Methods: We conducted a double-blind, randomized controlled study to evaluate the clinical efficacy and safety of Guardix-SG in the prevention of upper limb dysfunction after ALND. A total of 83 women with breast cancer were randomly assigned to one of two groups.

Result: In the Guardix-SG group (n = 37), a Guardix-SG was applied to the axillary region after ALND. In the control group (n = 46), ALND was performed without the use of Guardix-SG. The primary outcomes were ROM of the shoulder before surgery (T0) and 3 (T1), 6 (T2) and 12 months (T3) after surgery. Secondary outcomes included disabilities of the arm, shoulder, and hand (DASH) and motion-related pain assessed using a numeric rating scale measured and Assessment of lymphatic edema using body composition analysis. Compared with the control group, the Guardix-SG group showed pain was not reduced and ROM included coronal, scapular, horizontal and flexion was not improved. No adverse effect was observed in either group.

Conclusions: These results provide no evidence that Guardix-SG may provide pain relief and improve ROM of the shoulder without causing adverse effects. In order to obtain a clearer conclusion, the large-scale study must be investigated in further studies.

PO104

FIVE YEAR OVERALL SURVIVAL OF INTERVAL BREAST CANCERS WAS WORSE THAN NON-INTERVAL CANCERS WITH MAMMOGRAPHY SCREENING WOMEN: A REGISTRY-BASED RETROSPECTIVE STUDY FROM KOREA

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Background: Interval breast cancer (IBC)s made reliance of cancer screening decrease and examinees anxious. We investigated a large scaled breast cancer dataset for overall survival (OS) of IBCs compared to non-IBCs.

Methods: Twenty seven thousand one hundred forty one patients with breast cancer who have ever biannually national breast cancer screening programs between 2009 and 2013 were enrolled from Korean breast cancer registry. We compared IBCs group to non IBCs group according to clinicopathologic characteristics and analyzed a significant prognostic factors on overall survival by using multivariate Cox regression analysis.

Result: Incidence of IBCs was 1.3% (370/27141). IBCs were correlated with women aged between 45 and 55 years at diagnosis, higher educated women, early menopause (< 50 years), user of hormonal replacement therapy, and family history of breast cancer. Low to intermediate nuclear grade, early stage (stage 0–I), Her-2/neu overexpression, and low Ki-67 were correlated with IBC. IBCs increased risk of 5 years-mortality (HR 7.4; CI:1.85–29.66; $p = 0.005$) compared to non-IBCs. In women with breast cancer who have ever biannually breast cancer screening, lymph node metastasis, residence (Kyung-nam province), low education status, high histologic grade, and asymptomatic cancers increased risk of 5 years-overall mortality.

Conclusions: IBCs had clinically less aggressive tumors compared to non- IBCs. Though current study has short duration of follow-up and small number of events, 5 year OS of IBCs was worse than non-IBCs. Further longer observation and centralized review of medical information through big-data analysis were needed.

PO105

THE EFFECTS OF A 12-WEEK EXERCISE ADHERENCE PROGRAM ON PHYSICAL ACTIVITY LEVEL AND PHYSICAL FITNESS AMONG BREAST CANCER SURVIVORS - RESULTS FROM THE BLESS STUDY

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Background: Exercise is an important behavior related to a number of overall health benefits in cancer survivors. This study aimed to investigate the effects of a 12-week exercise adherence program (BLESS) on physical activity (PA) level and physical fitness among breast cancer survivors (BCS).

Methods: BCS with stage I-III were recruited for this quasi-experimental study and randomly assigned to the exercise or control group. The intervention group participated in the exercise adherence program, which consisted of combined supervised and home-based exercise, including stretching and resistance exercise specialized for BCS, with gradual increase in intensity. The control group was not prescribed a structured exercise program. PA level was measured using the Global PA Questionnaire and physical fitness was determined by the 30-second chair stand test (lower body strength).

Result: A total of 23 BSC (48.9%) participated in the exercise program with compliance to the program at 89.1%. The mean level of total PA was 73.05 ± 34.15 metabolic equivalent task (MET)-hour/week in the exercise group compared with 59.39 ± 43.04 MET-hour/week in the controlled group (mean difference, 16.22 ± 10.82 MET-hour/week, $p = 0.14$. The exercise program significantly increased muscular strengthening exercise (intervention: 2.22 ± 1.65 days vs. control: 1.23 ± 1.45 days, $p < 0.01$), and improved lower body strength (intervention: 2.41 ± 4.10 repetitions vs. control: -1.08 ± 2.43 repetition, $p < 0.01$).

Conclusions: This study found that the exercise adherence program improved PA level and lower body strength in BCS over 12 weeks, a much shorter period than previous studies for various fitness indices. The BLESS study is still underway and its effectiveness for PA and physical fitness will be followed over time.

PO106

INFLUENCE OF FINASTERIDE ON RECURRENCE AFTER SURGICAL TREATMENT OF GYNECOMASTIA

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Background: Finasteride is commonly used for treatment of alopecia. Gynecomastia is an adverse effect of finasteride. No studies have been performed to determine whether finasteride should be continued after mastectomy when gynecomastia occurs in patients taking finasteride. Therefore, we studied the effect of this drug on recurrence of gynecomastia.

Methods: We conducted a retrospective study of 1,673 patients with gynecomastia who underwent subcutaneous mastectomy with liposuction at Damsoyu Hospital from January 2014 to December 2016. Of these patients, those who received preoperative or postoperative finasteride were included in the study. Symptom recurrence was assessed either at the time of the visit or by phone counseling.

Result: In total, 71 patients received finasteride, and 52 of them responded to the survey. The average follow-up period was 31.0 ± 9.8 (range, 1,347) months. The mean duration of finasteride use was 47.2 ± 18.8 (range, 3,120) months, and the dose was 1 mg. Among all patients, only one (1.92%) reported intermittent pain, and physical examination and breast ultrasonography showed no evidence of breast enlargement or mammary tissue.

Conclusions: The use of finasteride seems to have little effect on recurrence in patients who have undergone surgical treatment of gynecomastia.

PO107

RECURRENT DIABETIC MASTOPATHY ARISING FROM TYPE II NON-INSULIN DEPENDENT DIABETIC MELLITUS: A CASE REPORT

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Background: Diabetic mastopathy is an uncommon tumor-like proliferation of fibrous tissue of the breast that usually occurs in a patient from type I diabetes mellitus of long duration.

Methods: Here we report a rare case of diabetic mastopathy that occurred in type II non-insulin dependent diabetes mellitus (NIDDM).

Result: A 63-year-old postmenopausal woman presented with a painless palpable mass from 4 months ago on left breast upper outer portion. She had NIDDM for a period of 33 years, complicated by bilateral diabetic retinopathy. Mammography revealed dense breast and ultrasonography showed an irregularshaped hypoechoic 3cm sized mass with an indistinct margin and acoustic posterior shadowing. The radiologic findings were similar to those of breast cancer. The core needle biopsy showed stromal fibrosis but surgical excision was performed because it was discordant with clinical findings. Pathology result demonstrated diabetic mastopathy with stroma fibrosis, perivascular lymphocytic infiltration, and prominent myofibroblast without evidence of malignancy. Six months after surgical excision, ultrasonography showed a nodular formation approximately 4 cm sized poorly defined hypoechoic lesion on resected site. For the next 4 years, the lesions were unchanged.

Conclusions: Breast surgeons should be aware of diabetic mastopathy when those encounter breast mass in patient with diabetes mellitus. If clinical findings and core needle biopsy suggested diabetes mastopathy, unnecessary surgical excision should be avoided because of the tendency for recurrence.

PO108

CASE REPORT: A CAVERNOUS HEMANGIOMA LOCATED IN THE AXILLARY AREA - CHALLENGES IN PREOPERATIVE DIAGNOSIS AND OPERATION

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Background: Cavernous hemangioma is not a true tumor, but rather a venous malformation. Although it has the potential to develop in all parts of the body, it is extremely rarely found in the axilla, with only two cases reported in the literature so far. We report a case of an axillary cavernous hemangioma.

Methods: A 30-year-old woman presented with a palpable mass in the axilla. She had no underlying diseases, traumatic history or breast surgery. Physical examination revealed a 4 cm-sized non-tender, easily movable mass with no remarkable findings in the bilateral breast and contra-lateral axilla. Ultrasonography showed a 4.8 cm sized well-vascularized solid mass with irregular margin, close to the axillary vessels. It was initially suspected to be either a lymphoma or a phyllodes tumor, graded BIRADS IV. A core needle biopsy was performed with an unexpected result of a cavernous hemangioma.

Result: To make a definitive diagnosis, surgical excision was performed. Intraoperatively, the mass was found to have infiltrative margins on the axillary vein, which had to be sacrificed after identification of collateral vessels. Microscopically, the mass consisted of dilated, thin walled vessels and immunohistochemical staining revealed positive expression for CD34, a marker for vascular endothelial cells. Based on these findings, pathological diagnosis of cavernous hemangioma was made. The patient developed postoperative ulnar nerve palsy and had no evidence of recurrence during a 23-month follow-up.

Conclusions: Cavernous hemangiomas in the axilla can involve large blood vessels. Therefore, particular attention on dissection as well as a detailed anatomic preoperative imaging should be taken into consideration.

PO109

I-II PHASE HER2 POSITIVE BREAST CANCER NEOADJUVANT THERAPY EFFICACY AND THE RELATED CLINICAL PATHOLOGIC FACTORS OF PROSPECTIVE STUDIES

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Background: Positive HER2 breast cancer is induced by human epidermal growth factor receptor 2 mutations. Recent studies indicated that positive HER2 breast cancer patients treated with neoadjuvant therapy included trastuzumab could improve the pCR rate. There are few relevant data about early breast cancer. Therefore, we classified the impact of TCH (docetaxel + carboplatin+trastuzumab) treatment on pCR rate in I-II phase HER2 positive breast cancer patients.

Methods: Forty eight patients with I-II phase HER2 positive breast cancer were enrolled and treatd with TCH neoadjuvant therapy, the efficacy of treatment was evaluated by imaging, If neoadjuvant therapy was effective (CR/PR), patients would undergo surgery after completing 6 cycle neoadjuvant therapy. Otherwise, patients would receive conventional treatment. Follow-up time was five years, and then we assessed the pCR rate, analyzed the clinicopathologic factors' effect on the rate of pCR and observed the disease-free survival (DFS) and overall survival (OS).

Result: The pCR rate was 66.7%, the pCR rates were significantly different according to HER2 gene amplification degree ($p = 0.015$) and ER/PR status ($p = 0.009$). However, no significant differences were noted in terms of age, tumor size, histological grade and lymph node status. Compared no-pCR group with pCR group, the five-year DFS were 62.5% and 87.5%, the five-year OS were 81.3% and 96.9% respectively.

Conclusions: I-II phase HER2 positive breast cancer by neoadjuvant therapy can achieve higher rates of pCR, HER2 gene amplification degree may have impact on pCR rates and pCR can improve DFS ($p = 0.032$) and OS ($p = 0.035$) of I-II phase HER2 positive breast cancer.

PO110

ROLE OF CIRCULATING TUMOR CELLS IN THE PROGRESSION OF BREAST CANCER

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Background: Breast cancer is the most common primary malignant carcinoma and is the leading cause of cancer-related mortality of women. Tumor invasion and metastasis greatly limit treatment options and result in poor outcomes, which is also true for breast cancer, but the metastatic mechanism is still unclear. Evaluation and characterization of circulating tumor cells (CTCs) has emerged as one of the hottest fields in translational cancer research. Objective is to explore the association between tumor clinicopathological characteristics and circulating tumor cells (CTCs) in breast cancer by using the Cell Search system.

Methods: We collected 110 cases of patients diagnosed with invasive breast cancer, who underwent fine needle aspiration biopsy or complete tumor resection surgery from 2010 to 2013 in Liaoning Cancer Hospital and Institute. CTCs were enumerated using the Cell Search system in peripheral blood of breast cancer patients. The expression of ER, PR, Her-2 and Ki67 protein in breast cancer was performed by immunohistochemistry. The statistical analysis was used to test the clinical relevance with CTCs in breast cancer.

Result: The statistical analysis showed there was no difference in age (Y), tumor size (T), ER, PR, Her-2 status and Ki67. Importantly, the CTCs was correlated with histologic grade, axillary lymph nodes state and TNM stage ($p < 0.05$). Additionally, the presence of CTCs was found among molecular subtype of Luminal B and TNBC ($p < 0.05$).

Conclusions: The results demonstrated that the presence of CTCs in breast cancer is associated with tumor molecular subtype and metastasis.

PO111

DISCOVERIES BEYOND BRCA1/2: MULTIGENE TESTING IN AN ASIAN MULTI-ETHNIC COHORT SUSPECTED OF HEREDITARY BREAST CANCER SYNDROME

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Background: Hereditary Breast Cancer (HBC) is a well-recognized entity attributed to germline mutations in BRCA1/2 and other cancer (CA) predisposition genes, but the spectrum of mutations in Asians is not well understood.

Methods: One thousand fifty six patients with suspected HBC were seen in our CA Genetics Clinic from 2000–2017, of which 460 underwent clinical-grade germline genetic testing. Patient characteristics and test results were analyzed.

Result: Of 460 tested probands, 93% were female, 61% Chinese and 90% had prior CA, of which 19% (77/414) had ≥2 primary CA. Median age at CA-diagnosis was 43y (range 17-83), most commonly Breast CA (BC, 70%) and Ovarian CA (OC, 25%). 34% had young-onset BC, 8% bilateral BC, and 4% BC & OC. Majority had family history of BC (53%) or OC (20%). 57% underwent multigene panel testing, 34% targeted testing, and 8% predictive testing for known BRCA1/2 mutations. 30% were found to have a pathogenic mutation (PM), 80% in BRCA1/2 with 8 novel mutations noted. Of 33 PM detected in non-BRCA1/2 genes, 61% were in 11 BC genes while 39% were incidental findings in non-BC genes suggestive of alternative CA syndromes. Panel testing was more likely to detect PM compared to targeted testing ($p < 0.001$), and extension of testing beyond BRCA1/2 impacted on management for one-fifth of mutation carriers.

Conclusions: Evolution of CA Genetics services from a single-gene to multigene approach has improved detection of PM in non-BRCA1/2 genes and aided in management. Panel testing is feasible and can be routinely offered in Asian patients with suspected HBC.

PO112

CAN WE ABATE THE PERSISTENT TREND OF NEWLY-DIAGNOSED LOCALLY-ADVANCED BREAST CANCER IN AN ADVANCED DEVELOPING ASIAN POPULATION?

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Background: Breast cancer is the most common cancer is women in Singapore, and its incidence is on the rise. Despite being recognised as an advanced developing country, LABC on presentation remains a persistent trend. The primary aim of our study is to better understand the patient, physician and systemic factors that contribute to diagnostic and treatment delay in T4 disease. Our secondary aim is to determine how we might intervene to improve this delay and suppress its negative impact on patient survival and quality of life.

Methods: Retrospective clinical-pathological analysis of patients diagnosed with T4 LABC, treated at SingHealth Duke-NUS Breast Centre from 2005 to 2014, and retrospective descriptive analysis utilising a comprehensive multi-domain 48-item questionnaire.

Result: We analysed 8,480 patients diagnosed with breast cancer over 10 years. 2.9% of patients presented with T4 disease, incidence of which remained persistent over time. 21.6% of these patients were metastatic on presentation. 66.53% were 50–74 years and 5.71% were less than 40 years-old on presentation. T4 disease existed proportionately amongst different races. 51.6% were of luminal A subtype and 12.2% were basal subtype.

Conclusions: Analysis of clinicopathological factors suggests this group of patients did not exhibit particularly aggressive subtypes, in line with our hypothesis that T4 disease on-presentation is largely a disease of neglect. The delay in patients seeking medical attention is multidimensional, encompassing misguided individual and shared community perception, particular medical/psychiatric conditions, social factors, blindspots in penetration of education surrounding screening and treatment, and preferences towards traditional or alternative therapies.

PO113

VARIATIONS IN THE RECEPTOR ACTIVATOR OF NUCLEAR FACTOR-κB (RANK) PATHWAY, NF-κB-RELATED GENES AND MAMMOGRAPHIC DENSITY IN PREMENOPAUSAL WOMEN

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Background: The receptor activator of nuclear factor-κB (RANK) pathway plays functional roles in breast development and may be associated with breast cancer risk. This pathway is a potential target for breast cancer prevention. As mammographic density is one of the strongest risk factors for breast cancer, we, therefore investigated the associations of single nucleotide polymorphisms (SNPs) in 12 RANK pathway, and NF-κB-related genes with mammographic density in 365 premenopausal women, who had screening mammography at the Washington University School of Medicine St. Louis, Missouri in 2016.

Methods: We assessed volumetric percent density (VPD), dense volume (DV), and non-dense volume (NDV) using Volpara software. Multivariate linear regression models (adjusted for age, body mass index, parity, and family history of breast cancer) were fitted on VPD, DV and NDV on logarithm scale with a SNP and beta coefficients (β) were evaluated. Significant SNPs were identified at the 5% Benjamini-Hochberg false discovery rate (FDR).

Result: Several SNPs were associated with mammographic density, but were not statistically significant after FDR adjustment. The strongest associations were observed between SNPs in NFKB2 (rs199513883, β = -0.67), TNF (rs3093660, β = -0.61), NFKB1 (rs4648061, β = -0.57), IKBKG (rs5986992, β = 0.47), TNFRSF11A (RANK) (rs118134297, β = 0.28) and VPD; NFKB2 (rs4919632, β = 0.57), TNFRSF13B (rs72553883, β = 0.53), NFKB2 (rs76894719, β = -0.43) and DV; TNFRSF11A (rs34005112, β = -0.50), NFKB1 (rs78492053, β = 0.44) and NDV.

Conclusions: RANK SNPs are associated with mammographic density. Because most of these variants are rare, larger studies are needed for validation. Findings could have important implications in breast cancer prevention since a well-tolerated RANKL antibody is already clinical use.

PO114

SOMATIC MUTATION PROFILING OF BREAST CANCER BY NEXT-GENERATION SEQUENCING

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Background: Despite the prominence in estimating cancer risk and risk-reducing intervention, lots of data support the improvement of disease free survival and overall survival through targeted therapy. Tumour profiling plays an important role in precision medicine and might provide markers for monitoring on therapeutic responses and relapse with possibly liquid biopsies. Considering the variations in mutation spectrum across ethnicity, it is worth studying the mutation profiling in Chinese population for future drug developments.

Methods: High risk breast cancer patients who were germline negative (BRCA1, BRCA2, TP53 and PTEN) were selected from Hong Kong Hereditary Breast Cancer Family Registry. 81 tumor DNA was subjected to 93 genes breast cancer panel by next-generation sequencing (NGS). Sequencing data were then analyzed by our in-house developed bioinformatic pipeline.

Result: Fifty one pathogenic/likely pathogenic variants and 18 VUS were identified, which correspond to 45 patients and 12 cancer predisposition genes. The most common mutated genes were TP53 (33.33%), PIK3CA (30.43%) and PTEN (7.25%). Among 45 patients with mutations, 26 patients (57.8%) identified a potential actionable drug target.

Conclusions: Our data suggests that NGS is useful in 57.8% of the cases, and one-third of the patients may benefit from targeted therapy. Different from ovarian cancer, neither BRCA1 nor BRCA2 somatic mutation has been detected. NGS allows better understanding of tumorigenesis which potentially broadens the therapeutic options and enhance molecular monitoring by liquid biopsy. The accumulated data contributes to a more comprehensive and applicable database of somatic mutation profiling in breast cancer of local population.

PO115

ANXIETY, DEPRESSION AND PERCEIVED STRESS AMONG BREAST CANCER PATIENTS: SINGLE INSTITUTE EXPERIENCE

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Background: Statistics reveal that the number of women diagnosed with breast cancer is increasing in Egypt. It is seen as a terrifying disease due to a high mortality rate, its impacts on self-image, and the sexual relationship. As Many patients experience psychological reactions, and may have psychiatric morbidities. The present study aimed to identify the prevalence and associated psychosocial factors of anxiety, depressive disorders and perceived stress in breast cancer patients.

Methods: This cross-sectional study was conducted in clinical oncology department in Menoufia University. Sixty patients were subjected to questionnaire for socio-demographic data ,structured psychiatric clinical interview to diagnose psychiatric diagnoses, Beck depression inventory (BDI-II) for measuring the emotional, cognitive and motivational symptoms of depression , Manifest Anxiety Scale to assess the anxiety state, and Perceived Stress Scale (PSS-10) to assess stress level.

Result: The prevalence of anxiety symptoms was 73.3%.The prevalence of depressive symptoms was 68.7%. While, the prevalence of perceived stress regarding Perceived Stress Scale was 78.1%. Moderate to severe anxiety, depression and distress were more prevalent among advanced disease patients (stage III and IV), patients underwent surgery, patients who was living in rural areas, among unemployed, illiterate and married patients but without statistically significant difference.

Conclusions: Anxiety, depressive disorders and perceived stress are common psychiatric disorders in breast cancer. Understanding these common psychiatric disorders and associated stress can help to plan for treatment and may result in more treatment success.

PO116

ANALYSIS OF THE AWARENESS OF BREAST CANCER IN THE MALAYSIAN POPULATION

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Background: Breast cancer is the most common cancer amongst women in Malaysia with 3,525 cases reported in 2006. The percentage of late presentation was 30–40%, Multiple breast cancer talks were given to the public in efforts to overcome this.

Methods: The talks were started in May 2014 till December 2017 and given by one breast surgeon. Questionnaires were distributed to the audience at the beginning of the talks. The questionnaires were collected at the end of the talks and analyzed using the Statistical Package for the Social Sciences (SPSS) software version 22.

Result: There were a total 2010 respondents from 51 centers. The participants were divided based on their location, into Hospital (10 or 19.6%), Varsity (Dental/Allied Health) (2 or 3.9%), Varsity (Others) (10 or 19.6%), Secondary Schools or Tuition Centers (5 or 9.8%) and Non academic (24 or 47.1%). Although the participants were aware of the existence of breast cancer, their knowledge was inadequate. The majority found the lecture beneficial and there was an improvement of their understanding of breast cancer.

Conclusions: Breast cancer awareness talks need to be continued to educate the public. Future analysis will need to be done to see if there is any decrease in the percentage of presentation of breast cancer in the late stages.

PO117

ASSOCIATIONS BETWEEN GERMLINE MUTATIONS IN PREDISPOSITION GENES AND CLINICOPATHOLOGICAL FACTORS INCLUDING BREAST CANCER SUBTYPES AND AGE OF PATIENTS WITH HIGH RISK FOR HEREDITARY BREAST CANCER

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Background: Genetic testing using multigene panels for hereditary breast cancer of individuals with a personal or family history of breast cancer has been widely used in clinical practice. Several mutations of the predisposition genes have shown strongly associated with specific subtypes of breast cancer.

Methods: We analyzed the associations between mutations in cancer predisposition genes and clinicopathological features in a cohort of 352 breast cancer patients tested for hereditary multigene panels that had been developed previously (We already reported a total of 59 pathogenic or likely pathogenic (P/LP) variants in 89 patients [25.3%]). The tumor histologic type categorized into HR-positive and triple negative. We estimated the associations between three cohorts; with mutations in BRCA 1/2 genes (A), with mutations in genes other than BRCA 1/2(B) and no mutation (C). The number of each cohort is 43, 46 and 263, respectively.

Result: The patients with mutations in BRCA 1/2 had significantly more triple negative tumors (34.9%) comparing with cohort B (15.2%) and C (14.4%). In contrast, we identified that HR-positive tumors accounted for 69.6% among the patients with mutation in genes other than BRCA1/2 (cohort B), it was similar figures in breast cancer without mutations in any predisposition genes. Additionally, the patients with mutations in BRCA 1/2 genes had developed the breast cancer in younger age; mean age at diagnosis was 40.7 in cohort A, 50.2 and 48.9 in B and C, respectively.

Conclusions: When we considered the genetic testing for patients who had any risk factors for familial/hereditary breast cancer, our results will aid the selection among lists of predisposition genes.

PO118

EVALUATION OF COMMON GENETIC VARIANTS FOR BREAST CANCER PREDICTION IN ASIAN BRCA MUTATION CARRIERS

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Background: Pathogenic mutations of BRCA1 and BRCA2 are related to high risk to develop breast and ovarian cancer. However, the estimated risk for breast cancer ranged from about 30% to 85% in BRCA1/2 mutation carriers. The large variability was partially caused by genetic modifiers and many studies identified a list of genetic variants influencing the breast cancer risk. However, the above studies were mainly on Western countries and these variants were less known their effect in Asian BRCA mutation carriers.

Methods: We searched for literatures and identify 135 genetic variants which were reported to influence the cancer risk of BRCA1/2 mutation carriers. We then genotyped them in 95 BRCA1/2 mutation carriers.

Result: The cumulative incidence of breast cancer was about 75%, 74.4% and 77.8% at 70 year-old among the entire cohort, BRCA1 and BRCA2 mutation carriers, respectively. Univariable analysis showed 18 genetic variants associated with breast cancer risk. Multivariable analysis revealed rs4973768 (HR = 2.91, 95% CI 1.47–5.76), rs9790517 (HR = 3.55, 1.11–11.33), rs9348512 (3.02, 1.55–5.89), rs527616 (6.10, 1.76–21.11), rs6678914 (2.08, 1.07–4.05), rs9393597 (2.57, 1.10–5.99), rs4135087 (2.63, 1.00–7.05) and rs167715 (6.37, 1.78–22.88) associated with increased breast cancer risk; variants rs16917302 (0.44, 0.21–0.93), rs10771399 (0.18, 0.08–0.43) and rs3803662 (0.12, 0.03–0.44) were related to decreased cancer risk. Using the weighted variants can construct a score to stratify mutation carriers into low, median and high risk to develop breast cancer ($p < 0.001$).

Conclusions: This preliminary data suggested a proportion of variants found in western population influenced the breast cancer risk in Asian patients; using them was helpful to accurately predict cancer risk.

PO119

SURVEILLANCE FOR PATIENTS WITH AND WITHOUT BREAST CANCER WHO HAVE BRCA MUTATIONS

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Background: It is known that 5-10% of all breast cancers are hereditary, and that the presence of BRCA 1/2 gene mutation increases the risk of suffering from breast and ovarian cancer. Regular examinations including breast MRI are recommended in NCCN guideline 2017 for BRCA 1/2 mutation positive cases.

Methods: From January 2010 to October 2017, we conducted a genetic test on 429 patients at our hospital. Among of those, 85 patients with breast cancer had BRCA1 or BRCA2 mutations. A genetic test was conducted in 42 members of 28 families without onset of breast cancer, and BRCA mutation was observed in 17 patients (5 males) (BRCA 1; 13, BRCA 2; 4).7 of 12 BRCA mutation positive women without cancer onset and 30 woman with breast cancer history underwent surveillance based on the NCCN guidelines at our hospital.

Result: Breast cancer was found in one unaffected woman with BRCA mutations by MRI screening so far. In this case, breast cancer was found in the first MRI screening and surgery was performed. And one BRCA1 mutation positive breast cancer patient, who had underwent annual MRI screening after the surgery was diagnosed MRI detected contralateral breast cancer after 4 years from the first breast cancer surgery.

Conclusions: Improving imaging and interpretation techniques of MRI are required. Also there could be the side effects due to long-term use of contrast agent. Further accumulation of cases and tracking of long-term results are needed.

PO120

CHANGING TREND IN CLINICOPATHOLOGICAL FACTORS AND TREATMENT PROFILE OF BREAST CANCER PATIENTS: SINGLE CENTER EXPERIENCE

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Background: The objective of this study is to evaluate change in clinicopathological factors and treatment profiles for breast cancer patients over the decades.

Methods: A detailed analysis was carried out with respect to age, menopausal status, family history, disease stage, surgery performed, histopathology, hormone receptor status, and use of chemotherapy or radiation therapy. Change in various clinicopathological factors and treatments of breast cancer cases was analyzed.

Result: Mean age at diagnosis was found to be older (50.7 yr vs. 46.2 yr, $p<0.001$) and mean BMI was higher (24.4 kg/m^2 vs. 23.0 kg/m^2, $p<0.001$) in 2000s compared with 1980s. The patients in 2000s had earlier stage tumors ($p<0.001$) and higher estrogen receptor positivity ($p<0.001$), higher frequencies of breast conserving surgery and radiation therapy, and lower frequency of chemotherapy, compared with those in 1980s. There was no significant difference in the frequency of family history and menopausal status, between those in 1980s and 2000s.

Conclusions: Our study has shown that there is increased incidence of breast cancer in older women over the decades, unlike common consensus. Change in mean age at presentation, mean BMI and stage at presentation was seen over the years. Earlier stage disease has increased, thereby the frequencies of breast conserving surgery and radiation therapy has increased and those of chemotherapy has decreased.

PO121

DIETARY PHYTOESTROGEN INTAKE AND THE RISK OF BREAST BENIGN DISEASE

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Background: Phytoestrogens are plant-derived xenoestrogens which exist in various foods. The effect was not clearly understood. The purpose of this study is to investigate the effect of dietary phytoestrogen intake on the progression of of breast benign mass

Methods: A questionnaire survey was conducted on the food intake behavior during the past 6 months of women with breast benign disease. We compared past breast ultrasound results with those when the patients filled out the questionnaires

Result: One hundred fifty two people participated in the study, and a total of 11 kinds of dietary phytoestrogen intake related information was collected. Except for flaxseed group, there was no relationship between food intake and breast benign disease, and the progression of the disease was lower in the flaxseed-intake group than in the flaxseed-non intake group

Conclusions: Overall, the intake of phytoestrogen-containing foods does not seem to be related to the progression of breast benign disease. However, considering the performing of this study through the questionnaire, the interactions between foods, and the various types of phytoestrogens, we think that more delicate research should be done in the future

PO122

WHEN AND WHAT IS OPTIMAL ADJUVANT TREATMENT OF BREAST CANCER AFTER SURGERY IN GERIATRIC PATIENT?

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Background: The overall survival of breast cancer has been dramatically prolonged up to now with the multidisciplinary approach to cure the disease. Geriatric breast cancer patients also increased during the development of medical science. However there is no therapeutic guideline for the geriatric patients in breast cancer disease and sub-optimal therapeutic decisions has often been made by clinicians and patients without standard guideline. It is important to define the proper old age in breast cancer patient in order to determine proper sub-optimal treatment.

Methods: We used the Korea Breast Cancer Society (KBCS) registry data during the period of 2005 to 2010 in age older than 75 years breast cancer women who received breast cancer surgery during that period. Cut off age of 75 years are on the basis of Korean women's average expected life during that period was 80 to 85. We verified 5 years overall survival among the patients who received standard adjuvant chemotherapy and attenuated treatment and omission of adjuvant chemotherapy.

Result: Total of 811 eligible patients, 65 received standard anthracyclin containing regimen, 106 patients received more attenuated regimen such as mono regimen or oral agent. 620 patients omitted adjuvant chemotherapy. 5 year survival rate in stage IIB was 83.3%, 71.4%, 79.1% each group and in stage IIIA was 83.3%, 71.4%, 49.7% each (p value: 0.991, 0.148). Other variables were analysed to compare the differences among sub groups.

Conclusions: The result showed that there is any dominant therapeutic regimen for the elderly advanced breast cancer patients whose expected life is limited within 10 years.

PO123

TUMOR SIZE IN RELATION TO THE OVERALL SURVIVAL OF PATIENTS WITH BREAST CANCER IN YOGYAKARTA, INDONESIA

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Background: Breast cancer is the most prevalent cancer in Indonesian women. The survival of patients depends on many factors, including patient- and tumor-related factors. Only few studies reported survival analysis on Indonesian patients. This study aimed to identify the factors that are associated with the overall survival (OS) of patients in Yogyakarta, Indonesia.

Methods: A retrospective cohort study was carried out at Dr Sardjito Hospital, Yogyakarta. Data of cases that were firstly diagnosed as breast cancer between January 2007 and December 2009 were analyzed. Socio-demographic and clinicopathological data were obtained from the medical and pathological records. The OS rate was calculated using Kaplan Meier method and factors that may impact on the survival were assessed using Cox regression.

Result: A total of 612 patients data were reviewed. The OS rate of the breast cancer patient was 78.14%. Kaplan-Meier plot showed that patients having tumor > 5 cm and HER-positive tumors had a worse OS compared to their counterparts ($p = 0.009$ and 0.023). Among all clinical and pathological variables identified, tumor size was the only predictor for the OS (HR = 5.631; 95% CI = 1.295–24.487, $p = 0.021$).

Conclusions: Tumor size at diagnosis had an impact on the survival of the local patients with breast cancer.

PO124

DIABETES AS A PROGNOSTIC FACTOR IN POSTOPERATIVE HER-2 POSITIVE BREAST CANCER PATIENTS TREATED WITH TARGETED THERAPY

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Background: Recent studies revealed that metabolic stress influences outcomes of breast cancer treatment. We sought to evaluate the prognostic effect of type 2 diabetes in postoperative HER-2+ breast cancer patients treated with HER-2 targeted therapy

Methods: We evaluated 190 HER-2+ (hormone receptor+/-) breast cancer patients (pT1-4N0-2M0) who were treated with surgical resection and trastuzumab (HER-2 targeted therapy) between 2006 and 2015. Survival outcomes and failure patterns were compared between such patients with (n = 12) and without (n = 178) type 2 diabetes.

Result: The median follow-up period was 42.4 months (range 12.0–124.7 months). Twenty-one patients (11.1%) showed relapse (including 9 patients with locoregional failure), and 3 patients (1.6%) died as a result of cancer relapse. One third of the patients with diabetes experienced relapse (4/12, 33.3%). The 3-year disease-free survival (DFS) and overall survival (OS) rates were 90.7% and 98.6%, respectively. Diabetic patients showed shorter DFS compared with non-diabetic patients ($p = 0.006$, 74.1% vs. 91.9%). OS was also shorter in diabetic patients compared with non-diabetic patients ($p = 0.017$, 91.7% vs. 99.1%). In additional immunostaining, HER-3 receptor and Neuregulin-1 were overexpressed in the tumor samples of diabetic patients.

Conclusions: Type 2 diabetes was associated with detrimental effects on survival in postoperative HER-2+ breast cancer patients who were treated with trastuzumab. The poor prognostic effect of diabetes in HER-2+ breast cancer patients should be considered in the context of secondary prevention.

PO125

COMPARISON OF HORMONE RECEPTOR AND HER2 STATUS AND TILS BETWEEN PAIRED PRIMARY AND RECURRENT TUMORS

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Background: It is known that there is discrepancy of hormone receptors (HR) and HER2 status between primary and recurrent tumors. Whether immunological microenvironment alters has been uncertain. The purpose of this study is to compare TILs and HR and HER2 status between paired primary and recurrent tumors.

Methods: The patients were eligible if they had primary surgery at our institute and their breast cancer recurred, and specimens of recurrent disease were available. High TILs were defined as ≥ 10%.

Result: Among 173 recurrent tumors, specimens were metastatic lesion to liver, lung, bone, skin or soft tissue, lymph nodes, and others in 19%, 27%, 16%, 15%, 14%, and 8%, respectively. In primary tumors, 86% were HR positive and 11% were HER2 positive. ER, PgR and HER2 status changed from positive in primary tumors to negative in recurrent tumors in 7%, 39%, and 6%, and changed from negative to positive in 25%, 20%, and 7%, respectively. TILs in primary tumors were significantly associated with breast cancer subtype. In 44% of recurrent tumors, TILs decreased compared with primary tumors, and were correlated with the site of metastasis; high TILs with liver 6%, lung 39%, bone 12%, skin or soft tissue 8%, lymph nodes 19%.

Conclusions: Hormone and HER2 status as well as TILs altered between primary and recurrent tumors. Immunological tumor microenvironment may depend on the site of recurrence and evaluation of recurrent tumors is required in the immunotherapy era.

PO126

CLINICOPATHOLOGIC SIGNIFICANCE OF ANDROGEN RECEPTOR EXPRESSION AND DISCORDANT RECEPTOR STATUS DURING PROGRESSION IN BREAST CANCER

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Background: The role of androgen receptor (AR) as a prognostic marker has been proposed in breast cancer. This study investigated AR status and its clinical significance in breast cancer, especially in triple negative breast cancer (TNBC). We also evaluated discordant AR status during the process of lymph node metastasis, locoregional recurrences (LRR) and distant metastasis.

Methods: From January 2005 to December 2010, we retrospectively reviewed 120 patients including 55 TNBC patients diagnosed as invasive carcinoma with no special type (NST), who were treated at the Kangbuk Samsung Hospital. Tissue microarray was constructed and immunohistochemical expression of AR was performed for 120 invasive carcinomas, NST specimens and matching samples from 28 lymph node metastasis, 2 LRR and 8 distant metastases.

Result: AR expression was found in 35.0% (42/120) of the total patients and 14.5% (8/55) of those diagnosed as TNBC. Positive expression of AR was significantly correlated with smaller tumor size, early T stage, fewer lymph node metastases, early AJCC stage, lower histologic grade, estrogen receptor/progesterone receptor positivity, more luminal A type, less TNBC, longer disease-free survival and overall survival, fewer distant metastasis and no deaths from breast cancer (all $p < 0.05$). AR was a favorable prognostic marker for disease free survival in univariate analysis ($p = 0.041$). The discordance rate of AR status between primary and recurrent/metastatic disease was 21.6%.

Conclusions: AR expression was associated with favorable clinicopathological outcomes in the whole study population. AR status can be altered during tumor progression.

PO127

LYMPHOCYTE ACTIVATING GENE-3 (LAG-3) EXPRESSION AND TUMOR INFILTRATING LYMPHOCYTES IN HER2-POSITIVE BREAST CANCERS

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Background: Lymphocyte activating gene-3 (LAG-3, CD223) is the third inhibitory receptor targeted in immunotherapy, followed by CTLA1 and PD1/PD-L1 axis. There are several ongoing clinical trials targeting LAG-3. The exact signaling downstream mechanism of LAG-3 remains largely unknown including breast cancers. Prognostic significance of tumor infiltrating lymphocytes (TILs) has been determined in breast cancers. We evaluated LAG-3 expression and TILs level in HER2+ breast cancers.

Methods: LAG-3 protein expression level of tumor cells and TILs was evaluated by immunohistochemistry among 167 HER2+ breast cancer. LAG3 mRNA expression level was compared between TILs low and TILs high HER2+ breast cancer using a NanoString assay (NanoString Technologies).

Result: High expression of LAG-3 in tumor cells was significantly associated with absence of hormone receptor expression ($p=0.031$) and high TILs level ($p=0.010$). High expression of LAG-3 in TILs was significantly correlated with high TILs level ($p=0.003$) and abundance of tertiary lymphoid structures around invasive component ($p=0.014$). High total immunoscore of LAG-3 both in tumor cells and TILs significantly associated with high level of TILs ($p=0.001$). High LAG-3 mRNA expression was correlated with high TILs level ($p=0.001$) by NanoString assay. Expression of LAG-3 was not a prognostic factor in HER2+ breast cancers.

Conclusions: LAG-3 expression in tumor cells and TILs are significantly associated with TILs level in HER2+ breast cancer, although it was not a prognostic factor.

PO128

CROSS-TALKING SYSTEM OF BREAST CANCER CELLS AND TUMOR ASSOCIATED MACROPHAGES

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Background: Levels of EGFR and/or HER2 expression are associated with prognosis of breast cancer patients. However, the tumorigenicity of these breast cancer patients and the interaction with tumor microenvironment are not fully elucidated. Here, we focused on the cross-talking systems between breast cancer cells and tumor associated macrophages (TAMs).

Methods: Total 950 breast cancer patients were selected from the clinical database of the Breast Cancer Center between January 1, 1995 and December 31, 2002 at Samsung Medical Center. Various secreted proteins were analyzed by Proteome Profiler Human Cytokine Array. Levels of mRNA and protein expression were analyzed real-time PCR and western blotting, respectively. The mature macrophage-like state was analyzed by adhesion capacity and confocal microscopy.

Result: Clinically, EGFR and HER2 positive breast cancer patients have poor prognosis comparing EGFR alone. We found that the levels of CCL2, CCL5, IL6 and IL8 are significantly increased in EGFR and HER2 positive breast cancer cells. These chemokines triggers differentiation of the human monocytes, THP-1, into macrophage-like cells. TAMs significantly increased the level of IL8 secretion. IL8 secretion by TAMs promoted cell growth and invasiveness of breast cancer cells.

Conclusions: Various secreted proteins by EGFR and HER2 positive breast cancer cells recruited monocytes and differentiated into TAMs. In addition, TAMs-induced IL8 secretion augmented cells growth and invasiveness of breast cancer cells. Therefore, we demonstrated that cross-talking between breast cancer cells and TAMs is involved with tumorigenicity of EGFR and HER2 positive breast cancer cells.

PO129

ROR1-MEDIATED ALTERNATIVE WNT5A SIGNALING REGULATES EMT IN BREAST CANCER CELLS

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Background: Receptor-tyrosine-kinase-like orphan receptor 1 (ROR1) plays a critical role on epithelial-mesenchymal transition (EMT) process. Wnt5a, one of ROR1 ligands, enhance proliferation and migration of various cancer cells. However, a role of Wnt5a and ROR1 complex is not well-known in breast cancer cells. In this study, we investigated a role of Wnt5a and ROR1 complex on breast cancer metastasis.

Methods: ROR1 was transiently silenced by specific siRNAs, whereas ROR1 overexpression was transfected by lentivirus system. The levels of protein expression were assessed using Western blotting and immunofluorescence. Breast cancer motility was assessed using migration and invasion assays.

Result: Silencing of ROR1 inhibits proliferation, EMT and migration capacity in MDA-MB 231. Conversely, overexpression of ROR1 enhanced expression of EMT and metastatic potential in MCF7 cells. Treatment of highly expressed ROR1 cells with a monoclonal antibody specific for ROR1 reduced expression of EMT marker protein and inhibited cancer cell migration and invasive activity.

Conclusions: ROR1 expression in breast cancer cell lines was associated with cancer cell invasion. We suggest that ROR1 could be as a potential therapeutic target. In further study, we will investigate the correlation between ROR1 expression and metastasis of breast cancers.

PO130

THE CLINICAL SIGNIFICANCE AND THE POSSIBILITY AS THERAPEUTIC TARGET OF EGFR IN HORMONE RECEPTOR-POSITIVE BREAST CANCERS

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Background: Although many researchers have been developing effective therapeutic strategies for treatment of hormone receptor positive [HR (+)] breast cancers, resistance of endocrine therapy occurs, either de novo or acquired resistance. Here, we investigated the clinical significance of EGFR and the possibility as therapeutic target for overcome endocrine resistance in HR (+) breast cancer models.

Methods: Using the clinical data of 2,166 patients with HR (+) and HER2 (-) breast tumors between January 2007 and July 2013, we analyzed the survival rates of breast cancer patients with tamoxifen. Levels of mRNA and protein expression were analyzed by real-time PCR and western blotting, respectively. Apoptotic cell death was analyzed by flow cytometry and phase contrast microscopy.

Result: EGFR expression was present in 109 patients (5%) and was involved with poor prognosis such as disease-free survival (DFS) and overall survival (OS) in HR (+) breast cancers. Levels of EGFR and its ligand, Transforming growth factor alpha (TGFA) expression were significantly increased in high risk breast cancer groups. Basal level of ER-α was decreased by TGFA treatment. When TGFA pretreatment, HR (+) breast cancer cells were occurred resistance by tamoxifen. However, down-regulation of ER-α by TGFA was reversed by gefitinib, a specific EGFR inhibitor. Apoptosis of HR (+) breast cancer cells was synergistically increased by combination of tamoxifen and gefitinib.

Conclusions: Aberrant EGFR expression is associated with poor prognosis in HR (+) breast cancers. EGFR could be a therapeutic target for overcome endocrine therapy resistance in HR (+) breast cancer patients.

PO131

ANNEX IN A1 TO THE BREAST TUMOUR MICROENVIRONMENT BY AIDING IN MACROPHAGE POLARISATION

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Background: Tumor-associated macrophages (TAMs) choreograph various aspects of the tumor microenvironment.Macrophages exhibit cellular plasticity and can be polarized to M1/M2 subtypes in presence of different microenvironment "signals". Annexin A1 (ANXA1), an anti-inflammatory protein is highly expressed in metastatic breast cancer.

Methods: The association between TAMs and breast cancer in the patients was assessed. Percentage of M1/M2 macrophages was evaluated in the breast tumors from MMTV mice. Macrophage education by breast cancer was assessed by ex vivo differentiation of bone-marrow derived macrophages (BMDMs) in the presence or absence of breast cancer conditioned media by flow cytometry,ELISA, and mRNA expression.

Result: Clinically, we found that M2 TAMs were highly enriched in Claudin-low breast cancer subtype and was strongly associated with ANXA1 gene expression. In the MMTV mouse model, M2 TAMs were higher in the breast tumors compared to the mammary tissues along with higher expression of ANXA1. Additionally, wild type BMDMs were skewed to a more M2 TAM-like phenotype upon co-culture with breast cancer cells, with enhanced migratory and invasive properties and phagocytic potential, which was reduced in the ANXAI-knockout BMDMs. Breast tumors isolated from the 4T1-orthotopic mouse model showed higher percentage of M2 TAMs in the wild type as compared to the ANXA1 KO mice.

Conclusions: This study demonstrates a novel role of ANXA1 in regulating the dynamic aspect of macrophage polarization in breast tumor microenvironment. RNA sequencing is underway to explore the unique signature molecules and the signaling mechanism involved in governing this entropic process. Secretome analysis (underway) of breast cancer conditioned media for the evaluation of various secreted proteins will also unveil important information pertaining to this dynamic process.

PO132

WHOLE EXOME SEQUENCING OF EXTREME RESPONDERS REVEALS LOW MUTATION BURDEN IN METASTATIC BREAST CANCER

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Background: Extreme responders to anticancer therapy are rarely encountered in the treatment of advanced breast cancer patients, but their treatment response have not been investigated on the whole exome level. We performed whole exome analysis to characterize genomic landscape of extreme responders in metastatic breast cancer patients.

Methods: Clinical samples were obtained from patients who showed exceptional response to anti-HER2 therapy or hormonal therapy. Non-responders were selected among those who did not respond. Matched breast tumor tissue (somatic DNA) and blood samples (germline DNA) were collected from a total of 18 responders (12 ER+, 6 HER2+) and 8 non-responders (6 ER+, 1 HER2+, 1 TNBC). Whole exome sequencing using Illumina HiSeq2500 was performed on the 26 patients (52 samples). Somatic single nucleotide variants (SNVs), indels and copy number variants (CNVs) were identified for each patient genome. Group specific somatic variants and mutation burden were statistically analyzed.

Result: Cancer exomes were characterized by 1,455 somatic single-nucleotide variants (1,327 missense, 80 nonsense, 36 splice-site, 12 start/stop-lost), 149 insertions/deletions (108 frameshift, 41 inframe), with a median of 1 mutations per Mb (0.2 to 2.7 mutations per Mb) in all patients. Responders harbored a significantly lower non-synonymous mutation burden than non-responders (median, 27 vs. 90.5, $p=0.01$), and copy number variation burden was also lower (median 23 vs. 31, $p=0.14$). Multivariate analyses of factors influencing progression-free survival showed that high mutation burden and visceral metastases were significantly related with progression.

Conclusions: Extreme responders of metastatic breast cancer are characterized by low nonsynonymous mutational burden.

PO133

CIP4 EXPRESSION IN BREAST CARCINOMAS AND ITS PROGNOSTIC SIGNIFICANCE

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Background: Cdc42 interacting protein 4 (CIP4) is an actin regulatory proteins in regulating cell invasion and tumor metastasis. Recent studies have shown that CIP4 is overexpressed in many types of cancer and may play a crucial role in metastasis. This study aimed to investigate the potential prognostic value of CIP4 in breast cancer.

Methods: Formalin-fixed, paraffin-embedded tissues from a cohort of 430 patients were used. The CIP4 expression in patients with breast cancer was analyzed by immunohistochemistry (IHC) in tissue microarrays and correlated with clinicopathologic characteristics to determine its prognostic implications.

Result: High CIP4 expression were found in 13.5% (58/430) patients. High CIP4 expression was significantly associated with invasive ductal carcinoma (IDC) histology ($p<0.001$), high histologic grade ($p<0.001$), negative estrogen receptor (ER) status ($p<0.001$), negative progesterone receptor (PR) status ($p=0.005$), positive cytokeratin 5/6 (Ck5/6) ($p=0.003$), positive epidermal growth factor receptor (EGFR) ($p<0.001$), high Ki-67 proliferating index ($p<0.001$), and positive p53 ($p<0.001$). However, high CIP4 expression were not associated with age, tumor stage, lymph node status, pathologic stage, or human epidermal growth factor receptor 2 (HER2) status. In intrinsic subtype analyses, high CIP4 expression correlated with HER2 type (24.1%) and basal TNBC (41.4%), although low CIP4 expression correlated with luminal A subtype (47.3%). Univariate survival analysis using the Kaplan-Meier method showed that CIP4 expression were not associated with disease-free survival (DFS, $p=0.444$) or overall survival (OS, $p=0.388$).

Conclusions: Our results indicated that breast tumors with high CIP4 expression are associated with HER2 and basal TNBC subtype. These findings suggest that CIP4 may be a promising biomarker for patients with breast cancer and may need to be analyzed, to obtain complete prognostic information.

PO134

SPLICING FACTOR HNRNPA2B1 CONTRIBUTES TO TUMORIGENIC POTENTIAL OF BREAST CANCER CELLS THROUGH STAT3 AND ERK1/2 SIGNALING PATHWAY

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Background: Increasing evidence has indicated that the splicing factor hnRNPA2B1 plays a direct role in cancer development, progression, gene expression, and signal transduction. Previous studies have shown that knocking down hnRNPA2B1 in breast cancer cells induces apoptosis, but the mechanism and other functions of hnRNPA2B1 in breast cancer are unknown. The goal of this study was to investigate the biological function, clinical significance, and mechanism of hnRNPA2B1 in breast cancer.

Methods: The expression of hnRNPA2B1 in 92 breast cancer and adjacent normal tissue pairs was analyzed by immunohistochemical staining. Stable clones exhibiting knockdown of hnRNPA2B1 via small hairpin RNA expression were generated using RNA interference technology in breast cancer cell lines. The effects of hnRNPA2B1 on cell proliferation were examined by MTT and EdU assay, and cellular apoptosis and the cell cycle were examined by flow cytometry. A nude mouse xenograft model was established to elucidate the function of hnRNPA2B1 in tumorigenesis in vivo. The role of hnRNPA2B1 in signaling pathways was investigated in vitro.

Result: Our data revealed that hnRNPA2B1 was overexpressed in breast cancer tissue specimens and cell lines. Knockdown of hnRNPA2B1 reduced breast cancer cell proliferation, induced apoptosis, and prolonged the S phase of the cell cycle in vitro. In addition, hnRNPA2B1 knockdown suppressed subcutaneous tumorigenicity in vivo. On a molecular level, hnRNPA2B1 knockdown decreased signal transducer and activator of transcription 3 and extracellular-signal-regulated kinase 1/2 phosphorylation.

Conclusions: We concluded that hnRNPA2B1 promotes the tumorigenic potential of breast cancer cells, MCF-7 and MDA-MB-231, through the extracellular-signal-regulated kinase 1/2 or signal transducer and activator of transcription 3 pathway, which may serve as a target for future therapies.

PO135

HOW MAMMOGRAPHIC DENSITY CONTRIBUTE TO MAMMARY TUMORIGENESIS: A PROOF OF CONCEPT EXPERIMENT

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Background: Mammographic density (MD) is a strong independent risk factor of breast cancer. Still less is known about the mechanism of how MD contribute to mammary tumorigenesis. We performed a proof of concept experiment to address if, 1) breasts with high MD consist of greater number of epithelial stem cells (ESC) resulting in greater number of cellular division, thereby 2) is accumulated with greater number of somatic mutations.

Methods: Sixty-five normal fresh mammary tissue were retrieved from surgical specimen of mastectomy/mammoplasty. ESCs were isolated by FACs sorting from EpCAM positive epithelial cell population. Cumulative population doubling (CPD) and colony forming assay (CFA) were performed to assess cellular division. Response to tamoxifen was tested by MTT assay, as tamoxifen reduces both MD and risk of breast cancer. In parallel, whole genome sequencing (WGS) was done from fresh normal mammary tissue of 10 high and 10 low density breast cases, whose blood-WGS were previously obtained.

Result: Though tissues with greater proportion of ESC (%) showed greater number of colonies and passages of cellular division, no association was found with MD. Tissue with greater proportion of ESCs displayed better tamoxifen response. Whole genome sequencing of normal mammary tissue revealed substantial number of somatic mutations including SNVs, indels. Though no significant association was observed between MD and somatic mutations, two patients with known BRCA germline mutations harbored greater number of somatic pathogenic mutations (mean 1.73 vs. 5.00, $p = 0.36$).

Conclusions: Though initial hypothesis were negative, in-depth analyses are ongoing to elucidate the mechanism of mammary tumorigenesis regarding mammographic density.

PO136

MK2206 POTENTIATES ANTICANCER EFFECT OF GEFITINIB VIA MTORC1 PATHWAYS IN MSL SUBTYPE TRIPLE-NEGATIVE BREAST CANCER CELLS

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Background: Triple-negative breast cancer (TNBC) cells show activated growth factor signaling and resistance to inhibitors for EGFR despite overly expressed EGFR protein which is related with malignant behavior and poor prognosis of cancer. To uncover the underlying mechanism of EGFR inhibitor resistance and identify signaling pathway target inhibitors that exert synergistic effect with EGFR inhibitor, we have screened the cell viability inhibitory effect of selected kinase inhibitors in combination with gefitinib in MSL subtype TNBC cell lines.

Methods: Screening of PKIs: Western blot analysis: mTOR, p-mTOR, ERK1/2, p-ERK1/2, SRC, p-SRC, 4E-BP1, p-4E-BP1, RPS6, p-RPS6, PRAS40, p-PRAS40, AKT, p-AKT, GSK-3β, p-GSK-3 β, RAPTOR, RICTOR, PARP1, cleaved PARP, cleaved caspase-3, XIAP, β-actin; β-tubulin. RPTOR was knock-downed and the synergisitc effect with gefitinib was anaylsed by cell proliferation assay

Result: The combination of gefitinib/MK-2206 exerted a prominent synergistic lethal effect in an MTT cell viability assay and a growth inhibitory effect in a long-term colony-forming assay in 2 MSL subtype TNBC cell lines (MDA-MB-231 and HS578T) and one basal-like (BL) subtype TNBC cell line (MDA-MB-468). Gefitinib/MK-2206 treatment synergistically decreased the mTOR signaling target substrates along with the downregulation of ribosomal protein S6 (RPS6), a marker of cell proliferation and target substrate of the AKT-mTOR signaling pathway. In addition, gefitinib markedly reduced the viability of MDA-MD-231 and HS578T cells when RPTOR was suppressed by siRNA-based knockdown.

Conclusions: RPTOR mediates, at least partially, the resistance to EGFR inhibition in TNBC cells. Targeting the (mTORC1) pathway may be a potential strategy for the treatment of EGFR-resistant TNBC.

PO137

THE RADIOSENSITIZING EFFECT AND IMMUNE-MODULATORY FUNCTION OF PI4K IIIα INHIBITION IN BREAST CANCER MODEL: A POTENTIAL MODEL OF DRUG REPOSITIONING

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Background: We investigated the radiosensitizing effect and immune-modulatory effect of PI4K IIIα inhibitor in vitro and in vivo and the mechanism of its interaction.

Methods: BT474 and MDA-MB-468 human breast cancer cells and 4T1 murine breast cancer cells were used. RNA interference, clonogenic assays, Western blotting, immunocytochemistry, in vitro kinase assays, wound healing assay and modified boyden chamber assay were performed. The in vivo radiosensitizing effect and immune-modulatory function were evaluated in in vivo xenograft models and immune-competent syngeneic murine tumor models.

Result: Specific inhibition of PI4K IIIα using siRNA showed significant radiosensitizing effect in breast cancer cells. Simeprevir, an anti-HCV agent, had an inhibitory effect of PI4K IIIα and exhibited radiosensitizing effect associated with prolonged γH2AX foci and down-regulated phospho-DNA-PKcs. Simeprevir led to eversion of the epithelial-mesenchymal transition as suggested by decreased invasion/migration. In BT474 human breast cancer xenograft models, simeprevir combined with radiation significantly delayed tumor growth compared to either treatment alone. Simeprevir enhanced the radiosensitizing effect of anti-programmed death-ligand 1 (PD-L1) and decreased the expression of PI3Kδ, phosphorylated-Akt, and PD-L1 in breast cancer cells co-cultured with human T-lymphocytes. Simeprevir showed significant radiosensitizing effect and immune-modulatory function in immune-competent syngeneic 4T1 murine tumor models by affecting the CD4(+)/CD8(+) lymphocyte ratio.

Conclusions: These findings suggest that targeting PI4K IIIα with an anti-HCV agent is a viable drug repositioning approach for enhancing the therapeutic efficacy of radiation therapy. The immune regulatory function of PI4K IIIα via modulation of PI3Kδ suggests a potential strategy for boosting radiosensitizing effect of immune checkpoint blockades.

PO138

TARGETING OF MICROENVIRONMENT TO IMPROVE EFFICACY OF CANCER METABOLISM TARGETED THERAPY IN BREAST CANCER CELLS

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Background: Metabolism of cancer cells is different from that of the normal cells. Therefore, targeting of cancer metabolism is a strategy that preferentially kills cancer cells without significant toxicity to normal cells. Dichloroacetate (DCA), an analog of acetic acid, is known to inhibit glycolysis. Metformin, an oral drug widely used in the treatment of type 2 diabetes, induces energy stress. Hypoxia is a common environmental phenomenon in many solid cancers and has been associated with the resistance of cancer cells to radiation- and chemo-therapy. Thus, we investigated that the effect of metabolic targeted drug, such as DCA or metformin, on MCF-7 breast cancer cell death in various tumor microenvironment, including hypoxia and glutamine deprivation.

Methods: Cell death was evaluated using by Annexin V and PI staining. Small interfering RNA (siRNA) was used for suppressing gene expression. The mRNA and protein levels were measured by RT-PCR and Western blot analysis, respectively.

Result: Co-treatment with DCA and metformin led to a dramatic induction of cell death in MCF-7 cells. However, HIF-1α activation in breast cancer cells suppresses DCA and metformin-induced cell death. These results suggest that targeting HIF-1α is necessary for cancer cell metabolism targeted therapy. Combination of metformin and lapatinib (the dual inhibitor of epidermal growth factor receptor and human epidermal growth factor receptor 2 tyrosine kinases) was also induced cell death in MCF-7 cells, but glutamine deprivation inhibits cell death induced by two drugs.

Conclusions: Based on these finding, we suggest that consideration of microenvironment regulation for cancer metabolism-targeted treatment in breast cancer cells.

PO139

INHIBITION OF BREAST CARCINOMA AMPLIFICATION SEQUENCE 1 (BCAS1) ENHANCES TAMOXIFEN SENSITIVITY IN BREAST CANCER CELLS

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Background: Breast cancer is most common cancer in women. Approximately 70% of breast cancer patients are ER positive and they are prescribed tamoxifen (Tam), selective ER modulators, used as adjuvant endocrine therapy. Among them, 30% of patients are acquired resistant to tamoxifen. The mechanism of tamoxifen resistance is unclear. Breast carcinoma associated sequence 1 (BCAS1) is high expressed in breast cancer, and amplified BCAS1 is associated with more aggressive tumor phenotypes. In the present study, effects of BCAS1 on tamoxifen resistance in breast cancer cells were investigated.

Methods: Cell viability and cell death was measured using MTT assay and the Annexin V-FITC Apoptosis Detection kit I, respectively. Protein expression levels were detected by Western blot. Mitochondrial membrane potential (MMP) was measured using JC-1. Mitochondrial morphology images were obtained using confocal microscope.

Result: For establishment of tamoxifen resistant (TR) cells, MCF-7 cells were treated with tamoxifen for 9 months. BCAS1 mRNA and protein levels in TR cells were higher compared to parental cells. BCAS1 suppression by siRNA increases tamoxifen-induced cell death and induced cleaved PARP protein. Mitochondrial morphology in TR cells was more tubular than parental MCF-7 cells. MMP and ATP production rate was higher in TR cells compared to parental MCF-7 cells. Down-regulation of BCAS1 in TR cells were also investigated. To confirm role of BCAS1, MCF-7 cells were overexpressed with BCAS1. BCAS1 overexpressed cells also increase MMP compared to parental cells and induce MMP-related protein expression.

Conclusions: Targeting BCAS1 could be strategy of overcoming tamoxifen resistance and improving breast cancer treatments.

PO140

COMBINATION OF CYSTINE DEPRIVATION AND TUMOR NECROSIS FACTOR-RELATED APOPTOSIS-INDUCING LIGAND UNDER HYPOXIA CONDITION INDUCES CELL DEATH IN MDA-MB-231 BREAST CANCER CELLS

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Background: Amino acid is possible new target for cancer therapy. Tumor frequently encounter hypoxic stress and hypoxic conditions lead to chemotherapy and radiotherapy resistance. In the present study, effects of amino acid deprivation in MDA-MB-231 cells were investigated in hypoxic condition.

Methods: Cell viability and cell death was measured using MTT assay and the Annexin V-FITC Apoptosis Detection kit I, respectively. RNA was extracted with TRIzol reagent, and total RNA (2 μg) was syntherzised with SuperScript II reverse transcriptase (Invitrogen). cDNA was amplified with a GoTaq G2 Flexi DNA Polymerase (Promega) using the specific primer pairs. Protein expression levels were detected by Western blot.

Result: MDA-MB-231 breast cancer cells were treated with medium containing individual amino acid deprivation for 48 h. Among individual amino acid deprivation, cystine deprivation induces approximately 90% cell death. Sulfasalazine, a potent inhibitor of cystine transporter (xCT), also increases the cell death in MDA-MB-231 cells. Other agents containing thiol such as mercaptoethanol and DTT recover sulfasalazine-induced cell death. However, hypoxia significantly reduces sulfasalazine-mediated cell death. Tumor necrosis factor-related apoptosis-inducing ligand (TRAIL) sensitizes sulfasalazine-mediated cell death in hypoxia; TRAIL alone did not induce cell death. We further investigated the mechanism.

Conclusions: The present study suggests that TRAIL sensitizes cystine deprivation-induced cell death in hypoxia.

PO141

PRECLINICAL MOUSE MODEL FOR METASTATIC BREAST CANCER

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Background: Breast cancer metastasis is the main cause of death of cancer patients. The metastasis model is modified for the evaluation and prediction of cancer progression. We describe two mouse models for investigating tumor metastasis.

Methods: In the first spontaneous metastasis mouse model, 4T1 mouse breast tumor cells are injected into the fourth mammary gland of host mice (BALB/c) and the metastasis of 4T1 tumor cells into the lung are examined with a colonogenic assay. Combined with the bioluminescence live tumor imaging, this mouse model allows tumor growth and progression to be monitored and quantified. As the spontaneous metastasis models recapitulate all the events involved in the multistep process of the metastatic cascade, they should help to improve our understanding of the mechanisms that regulate metastatic spread and growth. In the second experimental metastasis mouse model, luciferase-labeled MDA-MB-231 human breast tumor cells are injected into the left cardiac ventricle of nude mice (BALB/c Nude). Development of metastases was monitored by in vivo bioluminescence imaging (BLI), brain metastasis was monitored by high-field (9.4T) magnetic resonance imaging (MRI), and tumor-induced osteolysis was assessed by micro-computated tomography (μCT).

Result: We obtained serial images of 4T1-luc orthotopic model using IVIS Lumina system. After 4 weeks, bioluminescent signal was detected in lung, and then dead mice were began to occur. After 5 weeks, we observed lung nodule that was transferred from primary breast cancer. In the second metastasis mouse model, we confirm brain, knee, and rib metastases using optical imaging analyzer.

Conclusions: The use of experimental metastasis models has also been highly successful for investigating the tissue specificity of metastases, as well as their response to targeted therapies and the identification of possible relevant molecular drivers of metastatic disease. These two types of animal model might be a useful tool in assessing therapeutic implications and the efficacy of anti-cancer drugs.

PO142

PROSPECTIVE STUDY OF UDP-GLUCURONOSYLTRANSFERASE (UGT) 2B17 GENOTYPE AND EXEMESTANE (EXE) PHARMACOKINETICS (PK) AND PHARMACODYNAMICS (PD) IN ASIAN, HORMONE RECEPTOR (HR) POSITIVE, METASTATIC BREAST CANCER

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Background: The active metabolite of Exemestane, 17-dihydroexemestane (17DhExe), is glucuronidated by UGT2B17 to inactive exemestane-17-O-glucuronide (Exe17-O-glu). UGT2B17*2/*2 null genotype is 7 times more common in Asians than Caucasians and leads to reduced Exe glucuronidation in-vitro. We studied Exe Pharmacokinetics and Pharmacodynamics in metastatic breast cancer (MBC) patients genotyped for UGT2B17.

Methods: Eligible patients (HR+ MBC; ≥ 1 line of endocrine therapy) received Exe 25 mg OD till progression. UGBT2B17 genotype was correlated with day 29 (D29) steady-state PK (Exe and metabolites), change in PD biomarkers (estrone and androstenedione) at D29 vs. baseline (BL), objective response rate (ORR) [sum of complete and partial responses], and clinical benefit rate (CBR) [response or stable disease ≥ 24 weeks].

Result: In 64 patients enrolled, CBR was 25%; ORR was 3%. Frequencies of UGT2B17*2/*2, UGT2B17*1/*2 and UGT2B17*1/*1 were 72%, 26% and 2%, respectively. PD and PK data were available for 54 and 53 patients respectively. Mean Exe17-O-glu AUC and Cmax were significantly lower, and mean 17DhExe Cmax was numerically higher in patients with UGT2B17*2/*2 vs. other genotypes. 17DhExe Cmax was higher in patients with clinical benefit vs. none (5.6 vs. 3.8 ng/mL, $p = 0.02$). Frequency of desired PD effect (rise in androstenedione and fall in estrone at D29 vs. BL) was 22%. Exe plasma active index, defined as ratio of active vs. inactive metabolites, was higher in patients with a fall in D29 estrone vs. those without (14.7 vs. 9.5, $p = 0.05$).

Conclusions: UGT2B17 genotype affects Exe PK , and may have significant PD correlates. Larger studies to examine effects on clinical treatment efficacy are needed.

Poster Presentation

PO143

ADDITION OF TRASTUZUMAB TO NEOADJUVANT CHEMOTHERAPY MAY INCREASE OBJECTIVE RELEASE RATE IN EARLY BREAST CANCER WITH HER2 EQUIVOCAL

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Background: HER2 is considered an important prognostic marker in breast cancer. The anti-HER2 drug trastuzumab is widely recommended for patients who were defined as HER2 positive. And the addition of trastuzumab to neoadjuvant chemotherapy could reach rather high pathology complete release (pCR) rate. In 2007, ASCO/CAP HER2 testing guidelines defined a special kind of HER2 status, HER2 equivocal, and redefined it in the 2013 ASCO/CAP HER2 testing guidelines. In such cohort, the efficacy of adding trastuzumab is unknown. We conducted a retrospective study on HER2 equivocal patients, to investigate whether addition of trastuzumab could improve the benefit of neoadjuvant chemotherapy.

Methods: We retrospectively analyzed 26 consecutive patients who detected HER2 equivocal and underwent neoadjuvant chemotherapy in our hospital between 2012 and 2016. Eleven patients were treated with chemotherapy plus trastuzumab (PCH cohort) and 15 were treated with chemotherapy only (PC cohort). The clinical and pathological response between the two cohorts were evaluated to investigate the efficacy of additional trastuzumab in HER2 equivocal patients.

Result: Fifty four point five percent patients achieved pCR in PCH cohort, and 33.3% patients achieved pCR in PC cohort. Objective release rate (ORR) is signifigant higher in PCH cohort than in PC cohort (100% vs. 60%, $p = 0.024$).

Conclusions: Patients detected HER2 equivocal could achieve increased objective release rate from adding trastuzumab in neoadjuvant chemotherapy.

PO144

THE BREAST ABSCESS DRAINAGE AND IRRIGATION SYSTEM (BADIS TM): AN EFFECTIVE TREATMENT WITH GOOD COSMETIC OUTCOME

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Background: A breast abscess is commonest seen in a lactating woman. It may also occur in diabetics and those on immunomodifying medications. In breast reconstruction, it may occur post implant reconstruction. Small abscesses are easily aspirated. Large abscesses are more difficult to be completely aspirated, recur quickly and failure often leads to an incision and drainage procedure. This results in the need for many weeks of frequent dressing and eventually heal with unsightly scars.

Methods: The Breast Abscess Drainage and Irrigation System (BADIS TM), is a novel way of treating large breast abscesses. The patient undergoes one episode of general anesthesia or local anesthesia with sedation. We describe a case of a large breast abscess post implant reconstruction in a 40 year old woman. The total volume of pus drained was 1,100 mL. The infected implant was removed through an inframammary incision. The cavity was flushed repeatedly and the incision was sutured. Two surgical drains were left in place; one for entry and one for exit of flushing fluid which consisted of diluted hydrogen peroxide followed by normal saline.

Result: It resulted in an effective way of draining a large amount of pus with good cosmesis. Postoperative flushing was repeated in the ward to overcome incomplete pus drainage and prevent reaccumulation of pus.

Conclusions: BADIS TM is an economical yet effective treatment modality. It may be used for any large breast abscess irrespective of underlying cause. It is easily performed using regular surgical materials.

PO145

THE ROLE OF SHARP DISSECTION IN NIPPLE SPARING MASTECTOMY: A SAFE PROCEDURE AND NONE NECROSIS OF NIPPLE-AREOLA COMPLEX

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Background: Nipple sparing mastectomy (NSM) is becoming increasingly accepted for the treatment of breast disease, however, nipple-areola complex (NAC) necrosis, the frequent severe postoperative complication, inhibits popularity of this procedure. This study reported technical aspects and short-term postoperative outcome of NSM

Methods: A single-center, retrospective review of 77 patients treated with NSM at our institution from Nov 2015 and Sep 2017 was performed. The primary outcome was the incidence of the NAC necrosis

Result: A total of 95 NSM performed on 77 patients were included in our study. Median age of patients was 42 years. Among these patients, 53 (68.83%) for breast cancer 2 (2.60%) for flat epithelial atypia, 3 (3.90%) for papilloma 7 (9.09%) for hyperplastic pain1 (1.59%) for repeated multiple fibroma1 (1.59%) for serous mastitis3 (3.90%) for side effect after injecting Amazingel, 7 (9.09%) for gynecomastia. None of the 77 patients appeared NAC necrosis or mastectomy skin flap necrosis, NAC discoloration or ischemia with eschar formation presenting between the 3rd and 7th postoperative days in 6 nipples, 4 nipples had ischemia and 2 nipples showed discoloration. There was no infection happened among the 77 patients. After an average follow up of 12 months, all the NAC were intact and no local or systemic recurrences in those breast cancer cases.

Conclusions: NSM can be safely performed for properly selected patients. Through special surgical technique, nipple necrosis can be avoided and the other complication has an acceptable rate

PO146

INFLUENCE OF HYPOFRACTIONATED RADIATION THERAPY FOLLOWING MASTECTOMY ON COMPLICATION IN BREAST CANCER PATIENTS UNDERGOING TWO-STAGE PROSTHETIC BREAST RECONSTRUCTION

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Background: To compare the reconstruction-related complication risk between hypofractionated RT and conventional RT and identify a dosimetric predictor for the development of complications.

Methods: We identified 49 patients received expander placement with acellular dermal matrix immediately after mastectomy, then postmastectomy RT, followed by exchange of the expander for a permanent implant by a single surgeon. Of these patients, 19 underwent conventional 50 Gy RT. The remaining 30 patients underwent hypofractionated RT (40.05–42.56 Gy/15–16 fractions), of which 80% received arc-based intensity modulated-RT planning. The primary outcome was any reconstruction-related complication.

Result: Any complication rate was significantly higher in the conventional RT group than in the hypofractionated RT group (52.6% vs. 13.3%, $p = .003$). Patients with higher acute skin reaction during RT tended to experience more complications (grade 0–1 vs. 2-3; 13.5% vs. 75%, $p = .001$). Chest wall skin Dmax was the best dosimetric predictor for the development of any reconstruction-related complication as well as RT-related skin reaction. Mean Dmax were 44.6 Gy, 46.2 Gy, 48.6 Gy, and 54.8 Gy in patients received 40.05 Gy in 15 fraction without bolus, 40.05 Gy in 15 fraction with bolus, 42.56 Gy in 16 fraction with bolus, and 50 Gy conventional fractionation with or without bolus, respectively, in an equivalent dose of 2 Gy fraction using an α/β value of 4.

Conclusions: Hypofractionated RT may reduce reconstruction-related complication risk and Dmax can be its potential predictor. Despite the small sample size in our study, the promising results warrant further larger scale research.

PO147

STEREOTATIC VACUUM ASSISTED BIOPSY OF MAMMOGRAPHICALLY SUSPICIOUS MICROCALCIFICATIONS-THE INITIAL EXPERIENCE IN CHINA

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Background: Incidental indeterminate/suspicious microcalcification has become a more common encounter due to increased use of screening mammogram. However, open biopsy and surgical excision still remain the choice of diagnosis and treatment in many parts of Mainland China due to financial and technical reasons, particularly in rural areas. Stereotatic-guided vacuum-assisted biopsy (SVAB) under local anesthesia is becoming more popular in larger cities and with the aid of immediate imaging using TRIDENT specimen mammogram system.

Methods: All mammograms were reported by specialist radiologist and all SVAB were performed by specialist breast surgeon and radiologist. Retrospective review of a prospectively-maintained database was performed.

Result: From 1st December 2015 to 31st May 2017, 190 patients (192 procedures) with BIRADS 4 microcalcifications had undergone SVAB. Median age was 45 year-old (Range 24–81). Three patients had failed identification of microcalcification with the procedure abandoned. Median duration of procedure was 40 minutes (Range 10–90). There was no reported major complication, hematoma occured in 10 (5.2%) of patients. 23 (12%) of the biopsied specimens were malignant, including 19 ductal carcinoma in situ (DCIS), 1 microinvasive DCIS and 3 invasive ductal carcinoma (IDC). Fifteen-one hundred forty eight (10.1%) were mammographic BIRADS 4a lesions, 6/38 (15.8%) were BIRADS 4b and 2/6 (33%) were BIRADS 4c. Of note, there were 16 (8.3%) atypical ductal hyperplasia (ADH) detected in the current cohort, 6 patients received open excision, there was no upgraded diagnosis of DCIS or IDC.

Conclusions: Nearly 90% of BIRADS 4 mammographic lesions were benign, widespread introduction of SVAB in China can potentially decrease the public health budget burden.

PO148

THE USEFULNESS OF PEDICLED PERFORATOR FLAP IN PARTIAL BREAST RECONSTRUCTION AFTER BREAST CONSERVING SURGERY IN KOREAN WOMEN

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Background: The emergence of breast-conserving surgery combined with radiotherapy as the treatment of choice for early stage breast cancer has resulted in greater focus on oncoplastic breast surgery. The use of perforator flaps has particularly gained in reputation for its effectiveness in the reconstruction of partial breast defects in Korean women. Herein, we present our experience with the use of thoracodorsal artery perforator (TDAP) and lateral intercostal artery perforator (LICAP) flaps.

Methods: This study included 33 patients who underwent breast reconstruction using TDAP or LICAP flaps at our hospital from January 2011 to December 2014. Data from patient medical records, and patient satisfaction surveys, which were conducted 12 months postoperatively, were retrospectively analyzed and compared.

Result: TDAP and LICAP flap-based reconstructions were performed in 14 and 19 patients, respectively. Five patients developed complications that required additional intervention. Overall patient satisfaction was observed to be excellent in 15 (46%) patients, and good in 12 (36%).

Conclusions: Based on our experience, oncoplastic breast surgery using TDAP or LICAP flap is an effective remodeling technique for small-to-moderate breast defects in Korean women with smaller breasts.

PO149

A PHASE 2 STUDY OF POZIOTINIB IN PATIENTS WITH HER2-POSITIVE METASTATIC BREAST CANCER PREVIOUSLY TREATED WITH HER2-TARGETED THERAPIES

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Background: Poziotinib is a novel pan-HER inhibitor that irreversibly blocks the EGFR family of tyrosine-kinase receptors and inhibits the proliferation of tumor cells. This study evaluates the safety and clinical activity of poziotinib in adult patients with HER2-positive metastatic breast cancer who have received at least 2 HER2-therapies (trastuzumab and TDM-1).

Methods: Patients were treated with oral poziotinib 24 mg once daily for first 14 days in a 21-day cycle. Dose reduction was allowed if toxicity observed. Patients continued treatment until disease progression, death, intolerable adverse event (AE), or for 24 months. Tumor response was evaluated using RECIST v1.1 every 6 weeks. Safety assessments was performed throughout the study.

Result: Thirty three patients were enrolled; 6 ongoing and 27 discontinued treatment (16 PD, 2 deaths due to PD, 5 AEs). The median (range) age was 56 (29–94) years. Patients were heavily pretreated with the median (range) number of previous HER2-directed regimens was 5 (2–11) and 75% received pertuzumab in addition to trastuzumab and TDM-1. Five (15%) confirmed partial responses (PR), 2 (6%) unconfirmed PRs were observed along with 9 (27%) stable disease in the study. The most common AEs were diarrhea and rash. Overall, 22 (67%) patients had any AEs with Grade 3 or worse severity.

Conclusions: The most common AEs include diarrhea and rash as expected in EGFR inhibitors. Antitumor activity of poziotinib was observed in heavily pretreated patients with MBC with 5 confirmed and 2 unconfirmed PRs in 33 patients with 6 patients continuing treatment.

PO150

DIRECT-TO-IMPLANT BREAST RECONSTRUCTION WITHOUT THE ASSISTANCE OF ACELLULAR DERMAL MATRIX AFTER THERAPEUTIC MASTECTOMY

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Background: Direct-to-implant breast reconstruction has gained popularity these few years with the advantage of requiring fewer surgical procedures. However, traditional two-stage tissue expander/implant method provides means of reconstructing breasts of any size and decreases the rate of complication and implant loss compared with one stage approach according to the results of previous studies. The purpose of this study is to investigate that, with the improvement of mastectomy techniques in the past 10 years, if the traditional two-stage reconstruction still outperforms direct-to-implant method.

Methods: Retrospective, single-institution review identified patients undergoing immediate implant-based breast reconstruction from 2002 to 2017

Result: Three hundred sixty-one immediate breast reconstructions were performed in 350 women with an average follow-up of nearly 5 years. Three hundred twenty-three were direct-to-implant reconstructions while 38 were tissue expander/implant reconstructions. The overall complication rate, revision rate and implant loss rate in direct-to-implant reconstruction was 27.55%, 12.69%, and 13.0%, respectively. There was no difference in all 4 major outcome categories between direct-to-implant and tissue expander reconstruction (Complication rate: 27.55% vs. 26.32%; $p = 0.871$; Revision rate: 12.69% vs. 2.63%; $p = 0.103$; Implant loss: 13.0% vs. 18.42%; $p = 0.356$; Cancer recurrence rate: 4.02% vs. 2.63%; $p = 1.0$).

Conclusions: The 5-year overall complication rate, revision rate and implant loss rate in the direct-to-implant group were similar to the counterparts in tissue expander/implant reconstruction group. Capsular contracture was the only complication significantly associated higher overall revision rate. Infection and implant rupture were significant risk factors for implant loss.

PO151

THE GENE-EXPRESSION ASSAY AND WATSON FOR ONCOLOGY IN CLINICAL PRACTICE; 95 CASES OF BREAST CANCER

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Background: Personalized treatment has become the issue among the critics for cancer treatments, especially for therapeutic decisions in adding chemotherapy for the patients with Estrogen receptor (ER) positive, HER2 negative in the early stage of breast cancer (BC). With advancement of information technology (IT) and genomics, clinicians have reached therapeutic goal quickly and safely by differentiating subset which chemotherapy really needs indeed. IBM Watson for Oncology (WFO), which is a cognitive computing system to provide clinicians with evidence-based treatment options for cancer. WFO may be quite helpful in clinics and has been asked if it is more superior than human clinicians. We hypothesized that WFO would not be able to differentiate whether subset needs chemotherapy or not in ER positive, HER2 negative BC.

Methods: From December 2015 to July 2017, 95 patients with ER positive, HER2 negative BC who have been treated were retrospectively examined by WFO. The output was compared to real practices. Treatment options were suggested by WFO, and WFO recommendations were calculated by two manners, with or without gene-expression assay (GEA).

Result: WFO without GEA could not figure out which group doesn't need chemotherapy. There were concordant therapeutic options between real practices and WFO without GEA in 23.2 percentage of the whole patients. On the other hand, the results of WFO with GEA showed good clinical availability. The sensitivity, specificity, positive predictive value, and negative predictive value of WFO with GEA were 100, 80, 61 and 100%, respectively.

Conclusions: WFO without gene-expression assay has a limit for clinical use.

PO152

CLINICOPATHOLOGIC FACTORS AFFECTING RESIDUAL CANCER BURDEN IN BREAST CANCER

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Background: The patients who had low residual cancer burden (RCB, 0 or 1) after neoadjuvant chemotherapy (NAC) are well known to have good prognosis. In this study, we sought to determine clinicopathologic factors which affect RCB.

Methods: Institutional databases were reviewed to identify patients with stage IIA-IIIC breast cancer treated with NAC and BCS or mastectomy from June 2014 to February 2016. All patients received mammography, ultrasound and PET to evaluate clinical stage. Strain elastography was performed to measure the elasticity of tumor before NAC. Histologic type, TILs, tumor cellularity, HG, ER/PR/Her-2 status and Ki-67 were examined on core biopsy specimens before NAC. RCB were calculated based on final pathology.

Result: Seventy nine patients met our study criteria. Mean patient age was 46.29 ± 8.88 years, mean tumor size at presentation was 3.62 ± 2.07 cm and 39 (49.4%) patients presented with clinically node-positive disease. Breast cancer subtypes were determined according to the HR and Her2 status. Among all patients, pCR rate was 27.8% (22/79). Thirty eight percent (30/79) patients had low RCB (0 or 1) and 62.0% (49/79) pts had high RCB (2 or 3). On univariate analysis, high TILs level ($p = 0.034$) and HG III ($p = 0.028$) were significantly correlated with low RCB and subtype was correlated with RCB ($p = 0.052$). On multivariate logistic regression, HR+/Her2- subgroup was significantly correlated with high RCB ($p = 0.0118$). In HR+/Her2- subgroup analysis, high TILs level were correlated with low RCB ($p = 0.018$).

Conclusions: TILs, histologic grade and subtype of core biopsy specimen before NAC were related good tumor response. Those factors can help selecting good candidate for NAC.

PO153

ELEVEN CASES OF PREGNANCY-ASSOCIATED BREAST CANCER

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Background: Breast cancer is one of the most commonly diagnosed malignancies during pregnancy. In Japan, the average age of mothers having the first child is getting older at 30.4 years old. Prospective data about diagnosis, treatment, and outcome of pregnancy-associated breast cancer (PABC) is still limited, the management of PABC will become even more important.

Methods: A total of 11 patients with PABC were treated at our institution between 2003 and 2017. We searched the age and the gestational age of diagnosis, detection process, tumor histology, treatment during and after pregnancy and overall survival in each patient.

Result: The median age of diagnosis was 35 years old. 8 cases were found by breast self-examination. The lesions were at stage 1 in 1 case, stage 2 in 7 cases, stage 3 in 2 case and stage 4 in 1 case. Two cases were hormone receptor-positive, other 2 were HER-2 positive, 7 were triple negative type. Five cases underwent operation, 4 cases underwent chemotherapy during pregnancy, and the others started cancer treatment after delivery. In all cases, we had close information sharing with obstetrician and pediatrics, all babies were born with good Apgar scores.

Conclusions: The number of PABC in our hospital is not big, but it is tend to be said that PABC patients were found in later stage. Fortunately, there were no cases of abortion related to the cancer. Every case was treated depending on the situation such as gestational age and tumor histology. Therefore, treatment of PABC requires a multidisciplinary team approach.

PO154

IDENTIFICATION OF CANDIDATE GENES AND PATHWAYS IN HORMONE RECEPTOR POSITIVE YOUNG BREAST CANCER BY INTEGRATED BIOINFORMATICAL ANALYSIS

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Background: Studies had shown that the effect of age on survival of women with early breast cancer varied by breast cancer subtype and young age is associated with bad prognosis only in HR+ breast cancer. Currently, the involved signaling pathways and driven-genes are largely unclear.

Methods: This study integrated RNA sequencing and clinical data from TCGA data portal, including 46 aged younger than 40 years old pre-menopausal HR+ breast cancer cases and 414 aged older than 50 years old post-menopausal HR+ breast cancer cases. The differently expressed genes (DEGs) were identified between this two groups using the R language software. Protein-protein interaction (PPI) network was constructed with the identified DEGs afterwards. DAVID was used to perform the GO and KEGG pathway enrichment analysis of the most significant DEGs. The prognostic value of the weighted genes was confirmed by Kaplan–Meier survival analysis using Kaplan Meier Plotter (logrank *p*-value cut-off is 0.05).

Result: A total of 1,108 DEGs between the two groups (307 up-regulated and 801 down-regualted) were identified. GO function and KEGG pathway analysis revealed that the 20 DEGs' functions were mainly involved in cAMP signaling, Neuroactive ligand-receptor interaction, Chemokine signaling pathway. Survival analysis indicated that over expression of GPER1 and under expression of INS and SSTR5 were associated with worse overall survival .

Conclusions: Using integrated bioinformatical analysis, we have identified GPER1, INS and SSTR5 as candidate genes in Young HR+ breast cancer ,which could potentially improve our understand of the underlying mechanism.

PO155

IMPLEMENTATION OF NEOADJUVANT CHEMOTHERAPY FOR BREAST CANCER IN HKU-SZH: A REAL-WORLD SETTING WITH MULTIPLE DISCIPLINARY TEAM

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Background: The use of neoadjuvant chemotherapy is increasing in China but little has been reported. The current retrospective study aimed to evaluate the real-world implementation of neoadjuvant chemotherapy in Academic-based Southern China Hospital where regular MDT is in place.

Methods: Review of MDT records from July 2014 to July 2017 were performed. Final analysis included patients with locoregionally-advanced invasive breast cancer who were offered neoadjuvant at MDT. Compliance to MDT decision, scheduled treatment and clinical outcomes were described.

Result: Sixty-six female patients were included for analysis. The median age was 45 (range 31–66). Most of the patients were married (95.5%) and well-educated (secondary school or higher: 83.3%). The mean tumor size was 3.86 cm (range: 0.8–9.0 cm). The decision to receive neoadjuvant chemotherapy was mostly made jointly by the patients and their families (56.1%). The compliance to MDT decision was high (92.4%). Five patients refused neoadjuvant chemotherapy due to worry about delaying surgery or toxicity of chemotherapy. Fifty-two patients (78.8%) completed all curative treatment. Of the 9 patients who did not complete the planned neoadjuvant chemotherapy, 4 were due to suboptimal clinical response, 3 due to treatment-related toxicity and 2 due to patient preference. The PR+CR rate was 86.9% and pCR rate was 19.7%. After a median follow-up of 24.8 months, 4 patients relapsed and one of them died.

Conclusions: Implementation of neoadjuvant chemotherapy was feasible with high compliance rate and good efficacy in a MDT setting. Understanding of the decision-making process and reasons for default also improve patient compliance.

PO156

INTRAOPERATIVE RADIATION THERAPY (IORT) FOR BREAST CANCER IN VIETNAM

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Background: A total of 47 patients of breast cancer with stage I & II were collected from Hue Central Hospital from December 2012 to January 2016. Intraoperative radiation therapy (IORT) and oncoplastic surgery for breast cancer treatment was performed the first time in Vietnam.

Methods: IORT using the Intrabeam system was delivered to the tumor bed immediately after surgical excision during the anasthesia .The radiation dose received was to 20 Gy at the surface of the applicator. Oncoplastic breast surgery was performed after completion radiotherapy.. For nipple sparing mastectomy, using dose 8 Gy under the nipple areola and breast reconstruction immediately.

Result: Forty seven cases selected for IORT, mean age 51.26. Tumor size ranges from 10 to 30 mm, IORT in 39 (82.9%) single dose, 8 (17.1%) IORT cases required whole breast radiation therapy. Applicator size from 2.5–5.0 cm, 20 cases (42.6%) using applicator 4 cm, time of intra-operative radiation depends on dose delivered, maximum is 42 min. Wide local excision 23 (48%), donut 5 (10.6%), breast reduction 5 (10.6%), lateral mammoplasty 8 (17.0%), nipple sparing mastectomy 6 (12.8%).

Conclusions: IORT as a boost for breast conserving therapy and using single dose for selected patients. Combination between IORT and oncoplastic surgery give a chance to improve the quality of life for breast cancer patient.

PO157

VALIDATION ON USING SUPERPARAMAGNETIC IRON OXIDE PARTICLES FOR SENTINEL LYMPH NODE LOCALIZATION IN BREAST CANCER SURGERY

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Background: Injection of technetium sulphur colloid with or without combination of blue dye is gold standard for sentinel lymph node (SLN) biopsy. However, there are related risks and nuclear medicine facility availability is limited. A new system using SuperParagmagnetic Iron Oxide particle (SPIO, Sienna+) was developed since 2012 and had been used in more than 1,500 patients across Europe with promising results. We aim to compare Sienna+ in parallel to radioisotope in localization of sentinel lymph nodes.

Methods: This is a single center prospective validation study for patients with early stage breast cancer. Patients received both SPIO and radioisotope injection sequentially before operation. SLN was first harvested by identification of SPIO, followed by detection by radioisotope. SLNs were excised until the counts were < 10% of the highest count SLN. The primary endpoint of the study was the identification rate using SPIO and its concordance with radioisotope. Secondary end points were the rates of positive and false negatives SLNs between techniques.

Result: Between 4-26 September 2017, 20 patients underwent SLN biopsy using both tracers were analyzed. Difficulties with both techniques were encountered in patients who underwent neoadjuvant chemotherapy and second stage SLN biopsy. One patient with discordant findings was encountered, with SPIO identifying one more SLN than radioisotope. SPIO stained skin significantly, giving a bruise-like colour, which lasted for more than 3 months.

Conclusions: SPIO is non-inferior to radioisotope in identifying sentinel lymph nodes in breast cancer surgery. However, bruise-like stain of the skin by iron deposits is undesirable.

PO158

THROMBOCYTOPENIA CAUSED BY PEGFILGRASTIM IN PATIENTS WITH BREAST CANCER

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Background: The American Society of Clinical Oncology (ASCO) colony-stimulating factors (CSF) guideline recommends the use of primary prophylaxis of febrile neutropenia (FN) with a CFS for patients given chemotherapy with an approximate 20% or higher risk of FN. Thrombocytopenia is written to be a rare adverse event caused by pegfilgrastim, whereas there are no reports found in the literature. Here we describe the breast cancer cases with thrombocytopenia during the chemotherapy with prophylactic CSF.

Methods: We investigated the frequency of Grade3/4 thrombocytopenia and its clinical features in patients who were administered pegfilgrastim from January 2015 to November 2016.

Result: Among 537 patients administered pegfilgrastim, Grade3/4 thrombocytopenia was seen in five cases with the frequency of 0.9%. The chemotherapy regimens which were administered for these five patients were: CEF (cyclophosphamide, epirubicin, fluorouracil) for four patients and AC (adriamycin, cyclophosphamide) for one patient. The median of the minimum platelet counts was 1.6×10^4/l (0.5–3.5). Though three of the five planned the next cycle of chemotherapy, two of these three discontinued or decreased the chemotherapy. One of these three performed the next cycle as planned. In this case, pegfilgrastim was not administered and the amount of chemotherapy remained same.

Conclusions: In some cases, severe thrombocytopenia can be observed after administration of pegfilgrastim. The chemotherapy dosage does not have to be decreased as a result of the withdrawal of pegfilgrastim.

PO159

LOCAL TREATMENT IN ADDITION TO ENDOCRINE THERAPY IN HR-POSITIVE/HER2-NEGATIVE OLIGO-METASTATIC BREAST CANCER: A RETROSPECTIVE ANALYSIS

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Background: Recent trials provide robust evidence that endocrine therapy with/without targeted therapy (CDK4/6 inhibitors or mTOR inhibitors) effectively halts disease-progression in ER-positive/HER2-negative metastatic breast cancer. In ER-positive/HER-negative metastatic breast cancer patients who had very low metastatic volume and were treated with endocrine treatments as 1st line, we investigated survival impact of local treatments for metastatic lesions.

Methods: From prospectively constructed database of two institutes, we identified ER-positive/HER2-negative patients with oligo-metastatic breast cancer. De Novo patients were excluded. Oligo-metastatic disease was defined following stringent criteria: i) ≤ 2 metastatic lesions in single organ ii) maximal dimension ≤ 3 cm iii) involved organs: lung, liver, adrenal gland, bone, contralateral regional lymph nodes. Local treatments indicated surgery or radiotherapy. The progression-free survival (PFS) and the overall survival (OS) were investigated.

Result: Forty-six patients were included. Twenty-seven (58.7%) were treated with local treatments. Among the 27 patients receiving local treatments, 4 patients were treated with surgical resection, while 22 patients with radiotherapy. Both local treatments were carried out in 1 patient. Median PFS was significantly longer in patients with local treatments than in patients with endocrine treatments alone (39.0 vs. 16.6 months, $p = 0.004$). However, median OS did not differ according to local treatments (205.6 vs. 205.3 months, $p = 0.860$).

Conclusions: We showed that local treatments might bring a positive effect on tackling disease-progression in ER-positive/HER2-negative oligometastatic-breast cancer. A prospective trial warrants for this question for the role of local treatments in this subset of disease.

PO160

ADJUVANT CHEMOTHERAPY COMBINED WITH HUAIER GRANULE FOR TREATMENT OF POST-SURGICAL TRIPLE-NEGATIVE BREAST CANCER

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Background: In recent years, traditional Chinese medicine (TCM) have been rapid developments in cancer treatment. Huaier is a medicinal fungus which has been widely used in TCM for different kinds of cancers. A large number of clinical studies have shown that it has achieved good efficacy in the prevention of tumor recurrence and metastasis. Now we performed a case-control clinical study to further investigate the efficacy and safety of Huaier granules in post-surgical therapy for Stage IIII TNBC patients, and observed its effects on the post-surgical safety and survival rates of these patients.

Methods: Two hundred one TNBC patients underwent modified radical mastectomy were admitted to our hospital between October 2010 to September 2014. The patients were randomly allocated to the experimental group (101 cases) or the control group (100 cases). Patients in the experimental group received 20g oral Huaier granules 3 times a day, during and after chemotherapy for 6 or 18 months. The control group did not receive any TCM preparations during this process. The main outcome measures were disease-free survival (DFS) and overall survival (OS).

Result: The median follow-up time was 46 months. The 5-year DFS and OS of the 100 patients in the control group was 82% and 86%, and 5-year DFS and OS of the 101 patients in the experimental group was 87.1% and 90.1%; there was not statistically significant. However, Stage III patients in the control group showed a 5-year DFS of 53.8% and OS of 65.4%, Stage III patients in the experimental group had a higher 5-year DFS of 81.3% and OS of 87.5%; the difference was statistically significant. In the experimental group, 13 patients with 6-month medication showed disease progression, whereas only 3 patients with 18-month medication showed disease progression. The difference between the 2 groups was statistically significant.

Conclusions: Huaier granules play an important role in the post-surgical adjuvant therapy of TNBC patients. In particular, Huaier granules were able to effectively increase the DFS and OS of middle-stage to advanced breast cancer patients.

PO161

EFFECT OF CHEMOTHERAPY FOR EARLY, LUMINAL BREAST CANCER PATIENTS ON RECURRENCE AND SURVIVAL

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Background: The aim of this study was to identify whether adjuvant systemic chemotherapy has any benefit in early luminal breast cancer and to evaluate feasibility of endocrine therapy without adjuvant systemic chemotherapy in this group.

Methods: We analyzed data from 879 patients with early (stage I and IIA), HER 2 negative luminal breast cancer diagnosed between 2005 and 2011, and underwent adjuvant endocrine therapy with or without adjuvant systemic chemotherapy. During follow-up, the disease-free survival (DFS) and overall survival (OS) were compared between two groups.

Result: Of the 879 patients analyzed, 385 (43.8%) treated with chemotherapy and 494 (56.2%) treated without chemotherapy. The median follow-up period was 85.0 (1.0-143.0) months. In patients treated with chemotherapy, the 5, 10-year DFS rate were 96.0 and 89.5%, and the 5, 10-year OS rates were 99.2 and 95.2%. In patients treated without chemotherapy, the 5, 10-year DFS rate were 95.8 and 90.5%, and the 5, 10-year OS rates were 98.4 and 95.6%. No significant difference was observed in the DFS (adjusted hazard ratio [HR] 1.14; 95% CI, 0.70 to 1.84, $p=0.61$) and OS (HR 1.43; 95% CI, 0.67 to 3.05, $p=0.349$) rates between the patients who treated with chemotherapy and those who treated without chemotherapy.

Conclusions: This retrospective study suggests that adjuvant systemic chemotherapy might provide no benefit of recurrence and survival for early (stage I and IIA), HER 2 negative luminal breast cancer patients, although further prospective studies with randomization in a larger cohort are required to confirm these findings.

PO162

SENTINEL LYMPH NODE BIOPSY WITH SUPERPARAMAGNETIC IRON OXIDE : EXPERIENCE IN CHINESE POPULATION

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Background: The combined use of radioisotope and blue dye are the gold standard in sentinel lymph node (SLN) localization in early breast cancer. Superparamagnetic iron oxide (SPIO) has recently emerged to be a non-inferior new tracer in sentinel lymph node mapping with fewer disadvantages. This study represents the first and the largest cohort of superparamagnetic iron oxide in Chinese population.

Methods: From January 2016 to January 2017, a total of 100 breast cancer patients were recruited in Hong Kong and sentinel lymph node mapping was performed by SPIO. Patient characteristics, tumor characteristics and procedure success rate were analyzed.

Result: Mean age of patients was 55 years old (33–83). Mean tumor size was 2.0 cm (0.4 cm–9 cm) and 40% of patients had tumors located at upper outer quadrant. Of 100 patients, 44 underwent breast conservative treatment and 56 had mastectomy. All patients received injection of SPIO one day prior to operation. A total of 98 successful SLN biopsy procedures were undertaken with 512 SLN identified. Sixty-four (12.5%) of the SLN were positive for malignancy. There were 19 patients with macrometastases, 3 with micrometastases and 8 with isolated tumor cells. Twenty one patients underwent subsequent axillary dissection. Two patients failed SLN identification with SPIO, in which one of them has received neoadjuvant chemotherapy. The success rate of SPIO in SLN localization was 98%.

Conclusions: SPIO represents a feasible alternative in sentinel lymph node mapping with an equally high nodal detection rate. *An updated dataset analysis will be presented at the meeting

PO163

DISCREPANCY OF PATHOLOGIC COMPLETE RESPONSE AND OUTCOME BETWEEN BREAST TUMOR AND AXILLARY NODE IN HER2 POSITIVE BREAST CANCER AFTER NEOADJUVANT CHEMOTHERAPY

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Background: The pathologic complete response (pCR) rate in primary tumor and axillary node after different chemotherapy regimens of neoadjuvant chemotherapy (NAC) in HER2 positive breast cancer (BC) is unknown, the impact of pCR on disease free survival (DFS) and overall survival (OS) is still controversial.

Methods: A cohort of 350 HER2 positive BC (296 cytologically proved axillary node metastasis) received NAC with different regimens, antracyclin with taxotere (AT), docetaxel with transtuzumab (DT) and docetaxel with transtuzumab and pertuzumab (DTP) between 2005 and 2016 in a large medical center were analyzed retrospectively. The impact of pCR rates of breast and axillary node on DFS and OS were analyzed

Result: Median age was 50 years, median tumor size was 4.3 cm, the pCR rates of breast and axillary node were 16.2% and 28.7% in patients received AT (n = 130), 47.6% and 66.9% in patients received DT (n = 191), 65.5% and 77.8% in patients received DTP (n = 29). The 5-year DFS were 79.3% and 66.0%, 5-year OS were 89.5% and 76.6% in patients with breast pCR and non-pCR. The 5-year DFS were 75.7% and 58.4%, 5-year OS were 85.7% and 72.6% in axillary pCR and non-pCR patients.

Conclusions: Higher pCR rate in axillary node than breast was found in this cohort. Either pCR in axillary node or breast was associated with improved DFS and OS, but no difference of DFS and OS between breast and axillary pCR. The 5-year DFS in breast pCR received targeted therapy were significantly better than breast pCR patients received chemotherapy alone.

PO164

THE EFFICACY OF EVEROLIMUS IN ER-POSITIVE AND HER2-NEGATIVE ADVANCED/RECURRENT BREAST CANCER

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Background: Everolimus is effective for patients with ER+/HER2- metastatic breast cancer as a second-line treatment after recurrence. However, no predictive factors have been identified for the efficacy of everolimus. Moreover, the efficacy and safety of everolimus for heavily pretreated patients are still unclear.

Methods: Patients (n = 50) with ER+/HER2- metastatic breast cancer were enrolled in this study from April 2014 to April 2017. The median age was 64.5 years and the median number of previous regimens and time to everolimus after recurrence were 5 and 60 months, respectively. The efficacy of everolimus was evaluated in terms of the clinical benefit rate (CBR) and progression-free survival (PFS) in relation to the clinical characteristics.

Result: The duration of endocrine therapy before everolimus was < 3 months (19 cases), 3–6 months (14 cases) and > 6 months (17 cases). The clinical response rate was 22.0% (11/50) and the CBR was 44.0% (22/50). A higher CBR was seen in patients with a longer time to everolimus after recurrence. The median PFS was 159 days and a longer PFS correlated with a lower Ki-67 index value. Moreover, the duration of treatment before everolimus and the number of previous regimens were marginally associated with PFS. Two-thirds of the patients (33/50) had stomatitis (G3: 8.0%) and 18.0% had pneumonitis (G3: 8.0%).

Conclusions: Everolimus is effective even in heavily pretreated cases with ER–positive advanced breast cancer. Moreover, longer time to everolimus after recurrence and a lower Ki-67 value were significant predictive factors for the efficacy of everolimus.

PO165

UNDER 40 BREAST SYMPTOMATIC CLINIC, THE WAY FORWARD : SINGLE INSTITUTE EXPERIENCE IN UNITED KINGDOM

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Background: Experienced sonographers have extended their role within the symptomatic breast service. A study was undertaken to ascertain whether they could provide the radiology support to women under 40 years who do did not require mammograms. The aim is to measure the effectiveness of this breast clinic to ensure that radiology is providing a good service and to ensure that cancers are being detected within the population.

Methods: Under 40 years clinics started in August 2012. These included only female patients with symptoms referred by their GP. Sample size was 613 patients. Breast diaries were reviewed to ascertain core biopsies performed and reports of histological diagnosis.

Result: Sixty four (10%) core biopsies were taken 38 (59%) ultrasound guided by the sonographer and 26 (41%) freehand by the consultant surgeon. Three core biopsies (4.6%) were repeated. Three out of 613 patients (0.4%) showed breast cancer, one with high grade DCIS, one with grade III invasive ductal carcinoma and one with grade III invasive ductal carcinoma with metastatic lymph node which has been detected clinically and radiologically. 44 patients with fibroadenomas, five with fibrocystic changes, three with hamartomas, the rest with lipomas, phylloides tumour, inflammation, papillary lesion, fat necrosis, tubular adenoma, infarcted lymph node

Conclusions: Under 40 breast clinic led by a Surgeon and supported by sonographers is able to provide a comprehensive service with accurate diagnosis within all relevant guidelines. It is effective in ensuring cancers are being detected within the target population and in providing an excellent service.

PO166

ENDOCRINE THERAPY WITH OR WITHOUT ANTI-HER2 THERAPY FOR ER POSITIVE AND HER2 POSITIVE METASTATIC BREAST CANCER: A SINGLE INSTITUTE EXPERIENCE IN JAPAN

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Background: After CLEOPATRA trial showed a remarkable efficacy of pertuzumab, trastuzumab and docetaxel, taxane with dual anti-HER2 therapies became a standard induction treatment for HER2-positive metastatic breast cancer (MBC), and the position of endocrine therapy (ET) with or without anti-HER2 therapy became more unclear than before.

Methods: To reconsider this clinical question, we investigated the use and efficacy of these therapies for ER-positive and HER2-positive MBC patients.

Result: We found 74 MBC patients of this subtype who were treated in our institute after January 2000 with at least one trastuzumab containing regimen. Thirty-five patients were administered at least one ET with or without anti-HER2 therapy and there were 46 uses of these therapies among them. There were 17 uses of endocrine monotherapies with a median number of prior therapies of 0 (range 0–1). Overall response rate (ORR) and clinical benefit rate (CBR) were 11.8% and 41.2%. Median time to failure (TTF) was 6.5 months (2.4–34.8). Among 7 patients with clinical benefit, median TTF was 20.4 months(9–34.8). There were 29 uses of ET with anti-HER2 therapies, with a median number of prior therapies of 1 (range 0–9). ORR and CBR were 20.7% and 55.2%. Estimated median TTF was 12.8 months (1.8–127). Among 16 patients with clinical benefit, median TTF was 26.2 months (7–127).

Conclusions: These data were superior to past clinical trials and we speculate there may be selection bias. However, our data at least shows there is a subgroup of patients who could choose ET with or without anti-HER2 therapies for ER-positive and HER2-positive MBC.

PO167

LYMPHOVASCULAR INVASION CAN PREDICT PROGNOSIS IN BREAST CANCER TREATING NEOADJUVANT CHEMOTHERAPY

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Background: Lymphovascular invasion (LVI) has been indicated worse survival outcomes in breast cancer. However, the role of LVI after neoadjuvant chemotherapy (NAC) is unclear. The aim of this study was to examine association between lymphovascular invasion and survival outcomes and clinicopathological features in breast cancer patients treated with NAC.

Methods: We analyzed 187 breast cancer patients treated with NAC and surgery retrospectively between 2005 and 2013 in our institution. Kaplan-Meier analyses were used to assess recurrence-free survival (RFS) and overall survival (OS).

Result: Median follow-up was 57.9 months. Mastectomy (vs. BCS; hazards ratio [HR], 1.791; 95% confidence interval [CI], 1.022–3.139; $p=0.042$), ypN1-3 stage (vs. ypN0 stage; HR, 2.561; 95% CI, 1.247–5.261; $p=0.010$), and LVI (vs. no LVI; HR, 2.041; 95% CI, 1.170–3.562; $p=0.012$) were associated with worse RFS. Mastectomy (vs. BCS; HR, 2.759; 95% CI, 1.177–6.466; $p=0.020$), LVI (vs. no LVI; HR, 2.813; 95% CI, 1.335–5.928, $p=0.007$), and other molecular type (vs. luminal A type; HR, 7.962; 95% CI, 1.082–58.584; $p=0.042$) were associated with worse OS. The patients with LVI and negative for hormonal receptor had the worst RFS ($p<0.001$) and OS ($p<0.001$).

Conclusions: LVI in breast cancer assessed surgical specimens obtained after NAC was independent significant prognostic factor. The patients with positive for hormonal receptor and no LVI had favorable rate of recurrence and cancer related death. We suggest that the patients with negative for hormonal receptor and LVI should have short term follow-up and appropriate management.

PO168

HORMONAL EFFECT ON OVERALL SURVIVAL OF NEOADJUVANT CHEMOTHERAPY FOLLOWED BY TRASTZUMAB IN HER2-POSITIVE BREAST

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Background: Pathologic complete response (pCR) is considered as a surrogate endpoint for prediction of long term survival benefit in neoadjuvant chemotherapy (NAC). NAC with trastuzumab has significant higher pCR rates in HER2-positive breast cancer. But several studies did not demonstrate similar overall survival (OS) benefit in trial level. The essential explanation for this finding is hetergenicity of molecular subtype. We investigated the difference of overall survival of her2+ positive breast cancer patients received NAC with trastuzumab or without by hormonal receptor (HRc).

Methods: We compared treatment with trastuzumab with no tratsuzumab by HRc status from 2008 to 2013, in adult women with HER2-positive non metastatic breast cancer. All patients had been performed breast surgery followed by adjuvant chemotherapy with trastuzumab. The patients data was prospectively collected by Korean Breast Cancer Society.

Result: Of total 808 patients, 408 had positive HRc (trastuzumab 242, no trastuzumab 166) and 384 had negative HRc (trastuzumab 236, no trastuzumab 148). In HER2+, HRc+ breast cancer, trastuzumab group demonstrated a double pCR rate. (16.5% vs. 8.1%) and significant better overall survival (multivariate HR 0.53 [95% CI 0.30–0.92; $p = 0.041$]). In HER2+, HRc- patients, trastuzumab group had a higher pCR gain (28.8% vs. 11.8%) than HRc+ patients, but there was no statistical survival benefit (multivariate HR 0.66 [95% CI 0.37–1.18; $p = 0.164$]).

Conclusions: The addition of trastuzumab to NAC has same or better effect on overall survival benefit in HR+ her2+ breast cancer than HR- despite the lower pCR gain. We should investigate the other surrogate marker in addition to pCR.

PO169

TREATMENT PATTERNS AND OUTCOMES IN ELDERLY PATIENTS WITH METASTATIC BREAST CANCER: A MULTICENTER RETROSPECTIVE STUDY

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Background: There is little information regarding optimal treatment for metastatic breast cancer (MBC) in elderly patients. In this retrospective study, we examined a cohort of elderly patients with MBC receiving various treatments, in terms of clinicopathologic characteristics, treatment patterns, and outcomes.

Methods: Patients aged 65 years and older, and diagnosed with MBC between 2003 and 2015, were identified from the databases of three academic hospitals in South Korea. A total of 161 cases were eligible for inclusion. Based on age at MBC diagnosis, patients were divided into three groups: 65 to 69, 70 to 74, and ≥ 75 years.

Result: Most patients had received active treatment according to biologic subtype, although frequent dose modifications were observed during chemotherapy. The median overall survival (OS) for all patients was 30.3 months; age (≥ 70 years), Eastern Cooperative Oncology Group (ECOG) performance status (PS) (≥ 2), triple-negative cancer, and number of metastatic sites (≥ 2) were significant poor prognostic factors for OS in multivariate analyses. All types of systemic treatments conferred more prolonged OS in patients receiving the treatments. Patients aged ≥ 75 years were more likely to have a poor ECOG PS and advanced comorbidity, and tended to receive less intensive treatments.

Conclusions: Elderly patients with MBC should not be excluded from receiving active treatments. Future research plans for elderly patients, especially aged ≥ 75 years with breast cancer, should include a geriatric assessment that could be utilized to identify patients at risk for treatment-related toxicity and also to select patients who could benefit from active treatment.

PO170

COMPARISON OF SURVIVAL OUTCOMES AND TOXICITY AFTER MASTECTOMY ALONE VS. AUTOLOGOUS BREAST RECONSTRUCTION IN LOCALLY ADVANCED STAGED BREAST CANCER

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Background: For locally advanced stage to need more intensive chemotherapy and radiotherapy, the clinical effectiveness of immediate autologous breast reconstruction has not been frequently presented. Our study analyzed our experience.

Methods: From 2007 to 2014, our study enrolled patients with malignant breast cancer of clinically or pathologically proven stage II-III cancer. Age over 70 years. Out of 144 patients, 49 patients received immediate autologous breast reconstruction after mastectomy. All the patients received proper chemotherapy. Neoadjuvant chemotherapy and adjuvant radiotherapy were done in 22 patients and 48 patients, respectively. Loco-regional recurrence free survival, disease free survival and overall survival were calculated and compared with Kaplan-Meyer methods and log-rank tests, respectively.

Result: Median age was 46 years. Median follow-up period was 58.5 months. There is no loco-regional failure in stage II. For stage IIIb/IIIc of mastectomy group and reconstruction group, the 5-year loco-regional recurrence free survivals were 60.8% and 62.5%, respectively. The 5-year disease free survivals for stage II, IIIa and IIIb/IIIc for mastectomy group vs. reconstruction group were 93.0% vs. 84.8% ($p=0.214$), 57.5% vs. 88.9% ($p=0.240$) and 55.7% vs. 50.0% ($p=0.769$), respectively. In addition, a significant difference for overall survival between mastectomy group and reconstruction group was not observed. One patient with adjuvant radiotherapy had breast destruction due to surgical resection of extensive fat necrosis.

Conclusions: In early phase evaluation, immediate autologous breast reconstruction is compatible with total mastectomy for clinical survival. However, for the stage IIIb/IIIc to need adjuvant radiotherapy, one extensive fat necrosis observed and disease free survival fell short of its expectations.

PO171

IMPACT OF AGE ON LOCOREGIONAL RECURRENCE IN LOCALLY ADVANCED BREAST CANCER AFTER NEOADJUVANT CHEMOTHERAPY

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Background: Neoadjuvant chemotherapy (NAC) is the standard approach for downstaging of locally advanced breast cancer and can improve breast conservation rates. A pathological complete response (pCR) after NAC has favourable long-term outcomes and was well-mentioned. There is still a high locoregional recurrence (LRR) rate after NAC and the influence of age on LRR after NAC is less discussed in the literature. This study aimed to analyse the relationship of age and LRR after NAC.

Methods: Two hundred and sixty-three patients with invasive breast cancer who received NAC followed by mastectomy or breast conserving surgery (BCS) were enrolled. Concurrent weekly epirubicin and docetaxel was the standard NAC regimen.

Result: The median age was 48 years-old (range 18–75). The mean tumor size at diagnosis was 6.0 cm (range 2.0–22.0). The median follow up time was 54.6 months (range 9.2–126.9). Twenty-nine patients achieved a pCR after NAC in this study. No patients in the pCR group developed LRR compared with 31 patients in the non-pCR group. Eleven patients (6.9%) in age < 50 years group developed LRR compared with 20 patients (19.4%) in the age > 50 years group. In multivariate analysis, age < 50 years was the only independent prognostic factors for LRR.

Conclusions: Younger age can predict pCR and is an independent prognostic factor for LRR in locally advanced breast cancer patients after NAC as concurrent epirubicin and docetaxel.

PO172

IS NEOADJUVANT CHEMOTHERAPY BENEFICIAL IN METAPLASTIC CARCINOMA OF THE BREAST?

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Background: Metaplastic carcinoma (MC) of the breast is a rare pathologic entity accounting for <1% of all invasive breast cancers and is generally negative for hormone receptors and HER2. Although triple negative breast cancers (TNBCs) usually show good response to neoadjuvant chemotherapy (NAC) and pathologic complete response (pCR) rate of about 40%, chemoresponsiveness of MC to NAC is not well known. The aim of this study was to compare NAC response between MC and other TNBC.

Methods: Retrospective chart review of TNBC patients who underwent NAC and surgery at Seoul National University Hospital between January 2000 and January 2012 were included for analysis. Tumor size on ultrasound evaluation before NAC and pathologic size of residual tumor was used to assess responsiveness to NAC and categorized as complete response (CR), non-CR, and progressive disease (PD).

Result: Of 312 TNBC patients included in analysis, 29 (9.0%) were MC and 292 (90.96%) were non-MC. There was no statistically significant difference in response to neoadjuvant chemotherapy between the two groups. However there was a tendency for less CR (1 [3.4%] vs. 34 [11.6%]) and more PD (6 [20.7%] vs. 25 [8.6%]) in MC ($p = 0.058$).

Conclusions: Metaplastic carcinoma of the breast is associated with less CR and more PD after NAC compared to non-MC TNBC. Upfront surgery for MC may be more beneficial than NAC. Survival analysis (including larger number of MC cases) is warranted to determine the role of NAC in MC.

PO173

A MULTICENTER SURVEY OF BREAST CANCER RADIOTHERAPY IN CHINA FROM 2012-2016 BASED ON A CROSS-SECTIONAL QUESTIONNAIRE

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Background: This survey aims to evaluate the radiotherapy (RT) technology and indications for breast cancer (BC) in China from 2012 to 2016 and its correlation with update guidelines.

Methods: The questionnaire included information of adjuvant RT for BC patients with indication and the dose limitation of organs at risk.

Result: Fourteen centers responded to the survey, which represent 459.5 ± 312.8 patients receiving adjuvant RT in 2016. The number of BC patients receiving RT increased nearly 50% from 2012-2016. Almost all centers accept dose limit of heart as mean dose 6–8 Gy, with 8–10 Gy when RNI is given. Only one center had cardiac toxicity follow-up. Two centers suspended trastuzumab during RT. For BCS with N1, 8/10 in 2012 and 10/14 in 2016 chose RNI. PMRT was routinely carried for T1-2N1 in 8 centers and other 6 for poor prognosis patients. 10 centers chose chest wall RT for T1-2N0 with poor prognosis. PMRT in T3 and N2 patients were unified. 10/14 give IMN irradiation in central medial quadrant with N+, and more than ALN 4+ patients. Different levels of RNI is practiced for BCS with 1-2 SLN+ without ALND in 12centers. For T1-2 with SLN1-2+ without ALND after mastectomy, 13/14 centers believe that RT is required, and for SLN micrometastasis, only 7/14 centers think RT is required.

Conclusions: The indication of adjuvant RT for breast cancer in representative centers of China reflect the guidelines update. More attention has been paid to the individualized strategy patients with positive SLN without ALND. The sense of cardiac toxicity should call attention.

PO174

FEASIBILITY AND COSMETIC OUTCOME OF BREAST-CONSERVING SURGERY VIA CIRCUMAREOLAR INCISION FOR TUMORS LOCATED FAR FROM NIPPLE-AREOLAR COMPLEX

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Background: One of the most important goals of breast-conserving surgery is to improve cosmetic results after surgery and quality of life of patients. The skin incision dependent on location of the tumor can affect cosmetic outcome. Authors tried breast-conserving surgery using circumareolar incision for the tumor is placed far from the nipple-areolar complex (NAC) to maximize cosmetic outcome and to maintain oncologic safety.

Methods: Forty-two patients with ductal carcinoma in situ or invasive breast cancer located far from NAC underwent breast-conserving surgery via circumareolar incision from January 2017 to October 2017. If sentinel lymph node biopsy is required, another skin incision was created in the axilla using the conventional technique.

Result: Mean age of patients was 47.0 ± 9.6 years. Mean tumor size was 2.3 ± 1.1 cm (range, 0.7 to 4.5) on preoperative magnetic resonance (MR) imaging and mean distance from NAC to tumor was 5.9 ± 1.3 cm (range, 4.0 to 12.3). Patients with tumor located in the subareolar area were excluded even though distance from nipple was over 4 cm on MR imaging. Microscopic negative margins were obtained in all of patients. There was no surgical complication such as seroma, bleeding or infection. Any re-operation was not needed. All of patients received whole breast radiotherapy. After operation and radiotherapy, circumareolar incision scars were nearly invisible.

Conclusions: For tumors located far from NAC, breast-conserving surgery via circumareolar incision is a feasible technique and leads to superior cosmetic result in selective patients. Also it appears to be oncologically safe although long-term outcome is needed.

PO175

A PHASE II STUDY TO EVALUATE THE SAFETY AND EFFICACY OF PEGTEOGRASTIM IN KOREAN BREAST CANCER PATIENTS RECEIVING DOSE-DENSE DOXORUBICIN/CYCLOPHOSPHAMIDE (AC)

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Background: Dose-dense (dd) chemotherapy is a preferred (neo) adjuvant regimen in early breast cancer (BC). Although the results of the reported randomized trials are conflicting, recent meta-analysis showed dd-CT resulted in improved survival when compared to conventional schedules. However, there are no available safety data of dd chemotherapy with pegfilgrastim support from Korean patients. This phase II study was conducted to evaluate the safety and efficacy of pegteograstim in Korean BC patients receiving dd AC.

Methods: Subjects with operable histologically confirmed BC received four cycles of doxorubicin (60 mg/m^2) and cyclophosphamide (600 mg/m^2) on day 1 every 2 weeks. A subcutaneous injection of 6.0mg pegteograstim was given on day 2 of each chemotherapy cycle. The primary efficacy endpoint was the incidence of febrile neutropenia.

Result: Two of 63 subjects (3.2%) developed febrile neutropenia during all cycles of dd AC. One of 63 subjects (1.6%) developed febrile neutropenia during first cycle of chemotherapy. Dose delay was observed in 4 of 63 subjects (6.3%) and dose reduction was observed in 2 of 63 subjects (3.2%) during dd AC. The frequent AEs were nausea, alopecia, generalized muscle weakness, myalgia, mucositis, anorexia, dyspepsia, diarrhea, most of which were due to the chemotherapy. Adverse drug reactions (ADRs), wherein the causal relationship between the AEs and the pegteograstim could not be excluded, were 7.9%, and the ADRs were abdominal pain, bone pain, myalgia, generalized muscle weakness, and headache.

Conclusions: Dose dense AC chemotherapy with pegteograstim is a safe and feasible regimen in Korean breast cancer patients.

PO176

SKIPPING AXILLARY DISSECTION FOR PATIENTS WITH POSITIVE SENTINEL LYMPH NODE METASTASIS IS SAFE IN EVERY PATIENTS?

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Background: The ACOSOG Z11 trial reported that complete dissection of axillary lymph nodes may not be warranted in selected patients. According to the NCCN guidelines, it is recommended that in clinical node negative cases, selected patients based do not require axillary dissection, even if sentinel node is positive.

Methods: We reviewed our data retrospectively from July 2015 to July 2017 to examine risk factor of non-sentinel lymph node metastasis in cN0 cases. 910 patients underwent breast cancer surgery. 226 patients with neo-adjuvant chemotherapy were excluded from this analysis.

Result: In 585 patients with sentinel lymph node biopsy, 89 (15.2%) patients had sentinel lymph node metastasis. In the multivariate analysis, age, tumor size, lymphatic invasion, and mastectomy were related with sentinel lymph node metastasis, but not for subtype and grade. Among 88 patients with positive sentinel node, 27 (30.1%) patients had non-sentinel lymph node metastasis. In the univariate analysis, age and tumor size were related with non-sentinel lymph node metastasis, and in multivariate analysis, age remained significant. Out of those 27 patients, 19 patients had more than 2 positive non-sentinel lymph nodes. Moreover, 3 patients with invasive lobular carcinoma had 13, 15 and 16 non-sentinel lymph node metastasis.

Conclusions: ALND may be avoided for patients who have sentinel lymph node metastasis. However, several patients have massive non-sentinel lymph node metastasis, and special caution will be need before and during operation.

PO177

DIAGNOSTIC VALUE OF CONTRAST ENHANCED DIGITAL MAMMOGRAPHY VERSUS CONTRAST ENHANCED MRI FOR PREOPERATIVE EVALUATION AND SURGICAL MANAGEMENT OF BREAST CANCER

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Background: This study aimed to compare the pre-operative CEDM and MRI for the evaluation of diagnostic performance and effect to the surgical management in women with breast cancer.

Methods: From November, 2016 to October 2017, 84 patients diagnosed as invasive carcinoma and ductal carcinoma in situ (DCIS) underwent both CEDM and MRI were enrolled. We correlated the imaging findings and surgical management with pathologic results, and compared the diagnostic performance of both modalities in the detection of index and secondary cancers (multifocality, multicentricity) in breast with newly diagnosed cancer, and occult cancer in contralateral breast. We also evaluated whether CEDM or MRI made changes in surgical management of the affected breast.

Result: Eighty-four women with 85 index cancers were included for analysis (mean age, 50.9 years; range, 2,873 years). CEDM had similar sensitivity (92.3% [79 of 85 lesions] vs. 94.5% [81 of 85 lesions]), a significantly higher specificity (55.6% vs. 11.1%, $p=0.011$) and PPV (91.3% vs. 84.3%), a fewer false positive findings than MRI (18 vs. 26) in detecting index cancer. Both CEDM and MRI depicted 5 of 6 (83.3%) secondary cancers. Change in surgical management was lower in CEDM compared to MRI (36.5% vs. 41.2%) and change in surgical plan due to false positive finding was also lower in CEDM (17.6% vs. 22.4%).

Conclusions: CEDM depicted index, secondary cancer, and occult cancer in contralateral breast at comparable rate to that of MRI. The CEDM, caused by less false positive results, made less change in surgical management compared to MRI.

PO178

PREOPERATIVE MRI FEATURES ASSOCIATED WITH LYMPHOVASCULAR INVASION IN NODE-NEGATIVE INVASIVE BREAST CANCER: A PROPENSITY-MATCHED ANALYSIS

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Background: In node-negative disease, the presence of lymphovascular invasion (LVI) is reported to be an unfavorable prognostic factor. Thus, the aim of this study was to evaluate whether preoperative breast magnetic resonance imaging (MRI) features are associated with LVI in patients with node-negative invasive breast cancer by a propensity-matched analysis.

Methods: Among 389 patients with node-negative invasive ductal breast cancer who had preoperative breast 3.0-T MRI with precontrast T2-weighted fat-suppressed, pre- and dynamic postcontrast T1-weighted fat-suppressed sequences, 61 patients with LVI (LVI group) were matched with 183 patients without LVI (no LVI group) at a ratio of 1:3 in terms of age, histologic grade, tumor size, and hormone receptor status. Two radiologists reviewed the MRI features, following profiles of the focal breast edema (peritumoral, prepectoral, subcutaneous), intratumoral T2 signal intensity, adjacent vessel sign, and increased ipsilateral whole-breast vascularity, in addition to 2013 BI-RADS lexicon.

Result: The presence of peritumoral edema (45.9% [28/61] vs. 30.6% [56/183], $p=0.030$) and adjacent vessel sign (82.0% [50/61] vs. 68.3% [125/183], $p=0.041$) was significantly associated with LVI. Prepectoral edema was also more frequently observed in the LVI group than in the no LVI group with borderline significance (26.2% [16/61] vs. 15.3% [28/183], $p=0.055$). In cases of non-mass enhancement, regional enhancement was more frequently found in the LVI group than in the no LVI group (60.0% [3/4] vs. 5.9% [1/4], $p=0.042$).

Conclusions: Preoperative breast MRI features may be associated with LVI in patients with node-negative invasive breast cancer.

PO179

A NOVEL GENOMIC PANEL AS AN ADJUNCTIVE DIAGNOSTIC TOOL FOR PREOPERATIVE CHARACTERIZATION AND PROFILING OF BREAST FIBROEPITHELIAL LESIONS

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Background: Breast fibroepithelial lesions (FEL) encompass a spectrum of neoplasms from fibroadenomas (FA) to phyllodes tumors (PT). An accurate pre-operative diagnosis of FEL is essential in guiding appropriate surgical management. However, this is challenging due to overlapping morphological and clinical attributes, inter-observer variability between pathologists and the small volume of tissue obtained through pre-operative core biopsies (CB). A novel 16-gene panel assay identifies mutational differences across the spectrum, which may possibly assist in the diagnosis of problematic pre-operative CB.

Methods: DNA extraction and subsequently targeted sequencing using our customized 16-gene panel were performed on 211 formalin-fixed, paraffin-embedded (FFPE) breast FEL specimens (167 FA, 24 benign, 14 borderline and 6 malignant PTs) from Singapore General Hospital. A model was developed through machine learning to assist in the discrimination of FELs across the spectrum.

Result: Mutations in MED12 were observed in both FA and PT. Higher frequency of mutations were observed in TERT (47.7% vs. 3.6%), RARA (29.5% vs. 3.6%) and TP53 (9.1% vs. 1.2%) of PT as compared to FA. Machine learning identified seven genes (MED12, KMT2D, SETD2, TERT, RARA, FLNA and NF1) important in differentiating FELs across their spectrum.

Conclusions: We demonstrate the ability to extract quality DNA from FFPE CB specimens with successful characterization and profiling using a novel 16 gene panel assay. A prognostic scoring system can been modeled from our 16-gene panel assay. Larger numbers are required to validate this as an adjunctive diagnostic tool for breast CB yielding FELs in clinical practice.

PO180

THE NUMBER OF EXCISED LYMPH NODES OF PATIENTS IN EARLY BREAST CANCER PATIENTS WHO UNDERWENT MASTECTOMY HAS NO SIGNIFICANT IMPACT ON DISEASE FREE SURVIVAL AND OVERALL SURVIVAL

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Background: Sentinel lymph node biopsy (SLNB) can replace axillary lymph node dissection (ALND) in clinically lymph node negative breast cancer patients and can reduce morbidity. Especially in patients undergoing mastectomy, axillary ALND is recommended for SLNB-positive patients. The purpose of this study was to investigate the relationship between the number of excised lymph nodes and disease free survival (DFS) and overall survival (OS) when ALND was performed as a SLNB positive patients undergoing mastectomy for clinically lymph node negative breast cancer.

Methods: This study was retrospectively analyzed for patients who underwent mastectomy among patients with T1-2, no distant metastasis, and clinical negative lymph nodes from 2006 to 2010 in a single institution. Clinical pathologic features of two groups, N1 (n = 517) and N2-3 (n = 169). According to the number of excised lymph nodes, the patients were divided into three groups (10 or less, 11-20, 21 or more), and the disease free survival (DFS) rate and overall survival (OS) rate were analyzed.

Result: The local recurrence rate was 15.7% in the N1 group and 27.2% in the N2-3 group ($p = 0.0012$). There was a significant difference between the two groups. However, the DFS ($p = 0.982$) and OS ($p = 0.719$) among the three groups according to the resected lymph nodes in the N1 group did not show any significant difference. N2-3 group also showed similar results.

Conclusions: There is no correlation between DFS and OS according to the number of resected lymph nodes in patients with early breast cancer undergoing mastectomy.

PO181

NEGATIVE PREDICTIVE VALUE OF ULTRASONOGRAPHY AND FLUORODEOXYGLUCOSE POSITRON EMISSION TOMOGRAPHY/COMPUTED TOMOGRAPHY IN PREDICTING AXILLARY LYMPH NODE STATUS IN PATIENTS WITH BREAST CANCER

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Background: Axillary lymph node (ALN) status is important prognostic factor in patients with breast cancer. The aim of this study was to evaluate the negative predictive value (NPV) of preoperative ultrasonography (US) and fluorodeoxyglucose positron emission tomography/computed tomography (PET/CT) as non-invasive methods for predicting ALN status.

Methods: We reviewed the records of 230 patients with breast cancer who preoperatively underwent both US and PET/CT between February 2009 and August 2017 at Inje University Sanggye Paik Hospital. We retrospectively analyzed associations between sentinel lymph node biopsy (SLNB) results and clinicopathologic characteristics in 108 patients who had negative ALN both on preoperative US and PET/CT. We compared NPV of preoperative US+PET/CT in predicting ALN status with NPVs of SLNB from pre-existing studies.

Result: On univariate analysis, age (over 70 years $p=0.0092$, over 75 years $p=0.0247$) and size of tumor which was measured preoperatively via US (over 1.5 cm $p=0.0266$) were associated with positive SLN. On multivariate analysis, size of tumor which was measured preoperatively via US (over 1.5 cm $p=0.0202$) was associated with positive SLN. Seventy seven patients of 230 had size of tumor smaller than 1.5cm on preoperative US. Fifty four patients of 77 had negative ALN both on preoperative US and PET/CT. NPV of preoperative US+PET/CT in predicting ALN status was 96.3%.

Conclusions: Pre-existing studies reported NPVs of SLNB ranging from 90.1% to 96.1%. In conclusion in patients with breast cancer with size of tumor is smaller than 1.5 cm on preoperative US and negative ALN on both preoperative US and PET/CT, SLNB could be omitted.

PO182

APPLICATION OF BODY MRI COIL IN ADVANCED BREAST CANCER

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Background: Breast MRI coil is usually used to detect breast cancer individually using nipple Level as the center reference. The axillary zones are nearly outside the coil and images are usually suboptimal with noise. On the contrary, body coil have wider field of view (FOV), it can center at the axillary fossa, so combining two coils could evaluate the lymph nodes and chest wall more thoroughly.

Methods: When MRI sequences were completed using breast coil, patients were kept prone and were covered by body coil on the back. Delayed enhanced axial and coronal T1W and axial DWI (b = 50, 400,800 s/mm^2) sequences were performed by two coils, it took about 4 minutes altogether. Images of neck, axillary and chest were performed. Fifty three cases of pathologically proved breast cancer with axillay lymph nodes metastases were included in the study. A retrospective analysis and comparison of the positive rate of nodes on one and two coils images. The result were evaluated by Chi-square analyses with Fisher's exact test.

Result: The positive interpretation by single and two coils were 21 and 49 cases respectively, $p = 0.000$. Two coils sequences could see the full mapping of axillary nodes, with 3 additional cases of supraclavicular nodes metastases, 4 internal mammary nodal chain enlargement and 2 rib lesions, which were missed by single coil sequences.

Conclusions: Body MRI coil should be combined with breast coil for breast examination.

PO183

3D MRI FOR QUANTITATIVE ANALYSIS OF QUADRANT PERCENT DENSITY (QPD): CORRELATION WITH LOCATION OF BREAST CANCER GROWING IN DIFFERENT QUADRANTS

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Background: Whether higher cancer incidence is related to the greater amount of dense tissue is not known. The purpose of this study is to investigate the association between cancer incidence and density, by correlating the quadrant location of tumor in the diseased breast with the quadrant percent breast density (QPD) in the contralateral normal breast.

Methods: In total, 206 women (37 Western and 169 Asian women, mean age 46) with unilateral breast cancer were studied. The tumor was segmented and the quadrant location of the breast cancer in the diseased breast was determined using a computer-aided method based on the DCE-MRI sequence. The MR images of the contra-lateral normal breast were used for overall and quadrant breast density quantification. The MR density measurement was done with a template-based automatic segmentation method. The breast was divided into four quadrants: Upper-Outer (UO), Upper-Inner (UI), Lower-Outer (LO), Lower-Inner (LI).

Result: Breast cancer is more likely to grow in the upper-outer quadrant (88, 42.7%), in both Asian and Western women (43.2% vs. 40.6%). The highest QPD was noted most frequently in the UO quadrant in Western women (20/37 = 54.1%), but in the LO quadrant in Asian women (75/169, 44.3%). Overall, only 42 (42/206, 20.4%) had breast cancer occurring in the breast quadrant with the highest QPD.

Conclusions: The results showed that the development of breast cancer in a specific quadrant could not be explained by the density in that quadrant, and further studies are needed to find the biological reasons accounting for the higher breast cancer incidence in the UO quadrant.

PO184

CORRELATION OF MITOCHONDRIAL METABOLISM OF CANCER CELL AND FDG UPTAKE IN INVASIVE DUCTAL BREAST CANCER

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Background: Mitochondrial metabolism was determined by studying COX activity, expression of TOMM20 and MCT1. We studied the immunohistochemical expression of antibodies of mitochondrial metabolism in patients with IDC and the correlation with SUVmax of the primary tumor (pSUVmax) as well as other biological parameters. Prognostic significance of pSUVmax, HIF-1α, GLUT1 and CA IX for the prediction of progression-free survival (PFS) was also assessed.

Methods: One-hundred seventy four female patients with IDC who underwent pretreatment F-18 FDG PET/CT were enrolled. The pSUVmax was compared with clinicopathological parameters including ER, PR, HER2, axillary lymph node metastasis (LNM), stage, COX-4, TOMM20 and MCT1. The prognostic value of pSUVmax, COX-4, TOMM20 and MCT1 for PFS was assessed using the Kaplan-Meier method.

Result: PSUVmax was also significantly higher in higher stage ($p < 0.001$), ER-negative tumors ($p < 0.0001$), PR-negative tumors ($p = 0.0009$) and positive LNM ($p = 0.0283$). pSUVmax was significantly higher in patients with progression compared to patients who were disease-free (6.4 ± 3.5 vs. 4.1 ± 3.6, $p = 0.0045$). A receiver-operating characteristic curve demonstrated pSUVmax of 6.8, TOMM20 of 5 and MCT1 of 3 to be the optimal cutoff for predicting PFS (sensitivity; 53.6%, specificity; 86.0%, $p < 0.0001$; 60.9%, 72.2%, $p = 0.006$; 56.5%, 80.8%, $p = 0.0054$). Kaplan-Meier analysis identified pSUVmax ≥ 6.8 ($p = 0.0004$), TOMM20 ≥ 5 ($p = 0.0005$) and MCT1 ≥ 3 ($p < 0.0001$) as predictors of recurrence.

Conclusions: PSUVmax on pretreatment F-18 FDG PET/CT reflect expression of COX-4, TOMM20 and MCT1 and can be used as a good surrogate marker for the prediction of progression in patients with IDC. The amount of FDG uptake is determined by the expression of mitochondrial metabolism in breast cancer cell.

Poster Presentation

PO185

QUANTITATIVE ANALYSIS OF PERI-TUMOR INTERFACE FAT AND THE VOLUMETRIC FAT PERCENTAGE AND CONTRAST ENHANCEMENT IN THREE PERI-TUMORAL SHELLS TO DIFFERENTIATE MOLECULAR SUBTYPES OF BREAST CANCER

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Background: We analyzed degree of contrast enhancement in MRI and applied different morphological methods to quantitatively study the fat content on the tumor boundary and in different shells surrounding the tumor and compared among three molecular subtypes.

Methods: Ninety nine women (mean age 48.5 y/o) with solitary breast cancer were studied. 45 were Her2(-)HR(+), 44 were HER2(+), and 10 were TN. The tumor lesion, the breast, the fibroglandular and fatty tissue were segmented using well-established methods. The whole breast fat percentage and the peri-tumor interface fat percentage were measured. Three shells (SH1, SH2, SH3) surrounding the convex hall of the 3D tumor were defined and in each shell the volumetric percentage of fat was calculated. Additionally, the mean contrast enhancement from the fibroglandular tissue in the three peri-tumoral shells were calculated and compared among different subtypes.

Result: In the TN group, the fat percentage on the tumor boundary is 43 ± 19%, the highest among the three subtypes but not significantly different; and the fat percentage in SH2 and SH3 in the TN group is 82 ± 7% and 85 ± 7%, which is significantly higher compared to the two other two subtypes. The results remained after controlling for the whole breast fat percentage. The enhancement in SH1 closer to the tumor is higher than in SH2 and SH3, but not significant different among three subtypes.

Conclusions: Among the three subtypes, peri-tumor fat content is the highest in the most aggressive TN tumors. The method presented in this study provides a feasible tool for quantitative analysis of peri-tumoral tissue characteristics.

PO186

COMPARISON OF THE DIAGNOSTIC ACCURACY OF MAGNETIC RESONANCE IMAGING WITH SONOGRAPHY IN THE PREDICTION OF DUCTAL CARCINOMA IN SITU (DCIS) TUMOR SIZE

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Background: In order to effectively treat patients with ductal carcinoma in situ (DCIS), it is important to know the precise tumor size. We compared the rates of concordance of magnetic resonance imaging (MRI)-derived and sonography-derived breast cancer tumor size with histopathologically determined tumor size.

Methods: The preoperative breast MRI and sonography were analyzed in respect of the detection and assessment of the size of DCIS in 112. The MRI and sonography measurements were compared with the histopathologic size with using concordance correlation (Bland-Altan plot). We evaluated whether the hormone receptor status, the tumor nuclear grade, the presence of comedo necrosis and microinvasion influenced the MRI and sonography size estimates.

Result: A total of 112 patients comprised the study cohort. Mean tumor size was 19.1 mm ± 13.6 on histopathology, 14.9 mm ± 11.1 on sonography, and 26.5 mm ± 17.9 on MRI. Overall, breast MRI predicted tumor size more accurately than sonography (CCC = 0.74 vs. 0.64). In subgroup analysis, breast sonography had a higher concordance rate in cases where hormone receptor negative patients and tumor size were smaller than 20 mm. (CCC = 0.6 vs. 0.41, 0.44 vs. 0.34, respectively). However breast MRI was more accurate than ultrasound in most cases except the above cases.

Conclusions: Breast MRI was more accurate than breast ultrasound, regardless of microinvasion, microcalcification and tumor grade except when the tumor size was less than 20 mm and when the hormone receptor was negative.

PO187

PROGNOSTIC VALUE OF KI-67 IN ESTROGEN RECEPTOR-POSITIVE, STRONGLY PROGESTERONE RECEPTOR-POSITIVE BREAST CANCER PATIENTS: IS IT INDEPENDENT FACTOR?

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Background: Ki67 is one of the most useful parameters when it comes to the treatment and prognosis for breast cancer. Many studies link Ki67 to other clinicopathological markers when predicting the prognosis and tailoring the treatment for patients with breast cancer.

Methods: From January 2009 to December 2013 we conducted a retrospective review of the records of 1493 patients who underwent surgery for primary breast cancer at a single hospital. We analyzed the prognostic value of Ki-67 expression in relation to PR expression. The cut-off value for progesterone receptor (PgR) and Ki-67 were 20% and 25%, respectively. Kaplan-Meier analysis was used to evaluate the recurrence-free survival (RFS) as the primary end point.

Result: Of the 1,439 analyzed patients, the median follow-up time was 48 months. During follow-up, 172 patients had recurrence. In patients with low PgR expression, high Ki-67 expression group showed significantly worse prognosis compared to low Ki-67 expression group ($p = 0.008$). On the other hand, no significant difference was shown between low and high Ki-67 expression group when PgR expression was high ($p = 0.153$). Also, multivariate analysis demonstrated that high Ki-67 expression was an independent prognostic factor only when PgR expression was low.

Conclusions: Our study confirmed that high level of Ki-67 expression is directly correlated with risk of recurrence in early breast cancer patients only under low PgR expression. At high PgR expression, Ki-67 expression has no influence on breast cancer prognosis. Therefore, attention should be paid to correlation between PR and Ki-67 expression since it not an independent prognostic factor.

PO188

BREAST MICROCALCIFICATION TARGETING FOR DIFFERENTIAL DIAGNOSIS USING NEAR-INFRARED FLUOROPHORES

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Background: Differential diagnosis of breast microcalcifications is important in the treatment of breast cancer, because the mineral composition of breast calcification is directly associated with different pathological states. However, applying image-based modalities for the component identification of breast calcification remains challenging. The goal of this study was to create families of calcification-specific near-infrared (NIR) fluorophores and assess the types of microcalcifications in breast lesions.

Methods: Four different types of phosphonated NIR fluorophores were synthesized for 700 nm and 800 nm fluorescences. For in vitro calcium salts binding experiments hydroxyapatite (HA), calcium phosphate (CP), calcium oxalate (CO), calcium carbonate (CC) and calcium pyrophosphate (CPP) salts were incubated separately with fluorophores in PBS. And NIR microscopy images of breast microcalcifications were taken from the biopsy specimens of patients for ex vivo microcalcifications diagnosis. The mixture of fluorophores was administered intravenously into MCF7 cell line harvested mice that were mixed with HA, CO and imaged.

Result: We demonstrated the diagnostic potential of targeted NIR fluorophores to differentiate microcalcifications found in benign and malignant breast lesions. Additionally, using artificial mice models we confirmed subtle differences in the chemical composition of CO and HA calcifications occurring in benign and malignant breast lesions, respectively. This study provides the first evidence to distinguish benign calcification from malignant calcification via targeting the CO and HA using the combination of NIR fluorophores.

Conclusions: This novel technology shows significant potential for breast cancer diagnosis and image guided surgery performed with increased precision and efficiency by providing differential diagnosis of breast microcalcifications.

PO189

COMBINED FUNCTION MAGNETIC RESONANCE IMAGING (MRI) PARAMETERS AND MOLECULAR SUBTYPE PREDICT THE RESPONSE TO NEOADJUVANT CHEMOTHERAPY FOR BREAST CANCER: A SINGLE INSTITUTE EXPERIENCE

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Background: Neoadjuvant chemotherapy (NAC) is increasingly used in locally advanced breast cancer. Magnetic resonance imaging (MRI) and Ultrasound (US) are usually used to evaluate the response to NAC. This study aims to evaluate the correlation of MRI results with molecular features of the tumour, thus assessing the feasibility of response prediction to NAC.

Methods: Twenty six locally advanced breast cancer patients treated in HKU-SZH from 2014-2017 were recruited. Patients with distant metastasis and who had incomplete NAC were excluded. All patients received baseline and post-NAC MRI, and had both histological and immunohistochemistry (IHC) pathology pre- and post-NAC. Response to NAC was evaluated according to RECIST 1.1 protocol. Mean apparent diffusion coefficient (ADC mean) of MRI in non-pathologically complete response (pCR) cases were evaluated. Statistical analysis was performed with Mann-Whitney, Chi-square test and logistic where appropriate.

Result: Pathologically, four patients (15.4%) had pCR after NAC, 19 (73.1%) had partial response and 3 (11.5%) had static disease. The pre-NAC ADC and Ki-67 were 0.80 ± 0.17 and $42.2\% \pm 18.8\%$ respectively, while the mean augmentation of ADC and reduction of Ki-67 after NAC were $68.5\% \pm 61.2\%$ and $57.8\% \pm 69.5\%$. Multivariate analysis was performed to evaluate the prognosticators of tumor response to NAC. T stage ($\chi^2 = 27.231$, $p < 0.001$), N stage ($\chi^2 = 15.250$, $p < 0.001$), ER ($\chi^2 = 12.462$, $p < 0.001$), PR ($\chi^2 = 9.846$, $p = 0.002$) , Her-2 ($\chi^2 = 5.538$, $p = 0.019$) , ADC ($p = 0.014$) and Ki-67 ($p = 0.034$) prior to NAC were significantly associated with the pathological tumor size reduction.

Conclusions: In combination with clinical tumor characteristics, ADC information from MRI and Ki-67 is able to predict the response NAC for breast cancer.

Poster Presentation

PO190

FROZEN SECTION EXAMINATION OF SENTINEL LYMPH NODE SHOULD BE PERFORMED ON SELECTED PATIENTS WITH CLINICAL NODE NEGATIVE AND T1, T2 PRIMARY INVASIVE BREAST CANCER

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Background: Since the results of the American College of Surgeons Oncology Group Z0011 published, the criteria for applying axillary lymph node (ALN) dissection was relaxed among early breast cancer patients who were scheduled for breast conserving surgery, adjuvant chemotherapy therapy, and adjuvant radiation therapy. It is inefficient routinely to evaluate the sentinel lymph nodes by frozen section examination (FSE). Thus, it is necessary to predict three or more ALNs metastasis in breast cancer patients.

Methods: The records of 1650 patients with clinical node negative and T1, T2 primary invasive breast cancer who were treated between January 2013 and September 2016 were selected from the medical database of Yonsei University (Seoul, South Korea). Logistic regression analysis was performed to predict the three or more ALNs metastasis. The nomogram was developed with confirmed variables before surgery. Internal validation was carried out adopting bootstrap method by 500 times resampling.

Result: A total of 80 (4.8%) patients had three or more ALNs metastasis. Preoperative ALN suspicious image findings ($p = 0.029$), clinical tumor size ($p = 0.031$), ki67 ($p = 0.008$) were statistically significant predictors in multivariate analysis. The nomogram was constructed from these three variables, ca153, estrogen receptor status. It had good discrimination performance (area under the receiving operation characteristic curve [AUC] 0.75, 95% confidence interval [CI], 0.70 to 0.81) and calibration fit. The nomogram was validated, indicating good predictive power. (AUC 0.77, 95% CI, 0.71 to 0.82).

Conclusions: Our nomogram might help predict the ALN metastasis in breast cancer patients. Patients with a low probability of ALN metastasis could be spared FSE.

PO191

AWARENESS OF DYSGEUSIA AND QUALITATIVE AND QUANTITATIVE ASSESSMENT OF TASTE IN PATIENTS UNDERGOING CHEMOTHERAPY FOR BREAST CANCER

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Background: We analyzed the prevalence of gustatory test abnormalities in breast cancer (BC) patients undergoing chemotherapy.

Methods: We enrolled 43 BC patients undergoing chemotherapy and 38 BC patients who had never undergone chemotherapy (control group). Two gustatory tests were conducted: an instillation method examining the threshold for four basic taste stimuli and an electrogustometry method measuring the threshold for perception with electric stimulation at the front two-thirds of the tongue (cranial nerve VII) and at the back third of the tongue (cranial nerve IX). The results of the two gustatory tests and clinicopathological factors were compared between the chemotherapy and control groups and between patients with and without awareness of dysgeusia in the chemotherapy group.

Result: In the chemotherapy group, 19 (44%) patients were aware of dysgeusia. Although more patients had parageusia in the chemotherapy than control group, no significant differences in the results of the two gustatory tests were observed. Patients with dysgeusia awareness had a higher threshold at cranial nerve IX using the electrogustometry method than those without dysgeusia awareness; no significant differences in hypogeusia were observed using the instillation method. In fact, 74% (14/19) of patients with dysgeusia awareness could identify the four tastes accurately using the instillation method. Similar results were observed for the instillation and electrogustometry methods at cranial nerve VII.

Conclusions: While approximately half of the chemotherapy patients were aware of dysgeusia, 81% (35/43) of them could accurately identify the four basic tastes using the instillation method.

PO192

DOES GLUT-1 HAVE A ROLE IN PROGNOSIS OF BREAST CARCINOMA OF EGYPTIAN PATIENTS?

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Background: Breast cancer (BC) constitutes 38.8% of all malignant tumors among Egyptian females. Triple negative breast cancer (TNBC) has no confirmed therapeutic molecular target and has a poor prognosis. Glucose transporter-1 (GLUT-1) has important role in the transport of glucose in malignant cells and overexpressed in different types of human cancers. The aim of this work is to evaluate the role of GLUT-1 in breast carcinoma in Egyptian patients.

Methods: This is a retrospective study that included 79 invasive duct carcinoma (IDC) specimens, spanning the period between January 2010 and December 2016. All cases were stained for GLUT-1 antibody.

Result: Eighty percent of the studied cases showed positive GLUT-1 expression and 55% of positive cases were +3. There was a highly significant association between positive GLUT-1 expression and (+3) GLUT-1 positivity and advanced nodal stage ($p = 0.001$ and < 0.001 respectively), advanced T stage ($p = 0.000$ and 0.004 respectively). Furthermore, there was a highly significant association between its positive expression and poor degree of differentiation (Grade) ($p < 0.001$). Moreover, there was a statistical significant association between (+3) GLUT-1 positivity and advanced stage (III and IV) ($p = 0.018$). Also, there is a trend of significance between GLUT-1 expression and hormonal status as 94.1% of TNBC cases showed positive GLUT-1 expression ($p = 0.078$).

Conclusions: GLUT1 could be considered a poor prognostic marker in view of association between its positive expression and advanced stage (III and IV) and poor degree of differentiation. Furthermore, inhibition of GLUT-1 might play a therapeutic role for TNBC.

PO193

LUMINAL A SUBTYPE IS ASSOCIATED WITH EXCELLENT PROGNOSIS IN NODE-POSITIVE BREAST CANCER PATIENTS RECEIVING MASTECTOMY

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Background: Previous gene expression studies showed distinct molecular subtypes in breast cancer. Especially, luminal A subtype showed better prognosis than other subtypes in several publications. In this study, we evaluated prognostic factors including molecular subtypes associated with clinical outcomes in operable node-positive breast cancer patients who underwent mastectomy.

Methods: A total of 195 node-positive breast cancer patients who received mastectomy with axillary lymph node dissection between January 2005 and December 2010 were analyzed retrospectively. The intrinsic molecular subtypes were identified with estrogen receptor (ER), progesterone receptor (PR), HER2 status and Ki67 status using immunohistochemistry: luminal A subtype (ER and/or PR positive, HER2 negative, Ki67 ≤ 20%) vs. non-luminal A subtype. The clinical endpoints were locoregional recurrence-free survival (LRFS), distant metastasis-free survival (DMFS), invasive disease-free survival (iDFS) and overall survival (OS) in this study.

Result: The median follow-up was 72 months (range, 8–150 months). 109 of 195 patients (55.8%) were luminal A subtype. Luminal A subtype showed significantly higher 5-year LRFS than non-luminal A subtypes in univariate and multivariate analysis (98.1% vs. 91.6%, HR = 4.76, $p = 0.031$). Similarly, luminal A subtype was associated with excellent 5-year DMFS, iDFS and OS compared with non-luminal A subtypes (94.1% vs. 77.2%, $p = 0.002$; 92.2% vs. 75.6%, $p = 0.001$; 99.1% vs. 85.7%, $p = 0.005$, respectively).

Conclusions: Luminal A subtype was associated with lower rate of local recurrence, distant metastasis and death in patients who underwent mastectomy for node-positive breast cancer.

PO194

OUR EARLY EXPERIENCE WITH THE GENOMIC PARTNERSHIP PROGRAMME

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Background: The Genomic Partnership Programme (GPP) aims to help patients who require chemotherapy based on their Oncotype DX recurrence score. Patients with a recurrence score > 26 are eligible for refunding of their test cost.

Methods: A retrospective review of all patients who participated in this programme from January to September 2017 was performed.

Result: Thirty patients were identified. Their median age was 49.5 years old (range 27–69). All patients had early breast cancer with a median tumour size of 20mm (range 8-50). Most patients had T1c Grade 2/3 disease (n = 18, 60%) or T2 Grade 1/2 disease (n = 8, 27%). All the tumours were estrogen receptor and progesterone receptor positive, and HER-2 receptor negative with no nodal metastasis. Eight patients (27%) eventually received adjuvant chemotherapy. Six patients (20%) had refund of their test cost. The median number of days between surgery and Oncotype DX order was 23 days (range 12–58), 17 days (range 12–53) for the surgeon-initiated-test and 25 days (range 12–58) for the physician-initiated-test ($p = 0.05$). Among patients who had chemotherapy, there was a 16.5-day decrease in the median number of days from surgery to chemotherapy initiation in the surgeon-initiated-test group as compared to the physician-initiated-test group ($p = 0.286$). Compared to the same period in 2016, there was a 50% increase in the number of Oncotype DX tests following the introduction of GPP.

Conclusions: There was an increase in the number of Oncotype Dx test following the introduction of GPP. The interval between surgery and initiation of adjuvant chemotherapy may be reduced by surgeon-initiated testing.

PO195

USE OF PREOPERATIVE ENDOCRINE PROGNOSTIC INDEX SCORE IN BREAST CANCER PATIENTS WITHOUT NEOADJUVANT TREATMENT: COMPARISON OF MULTI-GENE PANELS RESULT

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Background: We investigated whether the preoperative endocrine prognostic index (PEPI) score, which was developed as predictor of response to neoadjuvant endocrine treated breast cancer patients, could be used as a prognostic factor before systemic treatment.

Methods: The PEPI score was evaluated in 59 patients who underwent a multi-gene panel study without receiving neoadjuvant treatment from October 2013 to December 2017 at KonKuk University Medical Center. PEPI score was compared with the results of the multi-gene panel study.

Result: The study included 59 patients with early breast cancer (T1-2, N0M0) with ER-positive, HER2-negative. 47 patients underwent EndoPredict and 12 patients underwent Oncotype DX. In multi-gene panel study, the study was divided into two groups, low risk group (n = 43) and high risk group (n = 16) which including intermediate result in Oncotype DX. The mean size of mass was 1.5 ± 0.4 cm in low risk group, 1.9 ± 0.6 cm in high risk group. The mean ER allred score was 7.9 ± 0.3 and 6.9 ± 1.9 in low and high risks group ($p = 0.046$). The mean value of ki-67 was 15.91 ± 1.2, 39.5 ± 29 in low and high risks group respectively ($p = 0.006$). PEPI score was 0 out of 59 patients, all belonged to low risk group ($p = 0.002$). There was a correlation between the PEPI score and the EpClin score in patients who underwent EndoPredict ($r = 0.620$, $p = 0.01$) and the PEPI score and RS score correlated significantly in patients who underwent Oncotype DX ($r = 0.887$, $p = 0.01$).

Conclusions: A PEPI score of 0 is considered to be a very strong prognostic factor in breast cancer patients without neoadjuvant endocrine treatment when compared with multi-gene panel.

PO196

PROGNOSTIC VALUE OF F-18 FDG UPTAKE BY PRIMARY-TUMOR ON PRETREATMENT PET/CT FOR DISEASE-PROGRESSION IN PATIENTS WITH HER2 POSITIVE INVASIVE DUCTAL BREAST CANCER

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Background: Although HER2 tailored therapy has changed the management of patients with HER2 positive breast cancer subtype, the majority of patients is either de novo resistant or acquires resistance to these therapies over time. The aim of this study was to evaluate prognostic significance of maximum standardized uptake value of primary-tumor (pSUVmax) on pretreatment PET/CT for progression-free survival (PFS) in HER2 positive breast cancer.

Methods: A total of forty-seven HER2 positive breast cancer patients who had undergone pretreatment F-18 FDG PET/CT and had Herceptin treatment were enrolled. To obtain the pSUVmax, a transaxial image representing the highest FDG uptake breast lesion was carefully selected, and a spherical region of interest was placed on the FDG-accumulating lesion. The prognostic value of pSUVmax for PFS was assessed using the Kaplan-Meier method.

Result: Fourteen of 47 patients (29.8%) experienced disease-progression during follow-up (median follow-up, 36 mo). pSUVmax was significantly higher in patients with disease-progression than in those who were disease-free (pSUVmax [Disease-progression group]: 10.3 ± 5.1 vs. pSUVmax [Disease-free group]: 6.4 ± 4.4, $p = 0.0125$). A receiver-operating characteristic curve demonstrated a pSUVmax of 6.1 to be the optimal cutoff for predicting PFS (sensitivity; 85.7%, specificity; 66.7%, area under the curve; 0.736). The patients with a high pSUVmax (more than 6.1) had significantly shorter PFS compared to patients with a low pSUVmax ($p = 0.0008$).

Conclusions: These results suggest that pSUVmax is associated with poor prognosis patients and pSUVmax might be incorporated into the risk assessment of patients with HER2 positive IDC.

PO197

SWITCHED PROGNOSIS OF TRIPLE POSITIVE BREAST CANCER AND TRIPLE NEGATIVE BREAST CANCER AFTER A CERTAIN CLINICAL TIME POINT

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Background: Triple negative breast cancer (TNBC) and triple positive breast cancer (TPBC) are two of the worst subtype of breast cancer. We tried to examine the differences in clinical courses of TNBC and TPBC.

Methods: We collected medical records of 628 breast cancer patients who diagnosed between 2004 and 2012 in single medical institute. We sorted out two subgroups, TNBC and TPBC as the expression of estrogen receptor, progesterone receptor, human epidermal growth factor receptor-2. We compared the variables such as age at diagnosis, TNM stage, operation methods, histologic grade (HG), nuclear grade (NG), lymphatic invasion (LI), vascular invasion (VI), neural invasion (NI), Ki67, Bcl-2 and metastatic sites. Survival analysis included the comparison of disease free survival (DFS) and overall survival (OS).

Result: Among total 628 patients, we sorted out the 91 TNBC and 81 TPBC patients. In univariate analysis, TPBC was showed higher proportion in lower HG ($p=0.0004$), lower NG ($p=0.0003$), Higher LI ($p=0.0385$) and NI ($p=0.0102$), lower Ki67 less than 20% ($p<0.0001$). In multivariate analysis, lower Ki67 ($p=0.0312$), higher LI ($p=0.0215$) were statistically significant different factors for DFS and bone metastasis ($p<0.0001$) was statistically significant different factors for OS. TPBC group was showed worse 10 years DFS ($p<0.0030$) and OS ($p<0.0398$) than TNBC, but additional 4-5 years after that, the OS curve were switched each other.

Conclusions: TNBC showed the better DFS and OS than TPBC after about 5 years from adjuvant therapy. Further larger scale clinical trials are needed to prove the results of our retrospective study.

PO198

A20 EXPRESSION AS A POOR PROGNOSTIC MARKER IN PATIENTS WITH BREAST CANCER

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Background: A20 protein, called TNFAIP3 (tumor necrosis factor α-induced protein 3) has the function of the ubiquitin-editing activities and acts as key regulator of inflammation and immunity. Previously, our group showed that A20 promotes tumor metastasis through multi-monoubiquitylation of SNAIL1 in basal-like breast cancer (Nature Cell Biology 2017). We aimed to investigate the difference in survival outcomes according to A20 expression in breast cancer patients.

Methods: We retrospectively analyzed patient data who were underwent surgery from 1996 to 2014 at Gangnam Severance Hospital. An immunohistochemistry (IHC) was performed using A20-specific antibody. A20 expression of 0~1+ were defined as low expression, 2~3+ as high expression. Survival curves were drawn using the Kaplan-Meier method and log-rank test was used to evaluate difference. Multivariate Cox proportional hazard model was used to exam risk factors which showed statistical significance in univariate analysis.

Result: The A20 expressions were confirmed in 442 patients. Their median follow-up period was 92.5 months and mean age was 48.4 years. High A20 expression was associated with pathologic T stage, pathologic N stage and under 35 years old at surgery. The RFS and OS differed significantly according to A20 expression in all patients ($p < 0.001$ and $p < 0.001$, respectively). In univariate analysis for RFS and OS, age under 35, node metastasis, lymphovascular invasion (LVI) and A20 were significant factors. Multivariate analysis of RFS and OS showed that A20, node metastasis and LVI were independent prognostic factors.

Conclusions: We found that A20 expression might be a poor prognostic marker in patients with breast cancer.

PO199

RESISTANCE TO TRASTUZUMAB IN HER2-POSITIVE MUCINOUS INVASIVE DUCTAL BREAST CARCINOMA

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Background: Incidence of Mucinous Breast Carcinoma (MBC) is approximately 1-6% among all cases of malignant breast carcinoma and overall prognosis is good. Human epidermal growth factor receptor 2 (HER2) is over expressed in approximately 4% of (MBC) which is associated with poor prognosis. Treatment with humanized monoclonal antibody (trastuzumab), should Improve the outcome. However, there were two previous case reports showed resistance to trastuzumab in HER2-positive MBC. Our aim is to evaluate the prognosis of HER2-positive MBC treated with trastuzumab in terms of overall survival (OS) and disease free survival (DFS).

Methods: A retrospective study at a single-Institution Samsung Comprehensive Cancer Center included 412 patients with MBC treated in our center and divided into two groups 396 patients with (HER2-negative) and 16 Patients with (HER2-positive treated with trastuzumab), from February, 1996 till July, 2017 with median follow up 42.2 months.

Result: Analysis included 412 patients (median age, 45 [Range 21–86] years). The OS was not significant between the two groups ($p = 0.66$) with no reported death in HER2-positive group, while 7 reported deaths In HER2-negative group (2 from breast causes and 5 from other causes). The DFS between the two groups was statistically significant ($p = 0.006$) with 5 years DFS for HER2-negative and HER-2 positive (93.3% and 69.9% respectively). One patient had metastasis from HER-2 positive group and 2 patients had recurrence (12.5%) while 18 patients (5.1%) from HER2-negative.

Conclusions: Patients with HER2- positive MBC has worse DFS than those with HER2-negative MBC, but the OS has no significant difference.

PO200

CLINICAL VALUE OF SERUM NEOPTERIN IN BREAST CANCER

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Background: Neopterin is an immune marker. The aim of the current study was to assess the relation between pre-chemotherapy serum neopterin level and clinical and pathological features of breast cancer.

Methods: This prospective study was conducted in clinical oncology department in Menoufia University. After informed consent, Sixty three patients with histologically verified breast cancer and 20 age and sex matched controls were enrolled. All patients were subjected to full history taking, through medical examination and full investigation. Venous blood sample were administrated from all participants for measurements of serum neopterin level. Serum neopterin level higher than 10 nMol\L was considered elevated.

Result: The mean Serum Neopterin level among the patients was 8.00 ± 7.43 and there was no statistically significant difference between Neopterin level in both patients and controls. Only 22 patients (34.9%) had elevated Serum neopterin level. Elevated Neopterin was mainly prevalent among older patients, IDC pathology, T3 and T4 tumors, N3 disease, grade III tumors and in patients who initially had both visceral and bone involvement. Neopterin was significantly elevated in patients with 2 or more metastatic sites (*p* value 0.01) but there was no significant relation between high Neopterin level and median time to progression and overall survival

Conclusions: Among breast cancer patients, the immune marker neopterin was significantly related the number of involved metastatic sites and it can be a potential marker for systemic tumor spread.

PO201

FAILURE PATTERNS ACCORDING TO MOLECULAR SUBTYPE IN PATIENTS WITH INVASIVE BREAST CANCER FOLLOWING POSTOPERATIVE ADJUVANT RADIOTHERAPY: PREDICTION OF DISTANT FAILURE IN CONTEMPORARY CLINICAL PRACTICE

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Background: This study evaluated the impact of molecular status on long-term patterns of failure in patients with non-metastatic breast cancer who completed postoperative radiotherapy (PORT).

Methods: We analyzed data from 1,181 individuals with non-metastatic invasive breast cancer undergoing surgery plus PORT from 2003 to 2011. Competing risks regression was used to explore subtype-specific recurrence patterns. A nomogram for predicting distant failure risks was constructed based on prognostic factors identified using a Cox proportional hazards model.

Result: The patients were classified into luminal A (LA) (38%), luminal B (LB)-human epidermal growth receptor 2 (HER2)(-) (21%), LB-HER2(+) (11%), HER2 (10%), and triple negative (TN) (19%) groups. In competing risks regression, initial development of distant metastasis was highest with TN tumors, followed by HER2, LB-HER2(-), and LB-HER2(+) subtypes (p = 0.005), even after adjusting for age and/or tumor stage. Regarding preferential sites of distant metastasis, the risk of initial brain metastasis was significantly higher with HER2 tumors, followed by TN tumors (p = 0.001). In distant metastasis-free interval, age (≥ 45 vs. < 45 years), molecular subtypes (LA vs. LB, HER2, and TN), T stage (T1 vs. T2-3 and T4), and N stage (N0 vs. N1 and N2-3) were independently associated (p < 0.05 for all). Regarding the significant factors, a well-validated nomogram was established (concordance index: 0.812).

Conclusions: The preferential and long-term risk of brain metastasis in the HER2 subtype underlines the importance of developing alternative anti-HER2 therapies. Our nomogram can be useful for predicting the individual probability of distant recurrence in breast cancer.

PO202

P-S6K1 AS A PROGNOSIS FACTOR OF PREMENOPAUSAL HORMONE RECEPTOR POSITIVE, HER2 NEGATIVE BREAST CANCER PATIENTS

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Background: Estradiol is produced through aromatization of androgens in the adipose tissues. Recently, some studies showed ribosomal protein S6 kinase-1 (S6K1) plays a critical role in early adipogenesis. It is possible that estrogen depletion therapy is more beneficial with phosphorylated S6K1 (p-S6K1) positive (+) tumor. In this study, we evaluated the possibility of p-S6K1 as a marker for using gonadotropin-releasing hormone (GnRH) agonist, in hormonal receptor (HR) (+) breast cancer.

Methods: We reviewed medical records of 473 premenopausal patients with HR positive, human epidermal growth factor receptor 2 (HER2) negative (-) primary invasive breast cancer. The p-S6K1 positive definded by immunohistochemical staining score 1+, 2+ and 3+ while a score of 0 was regarded as negative.

Result: A total of 360 patients (76.1%) had p-S6K1 (+) tumors. Among these patients, the mean disease-free survival (DFS) of the patients treated with GnRH agonist was significantly longer than that of the patients treated without GnRH agonist (107.0 months vs. 98.5 months, $p = 0.039$). Although GnRH agonist did not show an independent effect on DFS in multivariate analysis, there was a trend toward better DFS among patients with p-S6K1 (+) tumor (odd ratio 0.470; $p = 0.075$). In contrast, there was no beneficial effect of GnRH agonist in the patients with p-S6K1 negative tumor ($p = 0.788$).

Conclusions: In patients with high expression of p-S6K1, GnRH agonist significantly prolonged DFS. It suggests that p-S6K1 could be a potential biomarker for predicting the efficacy of GnRH agonist in premenopausal patients with HR(+)/HER2(-) premenopausal breast cancer patient.

PO203

IMPACT OF RECEPTORS DISCORDANCE IN RECURRENT METASTATIC BREAST CANCER PATIENTS AND ITS PREDICTIVE OUTCOME

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Background: Tumor phenotype may change during BC progression, Discordance in HR and HER2 status between primary tumors and metastatic sites for BC is well established. We conducted this single center retrospective study to evaluate the impact of receptors discordance between primary and recurrent metastatic patients and its impact on Pt outcome as prognostic and predictive factor

Methods: All metastatic recurrent BC pts diagnosed from November 2009 to December 2016 at King fahad hospital were identified in our database and reviewed by our pathologists. Pts were included if they had excision or core biopsy and were treated in our center

Result: A total of 428 patients were identified as metastatic recurrent BC cases, only 113 pts (26.4%) had a tissue biopsy. 42 pts (38%) were local recurrence and 71 pts (62%) were metastatic. 20.3% (23 pts) of these had discordant HRs or HER2 status when compared to the initial diagnosis. Discordance for ER, PR, and HER2 was 21.7%, 47.8%, and 17.4%, respectively. Initial Staging I, II, III was 21.7%, 52.2, and 26.1%. Mean time to progression (TTP) from initial diagnosis was 3.9 years (Range 1.5–8 years). LR was detected in 39.1%, mets was 91.3% and LR& mets were detected in 7 pts (30.4%). ≥2 metastatic sites were 47.8%. Refractory Disease and progression was 69.6% (16 pts). Median post progression Actuarial 1year OS was 47.4% (95% CI [26.4–68.2]) and 2 years was 13.3% (95% CI [8.7–35.3]).

Conclusions: Our study demonstrated the negative impact of receptors discordance on disease outcome. This selective group of pts needs more studies for treatment.

PO204

ANALYSIS OF PROGNOSTIC FACTORS FOR DISEASE-FREE AND POST-RECURRENCE SURVIVAL IN TRIPLE NEGATIVE BREAST CANCER

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Background: Triple Negative Breast Cancer (TNBC) has an unfavorable prognosis among breast cancer subtypes. In this study, we examined clinicopathological factors related to disease-free and post-recurrence survival in TNBC.

Methods: Patients (n = 308) with TNBC (Stage 1–3) who underwent surgery were enrolled from January 2007 to December 2016. Neoadjuvant chemotherapy (anthracycline +/- taxane) was performed in 42 cases, adjuvant chemotherapy in 188 cases, and no chemotherapy in 78 cases. Disease-free survival (DFS), overall survival (OS), survival after recurrence (ROS) were calculated using the Kaplan-Meier method and evaluated using the log-rank test and multivariate analysis.

Result: The DFS rates for 5 and 10 years after initial surgery were 86.2% and 83.4%, respectively. The OS for 5 and 10 years were 86.9% and 85.5%, respectively. The median ROS in TNBC patients (n = 43) with recurrence was 11 months. Multivariate analysis revealed that age (≤ 50 years), tumor size (≥ T2), lymph node metastasis and lymphatic invasion were significant prognostic factors. There was no significant correlation between DFS and grade, p53 overexpression and chemotherapy. Moreover, the multivariate analysis revealed that a shorter DFI (≤ 2 years) was a significant prognostic factor for post-recurrence survival.

Conclusions: In TNBC, the risk of recurrence was high in patients with larger tumor, younger age (< 50 years), lymph node metastasis and lymphatic invasion. Furthermore, a shorter DFI was a poor prognostic factor after recurrence. The findings suggest that appropriate and varied chemotherapy strategies are needed for TNBC patients.

PO205

IMPACT OF APPLICATION OF AJCC 8TH EDITION ON SURVIVAL RATE OF THE BREAST CANCER

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Background: The AJCC 8 edition has changed much. TNM stage, biologic marker (ER, PR, HER2), Histologic grade and multigene assays (oncotype Dx.) should be considered for staging, and it has been applied since January 1, 2018. Patients were recategorized and analyzed in order to know if this more complex classification helps to predict the real prognosis of the patients.

Methods: We review patients who were diagnosed and treated as breast cancer at Konyang Universty Hospital. we studied retrospectively 582 patients who were followed up and were able to review. Stage was classified according to AJCC 7th edition and AJCC 8th edition. survival rate of each stage were analyzed in both editions.

Result: Mean follow up period was 68.6 months. There was no change in the stage in 257 patients. In 195 patients, the stage was elevated and in 130 patients, the stage was changed down. When classified as AJCC 7th edition, the 5 year-survival rate was 95.9% in stage I, 97.9% in stage II, 93.1% in stage III and 89.9% in stage IV. However, when the AJCC 8th edition was applied, the 5-year survival rate was 97.9% in stage I, 96.9% in stage II, 92.2% in stage III, and 89.9% in stage IV.

Conclusions: The prediction of survival rate by stage was more accurate and the difference in survival rate of each stages was more clearly distinguished when The AJCC 8th edition was applied than AJCC 7th edition. AJCC 8th edition was reliable and useful for prediction of prognosis of breast cancer patient.

PO206

THE EXPRESSION OF ANDROGEN RECEPTOR AS A PROGNOSTIC FACTOR OF BREAST CANCER PATIENTS

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Background: Recently, several growth factors and proteins were studied as the factors related to the recurrence and survival rate of breast cancer. Androgen receptor (AR) has been of interest in the possibility of breast cancer as a prognostic and predictive factor. There has been several studies which found the relationship between AR expression and prognosis of breast cancer. In this study, we studied the association of AR with recurrence and survival of breast cancer patient.

Methods: We analyzed the pathologic findings of 363 tissue samples from breast cancer patients who received optimal treatment between January 1990 and December 2006 by using the tissue microarray. We measured the expression of ER and androgen receptor by immunochemistry staining. And we divided the breast cancer patient into 3 subgroup according to the molecular subtype, and analyzed the difference of recurrence and survival rate according to the presence of androgen receptor.

Result: In our study, Androgen receptor was shown in 40.1% of Luminal type, 30.1% of Her2 type and 6.4% of Triple negative breast cancer. We could not find any difference in recurrence rate with and without expression of the androgen receptor in all three groups. (Luminal type $p = 0.571$, Her2 type $p = 0.297$, Triple negative $p = 0.809$) And we also could not find any difference in survival rate with and without expression of the androgen receptor in all three groups, too (Luminal $p = 0.268$, Her2 $p = 0.674$, TNBC $p = 0.658$).

Conclusions: AR showed no significant difference in recurrence and survival in this study.

PO207

ASSESSMENT OF THE PROGNOSTIC STAGING SYSTEM OF AJCC 8TH EDITION FOR BREAST CANCER: A COMPARISON WITH THE CONVENTIONAL ANATOMIC STAGING SYSTEM

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Background: The 8th edition of AJCC manual introduced the prognostic staging system for breast cancer. The prognostic staging system incorporates biologic prognostic information into the anatomical staging system. The aim of the study is to evaluate changes of staging distribution and to ascertain the predictive power of new prognostic staging system

Methods: A total of 12,454 cases with breast cancer in the Severance Breast Cancer Registry were reviewed. All cases with breast cancer underwent surgery between 1978 and 2016. After exclusion of cases without complete anatomical staging data and/or prognostic staging information, 12,267 cases were included in the study.

Result: More than half of patients were age 50 or less (56.2%). T1 cancer is the most common, which was followed by T2, Tis, T3, T0, and T4. Approximately 70% of cases were node-negative breast cancer (69.5%). ER-positive and HER2-positive breast cancer were 62.2% and 17.0%, respectively. G2 tumors were more common than G1 and G3 tumors. Preoperative chemotherapy was performed in 13% of cases. LCIS cases was 3% of in situ cases. In the anatomic staging system, Stage 0 to IV were 20.7%, 38.9%, 30.7%, 9.0% and 0.8%, respectively. In the prognostic staging system, stage 0 to IV were 22.4%, 39.2%, 16.1%, 14.4% and 0.9%, respectively. There were 541 cases with missing stages in the prognostic staging system.

Conclusions: The prognostic staging system increased the proportion of stage I and III, whereas the proportion of stage II was decreased. Staging migrations were commonly observed in early breast cancer according to the prognostic staging system.

PO208

MOLECULAR COMPARISON OF MOLECULAR SUBTYPES OF TRIPLE-NEGATIVE BREAST CANCER DERIVED FROM REVERSE-PHASE PROTEIN ARRAYS AND MRNA ANALYSIS

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Background: Gene expression analyses have identified molecular subtypes of TNBC. However, these subtypes are not well defined enough to enable development of targeted therapy or new treatment strategies. In a previous study, we identified TNBC subtypes at the protein level using functional proteinomics; reverse-phase protein arrays (RPPAs) to move TNBC classification into clinical practice. In the present study, we compared them with mRNA-based molecular subtypes (TNBCtype-7, TNBCtype-4, and PAM50) using a single-institution data set unique in its results of both RPPA and mRNA analyses.

Methods: In the previous study, we identified two stable subtypes of TNBC using RPPAs: the DNA damage-related and inflammation and hormonal subtypes. Statistically, k-means cluster analysis enabled us to identify five RPPA subtypes. Fifty-seven RPPA samples had matching mRNA expression profiles. Normalized, annotated gene expression data were fed into the online subtyping tool TNBCtype to identify the subtypes in these TNBC samples. Association testing for the samples' classifications according to RPPA-based clusters and gene expression-based subtypes was carried out using the Fisher exact test.

Result: Comparison of the sample classification using the five RPPA-based k-means cluster subtypes and TNBCtype-7 demonstrated a significant association ($p = 0.017$). Both mRNA analyses and RPPAs identified the basal-like 1 (BL1) and BL2 molecular subtypes. Furthermore, we identified three additional TNBC subtypes using RPPAs. However, they were not concordant with mRNA-based molecular subtypes.

Conclusions: Both RPPA and mRNA analysis can classify the BL1, BL2, and non-basal subtypes of TNBC. Functional proteinomics demonstrated the potential for distinguishing more specific TNBC subtypes, such as inflammation and hormonal subtype.

PO209

ANALYSIS OF THE RELATIONSHIP BETWEEN MICRO-CALCIFICATION AND PROGNOSTIC FACTORS IN BREAST CANCER PATIENTS

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Background: To investigate the correlation between the prognosis of the breast cancer patients and mammographic calcification.

Methods: A total of 1035 breast cancer patients with complete clinical information were collected. According to mammographic calcification before operation, the cases were divided into calcification group and non-calcification group. The influence of calcification on the positive expression rate of ER, PR, Her-2, and the relationship between calcification and tumor size, axillary lymph node status, histological grade, molecular classification and prognosis were analyzed.

Result: The rate of calcification in the patients with axillary nodes metastasis was significantly higher than the group without lymphatic metastasis (53.6% ,47.1%) ($p < 0.05$); In Her-2 positive breast cancers, the rate of calcification was significantly higher than Her-2 negative group (63.3%, 45.3%) ($p < 0.05$); In molecular typing, the rate of Luminal A, Luminal B, Her-2 and triple negative breast cancer were 39.4%, 49.3%, 68.3% and 38.8%, showing significant differences among four groups ($p < 0.05$). In survival analysis, it had not found obvious difference between the calcification group and non-calcification group.

Conclusions: The breast carcinomas with micro-calcification in mammographic X-ray were associated with the expression of Her-2, molecular typing and axillary lymph node status, and it can provide reference for the development of breast cancer treatment strategies to a certain degree. But there was no significant correlation between calcification and survival, and the value in evaluating prognosis remains to be further studied.

PO210

E- BASED DECISION AID FOR WOMEN MAKING SURGERY TREATMENT DECISION AFTER BREAST CANCER DIAGNOSIS: DEVELOPMENT AND PILOT TEST

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Background: Women with earlier stage may receive breast conservative surgery. However, most women need to undergo mastectomy and having an option to receive breast reconstruction.The aim of this study was to examine the effect of E-based decision support on womens decision related outcomes.

Methods: Quasi-Experimental Designs with convenience sampling was used in this study. Women aged over 20 years, diagnosed breast cancer, and recommended for mastectomy by doctors were recruited. Paper-based education and E-based decision support which assisted women to clarify their needs and value via website were implemented. Outcomes including decisional conflict, preparation of decision making and satisfaction of appearance were measured before the intervention, after the intervention and the first outpatient visit after surgery.

Result: There were 15 women participated in this study, and 12 women completed all follow-up measures. The results showed that women's Decisional Conflict Scale score decreased significant after the intervention ($p = 0.003$). However, there were no significant difference on the preparation of decision making and satisfaction of appearance.

Conclusions: The study showed that the paper-based education combined with E-based decision support could decrease women's decisional conflict. Because of the small sample size and short-term follow-ups, the results of the effect of the intervention should be validated in the future.

PO211

TECHNOLOGICAL ISSUE IN USING WEB-BASED SURVEY SYSTEMS IN ASIAN AMERICAN CANCER RESEARCH

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Background: With an increasing number of racial/ethnic minorities in the cancer care field, the use of multiple languages in a web-based survey system becomes essential and frequently adopted to generate multilingual versions of web-based questionnaires. However, the challenges in the use of web-based survey systems in multilingual cancer research have rarely been reported. The purpose of this study is to explore challenges in generating multiple language versions (English, Mandarin Chinese, Korean, and Japanese) of a Web-based questionnaire in Asian Americans breast cancer survivorship research.

Methods: The REDCap system was used for the study. Throughout the study, team members kept written records of the issues. The issues were discussed in biweekly team meetings. Then, the written records and team meeting memos were analyzed using the content analysis to identify the themes reflecting the challenges in the system.

Result: Five themes of challenges were identified: a) necessities in modifying the instructions given by original instruments; b) necessities in managing different versions across institutes; c) limitations in system usages when using languages other than English; d) difficulties in ensuring consistencies (e.g., instructions, responses) across different languages; and e) lack of engineers with experience in multilingual survey. Future researchers need to a) check the instructions in existing instruments, b) be aware of technological limitations and strategize the methods to deal with the limitations, and c) set strategies to ensure consistencies across different languages and different versions of Web-based systems.

Conclusions: The use of Web-based systems is highly feasible for multiple languages. However, unexpected challenges need to be carefully considered.

PO212

THE EFFICACY OF JAPANESE SCALP-COOLING SYSTEM FOR THE PREVENTION OF CHEMOTHERAPY-INDUCED HAIR LOSS IN BREAST CANCER PATIENTS

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Background: Scalp cooling techniques have been applied to prevent or at least reduce chemotherapy-induced alopecia since the 1970s. I had the opportunity to exploit the computer-controlled chilled helmet-like silicon cap system. Therefore, in this setting, Id like to show the effectiveness of scalp cooling in preventing alopecia using our newly developed device called RV-01.

Methods: The RV-01 employs a digitized system for controlled scalp-cooling by an integrated refrigerator into a control unit. This contracts the blood vessels around hair roots or follicle, thus limiting the amount of cancer drugs reaching the hair follicles. 29 patients with operable primary cancer were subjected to scalp cooling during adjuvant chemotherapy administration using this system. Mean age was 48.0 (range 31 70) years. We used Deans scale and NCI-CTC scale as the visual analoge scale on hair loss for evaluation.

Result: None of the 29 patients treated with (F)EC regimen, 15 cases, DOC regimen (2 cases), DOC+H regimen (one case) and weekly Paclitaxel, 11cases ever used a wig. Hair loss in these patients ranged from G-0 to G-3 by NCI-CTC scale and G-0 to G-2 by Deans scale. Discomfort such as headache, being chilled, and scalp pain were also assessed but scalp-cooling was very well tolerated in our series of clinical trial.

Conclusions: In our experience, we proved that scalp hypothermia is one approach used to prevent hair loss especially for breast cancer patients. Scalp-cooling with RV-01 has also proven to be effective in the prevention of chemotherapy-induced hair loss.

PO213

CLINICOPATHOLOGIC FEATURES OF BREAST CANCER PATIENTS AND THE RELATIONSHIP BETWEEN QUALITY OF SLEEP, ANXIETY, DEPRESSION AND QUALITY OF LIFE OVER TIME DURING THE EARLY TREATMENT PERIOD

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Background: Quality of sleep (QOS), anxiety, depression and quality of life (QOL) are common issues among breast cancer patients. Prospective longitudinal studies of QOS, anxiety, depression and QOL in breast cancer patients are lacking. The aim of this study is to determine whether there is a proper treatment point associated with QOS, anxiety, depression and QOL during early treatment of breast cancer patients.

Methods: We used four self-report questionnaires about QOS, anxiety, depression and QOL. QOS was measured using Pittsburgh Sleep Quality Index, anxiety was measured with Beck Anxiety Inventory, depression was measured with Beck Depression Inventory, and QOL was measured with Quality of Life Enjoyment and Satisfaction Questionnaire - Short Form, respectively. Patients were assessed at the time of surgery, at the beginning of chemotherapy and the end of chemotherapy. Clinicopathologic information was collected for analysis.

Result: Fifty two patients were enrolled in this study, and 29 completed 3 times of self-report questionnaires. QOS, anxiety and depression showed no difference through the early treatment period. However, QOL changed during the same period ($p = 0.004$). Type of breast surgery (total mastectomy vs. breast conserving surgery) showed relationship with QOS through all the treatment period and with anxiety only at the time of surgery ($p = 0.002$).

Conclusions: QOL of breast cancer patients continuously changed during the early treatment period. Patients undergoing breast conserving surgery experienced other problems at different timing. In this study, we could identify other needs for breast cancer patients depending on the timing of early treatment.

PO214

EFFECT OF A COMBINED AEROBIC AND RESISTANCE EXERCISE INTERVENTION ON ENDOTHELIAL FUNCTION IN BREAST CANCER SURVIVORS

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Background: Mortality in breast cancer survivors (BCS) is largely attributable to cardiovascular diseases (CVD). Flow-mediated dilation (FMD) is the direct biomarker of endothelial function which measures diameter changes in arterial endothelium based on increased blood flow; reduced FMD is present in patients with CVD. The purpose of this study is to examine the effect of a 16-week combined aerobic and resistance exercise intervention on endothelial function in BCS.

Methods: BCS (Stage I-III) were randomized to the exercise (EX) or control (CON) groups. The 16-week exercise intervention consisted of 3 weekly aerobic sessions and 2 weekly resistance exercise sessions. FMD was measured using ultrasound; baseline diameter (D0) and peak diameter of 1min after cuff deflation (D1) [FMD (%) = (D1-D0) / D0 × 100]. Paired sample t-tests and repeated measures ANOVA were used to examine the effect of exercise.

Result: At baseline, the EX and CON groups did not differ by age (53.7 ± 8.9 years), BMI (27.8 ± 5.7 kg/m^2), and systolic/diastolic blood pressure (124.7 ± 23.1/78.9 ± 12.0 mmHg). Post-exercise, FMD increased from baseline in EX (7.01 ± 1.44% to 9.09 ± 1.13%; $p = 0.054$). FMD decreased from baseline (8.06 ± 2.24% to 6.78 ± 2.82%; $p = 0.34$) in CON. There was no group by time interaction in FMD following the 16-week intervention ($p = 0.053$).

Conclusions: Although endothelial function improvements did not reach statistical significance, possibly due to small sample size, our results provide evidence of the positive effects of exercise on improving endothelial function. Fully-powered studies are needed to determine whether exercise can be used to improve endothelial function, and if these improvements reduce CVD mortality in BCS.

PO215

RECURRENT NODULAR FASCIITIS OF BREAST MIMICKING BREAST CANCER

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Background: Nodular Fasciitis of breast is a rare benign proliferative lesion which resembles malignancy clinically and radiologically. It is known to resolve spontaneously. However, recurrence after wide excision has been rarely reported.

Methods: At 2011, a 51-years old woman visited our hospital due to an incidentally found left breast mass. Ultrasonography detected 1.7 cm-sized BIRADS 5 mass at upper-inner quadrant of left breast. Core needle biopsy (CNB) section of this lesion showed spindle cell proliferation and frequent abnormal mitosis suggesting malignant stromal cell tumor. She underwent breast conserving surgery. The tumor was composed of proliferation of spindle cells with minimal cellular atypia. The tumor cells were positive for smooth muscle actin and S-100. Based on these pathologic features, the tumor was confirmed as nodular fasciitis.

Result: After 6 years, the patient complained painful palpable mass at previous operation site. Ultrasonography revealed 4.1cm-sized hypoechoic, elastographically hard mass with irregular and spiculate margins arising at operation scar. The mass was extended toward posterior pectoralis major muscle. In spite of the strong assumption of malignant tumor, CNB section showed similar findings from previous slides. Muscle infiltration and nuclear positivity for B-catenin were additionally found at wide excision specimen. These differences made the diagnosis in favor of desmoid-type fibromatosis.

Conclusions: Nodular fasciitis of breast can be hard to distinguish from breast cancer especially when it recurs after surgery. Awareness of clinical, radiological, and histopathological characteristics of nodular fasciitis is important to make appropriate decision.

PO216

PRIMARY SQUAMOUS CELL CARCINOMA OF THE BREAST: A CASE REPORT

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Background: Primary squamous cell carcinoma of the breast is a very rare and constituting <0.1% of invasive breast cancers.

Methods: A 61-years-old woman presented to a palpable mass in the left upper breast which diagnosed 6 months ago and grows with pain from a month ago. Mammography showed an oval circumscribed hyperdense mass associated perilesional edema and overlying skin thickening in the upper portion of the left breast. Ultrasonography showed a 6 cm sized oval circumscribed heterogenous mass with angular margin in the upper portion of the left breast. US-guided core needle biopsy was performed on the left breast lesion and the histopathological examination of the biopsy specimen revealed epidermal cyst. Surgical excision was performed and pathologic examination showed epidermal inclusion cyst with focal squamous cell carcinoma. The patient underwent a wide local excision of the left breast and pathologic examination showed epidermal inclusion cyst with focal squamous cell carcinoma. Gross examination revealed a 6 cm tumor with huge central cystic space located in the upper portion of the left breast.

Result: Sections show a cyst in the dermis with a proliferating epidermal component and laminated keratin (black arrow) (Hematoxylin and Eosin stain, ×40). The proliferative areas are made up of squamous epithelium with nuclear atypia and adjacent infiltration into the surrounding dermis (Hematoxylin and Eosin stain, ×100).

Conclusions: We report a rare case of primary squamous cell carcinoma arising in proliferative epidermoid cyst of the breast in a 61-year-old female patient.

PO217

DERMATOFIBROSARCOMA PROTUBERANS OF THE BREAST

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Background: Dermatofibrosarcoma protuberans (DFSP) of the breast is an extremely rare malignancy with only a few cases reported in the literature. Confusion is possible with other primary breast lesions.

Methods: A 54-year-old woman presented with a 1-month history of a right breast mass. Mammography revealed a spiculated mass in the upper outer quadrant of her right breast. Breast sonography confirmed the presence of lesions measuring 1.9 cm and 1.2 cm. A percutaneous biopsy was performed, showing spindle cell tumor with bland spindle cells with fascicular growth pattern. The patient underwent wide excision of the tumor. Immunohistochemical and histological findings consisted with DFSP. Since surgical margins were free of the tumor, re-excision was not performed. There was no evidence of recurrence in annual follow up of mammography and sonography.

Result: However, three years after the surgery, a right breast mass was identified in self and clinical breast examination. The mass was found out to be a recurrent DFSP measuring 4.2 cm in Brest MRI. Radical mastectomy with immediate breast reconstruction using free transverse rectus abdominis myocutaneous flap was performed.

Conclusions: We present a rare case of DFSP of the breast. Awareness of this entity, immunohistochemistry and image studies, including breast MRI, is needed for proper diagnosis and complete surgical excision with wide margins is recommended for management of DFSP.

PO218

DERMATOFIBROSARCOMA OF THE BREAST: A CASE REPORT

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Background: Dermatofibrosarcoma protuberans (DFSP) is a locally aggressive malignant neoplasm of the subcutaneous tissue, frequently appears on the proximal extremities and the trunk. Its occurrence in the breast is extremely rare.

Methods: A 61-year-old female visited our breast clinic for palpable mass on her right upper-inner breast. After diagnostic work-up and excisional biopsy, she was diagnosed with DFSP and underwent wide excision with tumor free margin. The clinical records, imaging studies, and pathologic reports were reviewed.

Result: The patient presented hard, painless lump which was about 3 cm in diameter on the right upper inner breast on physical examination. The lump was rapidly growing for the past one month. On mammogram, about 2 cm sized lobulated contoured mass was identified on the right upper-inner breast. On sonogram, about 2 cm sized macro-lobulated mixed echoic mass was noted on RUI area. She underwent excisional biopsy and DSFP was diagnosed. Pathologic report with immunohistochemistry revealed 3 cm sized tumor composed of spindle cells arranged in storiform pattern and mitotic count was upto 9/10 HPF with positive resection margin. Breast MRI, bone scan, and PET-CT revealed no other lesion. To obtain a negative surgical resection margin, wide excision was performed. Immunohistochemistry showed positive CD34, Beta-catenin and negative SMA, Desmin, S-100, and CK5/6.

Conclusions: DFSP of the breast is a very rare disease and surgical resection obtaining negative resection margin is a treatment of choice. Axillary dissection is not indicated unless enlarged lymph nodes exist clinically. The role of adjuvant therapy is not established.

PO219

LONG TERM FOLLOW UP OF PRIMARY SMALL CELL CARCINOMA OF THE BREAST: 7-YEAR FOLLOW UP

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Background: Primary small cell carcinoma (SCC) of the breast accounts for less than 1% of primary breast cancers. Due to the rarity of this type of tumor and the lack of a standard treatment, we report here a case study of primary small cell carcinoma of the breast.

Methods: A 58-year-old female patient presented with a painless mass in right breast for 2 months. An ultrasound scan revealed solid and low heterogeneous echoes in the right breast. A mass was poorly differentiated with irregular borders.

Result: She underwent modified radical mastectomy. Microscopically, the mass was about 2.2 cm × 1.8 cm × 1.6 cm, which was diagnosed histologically SCC with glandular differentiation. Histological examination demonstrated 1 positive lymph node out of 25 axillary lymph nodes. A search for a non-mammary primary site was carried out, especially focusing on pathologic changes in the lungs. The result of CT scans of the neck, chest, and abdomen were all within normal limits. As a result, we concluded that the breast was the primary site. The patient was treated with doxorubicin in combination with cyclophosphamide followed by docetaxel. After the initial treatment, the patient was clinically monitored for disease relapse and metastasis. She is alive and well, 7-year after diagnosis and treatment.

Conclusions: Treatment for the SCC of the breast has not yet been established, and a consensus has yet to be reached. Role of surgery in local control and chemotherapy regimen of doxorubicin in combination with followed by docetaxel are showing excellent survival.

PO220

EXPERIENCE IN USING WATSON-FOR-ONCOLOGY AS A CLINICAL DECISION SUPPORTING SYSTEM (CDSS) FOR BREAST CANCER TREATMENT

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Konyang University Hospital, Korea

Background: One year after introduction of Watson for oncology (WFO) as a Clinical Decision Supporting System in cancer treatment. Recently, we tried to share the experience of using WFO in Konyang University Hospital to investigate the role of CDSS such as WFO in breast cancer treatment.

Methods: We retrospectively studied 100 patients who underwent adjuvant chemotherapy for breast cancer at Konyang University Hospital immediately before the introduction of WFO in April, 2017. We reviewed clinical data for 100 patients including age, stage, histologic characteristics, chemotherapy ect.

Result: The mean age of the 100 patients was 58.8 years (30–85). The stage was 43 patients in the first stage, 44 patients in the second stage, and 12 patients in the fourth stage. The concordance rate between actual chemotherapy and Watson's cancer treatment (recommendation + consideration) was 48% (48/100). Stage I: 17/43 (39.5%) stage II: 24/44 (55.8%) [stage 2A: 13/31 (41.9%), 2B: 11/13 (84.6% 7/12 (58.3%) and stage IV: 0/1 (0%), respectively. Most of the discrepancies between the chemotherapy proposed by WFO and the chemotherapy actually used were dose dense AC followed by paclitaxel.

Conclusions: We need to evaluate the clinical stability of the chemotherapy such as dose-dense regimen in Korea and to evaluate its benefit. Joint research on the use of AI-based CDSS such as WFO in the process of applying the system developed in the US to Korea, problem of authentication procedure for application of AI to medical treatment, medical stability problem, and development of Korean CDSS Interest is needed.

PO221

ANALYSIS OF SURVIVAL OUTCOMES BASED ON MOLECULAR SUBTYPES IN BREAST CANCER BRAIN METASTASES: A SINGLE INSTITUTIONAL COHORT

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Background: To evaluate the survival outcomes based on molecular subtypes of breast cancer in patients with brain metastasis.

Methods: We retrospectively reviewed 106 breast cancer patients treated for brain metastases, from January 2005 to May 2016. Patients were divided into four groups based on the tumor molecular subtype: Estrogen Receptor (ER)/Progesterone Receptor (PR) positive and human epithelial growth factor receptor-2 (HER2) negative, ER/PR and HER2 positive, HER2 (HER2 positive and ER/PR negative), and Triple negative (TNBC), respectively.

Result: The median follow-up time for surviving patients was 22 months (range: 11.2-51.1 months). The median survival of all patients was 14 months, with a 1-year overall survival (OS) rate of 57.5% and a 2-year OS rate of 32.1%. Thirty patients (28.3%) had a solitary brain metastasis while 62 (58.5%) patients had multiple metastases. A significant difference was observed in the survival rates of the two groups. Based on the Karnofsky performance score, the performance status of the patients at the time of brain metastasis was also found to affect survival. Patients with different molecular subtypes had different survival rates; the ER/PR positive and HER2 negative group showed the highest median survival (23.1 months), ER/PR/HER2 positive: 15.0, HER2: 12.5 and TNBC: 6.4 months, respectively, which was statistically significant ($p = 0.001$).

Conclusions: In breast cancer patients with brain metastasis, survival rates were different based on the molecular subtype of the tumor, despite various local and systemic treatments. Appropriate and tailored treatment approaches should, therefore, be considered for the different molecular subtypes.

REFERENCES
1. Ian Smith, Denise Yardley, et al. , J Clin Oncol 35, 2017
2. Jack Cuzick, et al. Lancet Oncol 2010; 11: 1135 - 41, 2010

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PRODUCT INFORMATION

【 성분 • 함량 】 1정(약 103mg)중 주성분 : 아나스트로졸 (별규) 1.0mg【 성 상 】 백색의 원형 필름코팅정【 효능 • 효과 】 1. 폐경기 이후 여성의 진행성 유방암의 치료(이 요법 이전의 타목시펜 치료시 암성반응을 나타내지 않는 에스트로겐 수용체 음성인 환자에서, 이 약의 유효성은 입증되지 않았다.) 2. 호르몬 수용체 양성인 폐경기 이후 여성의 조기 유방암의 보조 치료. 3. 조기 유방암의 보조 요법으로 2~3 년간 타목시펜을 투여 받아온 호르몬 수용체 양성인 폐경기 이후 여성 환자의 조기 유방암의 보조 치료.【 용법 • 용량 】 • 성인 : 아나스트로졸로서 1일 1회 1mg을 경구투여한다. • 소아 : 18세 이하 소아에게는 투여하지 않는다. • 신장애 환자 : 경증 또는 중등도의 신장애 환자는 용량을 변경할 필요가 없다. 중증 신기능장애 환자(크레아티닌청소율이 30 mL/min 이하인 환자)에서는 이 약을 투여하지 않는다. • 간장애 환자 : 경증의 간장애 환자는 용량을 변경할 필요가 없다. 중등도 이상의 간장 질환자에서는 이 약을 투여하지 않는다.【 사용상의 주의사항 】 1. 경고 1) 이 약은 폐경기 이전의 여성에게는 안전성 및 유효성이 입증되지 않았기 때문에 사용하지 않아야 한다. 폐경기 상태가 의심스러운 경우 폐경기 여부를 생화학적으로 확인 하여야 한다. 2) 이 약은 중등도 또는 중증의 간장애 및 중증의 신장애 환자(크레아티닌 클리어런스가 30mL/min 이하)에 대해서는 시험되지 않았다. 3) 이 약은 순환 에스트로겐을 낮추므로 골무기질 밀도를 감소시켜서 골절의 위험을 증가시킬 수 있다. 4) 골다공증 및 골다공증 위험이 있는 환자에게 치료 시작 및 그 후 일정한 간격으로 골밀도에 대하여 시험(예. DEXA scanning)하여야 한다. 골다공증 치료 및 예방법이 적절하게 시행되어야 하고 주의 깊게 모니터링 해야 한다. 5) LH-RH 계열과 아나스트로졸 병용에 대한 연구가 이루어지지 않았다. 이 병용요법을 임상에서 사용해서는 안된다. 2. 다음의 환자에는 투여하지 말 것. 1) 폐경기 이전의 여성 2) 임부 또는 임신하고 있을 가능성이 있는 여성, 수유부 3) 중증의 신장애 환자 (크레아티닌청소율이 30mL/min 이하인 환자) 4) 중등도 이상의 간장애 환자 5) 이 약 또는 이 약의 구성성분에 과민반응이 있다고 알려진 환자 6) 타목시펜 병용투여 환자 또는 에스트로겐을 함유하는 모법중인 환자(이 약의 약리작용을 감소시키기 때문에 병용해서는 안된다.) 7) 이 약은 락토오스를 포함하고 있다. 드물게 나타나는 갈락토오스 불내성(galactose intolerance), Lapp 유당분해효소 결핍증(Lapp lactase deficicy) 또는 포장-갈락토스 흡수장애(glucose-galactose mala-bsorption)등의 유전적인 문제가 있는 환자에게는 투여하면 안 된다.【 저장방법 】 밀폐용기 30℃ 이만에서 보관
【 포장단위 】 28정
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References

1. 뉴라펙프리필드시린지주 품목허가증 (제50228호) 2. ESMO Poster Session P1500 (2014) / Support Care Cancer (2016) 24:1709–1717

3. Invest New Drugs (2014) 32(4):636–643

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