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한국유방암학회
Korean Breast Cancer Society

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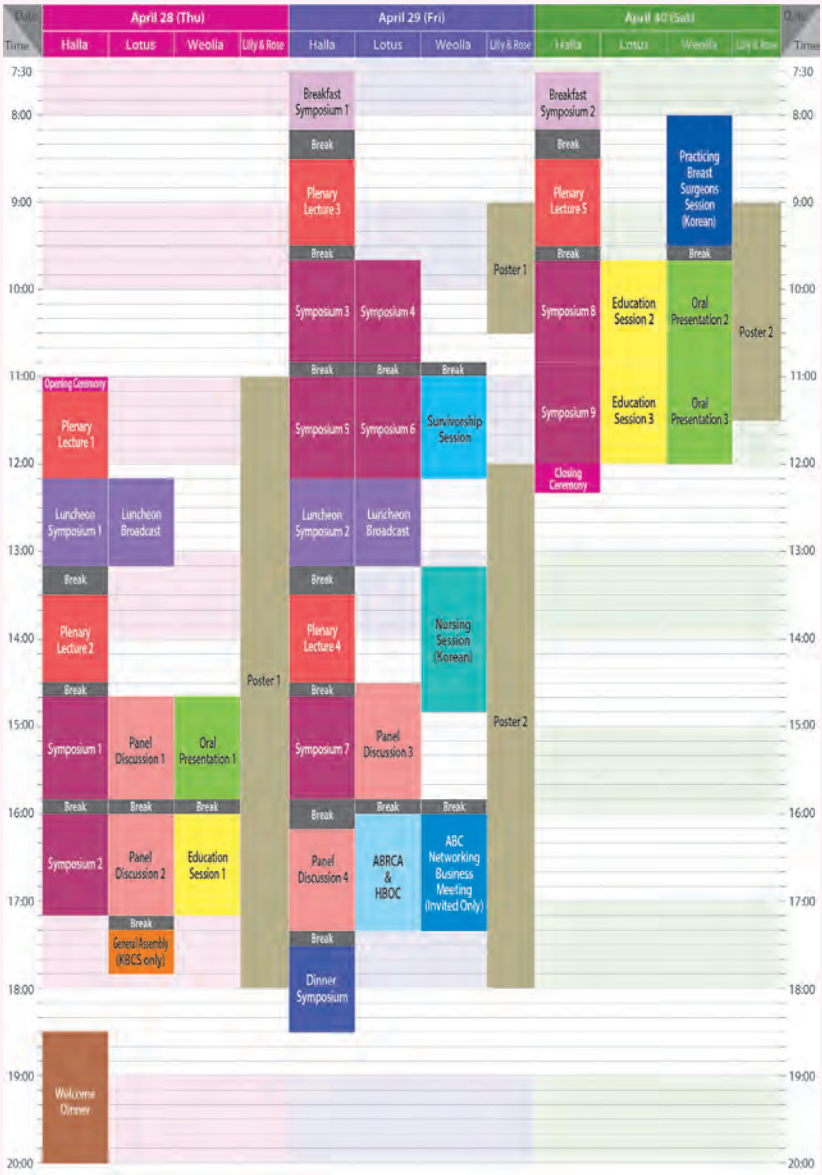
TABLE OF CONTENTS

PROGRAM AT A GLANCE



PROGRAM DETAILS

DAY 1

April 28(Thu)

Plenary Lecture 1 — 11:10-12:10

Current indications of Radiation Therapy — Halla

Moderator Doo Ho Choi
Samsung Medical Center, Korea

Speaker Bruce Haffty — 2
Rutgers Cancer Institute of New Jersey, U.S.A.

Luncheon Symposium 1 — 12:10-13:10

Optimized Endocrine Treatment Strategy in ER+ Post Meno ABC Management — Halla

Moderator Jung Han Yoon
Chonnam National University Hwasun Hospital, Korea

Speaker Antonio Llombart Cussac — 89
Medical Oncology Hospital Arnau de Vilanova in Valencia , Spain

Coffee Break 13:10-13:30

Plenary Lecture 2 — 13:30-14:30

Precision Medicine Based on Genomics in Breast Cancer — Halla

Moderator Young-Hyuck Im
Samsung Medical Center, Korea

Speaker Jorge Reis-Filho — 3
Memorial Sloan Kettering Cancer Center, U.S.A.

Coffee Break 14:30-14:40

Symposium 1 — 14:40-15:50

DCIS – What's New? — Halla

Moderator Thinh Dang Huy Quoc
Ho Chi Minh City Oncology Hospital, Vietnam

Moderator Yong-Sheng Wang
Shandong Cancer Hospital & Institute, China

Speaker So Yeon Park — 22
Molecular and Pathological Changes During Progression from in situ to Invasive Cancer
Seoul National University College of Medicine, Seoul National University Bundang Hospital, Korea

Speaker Jeong Eon Lee — 24
Personalized Treatment of DCIS
Samsung Medical Center, Korea

Speaker Mehra Golshan — 26
No Surgery for DCIS?
Dana Farber Cancer Institute, Brigham and Women's Hospital, U.S.A.

Panel Discussion 1 — 14:40-15:50

Circulating Tumor DNA – Myth or Reality? — Lotus

Moderator Eun Sook Lee
National Cancer Center, Korea

Speaker Jorge Reis-Filho 10
Clinical Utility of CtDNA in Breast Cancer
Memorial Sloan Kettering Cancer Center, U.S.A.

Speaker Seung Il Kim 11
Clinical Implications of Circulating Tumor Cells of Breast Cancer Patients: Role of Epithelial-Mesenchymal Plasticity
Yonsei University College of Medicine, Korea

Oral Presentation 01 — 14:40-15:50

Weolla

Moderator Jeong Soo Kim
The Catholic University of Korea Uijeongbu St. Mary's Hospital, Korea

Moderator Woo-Chan Park
The Catholic University of Korea Yeouido St. Mary's Hospital, Korea

Speaker Elif Candan 103
DETERMINATION OF ANTI-CANCER MECHANISMS OF GOSSYPETIN AND LUTEOLIN IN COMBINATION WITH CHEMOTHERAPEUTIC CYCLOPHOSPHOAMIDE ON MCF-7 HUMAN BREAST CANCER CELL LINES
Fatih University, Turkey

Speaker Govind Babu K 104
DEVELOPMENT AND VALIDATION OF PERSONALIZED EX VIVO PLATFORM MIMICKING PATIENT HETEROGENEOUS TUMOR MICROENVIRONMENT TO ENABLE PERSONALIZED TREATMENT FOR BREAST CANCER
Kidwai, India

Speaker Wei Xiong Wen 106
HI-PLEX FOR HIGH THROUGHPUT MUTATION SCREENING OF BRCA1, BRCA2, TP53, AND PALB2 IN BREAST AND OVARIAN CANCER PATIENTS
Cancer Research Malaysia, Malaysia

Speaker Alan Prem Kumar 107
DEAD-BOX RNA HELICASE DP103 AS A BIOMARKER FOR THERAPEUTIC RESPONSE TO DOCETAXEL
National University of Singapore, Singapore

Speaker Sun Young Min 108
THE BASIC FACTS OF KOREAN BREAST CANCER IN 2013 : RESULTS OF A NATIONWIDE SURVEY AND BREAST CANCER REGISTRY DATABASE
Kyung Hee University School of Medicine, Korea

Speaker Sang Hyeok Woo 109
IDENTIFICATION OF MOLECULES ASSOCIATED WITH TAMOXIFEN RESISTANCE THROUGH GENE EXPRESSION PROFILING OF TAMOXIFEN-RESISTANT BREAST CANCER CELLS
Korea Institute of Radiological & Medical Sciences, Korea

Speaker Rajiv Sarin 110
INHERITED PREDISPOSITION FOR BREAST CANCER IN DIVERSE HEREDITARY CANCER SYNDROMES: STRATEGIES FOR SYNDROME SPECIFIC GENETIC TESTING AND RISK MANAGEMENT
Tata Memorial Centre, India

Speaker Young-Hyuck Im 111
EFFICACY AND SAFETY OF EVEROLIMUS AND EXEMESTANE IN PATIENTS WITH ADVANCED BREAST CANCER FROM ASIA AND AFRICA: ASIAN SUBSET RESULTS FROM THE PHASE 3B EVEREXES STUDY
Samsung Medical Center, Korea

Coffee Break 15:50-16:00

Symposium 2 **16:00-17:10**
Optimal Breast Irradiation for Breast Cancer **Halla**

Moderator Kyung Hwan Shin
Seoul National University Hospital, Korea
Moderator Bruce Haffty
Rutgers Cancer Institute of New Jersey, U.S.A.
Speaker Won Park 27
Current Perspectives on Radiation Therapy in Autologous and Prosthetic Breast Reconstruction
Samsung Medical Center, Korea
Speaker Bruce Haffty 28
Regional Nodal Management in Breast Cancer: From Z11 to AMAROS
Rutgers Cancer Institute of New Jersey, U.S.A.
Speaker Sung-Ja Ahn 29
Tumor Bed Boost Integration during Whole Breast Radiotherapy: A Review of the Current Evidence
Chonnam National University Medical School, Korea

Panel Discussion 2 **16:00-17:10**
Biomarker Driven Clinical Trial Design in the Era of Precision Medicine in Breast Cancer **Lotus**

Moderator Janice Tsang
Queen Mary Hospital, University of Hong Kong, Hong Kong
Speaker Zhengyan Kan 12
A Molecular Portrait of Asian Breast Cancer: Multi-omics and Immune Profiling of a Prospective Breast Cancer Cohort Enriched in Young, Premenopausal Patients
Pfizer, Inc., U.S.A.
Speaker Yeon Hee Park 14
Innovative Clinical Trial in the Era of Genomics
Samsung Medical Center, Korea

Education Session 1 **16:00-17:10**
Current and Future Role of Neoadjuvant Therapy for Breast Cancer **Weolla**

Moderator Kyung Hae Jung
ASAN Medical Center, Korea
Moderator Visnu Lohsiriwat
Medicine Siriraj Hospital, Mahidol University, Thailand
Speaker Mehra Golshan 59
Surgical Issues in Patients with Breast Cancer Receiving Neoadjuvant Chemotherapy
Dana Farber Cancer Institute, Brigham and Women's Hospital, U.S.A.

Speaker	In Hae Park	61
	Neoadjuvant Therapy of Early Stage HER2-Positive Breast Cancer: Latest Evidence and Clinical Implications	
	National Cancer Center, Korea	
Speaker	Wonshik Han	63
	Neoadjuvant Endocrine Therapy in Breast Cancer	
	Seoul National University Hospital, Korea	

General Assembly (KBCS only) **17:20-17:50**
Lotus

Welcom Dinner **18:30-20:00**
Halla

DAY 2

April 29(Fri)

Breakfast Symposium 1 07:30-08:10

Getting Targeted Therapy Development Up-to-date in Breast Cancer — Halla

Moderator Kweon Cheon Kim
Chosun University Hospital, Korea

Speaker Joohyuk Sohn — 84
Yonsei Cancer Center, Korea

Coffee Break 08:10-08:30

Plenary Lecture 3 08:30-09:30

Maximizing Cosmetic and Oncologic Outcomes with Oncoplastic Techniques — Halla

Moderator Chanheun Park
Kangbuk Samsung Hospital, Korea

Speaker Jean-Yves Petit — 4
European Institute of Oncology, Italy

Symposium3 09:40-10:50

Additional Imaging Modality for the Management of Breast Cancer Patients — Halla

Moderator Woo Kyung Moon
Seoul National University Hospital, Korea

Moderator Louis Wing-Cheong Chow
Macau University of Science and Technology, Macau

Speaker Nariya Cho — 31
How to Use Magnetic Resonance Imaging Following Neoadjuvant Chemotherapy in Locally Advanced Breast Cancer
Seoul National University College of Medicine, Seoul National University Hospital, Korea

Speaker Sung-Eun Kim — 33
Current Role and Challenge of PET-CT in Breast Cancer
Korea University Anam Hospital, Korea

Speaker Sang Moo Lim — 34
PET/MR in Breast Cancer
Korea Institute of Radiological & Medical Sciences, Korea

Symposium 4 09:40-10:50

Breast Cancer Survivorship in Precision Medicine Era — Lotus

Moderator Min Hyuk Lee
Soon Chun Hyang University Hospital, Seoul, Korea

Moderator Janice Tsang
Queen Mary Hospital, University of Hong Kong, Hong Kong

Speaker Xiao-Ou Shu — 36
Influence of Lifestyle Factors on Breast Cancer Prognosis
Vanderbilt University, U.S.A.

Speaker John Hopper 37
Evidence that Germline Genetic Factors Influence Survivorship from the Australian Breast Cancer Family Study
University of Melbourne, Australia

Speaker Min-Woo Jo 38
Quality Adjusted Life Years Loss due to Breast Cancer in Korea
University of Ulsan College of Medicine, Korea

Coffee Break 10:50-11:00

Symposium 5 **11:00-12:10**
Role of Cytotoxic Chemotherapy in the Era of Personalized Medicine **Halla**

Moderator Keun Seok Lee
National Cancer Center, Korea

Moderator Paul Mainwaring
Mater Medical Center, South Brisbane, Queensland University, Australia

Speaker Stefan Glück 40
Nab-Paclitaxel in Breast Cancer: Clinical Development and Future Directions
Celgene Corporation, U.S.A.

Speaker Alison Jones 41
Eribulin Mesylate in the Management of Metastatic Breast Cancer
Leaders In Oncology Care, United Kingdom

Speaker Yee Soo Chae 42
Non-Anthracycline Adjuvant Chemotherapy
Kyungpook National University Medical Center, Korea

Symposium 6 **11:00-12:10**
Potential of Overcoming Resistance to HER2-Targeted Therapies **Lotus**

Moderator Jungsil Ro
National Cancer Center, Korea

Moderator Yoon Sim Yap
National Cancer Centre Singapore, Singapore

Speaker Seock-Ah Im 43
PIK3CA Mutations in HER2-Positive Breast Cancer
Seoul National University Hospital, Korea

Speaker Yoon Sim Yap 44
Overcoming HER2 targeted therapy: Ongoing Challenge
National Cancer Centre Singapore, Singapore

Speaker Tae-Young Yoon 45
Precision Medicine Guided By Single-Molecule Imaging
Yonsei University, Korea

DAY 2

Survivorship Session 11:00-12:10

Advanced Care and Research in Breast Cancer Survivorship — Weolla

Moderator Sung Hoo Jung
Chonbuk National University Hospital, Korea

Moderator Rajiv Sarin
Tata Memorial Centre, India

Speaker Juhee Cho — 74
Communication and Unmet Needs of Patients/Families/Caregivers
Sungkyunkwan University School of Medicine, Korea

Speaker Jung-Won Lim — 76
Patient Navigation Services for Breast Cancer Survivors
Kangnam University, Korea

Speaker Jong Won Lee — 77
M-Health Application beyond Quality of Life for Breast Cancer Survivors
ASAN Medical Center, Korea

Luncheon Symposium 2 12:10-13:10

Rethinking Neoadjuvant Therapy: Neoadjuvant Therapy as a Platform for Drug Development in HER2 Positive Breast Cancer — Halla

Moderator Nam Sun Paik
Ewha Womans University Cancer Center for Women, Korea

Speaker Jee Hyun Kim — 91
Seoul National University Bundang Hospital, Korea

Coffee Break 13:10-13:30

Nursing Session (Korean) 13:10-14:50

Current Issues for Management of Breast Cancer Treatment — Weolla

Moderator Mi Young Kang
Cheil General Hospital & Womens Healthcare Center, Korea

Speaker Jung A Do — 96
Nursing Care in Endocrine Therapy
Cheil General Hospital & Womens Healthcare Center, Korea

Speaker Jin-Hee Park — 97
Chemotherapy-Related Cognitive Function in Patients with Breast Cancer
Ajou University College of Nursing, Korea

Speaker Mi Sook Han — 98
Chemotherapy Induced Peripheral Neuropathy Breast Cancer Patients
Inha University Hospital, Korea

Speaker Onam Ok — 99
Nursing Care in Cardiotoxicity
Samsung Medical Center, Korea

Speaker Hyun Seo — 101
Nursing Management for Patients with Advanced Breast Cancer Wound
Ewha Womans University Mokdong Hospital, Korea

DAY 2

Plenary Lecture 4 — 13:30-14:30

What is the Next Goal of HER-2 Targeted Therapy — Halla

Moderator Sung-Bae Kim
ASAN Medical Center, Korea

Speaker Hope Rugo 6
University of California San Francisco Medical Center, Korea

Coffee Break 14:30-14:40

Panel Discussion 3 — 14:30-15:50

What is the Best in Breast Cancer Surgery? — Lotus

Moderator Jean-Yves Petit
European Institute of Oncology, Italy

Speaker Byung Ho Son 16
Surgery of the Primary Tumor in De Novo Metastatic Breast Cancer: To do or Not to do
ASAN Medical Center, University of Ulsan College of Medicine, Korea

Speaker Eun Sook Lee 17
Minimally Invasive, Maximal Outcomes in Breast Surgery
National Cancer Center, Korea

Speaker Anees Cagpar 18
Cavity Shave Margins : Method and Impact On Practice
Yale University School of Medicine, U.S.A.

Symposium 7 — 14:40-15:50

Challenging Treatment for TNBC — Halla

Moderator Gyungyub Gong
ASAN Medical Center, Korea

Moderator Seigo Nakamura
Showa University School of Medicine, Japan

Speaker Joon Jeong 46
Molecular Heterogeneity of TNBC and Methods of Classification
Gangnam Severance Hospital, Yonsei University, Korea

Speaker Masakazu Toi 48
The Future of Personalized Therapy in Triple-Negative Breast Cancer
Kyoto University Hospital, Japan

Speaker Naoto Ueno 49
New Treatment Directions for Triple-Negative Breast Cancer
The University of Texas MD Anderson Cancer Center, U.S.A.

Coffee Break 15:50-16:10

DAY 2

ABRCA & HBOC Session 16:00-17:20
Lotus

Moderator Sung-Won Kim
Daerim St. Mary's Hospital, Korea

Moderator Timothy Rebbeck
Harvard TH Chan School of Public Health and Dana Farber Cancer Institute, U.S.A.

Speaker Timothy Rebbeck 79
Precision Medicine for Cancer: the BRCA1/2 Paradigm
Harvard TH Chan School of Public Health and Dana Farber Cancer Institute, U.S.A.

Speaker Ava Kwong 80
Management of Hereditary Breast Cancer: Advances and Controversies
The University of Hong Kong, Hong Kong

Speaker Soo-Hwang Teo 81
Gene-Panel Sequencing in the Context of the Prediction of Breast-Cancer Risk in Asia
Cancer Reseaerch Malayisa, Malaysia

Asian Breast Cancer Networking Business Meeting (Invited Only) 16:00-17:20
Weolla

Panel Discussion 4 16:10-17:20
Challenging Treatments for CNS Metastasis from Breast Cancer
Halla

Moderator Joohyuk Sohn
Yonsei Cancer Center, Korea

Speaker Bora Lim 19
Current Challenges in Treating Breast Cancer Patients with Metastasis to Brain, Sneak Peak of Upcoming Biology
The University of Texas, MD Anderson Cancer Center, U.S.A.

Speaker Kyubo Kim 20
Current Issues in the Management of Brain Metastases from Breast Cancer
Ewha Womans University School of Medicine, Korea

Coffee Break 17:20-17:30

Dinner Symposium 17:30-18:30
Determining the Optimal Adjuvant Chemotherapy for Lower or Intermediate Risk of Breast Cancer - Who Should Receive Adjuvant Chemotherapy?
Halla

Moderator Sehwan Han
Ajou University Hospital, Korea

Speaker Kyoung Eun Lee 93
Ewha Womans University Mokdong Hospital, Korea

April 30(Sat)

Breakfast Symposium 2 — 07:30-08:10

Prophylaxis of Febrile Neutropenia: Experiences with Adjuvant TAC — Halla

Moderator Sung Yong Kim
Soon Chun Hyang University Hopital, Cheonan, Korea

Speaker Jihyoun Lee 86
Soon Chun Hyang University Hospital, Seoul, Korea

Coffee Break 08:10-08:30

Practicing Breast Surgeons Session (Korean) — 08:00-09:30

Ultimate Tips of VABB Device — Weolla

Moderator Heeboong Park
Park Surgical Clinic, Korea
Se Min Oh
Dr. Oh's Breast Center, Korea

Speaker Soo Jin Kim
Comparison of the Pros & Cons of VABB Devices, Bexcore, Mammotome and Encore
Chungdam Seoul Breast Clinic, Korea

Speaker Dong Seok Lee
Prevention and Management of VABB Complication
Bunhongbit Hospital, Korea

Speaker Jeong Kyeung Kim
Knowhow to Perfrom VABB for Technically Difficult Accessible Breast Masses
Subareolar Mass. Breast Mass Nearby Skin. Larger than 5cm Size Breast Mass
Maria Breast Clinic, Korea

Speaker Kyung Ho Cha
VABB Can Be an Excellent Tool for Biopsy of Microcalcifications:
Micropure Guided VABB, J Wire Guided VABB
Mamma Breast Clinic, Korea

Speaker Tae Ik Eom
Management of Premalignant Lesions after VABB.
ADH, ALH, LCIS, Flat Epithelial Atypia, Columnar Cell Change, Papillary Lesions, Phyllodes Tumor
HiU Breast Clinic, Korea

Speaker Junseok Lee
Legal Consulting for Running Breast Clinic: Medical Insurance Issues with Law Firm
Sunwoo LLC, Korea

Plenary Lecture 5 — 08:30-09:30

Two Decades at the NSABP - B27 to 57, and Unsolved Mysteries — Halla

Moderator Dong-Young Noh
Seoul National University Hospital, Korea

Speaker Soonmyung Paik 7
Yonsei University College of Medicine, Korea

Coffee Break 09:30-09:40

Symposium 8 09:40-10:50

Enhancing Endocrine Therapy for ER-Positive Breast Cancer: Co-Targeting Signaling Pathways — Halla

Moderator Jin Seok Ahn
Samsung Medical Center, Korea

Moderator Hideko Yamauchi
St. Luke's International Hospital, Japan

Speaker In-Chul Park 51
Sensitization of Breast Cancer Cells to Chemotherapeutic Drugs by Metabolic Regulation
Korea Institute of Radiological & Medical Sciences, Korea

Speaker Young-Jin Suh 52
Cross-Talk between Adiponectin and IGF-IR in Breast Cancer
The Catholic University of Korea, Vincent's Hospital, Korea

Speaker Joohyuk Sohn 53
Bidirectional Crosstalk between the ER and HER2 Signaling Pathways : From Bench to Bedside
Yonsei Cancer Center, Korea

Education Session 2 09:40-10:50

Immune-Oncologic Approaches as Innovative Therapeutic Strategy for Refractory Breast Cancer — Lotus

Moderator Tae Hyun Kim
Inje University Busan Paik Hospital, Korea

Moderator Leisha A Emens
Johns Hopkins University-School of Medicine, U.S.A.

Speaker Hee Jin Lee 64
Value of Immune Infiltration to Predict Therapeutic Outcomes
ASAN Medical Center, University of Ulsan College of Medicine, Korea

Speaker Leisha A Emens 65
Immune Targeting in Breast Cancer
Johns Hopkins University-School of Medicine, U.S.A.

Speaker David Page 67
Combination Immunotherapy Approaches: Chemotherapy, Radiation Therapy, and Dual Checkpoint Therapy
Providence Portland Cancer Center, Earle A. Chiles Research Institute, U.S.A.

Oral Presentation 2 09:40-10:50 — Weolla

Moderator Young Up Cho
Inha University Hospital, Korea

Moderator Ho Yong Park
Kyungpook National University Hospital, Korea

Speaker	Tutku Ozarpaci	113
	INVESTIGATION OF CYTOTOXIC AND APOPTOTIC EFFECTS OF URTICA DIOICA AGGLUTININ ON MCF-7 AND L929 CELL LINES *Fatih University, Turkey*	
Speaker	Bo Hwa Choi	114
	SCREENING BY ABBREVIATED BREAST MAGNETIC RESONANCE IMAGING (MRI) IN WOMEN WITH A HISTORY OF BREAST CANCER OPERATION *Konkuk University Medical Center, Korea*	
Speaker	Jae Yang Lim	115
	ANALYSIS OF INTERVAL BREAST CANCER WITH A SINGLE CENTER DATASET *Dr. Lim's Breast Clinic, Korea*	
Speaker	Hideko Yamauchi	117
	ESTIMATING THE COST OF WORK LOSS OF CANCER SURVIVORS IN JAPAN *St. Luke's International Hospital, Japan*	
Speaker	Yun Gyoung Kim	118
	THE RISK FACTORS OF PREGNANCY-ASSOCIATED BREAST CANCER IN KOREAN WOMEN *Korea Cancer Center Hospital, Korea*	
Speaker	Tsutomu Takashima	119
	EFFICACY OF DOCETAXEL, TRASTUZUMAB AND PERTUZUMAB COMBINATION REGIMEN FOR HER2-POSITIVE METASTATIC BREAST CANCER *Osaka City University Graduate School of Medicine, Japan*	
Speaker	Il Yong Chung	120
	INFLUENCE OF BODY MASS INDEX AT DIAGNOSIS IN RELATION TO HORMONE RECEPTOR, MENOPAUSAL AND NODAL STATUS ON BREAST CANCER PROGNOSIS *ASAN Medical Center, Korea*	
Speaker	Heewon Kim	121
	THE DISTRIBUTION OF PROBANDS AND BRCA CARRIERS FROM 4 ASIAN BREAST CANCER STUDIES (SINGAPORE, CHINA AND KOREA) *Seoul National University College of Medicine, Korea*	

Symposium 9 — 10:50-12:00

New Area for Anti-Cancer Drug Development in Breast Cancer — Halla

Moderator	Jin-Hee Ahn *ASAN Medical Center, Korea*	
Moderator	Christina Galvez *St Luke's Medical Center, Global, Philippines*	
Speaker	Soohyeon Lee	55
	Combination Strategy in Cancer Immuno-Oncology Drug Development *Pfizer Korea, Korea*	
Speaker	Hyeong-Gon Moon	56
	The Tumor Microenvironment: A Driving Force for Breast Cancer Progression *Seoul National University College of Medicine, Korea*	
Speaker	Elgene Lim	57
	Targeting the Androgen Receptor in Breast Cancer *Garvan Institute of Medical Research, Australia*	

DAY 3

Education Session 3 — 10:50-12:00

New Paradigm for Overcoming Endocrine Resistance — Lotus

Moderator Sei-Hyun Ahn
ASAN Medical Center, Korea

Moderator Masakazu Toi
Kyoto University Hospital, Japan

Speaker Jee Hyun Kim — 68
New Paradigm for Overcoming Endocrine Resistance - Targeting CDK 4/6
Seoul National University Bundang Hospital, Korea

Speaker Woochul Noh — 70
PI3K/mTOR Pathway
Korea Cancer Center Hospital, Korea

Speaker Kyong Hwa Park — 71
ESR1 Mutations-A Mechanism for Acquired Endocrine Resistance in Breast Cancer
Korea University Anam Hospital, Korea

Oral Presentaion 3 — 10:50-12:00

Weolla

Moderator Jeong Eon Lee
Samsung Medical Center, Korea

Moderator Lee Su Kim
Hallym University Sacred Heart Hospital, Korea

Speaker Zeynep Ulker Akal — 122
SYNTHESIZATION, CHARACTERIZATION OF FOLIC ACID AND QUERCETIN FUNCTIONALIZED MAGNETIC NANOPARTICLES RESEARCH ON BREAST CANCER CELL LINE FOR HYPERTHERMIA AND TARGETED DRUG DELIVERY APPLICATIONS
Fatih University, Turkey

Speaker Kevin Nguyen — 123
BREAST CANCER RISK ASSOCIATIONS WITH DIGITAL MAMMOGRAPHIC DENSITY BY MAMMOGRAPHY DENSITY THRESHOLDS AND MAMMOGRAPHY SYSTEM
The University of Melbourne, Australia

Speaker Vivian Shin — 125
TARGETING A NOVEL CHEMORESISTANCE GENE, ZBTB2, TO OVERCOME CISPLATIN-RESISTANCE IN TRIPLE-NEGATIVE BREAST CANCER
The University of Hong Kong, Hong Kong

Speaker Jeeyeon Lee — 127
THE ROLE OF PREOPERATIVE BREAST MAGNETIC RESONANCE (MR) IMAGING FOR SURGICAL DECISION IN PATIENTS WITH TRIPLE-NEGATIVE BREAST CANCER
Kyungpook National University Hospital, Korea

Speaker Jong Oh Lee — 128
CHANGES OF ABDOMINAL FAT DISTRIBUTION AFTER ENDOCRINE THERAPY IN BREAST CANCER PATIENTS
Hanyang University College of Medicine, Korea

Speaker Hong Kyu Jung — 129
DEVELOPMENT OF SECOND PRIMARY CANCERS IN KOREAN BREAST CANCER SURVIVORS
Soon Chun Hyang University Hospital, Seoul, Korea

Speaker	Moo Hyun Lee	130
	THE PRECISE QUANTIFICATION OF PROGESTERONE RECEPTOR COULD BE AN ALTERNATIVE TO THE RECURRENT SCORE IN HORMONE RECEPTOR-POSITIVE EARLY BREAST CANCER *National Cancer Center, Korea*	
Speaker	Takafumi Sangai	131
	SIX-YEAR FOLLOW UP OF BREAST-CONSERVING SURGERY USING SUPINE MAGNETIC RESONANCE IMAGING IN BREAST CANCER PATIENTS RECEIVING PRIMARY SYSTEMIC THERAPY *Chiba University, Japan*	

Closing Ceremony **12:00-12:30**

Halla

POSTER EXHIBITION

- **GBCC Abstract Book**
- **GBCC Publication Committee**
  Editor-in-chief: Chang Wan Jeon
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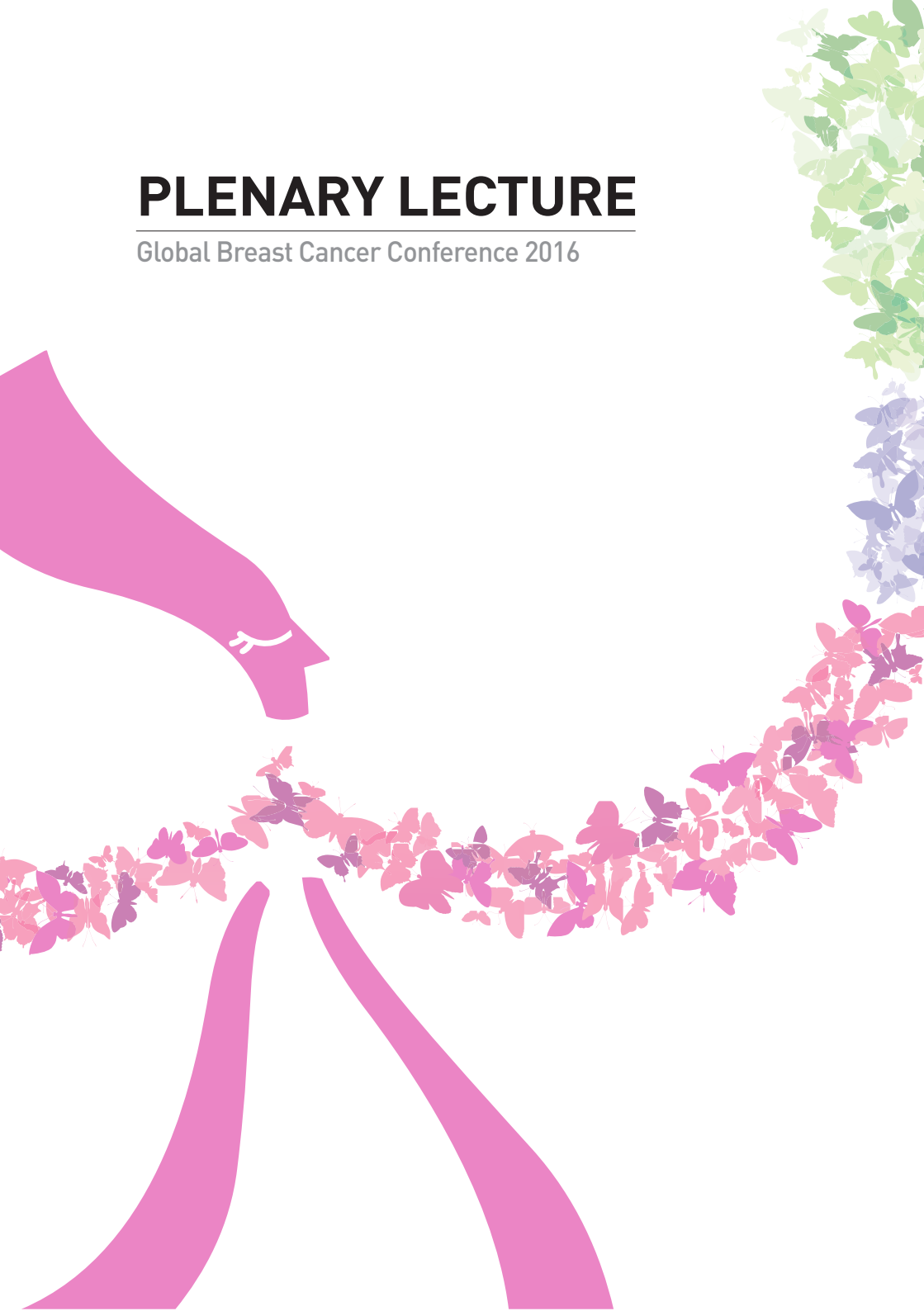
PLENARY LECTURE

Global Breast Cancer Conference 2016



CURRENT INDICATIONS OF RADIATION THERAPY

Bruce Haffty

Department of Radiation Oncology, Rutgers Cancer Institute of New Jersey, U.S.A.

The past 10 years has been accompanied by a major shift in the approach to whole breast irradiation. Traditionally, after breast conserving surgery, radiation is delivered to the whole breast over the course of 6-7 weeks using fraction sizes of 180-200 cgy daily. While this approach has been the accepted standard, recent approaches including hypofractionated whole breast radiation over the course of 3-4 weeks, accelerated partial breast irradiatiaon over the course of 1-2 weeks, and intraoperative radiation have evolved. During this lecture we will discuss the various approaches to radiation after breast conserving surgery, the available data, controversies, risks and benefits of each of these approaches. Avialable prospective randomized and evolving data will be discussed as will current national guidelines and standards. Selection criteria and relative contraindications for each of these approaches will be presented and future directions for research will be discussed. Elimination of radiation in selected patients after breast conserving surgery will also be discussed. At the completion of the lecture the participant should have gained an understanding of all of the available options for radiation after breast conserving surgery and have a better understanding of the risks and benefits of each of these approaches.

PRECISION MEDICINE BASED ON GENOMICS IN BREAST CANCER

Jorge Reis-Filho

Department of Pathology, Memorial Sloan Kettering Cancer Center, U.S.A.

MAXIMIZING COSMETIC AND ONCOLOGIC OUTCOMES WITH ONCOPLASTIC TECHNIQUES

Jean-Yves Petit

Department of Plastic Surgery, European Institute of Oncology, Italy

In Europe, oncoplastic surgery usually refers to any type of plastic procedure performed to improve the results of the conservative treatment. Now Breast Conservative Treatment (BCT) is widely accepted to treat T1 and small T2 breast cancer. However; in large breast a conservative treatment can also be proposed for tumours larger than T2. The quadrantectomy can induce breast volume asymmetry and local deformities. Glandular defects or scar retraction as well as nipple areola complex (NAC) dislocations are other types of cosmetic failures. To better evaluate these deformities, both breasts should be prepped up and draped and the patient should be elevated in a sitting position at the end of the BCT procedure. Most of the deformities can be avoided immediately by using simple tricks, which can be performed by breast surgeons without any training in plastic surgery: optimal positioning of the scar, transposition of the NAC to avoid dislocation, better evaluation of the symmetry. In our experience at the EIO, only 10 to 15% of BCT require a more sophisticated plastic surgery procedure to improve the final cosmetic result. When this reconstruction is performed after completion of BCT, the most convenient technique to replace the volume is a lipo-transfer.. The procedure can be performed usually with local anesthesia with minimum scarring. Different ongoing studies are performed in our institute to demonstrate the safety of lipo-transfer in cancer patients. The difficulties of delayed glandular reshaping after breast irradiation justify immediate partial reconstruction. In these cases, trained plastic surgeons should be called upon immediately to improve the partial reconstruction. In such cases, the plastic surgeon should be involved in the preoperative planning with the cancer surgeon and the patient. The glandular reconstruction can be performed with volume displacement or volume replacement techniques. Volume displacement with glandular flaps is easily feasible and safe in very dense breasts (mainly glandular as shown on the mammogram). But when the breast is fatty, with a low radiologic density, these glandular flaps should be avoided, because there is a high risk of necrosis after fat undermining and mobilization. In case of fatty breasts and large resection, classic mammoplasty procedures should be preferred if simple closure of the lumpectomy cavity is not feasible. In theory, volume replacement could be done with prosthesis, but

implants are not recommended during BCT because postoperative radiotherapy will increase the risk of capsular contracture and poor cosmetic results. Latissimus dorsi, such as the miniflap technique, is a good solution to replace the resected volume. Local perforator flaps have been described recently; delicate dissection of small perforator vessels can allow the rotation of axillar skin flaps inside the breast to fill up the defect.

WHAT IS THE NEXT GOAL OF HER-2 TARGETED THERAPY

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The last almost two decades have brought about a marked change in the treatment and prognosis of HER2 positive disease in both the early and late stages, with the now routine use of trastuzumab as well as increasing use of novel antibodies, tyrosine kinase inhibitors and immunotoxins. Despite these new and effective treatments, there remain significant challenges. The most critical area is to be able to understand and identify mechanisms of resistance, and apply appropriate combination therapies early enough to make an impact on disease outcome. This has proven to be a greater challenge than initially expected, although a series of new agents have demonstrated efficacy in trastuzumab resistant disease including novel antibodies, tyrosine kinase inhibitors, and toxins. Additional challenges include understanding the biologic differences between hormone receptor negative and hormone receptor positive disease. Ideally, this information would then be used to provide a more individualized treatment approach. For hormone receptor positive disease, new therapeutic approaches may reduce resistance to hormone therapy with prolonged overlap of HER2 targeted agents with hormone therapy in the adjuvant setting showing intriguing results. Preventing and treating brain metastases remains an important issue; newer tyrosine kinase inhibitors such as ONT380 may offer hope and are being actively investigated. In addition to evaluating new therapies, it is critical that less toxic options be explored. All patients clearly do not need all therapies, and less may be more in patients with early stage, highly responsive disease reducing both toxicity and cost. An abbreviated course of chemotherapy combined with trastuzumab has been demonstrated to be highly effective and well tolerated as adjuvant therapy for small cancers, and combinations of antibodies without chemotherapy may also be a possible option, as we continue to struggle with trying to identify which patients can avoid anthracyclines without compromising efficacy. Short course neoadjuvant therapy with the immunotoxin trastuzumab emtansine has results in impressive rates of pathologic complete responses in hormone receptor positive disease. In the ATTEMPT trial, trastuzumab emtansine is being compared to short course paclitaxel with a year of trastuzumab as treatment for stage I HER2 positive disease. In this talk, many of the issues outlined above will be explored in the context of evolving therapies and clinical trials.

TWO DECADES AT THE NSABP - B27 TO 57, AND UNSOLVED MYSTERIES

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Fisher brothers' publication about the failure of regional lymph node as a barrier to cancer cell spread in 1966 challenged Halsted-Virchow dogma. Through NSABP trials B-04 and B-06, which was conducted with great difficulty in the face of heavy resistance from the disciples of Halsted, the dogma was finally disproven. However, the results from these two trials further underscored the need to develop systemic therapies even for node negative breast cancer as evidenced in 25-year follow up of NSABP B-04 by Bernard Fisher.

Through the efforts of William McGuire and many others, breast cancer became the first solid tumor for which molecular subtype specific systemic therapy was developed based on estrogen receptor status. Hence by the time Fisher designed trials for node negative breast cancer, two trials had to be designed based on ER status, one for ER+ (NSABP B-14) and the other for ER- (NSABP B-13). Both trials were positive but 20% recurrence rate at 10 years for tamoxifen treated ER+ patients stimulated testing of adding chemotherapy to tamoxifen for ER+ node negative breast cancer (NSABP B-20). Positive results from B-20 and decreased incidence of contralateral breast cancer in tamoxifen treated patients in B-14 together with preclinical data convinced Fisher that breast cancer treatment can be unified into a common theme of neoadjuvant chemotherapy followed by post-neoadjuvant tamoxifen (NSABJP B-18) with pCR as a surrogate marker for long term chemotherapy benefit. He wanted to demonstrate that delta-pCR predicts delta-survival by testing the addition of taxane to AC (B-27). I joined Fisher when B-27 was being discussed in 1995. By then, breast cancer specialists have begun to realize the necessity of big Ns for for clinical trials testing new drugs due to excellent baseline prognosis. The solution to these dilemmas was delivered through a totally unexpected route.

During the conduct of NSABP B-31 for trastuzumab, accuracy of companion diagnostics has become an issue and that experience led to founding of Genomic Health Inc. by Steve Shak who was the program director for trastuzumab at Genentech. We collaborated to develop methods to multiplex mRNA expression analysis using degraded

RNA extracted from formalin fixed paraffin embedded (FFPE) tumor tissue - leading to the development of OncotypeDx. While OncotypeDx is now in routine use in USA and some other countries, there are many unsolved issues; 1) high cost prevents its global utilization - can we develop a robust test that costs below $500? 2) Many competing gene expression-based assays have been just endorsed by ASCO for the same clinical utility. Indeed, this decision was supported by a meta-analysis by Wirapati et al which demonstrated that these tests all robustly identify low proliferating ER+ tumors as low risk. However, in reality, there is a significant problem. Unlike in meta-analysis in which all cases were normalized and genes were standardized before applying various prognostic algorithms, real testing involves different technical platforms and single sample classifier algorithms that utilize within sample reference genes. As a result, they do not agree with each other in as much as 30-40% of the time. What do we do when the same patient is classified as low risk by OncotypeDx and high risk by ProSigna? Then there are important unsolved mysteries involving lobular invasive carcinoma; 1) should lobular invasive ca treated with chemotherapy? 2) can we apply OncotypeDx to lobular invasive ca? 3) if tamoxifen is inferior to AIs as suggested by BIG 1-98, should we use ovarian suppression plus AI instead of tamoxifen for premenopausal lobular invasive ca?

While inaccuracy of companion diagnostics surfaced as a result of a central review and translational studies of the archived tumor samples from NSABP B-31, ironically it also suggested the unthinkable - HER2 negative patient may also benefit from trastuzumab, possibly as an anti-stem cell therapy. This is being tested in NSABP B-47.

Whether we can use delta-pCR as a surrogate of delta-survival remains unanswered, especially for triple negative breast cancer, for which neoadjuvant trials are most needed as illustrated by FDA meta-analysis. Genome sequencing of residual TNBCs revealed what a daunting problem we are facing - many tumors are dark matters and otherwise every tumor has a unique potentially actionable targets. Unfortunately, total mutation burden of most TNBCs do not reach a level of sensitivity to immune checkpoint therapy.

Unsolved mysteries abound, breast cancer remains a fertile ground for clinical and translational research for young investigators.

PANEL DISCUSSION

Global Breast Cancer Conference 2016

CLINICAL UTILITY OF CTDNA IN BREAST CANCER

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CLINICAL IMPLICATIONS OF CIRCULATING TUMOR CELLS OF BREAST CANCER PATIENTS: ROLE OF EPITHELIAL-MESENCHYMAL PLASTICITY

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Circulating tumor cells (CTCs) are defined as tumor cells circulating in the peripheral blood of patients, shed from either the primary tumor or a metastatic site. The presence of CTCs in the peripheral blood of cancer patients was recognized more than a century ago. In patients with breast cancer, metastasis is the main reason for cancer mortality. Although the survival rate has increased, thanks to early detection and improved adjuvant therapy, the occurrence of distant metastases remains high. Distant relapse after definitive local treatment indicates that there might be undetected spread of the tumor at the time of primary local treatment. It has been shown that cells can be shed from the tumor at all stages of the disease, and these cells may remain in the patients circulation for lengthy periods after initial treatment of the primary tumor. For this easons, researchers have been interested in CTCs because these cells could represent an important link to the process of metastasis. In addition, CTCs may become a valuable tool to refine prognosis. Several clinical trials have established the correlation between the presence of CTCs at diagnosis and decreased progression free survival and overall survival in patients with breast cancer. Furthermore, a potential role of CTCs for the prediction of esponsiveness of systemic chemotherapy in adjuvant setting has been rapidly expanding. Finally, CTCs are a potential source of biological information that can be used to predict responsiveness to various targeted agents. In this way, a paradigm shift may be introduced in the treatment strategy, from the present one that is based only on primary tumor characteristics to the future one that considers molecular characterization of CTCs as well. Here we will discuss the technical aspects of different detection methods and possible clinical application of CTCs in patients with breast cancer. In conclusion, current prognostic and predictive factors are inefficient and the information regarding CTCs could Circulating Tumor Cells 129 provide an additional clue. Although CTCs research in breast cancer has rapidly expanded, the clinical relevance of CTCs has not been firmly established. Further optimization and standardization of CTCs detection techniques could lead to the inclusion of CTCs detection in daily clinical practice. Molecular characterization of CTCs might open the new horizon in improving tailored treatment.In the future, identify circulating cancer stem cell may clarify the metastatic cascade and may help develop new targets in cancer treatment.

A MOLECULAR PORTRAIT OF ASIAN BREAST CANCER: MULTI-OMICS AND IMMUNE PROFILING OF A PROSPECTIVE BREAST CANCER COHORT ENRICHED IN YOUNG, PREMENOPAUSAL PATIENTS

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Breast cancers (BC) in younger, premenopausal patients (YBC) tend to be more aggressive with worse prognosis, higher chance of relapse and poorer response to endocrine therapies compared to breast cancers in older patients (OBC). The proportion of YBC (age ≤ 40) among BC in East Asia is estimated to be 16-32%, significantly higher than the 7% reported in Western countries. Genomic and molecular characterizations have deepened our understanding of breast cancer biology in areas ranging from intrinsic subtypes to treatment responses, however, the molecular bases of Asian YBC remains poorly characterized. We have performed whole-exome sequencing (WES), whole-transcriptome sequencing (WTS) and high coverage targeted sequencing on tumor and matched normal samples from 133 Korean BC patients consisting of 74 YBC cases (age ≤ 40). We further performed immunohistochemistry (IHC) analyses to characterize tumor-infiltrating lymphocytes (TILs) in 46 tumors using four markers (CD45, CD4, CD8 and CD163). We found that BRCA1/2 germline deleterious mutations are enriched in YBC and the ER+/HER2- subtype, indicating that Asian ER+ YBC has a significant germline contribution. MutSig analysis4 identified ARID1A as a significantly mutated gene, implicating chromatin modeling as a cancer driver in Asian BC. Differential expression analyses suggested that Asian YBC differ in energy metabolism and are more active in protein synthesis than OBC tumors, whereas OBC is more proliferative than YBC. Using gene expression signatures representing distinct immune cell types and immunohistochemistry, we classified our cohort into four subtypes of varying TIL activities: high, medium, low and quiet. The majority of immunogenic cases with high TIL levels lie in ER+ or HER2+ subtypes although higher proportion is seen in TNBC. Moreover, YBC tumors appear to harbor lower levels of TIL activities than OBC, suggesting that younger patients may be less likely to benefit from immuno-

modulatory therapies than older patients. To our knowledge, this is the first large-scale multi-omics study of Asian breast cancer and would significantly contribute to the compendium of molecular data available for young, premenopausal breast cancer. While the major landmarks in the molecular and immune landscape of Asian BC look similar to that of the predominantly Caucasian BC cohorts, we have identified a number of distinguishing characteristics pointing to distinctive oncogenic mechanisms underlying Asian BC.

INNOVATIVE CLINICAL TRIAL IN THE ERA OF GENOMICS

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Precision medicine, employing genome-guided biomarkers and theranostics, has changed the clinical trial recruitment and reporting landscape. An increasing number of clinical trials have an eligibility component requiring the absence or presence of a specific molecular variant to validate predictive biomarkers, which are defined as gene variants that inform or recommend therapeutic action. For example, basket trials and umbrella trials both recruit on the basis of predictive biomarkers but the study designs differ. Basket trials test one drug based on one molecular target in a variety of tumor types, whereas umbrella trials test a variety of drugs, with several molecular targets in a single tumor type. The actionability of predictive biomarkers with respect to patient treatment options differentiates them from biomarkers used for diagnostic and prognostic purposes.

Genomic studies have shown that breast cancer includes large number of rare genomic segments. This led to the development of precision medicine where sequencing could be used to identify drivers in individuals, who would be treated accordingly. Ten to twenty molecular alterations are being investigated in the context of biomarker-driven therapeutic trials. This includes PIK3CA, AKT1, ERBB2, PTEN, BRCA1/2, ESR1 mutations, FGFR1, CCND1 amplifications, AR expression. Beyond the question of clinical utility of detecting these variants, there are several challenges that precision medicine is facing in breast cancer.

However, given the genetic and epigenetic instability of cancer cells, it is likely that each new drug or combination of drugs targeting the tumor cells will meet with more complex mechanism fo acquired resistance. The recent failures of prospective trials testing precision medicine (SAFIR01, SHIVA) highlights the need to better understand what defines a targetable alteration. These trials also pointed out the need to target the molecular alterations, rather than the pathway. Also, its important to better understand the role that alterations on multiple drivers could play on resistance. Furthermore, breast cancers as other solid tumors exhibit inter-patient and intra-tumoural genomic variability which underpins our understanding of intrinsic drivers of the disease.

Now, one of the major challenges will be to integrate immunotherapeutics in the application field of precision medicine especially for innovative adaptive clinical trials. High mutational loads and neoantigen expression could predict efficacy of immunotherapeutics. Further combination with targeted therapies should be rationalized based on genomics. The T cell response is adaptable and can accommodate not only tumor heterogeneity but also responses to novel antigens expressed by recurring tumors.

In summary, while candidate biomarkers exist and technologies are available, clinical trials of precision medicine failed to deliver until now for patients with breast cancer.

In conclusion, now we face the era of incorporation of immune-oncology into precision medicine, though there are still ongoing randomized trials testing drugs according to genomic alterations.

SURGERY OF THE PRIMARY TUMOR IN DE NOVO METASTATIC BREAST CANCER: TO DO OR NOT TO DO

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The true value of the surgical removal of the primary tumor in patients with de novo metastatic or stage IV breast cancer is currently unknown. Retrospective studies have showed mixed conclusion on this issue although some reported survival advantages. The recently published RCT data did not show survival benefit from surgical resection of the primary tumor in de novo metastatic breast cancer, however, this study has a few limitations.

About 5%-10% of patients with newly diagnosed breast cancer have distant metastases at first presentation, and these patients are primarily given systemic therapy, which includes chemotherapy, endocrine therapy, and target therapy. What about surgery of the primary tumor after responding to these therapies?

So far, there are no guidelines on how to manage these patients with de novo metastatic or stage IV breast cancer, and the treatment decisions are often made upon clinicians experience or patient preference. Until strong evidences are available, ABC2 recommends that surgery of the primary tumor should not be offered as a routine practice but can be discussed on a case-by-case basis and offered to selected patients.

There are some points of consideration related to surgery of the primary tumor, which includes surgery type and timing, patient selection, small metastatic lesions detected on modern CT or PET-CT, and new targeted drugs, etc.

Overview of literature about surgery of the primary tumor in de novo metastatic breast cancer and discussion on the question - to do it or not to do it - are intended to do.

MINIMALLY INVASIVE, MAXIMAL OUTCOMES IN BREAST SURGERY

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There is longstanding controversy that does the local therapy influence mortality. The concept of tumor biology Fisherian paradime appeared a worthy successor to the Halstedian centrifugal spread of cancer. However, there is increasing evidence that not all the breast cancer are systemic disease. Prevention of local recurrence can save lives, local control does matter.

Recently, onco-plastic breast surgery has revolutionized the field of breast conserving surgery. The final aims of this technique are to obtain an adequate resection margin that will reduce the rate of local recurrence while simultaneously improving cosmetic outcomes. The use of skin and nipple areolar sparing mastectomy with autologous tissue or implant reconstruction is markedly increasing along with magnetic resonance imaging (MRI) assessment of the breast. A latissimus dorsi flap is known to be a feasible option for reconstruction of breast volume in total mastectomy, breast conservation surgery after large volume excisions for women with relatively larger or multi-centric operable breast cancer, and in some locally advanced breast cancers post neo-adjuvant chemotherapy.

Our hospital of NCC, Korea performed 153 cases of skin sparing mastectomy and immediate breast reconstruction using latissimus dorsi pedicled flap between March 2003 and September 2013. The median follow up period was 64.6months. The mean age was 42.8 years. The average hospital stay was 10.9 days. There were four cases of reoperation due to three skin necrosis and one partial flap necrosis. Seroma is a main postoperative complication (42.4%), but that was well controlled with conservative management. The other complications were arm edema (2.0%), limited range of motion (2.6%) and wound infection (3.3%). Most of patients were satisfied with the cosmetic results. We also conducted 325 cases of NAC sparing mastectomy with implant reconstruction.

Skin sparing mastectomy and immediate breast reconstruction can be reliable and useful, with low morbidities, and produced a sufficiently high level of patient satisfaction.

CAVITY SHAVE MARGINS: METHOD AND IMPACT OF PRACTICE

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Positive margin rates after partial mastectomy (breast conserving surgery) have been reported to be 20-40%. A number of retrospective studies had suggested that resection of cavity shave margins may reduce positive margin and re-excision rates. We will discuss the results of a randomized controlled trial of routine cavity shave margins on positive margin and re-excision rates, recently reported in the New England Journal of Medicine. In this study of 235 patients with stage 0-3 breast cancer, surgeons were instructed to perform their standard partial mastectomy with or without resection of selective margins. Patients were randomized intraoperatively to either resect further tissue circumferentially around the cavity (shave) or to have no further tissue taken (no shave). Groups were well-matched in terms of baseline characteristics. Prior to randomization, the rates of positive margins and the volume of tissue taken were not significantly different between the two groups. After randomization, patients in the shave group were significantly less likely to have a positive margin (19% vs. 34%, $p = 0.01$) and to require a second surgery for margin clearance (10% vs. 21%, $p = 0.02$). The technique did result in a higher volume of tissue resected, but this did not affect patient-reported cosmetic outcome. Furthermore, while taking cavity shave margins was associated with an incremental operative time of 10 minutes and additional tissue for pathologic evaluation, the cost associated with this was offset by the significant reduction in reoperative surgery. We will discuss the technique, and the ongoing multicenter trial to validate the findings of this Yale trial.

CURRENT CHALLENGES IN TREATING BREAST CANCER PATIENTS WITH METASTASIS TO BRAIN, SNEAK PEAK OF UPCOMING BIOLOGY

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Aggressive breast cancers, e.g., IBC, TNBC and HER2 positive breast cancer present with high rate of CNS metastasis. While patients with stage IV breast cancer survive longer than ever, the median overall survival (OS) of breast cancer patients with brain mets (BCBM) and leptomeningeal disease (LMD) are only around 2 years, mandating the development of better CNS targeted therapy.Once cancer is metastasized to the CNS space - including brain parenchyma or leptomeninges, the response to conventional systemic therapy is poor, and radiation therapy - either WBRT or local targeted radiation therapy remain to be the main modality of treatment. With improvement in the filed of cancer biology, there is slow but increasing understanding of the difference in CNS metastatic breast cancers. For example, detection of specific signature in the disseminated cancer cells, specific gene mutation that may be related to the CNS specific metastasis, have been studied by different researchers. More importantly, active development of novel targeted agents that penetrates the blood-brain-barrier shed the light into developing novel CNS targeted systemic therapy. In HER2 positive breast cancer, there are multiple efforts ongoing to develop small molecule HER2 targeting agents. Brain metastasis targeted preclinical model development also has helped the field to move forward and to validate novel targeted agents prior to application in clinical setting.

Despite some progress made in targeted therapy and possible biomarker development that made in the field, the prognosis of patients with breast cancer with CNS involvement remains to grim. Team science based development of translational effort to strengthen the research to develop preclinical model, combined with novel targeted therapeutics that can be tested in targeted group of patients with strong translational component, would be the most important step to make true difference in patients with dismal disease, who are in great need of better therapy.

CURRENT ISSUES IN THE MANAGEMENT OF BRAIN METASTASES FROM BREAST CANCER

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The incidence of brain metastasis from breast cancer is reported to be 30-40% in the autopsy series. Although clinically diagnosed brain metastasis is fewer, that is, 10-20% of the metastatic breast cancer patients, the incidence has been increasing with the advanced neuroimaging studies and improved survival due to recent developments in the cancer treatment.

According to the NCCN guidelines, surgical resection followed by whole brain radiotherapy (WBRT) is recommended as category 1 in the limited (1-3) metastatic lesions with resectability. However, in the unresectable disease or multiple (> 3) lesions, WBRT or stereotactic radiosurgery (SRS) alone is equally recommended as category 2A.

Currently, more physicians prefer SRS alone for avoiding neurocognitive decline caused by WBRT. However, the omission of WBRT results in the increase of local recurrence and/or distant brain metastasis, and therefore, may cause the overall decline in the quality of life due to the salvage treatment. A smaller fraction size, hippocampus avoiding WBRT, or concomitant use of memantine with WBRT is being tried for the preservation of neurocognitive function along with the intracranial control.

Recently, it is suggested that the improved intracranial control with WBRT translates to a survival advantage for patients with favorable prognosis. This is contrary to the current trend of reserving WBRT for those patients with unfavorable prognosis. Further studies are needed for defining the optimal indication of WBRT.

SYMPOSIUM

Global Breast Cancer Conference 2016

MOLECULAR AND PATHOLOGICAL CHANGES DURING PROGRESSION FROM IN SITU TO INVASIVE CANCER

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Ductal carcinoma in situ (DCIS) is an early pathologic stage of breast cancer characterized by proliferation of tumor cells within the ductal-lobular system but not extending through the basement membrane. Like invasive breast cancer, DCIS comprises a highly heterogeneous group of diseases with diverse histologic features, molecular alterations and risks of progression to invasive cancer. Molecular studies have revealed that in situ lesions preferentially cluster with invasive lesions of the same grade in gene expression profiling, and that the in situ and invasive components of the same tumor exhibit similar patterns of genetic alterations, suggesting that DCIS are precursors of invasive cancers of similar grade.

However, the natural history of DCIS is poorly understood, although it is known that 14% to 53% of in situ lesions evolve to invasive cancer over a period of 10 or more years if left untreated. Moreover, the mechanisms by which DCIS progress to invasive carcinomas are not well understood, and robust biomarkers capable of stratifying the aggressive forms of DCIS from the indolent forms are lacking. In a previous study, we have studied the amplification frequencies of HER2, C-MYC, CCND1, and FGFR1 in a large series of pure DCIS, DCIS associated with invasive carcinoma and invasive carcinomas, and found that HER2, C-MYC CCND1, and FGFR1 amplification status was in most cases concordant in the matched invasive and DCIS components of the same tumors, pointing to their early roles in the development of breast cancer. However, FGFR1 amplification was more frequent in invasive carcinomas than in pure DCIS, and in the invasive components of the same tumors, suggesting that FGFR1 amplification play an important role in the in situ-to-invasive transition as well as tumor initiation.

Furthermore, in pure DCIS, heterogeneity of gene amplification was found in 3.7% (2/52) for HER2, 11.8% (2/17) for C-MYC, 22.7% (5/22) for CCND1, and 10% (1/10) for FGFR1 amplified cases. These findings suggest that intra-tumoral genetic heterogeneity is already present in the DCIS and that progression of DCIS to invasive carcino-

mas may result from selection of subpopulations of tumor cells. In another previous study, we also reported that the differences in molecular subtypes among the invasive tumor foci of multifocal/multicentric breast cancers was associated with mixed molecular subtypes in the DCIS components, suggesting that heterogeneity within the DCIS followed by selection of different clones might give rise to the different phenotypes in multicentric/multifocal breast cancers.

The progression from in situ to invasive carcinoma is thought to be a complex process, depending on changes in tumor cell properties, myoepithelial cells and tumor microenvironment. As epithelial-mesenchymal transition (EMT) promotes tumor invasion by facilitating tumor cells to escape from the rigid constraints of the surrounding tissue architecture, such as basement membrane, it is expected to play an important role in the progression of in situ to invasive carcinoma. A gene expression profiling study revealed that the genes associated with EMT were enriched in invasive cancer relative to pure DCIS. Recently, we have shown that expression of EMT markers is greater in invasive carcinomas than in pure DCIS, especially in basal-like subtypes, and in the invasive component of basal-like breast cancers, suggesting that EMT is involved in the progression from in situ to invasive basal-like breast cancer.

Personalized Treatment of DCIS

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Personalized medicine may separate patients into different groups based on their predicted response or risk of disease progression. Since the subgrouping of invasive breast cancer (IBC) according to the mRNA expression in 2000, it has been widely accepted that the patients with IBC have different prognoses and drug responses according to the subgroup. Although we are not so successful to find clinically feasible molecular markers other than hormonal receptors and Her-2 receptor yet, each breast cancer subtypes has their own differently optimized treatment options.

Ductal carcinoma in situ (DCIS) is very well known as one of the non-obligatory precursors of IBC, and the management of DCIS has been debated. One of the reasons for this debate is based on the fact that most DCIS patients will not develop subsequent IBCs.

There are varieties of modalities to treat DCIS patients, such as surgery (lumpectomy or mastectomy with or without reconstruction), radiation treatment, and hormonal treatment in DCIS with hormonal receptor expression. According to the previous clinical studies, radiation may reduce ipsilateral local recurrence of IBC or DCIS by roughly 50%, and tamoxifen may reduce bilateral breast events by almost 30%. It seems like that the aromatase inhibitors may generate the similar effect in postmenopausal women. Even we may provide skin sparing mastectomy with or without preservation of the nipple areolar complex plus immediate reconstruction, we need to think of risk-benefit ratio to avoid unnecessary under- or over-treatment based on their known probable adverse effects.

Although we are living in an era in which genome based tests are available, little has been known about any specific genetic alterations which drive DCIS to invasive progression or recurrence. As a scoring system based on age, tumor size, margin width, tumor grade and necrosis, University of Southern California/Van Nuys Prognostic Index (USC/VNPI), seems to be one of the tools to help the decision for adjuvant radiation treatment after breast conserving surgery for DCIS. However, this is solely based on the clinical and phenotypical characteristics. As a result, traditional biomarkers (ER, PR,

HER2, Ki-67, etc.) to classify IBCs have been introduced to the decision making for DCIS patients. So far, it looks like that Hormone receptors (+) Her-2 (-) DCIS is the most indolent subgroup, but there has been debate on the role of Her-2 receptor expression for the recurrence of DCIS. Multigene expression assays such as the 12-gene Oncotype DX DCIS score has been recently introduced to select the patients with low-risk DCIS treated by breast-conserving surgery (BCS) alone who requires adjuvant radiation in condition of free surgical margins, but the indication and experienced is still greatly limited.

Because there is no sufficient protein biomarkers or genetic characteristics to predict prognosis of DCIS, traditional factors are still of importance to make a decision for personalized treatment of DCIS patients. Surgery type, resection margin status is one of important factors related to the local recurrence. In a recent study based on SEER database, the prognostic score with age, size, and tumor grade is associated with the benefit in survival offered from radiation after breast conserving surgery.

It is important to understand the risk-benefit ratio of the treatment modalities and the amount of benefit to provide the personalized treatment for the patients with DCIS. Considering the recent findings regarding to the relationship between subtypes and prognosis in IBC, we may consider the application of molecular markers or genetic assays to find the best personalized treatment for DCIS patients for the future.

NO SURGERY FOR DCIS?

Mehra Golshan

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Ductal carcinoma in situ (DCIS) is a breast lesion defined as a proliferation of monoclonal epithelial cells in breast ducts without evidence of invasion in the basement membranes. Because the prevalence of breast cancer screening has increased, early detection has contributed to a dramatic increase in the incidence of DCIS, which has risen from 5.83 per 100,000 women in 1973 to 35.54 per 100,000 women in 2011. Assuming constant incidence and survival rates, it is estimated that by 2020, more than 1 million women living in the United States will have a diagnosis of DCIS. Ductal carcinoma insitu displays a wide spectrum of histological diversity along a continuum, ranging from very well to very poorly differentiated, and nuclear grade has accurately conveyed this diversity. Approximately 25% to 50% of DCIS cases will likely progress to invasive ductal carcinoma. Ozanne etal established a simulation model to predict the progression rate of DCIS to clinically significant invasive breast cancer. Ozanneet al estimated that the rate of progression from DCIS to invasive cancer across a 10-year period is 60% for high-grade DCIS (for patients younger than 45 years with lesions larger than 1 cm) and 16% for low-grade DCIS (for patients older than 45 years with lesions larger than 2.5 cm). After local therapy for DCIS, nuclear grade was a proven predictive factor of ipsilateral breast cancer recurrence in a randomized clinical trial and meta-analysis.

An optimal strategy for DCIS management would be based On individual risk factors that predict subsequent invasive ductal carcinoma to avoid overtreatment. Although surgical management usually with radiation therapy is the current standard of care for all grades of DCIS, to our knowledge, the survival benefit of surgical resection and/or radiation has not been examined. Therefore, we investigated the survival benefit conferred by surgical treatment and radiation in patients with DCIS using survival data in the Surveillance, Epidemiology, and End Results (SEER) database. We hypothesized that breast cancer specific survival (BCSS) for patients with low-grade DCIS is independent from surgical treatment at the time of diagnosis.

CURRENT PERSPECTIVES ON RADIATION THERAPY IN AUTOLOGOUS AND PROSTHETIC BREAST RECONSTRUCTION

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Multi-disciplinary approach for breast cancer reduces breast cancer mortality and improves overall quality of life with the addition of breast reconstruction. Despite advanced techniques, adjuvant therapies may adversely affect reconstructive outcomes.

Post-mastectomy radiotherapy (PMRT) after breast reconstruction is an undesired treatment, although it is not an absolute contraindication. PMRT related toxicities have been shown to increase rates of capsular contractures, infection and loss of prosthesis in implant reconstruction. In autologous reconstruction, other adverse events such as fibrosis, distortion, volume loss and fat necrosis have been demonstrated. The extent of toxicities after radiotherapy with reconstruction is dependent on radiotherapy dosage, treatment length, interval from radiotherapy to reconstruction and method of reconstruction.

The appropriate time to perform the permanent implant in order to allow for sufficient healing from PMRT injury remains in question. Overall, sufficient time between PMRT and the permanent implant may increase a successful prosthetic reconstruction. And, compared with PMRT to tissue expander, PMRT to permanent implant reduces the rate of reconstructive failure. Despite this, PMRT to tissue expander remains common as many patients that receive neo-adjuvant chemotherapy are not candidates for delaying PMRT until after permanent implant.

Autologous reconstruction had been the cornerstone reconstruction of choice in the setting of radiotherapy. Multiple studies have demonstrated reduced complications and failure rates with autologous reconstruction, as compared to implant prosthesis. Also, increased aesthetic outcomes and patient satisfaction have been documented when compared to prosthetic reconstruction.

REGIONAL NODAL MANAGEMENT IN BREAST CANCER: FROM Z11 TO AMAROS

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Breast cancer regional node management has witnessed many changes over the last decade. There have been recent landmark studies reported that significantly impact clinical practice in the regional nodal management of breast cancer. The introduction of sentinel node sampling and subsequent publications of the Z0011 trial and AMAROS trial have significantly impacted the use of full axillary dissection. This, along with recent randomized trials demonstrating a continued benefit to regional nodal irradiation, and recent data suggesting a benefit to internal mammary radiation, have all had a substantial impact on practice and how the radiation oncoogist approaches the regional lymph nodes. Controversies exist and there continues to be debate surrounding the optimal approach. In addition to the controversies in managent of the regional lymph nodes on the primary management of breast cancer, the increasing use of neoadjuvant systemic therapy has also significantly impacted on regional nodal management. Whether to approach the regional nodes based on original prresentation or based on the response to therapy continues to be an area of controversy and debate.

During this lecture we will present the evolution in the managment of the regional lymph nodes from the radiaton oncology perspective, discuss the various controversies, data supporting various approaches and ongoing trials that are attempting to address unresolved issues.

TUMOR BED BOOST INTEGRATION DURING WHOLE BREAST RADIOTHERAPY : A REVIEW OF THE CURRENT EVIDENCE

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Randomized clinical trials in patients with early-stage breast cancer have demonstrated that following breast-conserving surgery, adjuvant whole breast irradiation (WBI) lowers the relative risk of ipsilateral breast tumor recurrence and improve the absolute overall survival. Historically, conventional fractionated (CF)-WBI, a dose per fraction of 1.8-2.0 Gy in 25 fractions over 5-6week treatment has been recommended on the basis that a high total dose delivered in small fractions keeps the normal tissue damage to a minimum while gaining the maximum level of tumor control. This perception was strengthened when early studies of hypofractionation (HF), which did not use adequate reductions in total dose, reported unacceptably high rates of normal tissue injury. Despite its proven effectiveness and safety, CF-WBI has certain shortcomings, including inconveniences to patients associated with prolonged daily treatment for 6-7 weeks. HF-schemes for breast treatment, a shorter treatment period while maintaining cosmetic and patient disease-free survival rates, are attractive for early-stage breast irradiation.

Through empiric observation, it has become clear that the therapeutic ratio, the balance between tumor cell kill and normal tissue damage, is affected not only by fraction size but also the total dose of radiation and in some instances overall treatment time and the volume of tissue irradiated. Currently, the mostly commonly used linear-quadratic model predicts that the biological effect of radiation will be directly proportional to total dose and fraction size. The effect of fraction size will be modified by the inherent fractionation sensitivity or α/β ratio of the tumor or normal tissue in question. When the α/β ratio of the tumor is the same or less than that of the critical normal tissue, then a larger dose per fraction (hypofractionation) with a modest decrease in total dose may be equally or potentially more effective than conventional fractionation.

Recently, the analysis of the available clinical data from multiple institutions supports that breast cancer has a low ratio of α/β, encouraging hypofractionated radiotherapy regimens for breast cancer. The α/β ratio of breast cancer has been under study with

more recent data suggesting it to be around 4, which implies the hypofractionated regimens should perhaps be more effective for local control of breast cancer as compared with the conventional 2 Gy fraction schedule. There are now long-term data from randomized trials to support the concept that modest hypofractionation can be used to treat the whole breast after breast conserving surgery with similar rates of local control and radiation morbidity as seen with conventional fractionation.

Current guidelines by the NCCN suggest that a boost may be required in part of patients. In randomized trials testing HF-WBI, the issue of boost radiation was not addressed and given by conventional fraction as an option after HF-WBI, reducing the gain in scheduling time. To preserve the convenience of HF-WBI and the benefit of boost therapy, we can consider daily incorporation of a tumor bed boost with HF-WBI rather than a standard sequential boost. IMRT enables the simultaneous delivery of different dose prescriptions to different target volumes in the same treatment fractions. Short-term data showed that HF-WBI with simultaneous integrated boost (SIB) was feasible and comparable in their toxicities with CF-WBI. Modulation of fraction size across the breast is potentially superior to modulation of fraction numbers as a way of matching of dose intensity to tumor recurrence risk. Currently, target volume delineation can be considered as the weakest part of the quality chain in IMRT. To minimize this, consensus guidelines for target volume delineation in early breast cancer must be defined. Furthermore, there is the issue of delivering a SIB, giving an even higher daily dose to the tumor bed. The challenge is to quantify the effect of reduced volume effects when applying HF-WBI dose response data to HF-SIB. Several clinical trials have been undergoing testing the limits of HF-WBI and the volume & fractionation effects needed to compensate for the adverse effects of dose escalation.

HOW TO USE MAGNETIC RESONANCE IMAGING FOLLOWING NEOADJUVANT CHEMOTHERAPY IN LOCALLY ADVANCED BREAST CANCER

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Neoadjuvant chemotherapy (NAC) has been increasingly used in patients with operable breast cancers as well as locally advanced breast cancers, as studies have shown that survival outcomes and locoregional control with NAC are similar to those with adjuvant chemotherapy, In addition, NAC reduces tumor volume to allow more breast-conserving surgery (BCS). A meta-analysis of 14 prospective randomized trials suggested that NAC was associated with an absolute decrease in the mastectomy rate of 16.6%. Selection of candidates for BCS after NAC is based on the tumor size at baseline, amount of reduction of tumor size, and its subtype. Negative estrogen receptor, smaller initial tumor size, higher Ki-67 level, absence of in situ component, and residual tumor size ≤ 3 cm are associated with predicting BCS. With the advent of newer therapeutic agents and targeted therapies, the rates of pathological complete response (pCR) have increased, however, the rate of BCS has not been increased in multiple studies. This might be attributed to the limitation in evaluation of residual disease extent after NAC.

MRI has been shown to be the most accurate in determination of residual disease after NAC, when compared with clinical examination, mammography, and ultrasonography. However, overall accuracy of MRI for the selection of surgical therapy after NAC was 76%. Under- or over estimation of residual disease extent after NAC might lead to positive margins after BCS or unnecessary total mastectomy. Main reason for these inaccuracies is that identification of scattered microscopic foci of residual cancer after NAC is problematic at MRI. Although MRI is accurate for evaluation of unicentric, high-grade, ER negative breast cancer, it is inaccurate for the evaluation of ER positive tumors. Accuracy of MRI is not only influenced by ER, PR, HER2 status of the tumors, but also influenced by the chemotherapeutic agent. Decreased contrast enhancement after Taxane or HER2 targeted agents might lead to underestimation of residual disease extent. In addition, patients with malignant calcifications, although lumpectomy after NAC does not need to remove the entire volume of breast tissue initially occupied by

the tumor, presence of residual disease cannot be reliably excluded for the residual malignant calcifications. These factors should be considered for planning BCS after NAC.

CURRENT ROLE AND CHALLENGE OF PET-CT IN BREAST CANCER

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Positron Emission Tomography (PET) is one of the imaging modalities which become successful not just in the staging of the disease, but in the therapeutic response evaluation, as well. The hybrid PET-CT imaging is a unique tool in the field of diagnostic imaging modalities: its main advantage is the ability to measure not just morphological, but also metabolical properties and even biological behavior of the tissues. These benefits increase the role of PET-CT diagnostics in oncology, especially in breast cancer diagnostics. In PET-CT imaging the most widely used radiotracer is the 18F-fluoro-deoxi-glucose (FDG). FDG is a radio-labeled glucose analogue molecule which acts like a regular glucose until intracellular uptake via the glucose transporters (GLUTs) of the cell membrane. As the hexokinase enzyme phosphorylates the FDG, it is stuck in the cell, accumulating and reflecting the higher metabolic rate and glucose consumption of tumor tissues (the Warburg effect itself). With the additional CT imaging technique the sensitivity and specificity of FDGPET-CT imaging is become remarkable in the staging of the disease, the detection of distant metastases and tumor recurrence as well. Although in most countries in the daily clinical practice only FDG is available for PET-imaging, but the evolving new PET-CT tracers can give a new perspective in the determination of stage and in the evaluation of therapeutic response of tumors.

To understand better the biological behavior and therapeutic response of breast cancer, new tracers and targets of molecular imaging are under investigation. The mainstream of these researches, the tracers were divided into three main groups: Tracers in connection to the unique therapeutic agents of breast cancer, such as hormonal or anti-HER2 (Human Epidermal Growth Factor Receptor 2) therapiesspecific breast cancer tracers

Tracers which arelike FDG itselfrelated to cell proliferation and metabolism non-specifically for breast cancer, and Tracers linked to other pathways of tumor metabolism, such as the markers and inhibitors of angiogenesis, or to growth factor receptor families. (mostly under investigation).

These tracers may lead to non-invasive evaluation of the main, leading therapeutic decision-maker properties of metastatic breast cancer such as receptor status, proliferation activity and therapy resistance, and could also become predictive markers in the early measurement of therapeutic response in the neoadjuvant treatment of locally advanced breast cancer. However, these new agents are currently not available in the daily practice; the preliminary results are promising.

PET/MR IN BREAST CANCER

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It has been tried to achieve an early assessment of response to anti-cancer treatment because early prediction assist to make a right decision for further treatment. When the inefficacy of treatment become apparent, the treatment modality should be modified to improve the patients survival. Information from interim treatment assessment can provide significant suggestion to predict the patients prognosis. Also, proper assessment of cancer treatment enables the society to allocate the medical property in a right way.

FDG-PET has demonstrated the excellent capability to distinguish between treatment responder and non responder in many malignant diseases. Functional imaging shows better outcome than anatomical imaging because anatomical imaging cannot differentiate between fibrotic tissue and viable tumor. As the MRI technologies are developed widely, diverse functional parameters can be obtained from MRI. There are many functional imaging techniques such as dynamic contrast enhancement (DCE) MRI, diffusion weighted (DW) MRI, 1H-MR spectroscopy (MRS), and blood oxygenation level-dependent (BOLD) MRI. They are expected to detect the biological changes early and to supply complementary information other than PET. First model of PET-MRI was parallel type. Afterwards, integrated PET-MRI system was developed. However, the parallel PET-MRI system can be applied in similar ways in comparison with the integrated PET-MRI system with more flexible operation of PET and MRI separately.

Many researchers have applied these functional parameters in the clinical situation. However, the effectiveness is controversial, and depends on each researcher. When it comes to considering MRI functional parameters, there are some points which should be considered. Regarding DW MRI, it takes much time to acquire the image and the resolution of image is limited. In case of spectroscopy, it also takes much time to get the image and the information tends to mix with some noises. Many parameters were induced from DCE MRI such as transfer constant, outflow rate constant. These DCE MRI parameters are expected as promising biomarkers because of precise quantification, although further researches are necessary.

To take a glance at the further detailed information, there are some studies which showed the usefulness of combination PET and MRI. Our study revealed that func-

tional 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. We 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, $p<0.0001$). Regarding the ability to classify a high-risk group in terms of hazard ratio (HR), in our study two modalities combined predicted DFS more robustly than a single modality alone. This superiority of two modalities combined can be demonstrated by comparing the data with those of previous studies. The most powerful parameters from previous studies showed a lower HR than that the two modalities combined. The transfer constant (HR 1.03, 95% CI 1.01-1.06, $p=0.043$) for DFS and tumour volume (HR 2.62, 95% CI 1.77-3.88, $p<0.001$) for recurrence-free survival from MRI showed lower HR, and the rate of decrease in SUV (HR 4.29, 95% CI 0.5-36.7, $p=0.18$) for DFS from PET also showed a lower HR.

Beyond the FDG-PET, targeting and imaging tumor marker has been attempted using radiolabelled antibody. Some clinical trials have been tried using Cu-64 trastuzumab to target HER2 in breast cancer and they demonstrated thte effectiveness of targeting. In near future, PET-MRI may show better soft tissue contrast with specific protein expression visualization.

This presentation will summarize studies which have suggested the usefulness of parallel PET-MRI in breast cancer in terms of diagnosing, assessing treatment response and predicting prognosis. These results strongly indicate that the combination of functional parameters from PET-MRI may improve the diagnosis, the prediction of treatment response and prognosis in breast cancer.

INFLUENCE OF LIFESTYLE FACTORS ON BREAST CANCER PROGNOSIS

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Breast cancer is one of the most common cancers in the US and many countries in the world, with approximately 1.7 million new cases diagnosed each year worldwide. While the incidence of breast cancer is much higher in North American and European countries, it has been increasing rapidly among Asian countries in the last 2 decades. The five-year survival rate for breast cancer varies widely internationally and across ethnic groups within a country. Known prognostic factors for breast cancer include type of breast cancer, age at diagnosis, grade and stage of cancer, and cancer treatment, as well as co-existing health condition(s) at diagnosis. However, inter-individual variation in breast cancer prognosis still exists even after these clinical predictors are accounted for, suggesting that other factors, such as those involved in lifestyle, may play an important role in breast cancer prognosis. This presentation will introduce the current knowledge on the association between lifestyle factors and breast cancer survival, focusing on the role of exercise, dietary intake, and obesity in breast cancer prognosis. This knowledge provides a basis for health care providers and breast cancer survivors to take proactive measures to improve survival rates and quality of survival.

EVIDENCE THAT GERMLINE GENETIC FACTORS INFLUENCE SURVIVORSHIP FROM THE AUSTRALIAN BREAST CANCER FAMILY STUDY

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It is not established if genetic factors influence survival after breast cancer.

We conducted a population-based study of 1,196 Australian women diagnosed with invasive breast cancer before age 60 years (half before 40 years). Cases were from the Victorian and New South Wales Cancer Registries, unselected for family history, and diagnosed between 1992-1999 (response ~70%). Cases were interviewed and we recruited first- and second-degree relatives to establish cancer family history from multiple sources and attempted to verify reported breast cancers. We used the BOADICEA software, validated using our Australian data, to estimate lifetime genetic risk from family data. Cases were last followed-up in 2014 by interviews and linkage to the National Death Index. We collected pathology material and cancer registry records on immunohistochemistry. Hazard ratios (HR) were estimated using Cox regression.

There were 375 deaths over a total of 14,717 person-years follow-up. Age at diagnosis, estrogen receptor status, tumour grade, tumour size and lymph node status and log(BOADICEA) were all univariably associated with survival. The latter HR for family history decreased from 4.15 (2.42-7.14) to 1.65 (0.65-4.19) after adjustment for age, estrogen receptor status and tumour grade.

Our data are consistent with family history being associated with survival in part due to genetic factors being implicated in early-onset disease, which is more likely to be estrogen receptor negative with a direct influence on tumour grade and poorer outcomes, at least in the first 5 years after diagnosis. There was also a suggestion that there are genetic factors specific to survival.

QUALITY ADJUSTED LIFE YEARS LOSS DUE TO BREAST CANCER IN KOREA

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Breast cancer is one of substantial health issues in many countries. Especially in Korea, breast cancer incidence has been increasing since 1999. Five-year mortality of breast cancer patients has improved but their health-related quality of life (HRQoL) is still an important issue in caring them.

Both HRQoL and traditional clinical outcomes (i.e., mortality or tumor responses) are considered as significant outcomes of cancer care. Because breast cancer treatment could be closely related with keeping femininity, their HRQOL could be a hot issue in a clinical decision making of breast cancer patients.

There are several approaches to measure HRQoL. Frequently, researchers use structured survey forms which are classified into disease-specific instruments like FACT-B and generic instruments such as SF-36v2. Preference-based instruments like EQ-5D is useful to make a summary score called an utility which is used to calculate quality-adjusted life year (QALY).

QALY is a generic measure of disease burden, including both quality and the quantity of life. This term is also utilized in cost-utility analysis, which is a kind of economic evaluation to assess economic efficiency of healthcare interventions. To calculate QALY, it is needed to estimate utilities on health states that can be obtained indirectly by preference-based instruments or directly by valuing health states using valuation methods like the standard gamble method.

Several studies use QALY to investigate the burden of non-communicable diseases (NCDs), such as stroke, diabetes, and cancer. Recently, in Korea, QALY losses due to 13 NCDs were calculated from a national representative study that was the Korean Community Health Survey (KCHS) 2010. Unfortunately, there was no data for breast cancer in Korea.

This presentation will deal with QALY loss of breast cancer patients in Korea. Firstly, I

will introduce the concept of HRQOL and QALY. Secondly, some HRQOL study results on breast cancer patients will be presented including utility studies in Korea. Lastly, QALY loss of breast cancer patients in Korea will be interpreted in this presentation.

NAB-PACLITAXEL IN BREAST CANCER: CLINICAL DEVELOPMENT AND FUTURE DIRECTIONS

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Nab-Paclitaxel (nab-P) is a solvent free formulation of Paclitaxel without the need of premedication, distinct pharmacokinetics, unique distribution in and ability to dose escalate and to deliver the active compound (Paclitaxel) in higher doses to the malignant tissues.

Nab-P is approved by the US-FDA in 3 indications (metastatic breast cancer, advanced Pancreatic cancer and metastatic and advanced NSCLC). Additional studies show that a number of different doses and schedules are very active and that nab-P outperformed in a large randomized controlled trial (RCT) the standard of care form metastatic melanoma.

In the NeoAdjuvant setting, recently a RCT (GeparSepto) of over 1200 patients showed that replacing solvent based (sb) P with nab-P resulted in a statistically significant and clinically meaningful increase of pathologic complete responses, especially in the triple negative subset. This trial is now one of the new backbones of studies investigation novel compounds.

More recently, nab-P was chosen as a cytotoxic compound of choice in combination with novel immuno-oncology compounds like immune-checkpoint inhibitors (ICI). An array of studies was initiated by many investigators and few companies to show the superior efficacy of such combinations.

ERIBULIN MESYLATE IN THE MANAGEMENT OF METASTATIC BREAST CANCER

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Eribulin mesylate (E7389) is a non-taxane inhibitor of microtubule dynamics of the halichondrin class of cytotoxic drugs. It is a structurally modified synthetic analogue of halichondrin B, a natural product isolated from a marine sponge. Eribulin has a novel mode of action that is distinct from other tubulin-targeting agents. It inhibits the microtubule growth phase without affecting the shortening phase, and causing tubulin sequestration into non-productive aggregates hence mitotic arrest. Phase1/2 studies defined the dose as 1.4mg/m2 Day 1 and 8 every 21 days with dose modification for mild to moderate hepatic dysfunction and with less neuropathy than taxanes. The predictable side effects were neutropenia and fatigue and alopecia is seen in approximately 50% of patients. The activity of eribulin was shown in a phase III trial (EMBRACE) of 762 heavily pre-treated patients who were randomly assigned to treatment with eribulin or other chemotherapy (based on physicians and patients choice). Treatment with eribulin significantly improved OS (median, 13.1 vs. 10.6 months). The primary toxicity with eribulin was neutropenia, with grade 3 and 4 neutropenia in 45 percent of patients, and grade 3 and 4 febrile neutropenia in 5 percent. There may be a higher incidence of neutropenia in the East Asian population. Peripheral neuropathy was the most common adverse event leading to discontinuation of eribulin, occurring in 5 percent of patients. Of note, a subsequent randomized trial was performed in women with metastatic breast cancer who had received prior anthracycline and taxane therapy with an aim to formerly evaluate eribulin versus capecitabine as first, second, or third-line therapy. Unlike the earlier trial, there was no difference between eribulin and capecitabine in terms of PFS (four months in each) or overall response rates (11 and 11.5 percent, respectively). In addition, there was no clinically meaningful difference in OS (15.9 vs. 14.5 months, respectively; HR 0.88, 95% CI 0.77-1.00). For patients with TNBC, the median OS was 12.9 months with eribulin compared with 8.2 months in the control (HR = 0.74; 95% CI, 0.60-0.92, $p = 0.006$). A statistically significant benefit was not seen in patients with HER2-positive disease. For this population, the median OS with eribulin was 13.5 versus 12.2 months (HR = 0.82; 95% CI, 0.62-1.06, $p = 0.135$). Studies have shown activity of eribulin in earlier stage metastatic breast cancer and also predictable activity in combination with Trastuzumab in metastatic HER2 positive breast cancer. Combination doublets outside clinical trials are not currently recommended. Eribulin is a valuable drug in metastatic breast cancer.

NON-ANTHRACYCLINE ADJUVANT CHEMOTHERAPY

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Anthracyclines have been considered as a main component in the adjuvant treatment of early-stage breast cancer. However, with the increasing use of other active drugs-mainly taxanes and trastuzumab in HER2-positive diseasecoupled with concerns about anthracycline-associated toxicities including cardiac failure and secondary malignancies, there has been tremendous debate about whether anthracyclines are still needed. Although there is still consensus of using anthracycline-taxane regimens particularly in women with high-risk disease, non-anthracycline regimens have proven clinical benefit for early breast cancer based on balance between risk and efficacy in large clinical trials (USO9735 and BCIRG006). Therefore, non-anthracycline regimens for early breast cancer became standard in US and Europe and is increasing as the need of adjuvant chemotherapy has proven for small-sized, node negative early breast cancer with unfavorable histology such as triple negative, HER2-overexpressed and Luminal B type. Currently, there is no standard guideline or biomarkers for the use of non-anthracycline regimens in spite of wide range of molecular works. This presentation aimed to identify which biomarkers and characteristics are known to be associated with benefit from non-anthracycline regimens.

PIK3CA MUTATIONS IN HER2-POSITIVE BREAST CANCER

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PIK3CA is among the most commonly mutated oncogene in breast cancer and is present in about one-fourth of all HER2-positive metastatic breast cancers (mBC). Preclinical studies using HER2-positive cell lines have shown that an additional mutation in PIK3CA, the alpha-catalytic subunit of PI3K, results in downstream constitutive signaling, making breast cancer cells that harbor both aberrations resistant to trastuzumab and lapatinib. In HER2+ mBC, pertuzumab consistently showed a PFS benefit, independent of biomarker subgroups (hazard ratio < 1.0), including estrogen receptornegative and positive subgroups in the CLEOPATRA study. High HER2 protein, high HER2 and HER3 mRNA levels, wild-typePIK3CA, and low sHER2 showed a significantly better prognosis ($p < 0.05$). PIK3CA showed the greatest prognostic effect, with longer median PFS for patients whose tumors expressed wild-type versus mutated PIK3CA in both the control (13.8 vs. 8.6 months) and pertuzumab groups (21.8 vs. 12.5 months).

Role of PIK3CA mutation in NeoALTTO trial was reported that the PIK3CA mutations are associated with a decreased benefit to neoadjuvant HER2-directed therapies. The women with wild-type PIK3CA tumors treated with the combination therapy had a 53.1% pCR rate compared with 28.6% for the women whose tumors harbored a PIK-3CA activating mutation ($p = 0.012$). However, PIK3CA mutation status did not affect overall survival outcomes ($p = 0.014$). Meta-analysis confirms a significantly lower pCR rate in HER2+, PIK3CA mutant tumors after anti-HER2 treatment. Patients with a HER2+/HR+/PIK3CA mutant tumor had a pCR rate of 5.5% only when treated with double-blockade and might be considered for alternative treatment. In addition, the PIK3CA mutations did not affect outcomes for HER2-positive patients receiving adjuvant trastuzumab treatment. Current data suggest that results from the metastatic and neoadjuvant setting may not be always applicable to the adjuvant setting.

OVERCOMING HER2 TARGETED THERAPY: ONGOING CHALLENGE

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The advent of HER2-targeted therapies has significantly improved treatment outcomes for patients with HER2-positive breast cancer in this millennium. However, treatment resistance remains a problem for most patients, and there is still an unmet need to develop better therapies. Understanding the biology of HER2-positive breast cancers, the mode of action of various therapies, as well as the mechanisms of resistance, are critical. To evade HER2 inhibition, HER2+ breast cancer cells may reactivate the HER pathway or its downstream signaling via various mechanisms, or may switch to alternative survival pathways. The host and tumour microenvironment may also play a role in treatment resistance. In this session, we will discuss the challenges we face in treating patients with HER2-positive breast cancers, in addition to novel treatment strategies which have been or are being explored.

SP06-3

PRECISION MEDICINE GUIDED BY SINGLE-MOLECULE IMAGING

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Analysis of cancers at the protein-protein interaction (PPI) level can reveal whether a genomic mutation is the driver or passenger for individual cancers. In the absence of genomic mutations, the PPI analysis preserves the capability to stratify cancers and predict their responses to targeted therapy, although this is yet to be realized in clinical practice. I will talk about single-molecule co-IP profiling of receptor tyrosine kinase (RTK) signaling, which allows quantitative prediction of the responses of cancers to RTK-targeted drugs. For individual cancers, human epidermal growth factor receptors (HER) and MET receptors were separately pulled down on to the imaging plane of single-molecule fluorescence microscope. Formation of single PPI complexes between the pulled-down RTKs and fluorescently labeled downstream proteins generated diffraction-limited spots, the number of which was used to gauge the PPI strengths. The weighted sum of major downstream PPIs showed a high correlation with drug susceptibility of individual cancers. Application of this method to two current RTK-targeted cancer therapies, specifically, prediction of response of lung adenocarcinoma and breast cancers to epidermal growth factor receptor (EGFR)- and HER2-targeted drugs, was successfully demonstrated. In addition, this single-molecule PPI profiling facilitated prediction of the response to an EGFR tyrosine kinase inhibitor in lung squamous cell carcinoma (SQCC) patient-derived tumor xenografts (PDTXs), for which no current predictive markers are available. In conclusion, our approach provides a strategy to develop predictive PPI markers for RTK-targeted drugs, especially in cancer types without actionable genomic mutation, which may significantly expand the scope of the targeted cancer therapy.

MOLECULAR HETEROGENEITY OF TNBC AND METHODS OF CLASSIFICATION

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Tumor heterogeneity of triple-negative breast cancer (TNBC) has been main barrier in conquering breast cancer. To dissect molecular diversification and discover therapeutic targets in TNBCs, intensive research has been focused. Since Perou et al. published their landmark study categorizing breast cancer by gene expression profiling into intrinsic subtypes, gene-expression profiling analyses has been widely adopted in classifying and discovering relevant therapeutic targets since among the various ways using genomic data [1]. Several molecular classifications based on gene-expression profiling are suggested in this perspective.

In 2011, the researchers of the Vanderbilt University reported the seminal study classifying TNBC into distinct subtypes [2]. Using gene expression analyses from 587 TNBC tumors, they illustrated that 6 distinguished subtypes consist of TNBC and display a unique biology that responds differentially to various therapies. By k-means and consensus clustering, they found 6 subtypes including 2 basal-like subtypes, 1 with increased cell cycle and DNA damage response gene signatures (BL1) and the other one with high expression growth factor pathway and myoepithelial markers (BL2); 2 mesenchymal subtypes with up-regulated gene signatures associated with cell differentiation and growth factor signaling (M and MSL); an immunomodulatory (IM) type with enriched immune cell processes; and a luminal androgen subtype characterized by androgen signaling (LAR).

In 2014, there is another classifier of TNBC proposed by the researchers of the Baylor University [3]. By integrating mRNA expression and DNA profiling from 198 TNBC tumors, they tried to classify the molecular subtypes of TNBC and discover therapeutic targets in each subtype. By non-negative matrix factorization (NMF) method, they discovered classifier panels comprising 80 core genes. Training and validation. They classified TNBC tumors into four distinct subtypes: (a) LAR, (b) mesenchymal (MES), (c) basal-like immunosuppressed (BLIS), and (d) basal-like immune-activated (BLIA). In overall subtypes, tumors with BLIS subtype showed a worst prognosis, whereas tumors with BLIA showed a best prognosis. The prognosis of MES and LAR was in the middle

between BLIA and BLIS.

Another subtyping in TNBC was reported by the researchers of the Unicancer center in France [4]. Likely to earlier studies on subtyping, they used gene expression profiling from 194 TNBCs and adopted fuzzy clustering. They discovered 3 subtypes (C1, luminal androgen receptor, 22.4%, ;C2, basal-like with low immune response and high M2-like macrophages, 44.9%;C3, basal-enriched with high immune response and low M2-like macrophages, 32.7%) in training set (n = 107) and validated these subtypes in other cohort (n = 87). They found that grade and Nottingham prognostic index were higher in C2 and C3 than in C1. Their functional analyses informed that luminal androgen signaling was enriched in C1 as like LAR in the Vanderbilt and the Baylor. C2 type consisted of an almost pure basal-like cancer by PAM50 assay. Claudin-low subtype was noted in 26% of C3 type, as well as basal-like type. Furthermore, immune response signaling which is associated with high immune response and low M2-like macrophage is enriched in C3, that has similarities with IM subtype of the Vanderbilt or BLIA of the Baylor. Their findings highlighted that targeting immune response genes and lowering macrophages would be an effective therapeutic strategy in TNBCs.

Overall these three studies exemplify the challenges of subtypes in gnomically complex TNBCs. These molecular classifications elucidate that TNBCs are separated into several distinct subtypes having specific biologic pathway that is therapeutically targeted. Although discrepancy of these classifiers still remains, these efforts may offer subtype-tailored therapies in TNBC. In future, simplified classifying kit will be incorporated into clinical practice that may lead to precision medicine for women with TNBC.

THE FUTURE OF PERSONALIZED THERAPY IN TRIPLE-NEGATIVE BREAST CANCER

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Triple negative breast cancer (TNBC) contains a variety of subpopulations with respect to biological characteristics. It would be reasonable to consider therapeutic strategies for TNBC based upon the tumor biology. For instance, PARP inhibitors may be useful for tumors having BRCA related dysfunctions. Among chemotherapies, platinum and eribulin may provide unique property in the treatment of TNBC. Immune therapies such as anti-PD1 antibody are known to drive a significant tumor response according to recent studies. In addition, response-guided approach can be also incorporated in the treatment of primary TNBC. Adjuvant metronomic chemotherapy with oral FU has been demonstrated to act as an effective tool for controlling residual invasive diseases after neoadjuvant cytotoxic chemotherapy.

NEW TREATMENT DIRECTIONS FOR TRIPLE-NEGATIVE BREAST CANCER

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The University of Texas MD Anderson Cancer Center has launched the Moon Shots Program, an unprecedented effort to dramatically accelerate the pace of converting scientific discoveries into clinical advances that reduce cancer deaths. The Moon Shots Program is built on a disruptive paradigm that brings together the best attributes of both academia and industry by creating cross-functional professional teams working in a goal-oriented, milestone-driven manner to convert knowledge into tests, devices, drugs, and policies that can benefit patients as quickly as possible. One of the disease areas is represented by triple-negative breast and ovarian cancers, which are cancers linked at the molecular level. Each moon shot has been receiving an infusion of funds and resources needed to work on ambitious and innovative projects prioritized for patient impact, ranging from basic and translational research to biomarker-driven novel clinical trials to behavioral interventions and public policy initiatives. Over its first 10 years, the cost of the Moon Shots Program may reach $3 billion. In 2016, the state of the Union by President Obama recognizes the importance of Moon Shots approach to fight cancer.

In patients with triple-negative breast cancer (TNBC), poor outcomes result from recurrent disease owing to metastasis. Metastasis may result in part from the resistance of TNBC to therapy, which can be classified into three types: 1) intrinsic resistance owing to molecular characteristics present before chemotherapy is initiated, 2) adaptive resistance owing to molecular changes soon after chemotherapy is initiated, and 3) acquired resistance as indicated by residual or recurrent disease after prolonged chemotherapy. Most likely, all three types of resistance contribute to a lack of pathologic complete response (pCR) to preoperative chemotherapy in TNBC patients.

Understanding the three types of resistance will lead to the development of novel targeted therapy for TNBC that may be incorporated into neoadjuvant chemotherapy. We will address unanswered clinically relevant questions by creating a comprehensive novel translational research program.

Currently, we can identify intrinsic molecular characteristics that determine pCR rates

for TNBC after neoadjuvant chemotherapy. For example, using gene profiling, Lehmann et al. (J Clin Invest 121:2750-2767, 2011, PMID: 21633166) found that TNBC can be classified into six clustersbasal-like 1, basal-like 2 (BL2), immunomodulatory, mesenchymal, mesenchymal stem-like, and luminal androgen receptorplus an unstable cluster. In our data set, the basal-like 1 subtype had the highest pCR rate (52%), whereas the BL2 and luminal androgen receptor subtypes had the lowest rates (0% and 10%, respectively). TNBC subtype and pCR status were significantly associated with each other ($p = 0.044$), and TNBC subtype was an independent predictor of pCR status ($p = 0.022$) according to a likelihood ratio test (Clin Cancer Research 19:5533, 2013, PMID: 23948975). Use of Lehmanns subtype predicted pCR status better than did use of the PAM50 intrinsic subtypes (basal-like versus non-basal-like). We speculate that an androgen receptor pathway drives the luminal androgen receptor subtype. For BL2, the drive may result from epidermal growth factor receptor or mitogen-activated protein kinase pathways. These findings helped us developing innovative personalized medicine strategies for patients with TNBC.

The learning objective of this talk is to provide our comprehensive research plan based on the current knowledge of TNBC molecular changes contributing to treatment resistance and how the Moon Shots Program has evolved over that past 3 years.

SENSITIZATION OF BREAST CANCER CELLS TO CHEMOTHERAPEUTIC DRUGS BY METABOLIC REGULATION

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Background: Targeting of tumor glucose metabolism is highlighting as a novel therapeutic strategy against cancer. Tamoxifen is the standard endocrine therapy for ER+ breast cancer, however, many women still relapse after long-term therapy. The aim of present study was to evaluate the possible augmentation of the tamoxifen resistance via reprogramming of cancer metabolism and to investigate the its underlying mechanism(s).

Methods: We established the tamoxifen resistant MCF breast cancer cells by maintaining the cells in media including tamoxifen for 6 months. Cell death by combined treatment of dichloroacetate (DCA), an inhibitor of pyruvate dehydrogenase kinase, and tamoxifen was evaluated using by PI and annexin V staining.

Result: In the present study, we found that combined treatment of DCA and tamoxifen synergistically induced cell death in MCF7 breast cancer cells. Furthermore, combination regimen enhanced cell death in tamoxifen resistant MCF7 cells. These effects were correlated with downregulation of EGFR protein levels. These results were further confirmed by the treatment of tamoxifen and EGFR inhibitors.

Conclusions: Based on these finding, we propose that metabolic regulation with DCA could enhance the tamoxifen-induced cell death and overcome tamoxifen resistance in breast cancer cells.

CROSS-TALK BETWEEN ADIPONECTIN AND IGF-IR IN BREAST CANCER

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Obesity is becoming one of the epidemic morbidities which is a chronic as well as a multifactorial disorder. It becomes evident through two characteristic phenotypes by an enlarged mass of adipose tissue caused by a combination of size increase of preexisting adipocytes (hypertrophy) and de novo adipocyte differentiation (hyperplasia). Obesity is correlated with many metabolic diseases such as hypertension, type 2 diabetes, metabolic syndrome, and cardiovascular disease, and it is well known and asserted to be associated with an increased risk of cancer development in different tissues including breast and the body of evidence becomes swollen. Adipose tissue is now regarded as not only a storage reservoir for excess energy, but rather also an endocrine organ with specific metabolism, secreting lots of bioactive molecules also known as adipokines. Among these adipokines, adiponectin outstands the most ubiquitous adipose tissue-excreted protein, which exerts insulin sensitizing, anti-inflammatory, and anti-atherogenic characteristics. The serum concentrations of adiponectin are inversely correlated with body mass index. Recently, low levels of plasma adiponectin have been associated with an increased risk for obesity-related cancers and development of more aggressive phenotype, concomitantly with alterations in the bioavailability of insulin-like growth factor- I (IGF-I) and IGF-I receptor (IGF-IR) signaling pathways. Today, I will discuss the cross-talk between adiponectin/AdipoR1 and IGF-I/IGF-IR in breast cancer. Adiponectin has surfaced as a crucial adipokine involved in breast carcinogenesis in women with obesity. In ERα-positive breast cancer cells, the interaction of adiponectin with its specific receptor induces the activation of multiple pathways, through the interplay between ERα and IGF-IR. This leads to (i) increased activation of MAPK and upregulation of genes involved in proliferation and inhibition of apoptosis, (ii) induction of cell migration, which may culminates into metastasis. On the basis of current and recent findings and understanding, I may conclude that adiponectin differently modulates IGF-I stimulatory effect in breast cancer cells in relationship to ERα status. Indeed, the antagonistic effects exerted by adiponectin on IGF-IR signaling are evident only in ERα-negative breast cancer cells. Thus, only in the latter circumstance, adiponectin sounds to be exploited in novel therapeutic strategies for breast cancer treatment.

BIDIRECTIONAL CROSSTALK BETWEEN THE ER AND HER2 SIGNALING PATHWAYS : FROM BENCH TO BEDSIDE

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Gene expression profiling studies suggested that HER2+/HR+ and HER2+/HR- tumors are two different subtypes, naming luminal B and HER2 enriched subtypes, respectively. It has been reported that around half of HER2 positive tumors are also HR positive. With regards to treatment, it is commonly believed that anti-HER2 therapies are active in patients with HER2+ disease, irrespective of HR status. However, endocrine therapies are less beneficial in HER2+/HR+ patients than HER2-/HR+ patients. Also, there is quite solid evidence that anti-HER2 therapies have more magnitude of benefit in HER2+/HR- than HER2+/HR+ patients. Therefore, increasing therapeutic benefit in HER2+/ER+ (triple positive in case that PR is also positive) would be another challenge in breast cancer.

Triple positive breast cancer (BC), namely ER/PR/HER2 positive tumors seems to be closer to HER2-/HR+ tumors rather than HER2+/HR- tumors in terms of not only tumor biology determined by gene expression profiles but also its good prognosis which is similar to hormone positive breast cancer rather than HER2+/HR- breast cancer. However, it also seems to be distinct group of BC from HR+/HER2- subtype considering anti-HER2 therapies are getting benefit in this subtype in contrast with in HR+/HER2- subtype.

Clinical trial results shows in this triple positive BC, combination of anti-HER2 and endocrine therapy is better than endocrine therapy alone but it shows shorter progression free survival than chemotherapy plus anti-HER2 therapies through indirect comparison. However, it needs to be questioned if we should use chemotherapy based anti-HER2 therapies as an upfront therapy in this disease with good prognosis. Also, it needs to be clarified who could get the critical benefit with endocrine therapy based anti-HER2 treatment. Finally, the other targets such as EGFR, PI3K, etc need to be studied to improve its prognosis.

In this presentation, available literature data will be discussed on differences in tumor biology and clinical outcomes based on ER and PR status in HER2 positive early and advanced breast cancer.

SP09-1

COMBINATION STRATEGY IN CANCER IMMUNO-ONCOLOGY DRUG DEVELOPMENT

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Breast cancer has not been perceived as an immunogenic tumor when compared with diseases such as melanoma, renal cell carcinoma and non-small cell lung cancer. However there is increasing evidence to support that certain breast tumors are intrinsically more immunogenic than others. The ability to profile many breast cancer tumors on a molecular level has revealed that certain tumors demonstrate a high level of immune-regulatory gene activation. Tumors that elicit more potent cytotoxic T-cell responses tend to have a more favorable prognosis and respond better to chemotherapy than less immunogenic tumors. Additionally, it is necessary for breast oncologists to think that immunogenicity appears to differ between subtypes. For instance, in triple negative breast cancer and HER2-positive breast cancer tumor infiltrative lymphocytes (TILs) are prognostic and predictive for response to chemotherapy containing anthracycline, but in other subytpes they are not.

Many standard treatments used in breast cancer rely in part on their immunogenic effects for their success in eradicating disease. Understanding how to use these agents to effectively augment the antitumor immune response may lead to better outcomes. Finally, many new immune-modulatory agents and vaccines that can reverse the immunosuppression caused by established tumors are in development. Combining these novel agents with current therapies may boost their efficacy. This review discusses the available data regarding the immune-modulating effects of various treatments and how they can be utilized in the treatment of breast cancer based on intrinsic subtype.

THE TUMOR MICROENVIRONMENT: A DRIVING FORCE FOR BREAST CANCER PROGRESSION

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The development and progression of breast cancer are complex processes involving a diverse interaction between the cancer cells and the cells in the microenvironment. The microenvironment of breast cancer is comprised of various cell types and extracellular matrix molecules which can exert various effects to the cancer cells. Traditionally, many focus has been made against the roles of fibroblasts and immune cells. However, recent studies indicate that the adipocytes can also contribute to the cancer cells phenotypes.

In this talk, I will summarize the recent efforts of modulating cancer microenvironment for targeting breast cancer cells behaviors. Also I will briefly introduce our ongoing researches on the biologic roles of cancer-associated adipocytes. The adipocytes in the vicinity of cancer cells show a phenotypic changes in gene expression and protein secretions. These changes indicate a complex cell-cell interactions between the epithelial cancer cells and the microenvironmental adipocytes. Furthermore, our recent studies indicate the normal mammary epithelial cells around the cancer cells may undergo molecular reprogramming and transition to more proliferative state.

TARGETING THE ANDROGEN RECEPTOR IN BREAST CANCER

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The androgen receptor (AR) is expressed in the majority of breast cancer and across the three main breast cancer subtypes. Progesterone Receptor (PR) on the other hand, is expressed primarily in Estrogen Receptor (ER) positive luminal breast cancer. Gene expression profiling and chromatin immunoprecipitation followed by gene sequencing techniques have significantly increased our understanding of ER signalling in breast cancer. The functional role of PR and AR on the other hand is relatively poorly understood up to now. There is substantial interplay between PR and ER, as well as AR and ER. AR is present in nearly all ER+ and ER-HER2+ breast cancers, and in ~75% of metastases. It is also present in a smaller proportion of triple negative breast cancers (TNBC). The signalling effect of AR is likely to be different across breast cancer subtypes, and particularly important is its interaction with ER signalling as AR and ER extensively co-occupy chromatin in breast cancer cells and share similar cofactors. Older trials of AR-directed therapies in breast cancer have had generally been disappointing. More recently, potent, next-generation, AR-directed therapies have been developed in the context of prostate cancer and early phase clinical trial data have emerged with the use of AR antagonists in TNBC. I will discuss the rationale and clinical context in which AR may be potentially targeted in breast cancer.

EDUCATION SESSION

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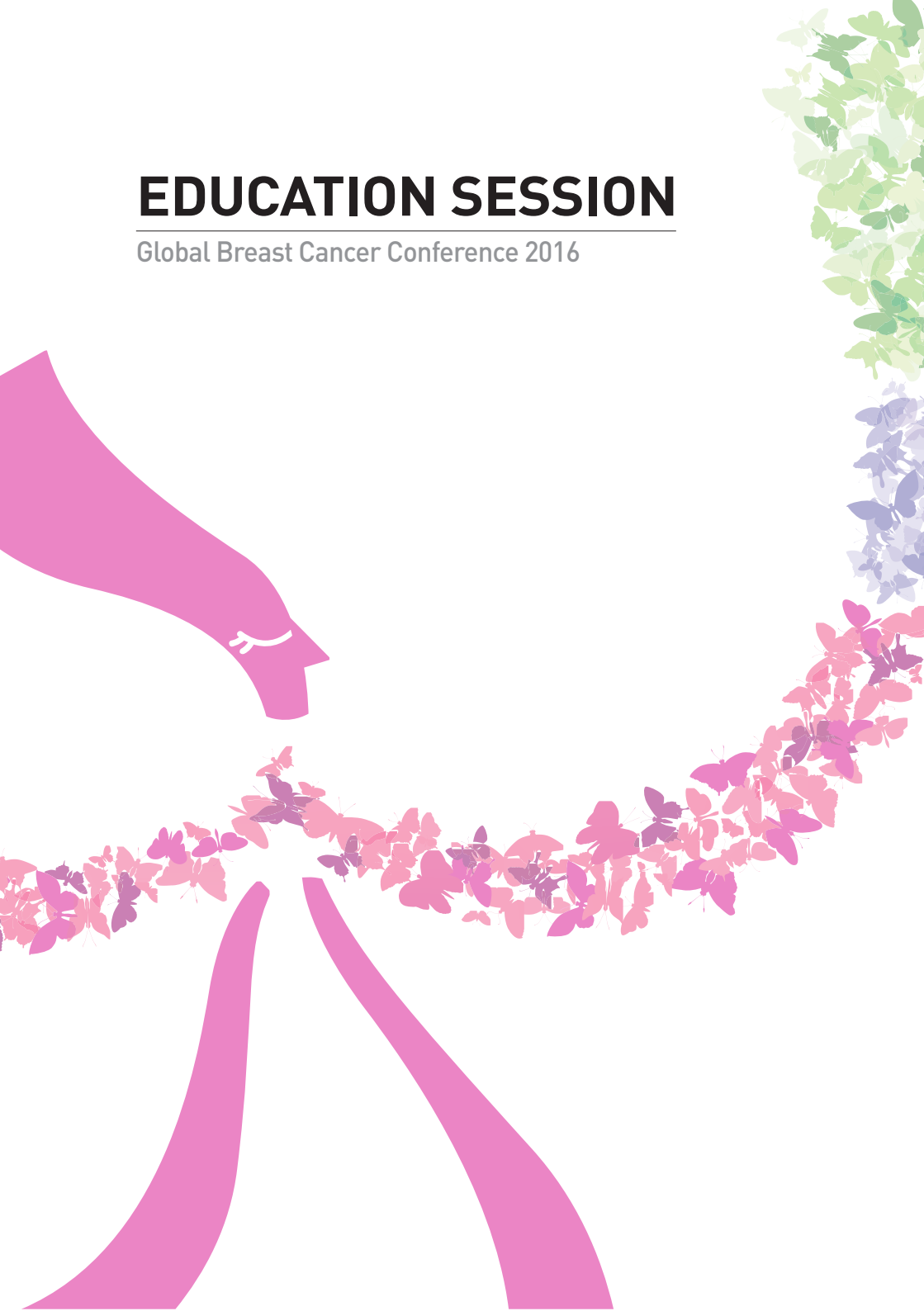

SURGICAL ISSUES IN PATIENTS WITH BREAST CANCER RECEIVING NEOADJUVANT CHEMOTHERAPY

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Data from randomized trials examining neoadjuvant treatment in operable breast cancer (BC) have shown that neoadjuvant systemic therapy (NST) achieves disease-free and overall survival results equal to adjuvant systemic therapy, making the neoadjuvant approach an option, especially in BC subtypes such as human epidermal growth factor receptor 2 (HER 2)-positive and triple negative breast cancers (TNBC) where the need for systemic therapy is clearly indicated. The sole and compelling clinical rationale for NST, as opposed to adjuvant treatment, is to provide effective systemic treatment while surgically downstaging the cancer at presentation. NST can render patients operable who had been inoperable, and can facilitate breast conserving therapy (BCT) when patients had previously needed mastectomy. NST also offers the potential advantage of gauging the sensitivity of the tumor to systemic therapy and the outcome of NST, particularly, pathological complete response (pCR) to systemic therapy is a prognostic marker for long-term survival, in patients with HER2-positive and TNBC disease.

However, the goal of NST is neither to achieve a pCR nor to establish a refined prognosis. The goal is to improve surgical options for the patient while delivering effective adjuvant therapy.

The likelihood of having surgical options affected by BCT depends on the stage at presentation, the response to treatment, and the patients preferences. Women who are candidates for breast conservation at baseline will not have their surgical choices affected by even a good response to NST. By contrast, women with extensive cancer throughout the breast will likely require mastectomy regardless of treatment response. Women who prefer a mastectomy for personal reasons, risk of hereditary BC, or consideration of cosmetic outcomes will again not have their surgical choices affected by the response to therapy. Increasingly, the ability of NST to downstage the axilla is becoming a potential rationale for NST, as patients with metastatic cancer to the axilla who have excellent treatment responses, and who are likely to have postsurgical radiation, may be able to avoid completion axillary dissection.

In this review, we aim to discuss the surgical benefits offered by the NST with modern era therapies and examine whether we are continuing to achieve the advantage of offering less extensive breast surgery.

NEOADJUVANT THERAPY OF EARLY STAGE HER2-POSITIVE BREAST CANCER: LATEST EVIDENCE AND CLINICAL IMPLICATIONS

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Neoadjuvant chemotherapy has been used in breast cancer to treat patients with locally advanced disease to facilitate surgical resection and to allow breast-conserving surgery. Further, the complete eradication of invasive tumor in the primary breast lesion and lymph nodes (pathologic complete response, or pCR) in response to neoadjuvant chemotherapy is a known prognostic factor, especially in HER2 overexpressed breast cancer.

Recently, trastuzumab has been combined with chemotherapy in the neoadjuvant setting, conferring benefits similar to those observed in the adjuvant setting in HER2 positive breast cancer. The NOAH trial compared neoadjuvant chemotherapy with or without concurrent trastuzumab followed by adjuvant trastuzumab to complete 1 year in 235 women with locally advanced/inflammatory HER2-positive breast cancer. In this study, trastuzumab significantly improved the event-free survival (EFS) rate (HR = 0.59; 95% CI = 0.380.90; $p = 0.013$), and the pCR rate in the breast and lymph nodes. Follow-up results after a median of 5.4 years confirmed the EFS benefit in the trastuzumab arm (5-year EFS, 57.5% vs. 43.3%; HR = 0.64; $p = 0.016$). The difference was particularly notable in patients who achieved a pCR with trastuzumab treatment : the 5-year EFS in these patients was 86.5%. There was also a trend toward an OS benefit with the addition of trastuzumab (5-year OS, 73.5% vs.62.9%; HR = 0.66; $p = 0.055$).

There is also significant emerging data on the use of combined HER2-targeted therapy in the neoadjuvant setting. In NeoALTTO, 455 patients with HER2-positive breast cancer and tumors >2 cm were randomized to receive trastuzumab alone, lapatinib alone, or the two agents in combination. Adjuvant therapy consisted of 3 cycles of FEC and the same anti-HER2 therapy to which the patient had previously been randomized to complete 1 year. In the NeoALTTO trial, the pCR rate in the breast was significantly higher with the combination of lapatinib and trastuzumab compared with trastuzumab alone (51.3% vs.29.5%; $p = 0.0001$).

In this study, there was no improvement in 3-year EFS or OS with the combination of trastuzumab plus lapatinib compared with trastuzumab alone (HR = 0.78; $p = 0.33$ and HR = 0.62; $p = 0.19$, respectively). However, the 3-year EFS and OS rates were significantly higher in patients who achieved a pCR (86% and 94%, respectively) than in those who did not (72% and 87%, respectively; $p = 0.0003$ and $p = 0.005$, respectively). For the subgroup of patients who achieved a pCR, the improvements seen in EFS and OS were driven by those patients who had hormone receptornegative disease, reinforcing the notion that the hormone receptorpositive/HER2-positive and hormone receptornegative/HER2-positive subgroups represent distinct disease subtypes.

Pertuzumab is a monoclonal antibody that targets a different extracellular domain of the HER2 receptorspecifically, the dimerization region with HER3. These heterodimers, particularly HER2-HER3, are thought to be important in driving breast cancer cell proliferation. In the phase II Neoadjuvant Study of Pertuzumab and Herceptin in an Early Regimen Evaluation (NeoSPHERE) trial, patients with HER2-positive breast cancer with tumors >2 cm were randomized to one of four treatment arms: A) docetaxel plus trastuzumab and pertuzumab, B) docetaxel plus trastuzumab, C) docetaxel plus pertuzumab, or D) pertuzumab plus trastuzumab alone (without chemotherapy)all of which were given every 3 weeks for 4 cycles. All patients then received adjuvant trastuzumab to complete 1 year. A statistically significant difference in the in-breast pCR rate was noted in patients who received trastuzumab and pertuzumab plus docetaxel compared with the combination of trastuzumab and docetaxel (45.9% vs.29%; $p = 0.014$). As reported in prior studies, pCR rates were higher in patients with hormone receptornegative tumors. Notably, even in the absence of cytotoxic chemotherapy, 16.8% of patients in the dual anti-HER2-alone arm achieved a pCR. Similarly, TRYPHAENA, a phase II study, evaluating the neoadjuvant use of pertuzumab in patients with operable, locally advanced breast tumor showed that combination of pertuzumab and trastuzumab induced higher pCR rate compared to other regimens.

Several clinical trials are currently underway to further evaluate the value of new drugs in the neoadjuvant setting such as PI3K targeting agents, T-DM1, etc. According to these data, different strategies will be emerged for HER2 positive early breast cancer.

NEOADJUVANT ENDOCRINE THERAPY IN BREAST CANCER

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Neoadjuvant endocrine therapy (NET) is increasingly becoming an integral part of preoperative breast cancer management especially in postmenopausal women with ER+, HER2- breast cancer. NET is associated with a higher rate of breast conserving surgery (BCS), may reduce the need for adjuvant chemotherapy and enables a delay of surgery for medical or practical reasons. There is much more experience in postmenopausal than premenopausal women. Aromatase inhibitors are generally the agent of choice. NET could downsize large tumors although pathologic complete response is not common, as well as it provides an early measurement tool for evaluating response to endocrine therapy. Despite the little evidence comparing NET against neoadjuvant chemotherapy (NCT), NET could be a safe alternative to NCT for certain patients. While duration of endocrine treatment in clinical trials has usually been standardized at around three to four months, it is clear that volume reductions continue to occur beyond that time in multiple studies and routine clinical practice is often to treat to maximum response. Change in Ki67 is accepted as a validated endpoint for comparing endocrine neoadjuvant agents. Levels of Ki67 during treatment are more closely related to long-term prognosis than pretreatment Ki67. The Preoperative Endocrine Prognostic Index (PEPI) that combines residual Ki67 score with measures of on-treatment ER and other clinicopathologic factors has also found application in clinical trials. Neoadjuvant endocrine therapy provides a unique opportunity for studies of endocrine responsiveness and the development of new experimental drugs combined with systemic hormonal treatment. I will also introduce ongoing NET in Korean women (NEST and METEOR study) in this presentation.

VALUE OF IMMUNE INFILTRATION TO PREDICT THERAPEUTIC OUTCOMES

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The importance of tumor-infiltrating lymphocytes (TILs) in adjuvant and neoadjuvant settings has been determined for breast cancer. In general, increased lymphocytic infiltration in tumors is inversely correlated with estrogen receptor and/or progesterone receptor expression, but is positively correlated with the pathologic complete response rate and increased patient survival. Although different methods have been used for assessing the presence of TILs in various studies, TILs have a strong prognostic and predictive significance, particularly in triple-negative and HER2-positive breast cancer. Recently, a standardized method for evaluation of TILs with hematoxylin and eosin stained tissues of breast cancer by a group of professionals (the International TILs Working Group) has been suggested and validated with a large number of tumor samples. However, which subset of immune infiltration is important for predicting therapeutic outcomes is still needed to be defined. Triple-negative breast cancer has no definite targeted treatment but a growing body of evidence suggests that immunotherapy shows great potential for combating the disease. Therefore, a better understanding of TILs and related features could facilitate the development of efficient immunotherapeutic approaches.

IMMUNE TARGETING IN BREAST CANCER

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Breast cancer has historically been considered immunologically silent. Recent efforts to characterize breast cancer-associated immune infiltrates demonstrate that some breast tumors contain T cell infiltrates (TILs), with greater numbers of immune cells present in breast cancers that are triple negative or HER-2+ relative to breast cancers that are ER+. Furthermore, data increasingly support a relationship between endogenous T cell infiltrates, pathologic response to neoadjuvant therapy, and survival in patients with triple negative or HER-2+ breast cancers. Extending these observations, it has also been recognized that multiple standard breast cancer therapies work in part by harnessing the immune system. Thus, enhancing breast cancer-specific immune responses--especially T cells--is a highly promising strategy for further improving clinical outcomes for breast cancer patients.

Multiple cancer vaccines have been tested in breast cancer with modest success. Vaccines are designed to induce T cells highly specific for a tumor antigen (HER-2, for example) expressed at high levels by tumor cells relative to normal tissues. Tumor-specific T cells are activated by two signals, one provided by the tumor antigen and the second provided by an array of accessory molecules that transmit a collection of positive and negative signals that together determine the magnitude and quality of T cell activation. Two of the major negative signaling pathways are regulated by the cell surface receptors cytotoxic T lymphocyte antigen-4 (CTLA-4) and programmed cell death receptor-1 (PD-1). Ipilimumab, a monoclonal antibody specific for CTLA-4, is approved for melanoma and was the first immune checkpoint antagonist available in the clinic. Currently, monoclonal antibody antagonists of PD-1 or its ligand PD-L1 are revolutionizing cancer therapy. They are well tolerated, and produce durable response rates of 10-50% or more in a wide range of tumor types. Current data suggest that PD-L1 expression within the tumor enriches for responders, but PD-L1 negative tumors can also respond. In breast cancer, early data suggest these response rates range from 5-19%, depending on the breast cancer subtype and level of PD-L1 expression by the tumor. The response rate for PD-L1-selected triple negative breast cancer is about 19% for both the PD-1 antagonist pembrolizumab and the PD-L1 antagonist atezolizumab. This represents an important advance for this highly aggressive breast cancer subtype, and clinical trials combining these drugs

with chemotherapy are underway. Defining predictive biomarkers of response and resistance, and developing combination strategies that incorporate other immune-based drugs or standard breast cancer therapies to further enhance response rates are high priorities for clinical development. Optimizing breast cancer immunotherapy is certain to improve therapeutic efficacy, enhancing quality of life and promoting cure.

COMBINATION IMMUNOTHERAPY APPROACHES: CHEMOTHERAPY, RADIATION THERAPY, AND DUAL CHECKPOINT THERAPY

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Immune checkpoint blockade antibodies, for example anti-programmed death 1/ligand 1 (anti-PD-1/L1) antibodies pembrolizumab and atezolizumab, are clinically active in metastatic breast cancer. Objective response rates ranged from 5-19% across four phase I clinical trials, highlighting the possibility that the majority of breast cancers will not respond to anti-PD-1/L1 alone. Conventional breast cancer therapies such as radiation therapy or chemotherapy have immunostimulatory properties, and may be combined with immunotherapy to enhance clinical benefit. The pre-clinical rationale and current clinical trial landscape of combination immunotherapy will be reviewed, as well as promising novel immunotherapy agents that are designed to overcome immune tolerance in breast cancer.

NEW PARADIGM FOR OVERCOMING ENDOCRINE RESISTANCE - TARGETING CDK 4/6

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Cyclin Dependent Kinases 4 and 6 have crucial role in cell cycle regulation by regulating the transition from the G1 phase to the S phase of the cell cycle. CDK4/6 form activating complexes with cyclin D1 and phosphorylates pRb, which relieves repressive activities of pRb and results in transcription of S-phase specific target genes. Cyclin D1 and CDK 4/6 amplification has been reported in 15-25% of breast cancer, more frequently in luminal A, B and HER2 enriched subtypes. ER and HER2 signaling pathways exert their downstream effects on the cyclin D;CDK4/6 pathway. Data suggest that endocrine acquired resistance may be mediated by deregulation of multiple alternative mitogenic pathways that can potentiate cyclin D1:CDK4/6 signaling in an ER-independent fashion, making CDK 4/6 a promising target for overcoming endocrine resistance.

However, efforts to develop CDK inhibitors in the past halted due to poor efficacy and overlapping toxicities with cytotoxic chemotherapy, most notably neutropenia. These first-generation CDK inhibitors were less specific and broad pan-CDK inhibitors. Recently, more specific CDK inhibitors were developed Palbociclib was the first in class which was approved by FDA - for use in first-line, HER2(-) HR (+) postmenopausal breast cancer with letrozole. Preclinical studies showed potent inhibition of tumor cell proliferation, accompanied by G1 arrest, and decrease in E2F-dependent gene expression. Large panel of cell lines were tested in vitro, and luminal, ER+ or HER2 amplified cells were most sensitive to palbociclib. Palbociclib also demonstrated synergistic growth inhibitory activity with tamoxifen or trastuzumab in ER+ and HER2 + cell lines. Phase 1 studies showed good bioavailability and mild to moderate toxicities, mainly myelosuppression. Phase 2 study was performed in post-menopausal ER+ metastatic breast cancer with PFS as primary endpoint. Patients were randomized to letrozole alone or letrozole plus palbociclib. Median PFS was significantly improved, from 10.2 months in letrozole alone arm to 20.2 months in combination arm (HR 0.488, 0,1319-0.748, $p < 0.001$). Most common AE was neutropenia, fatigue, leukopenia, but neutropenic fever was not reported. Phase 3 studies followed in other settings; PALOM-3 study compared PFS in palbociclib and fulvestrant vs. fulvestrant and placebo in HR+ MBC patients progressing on AI. The PFS was 9.2 vs.3.8 months in the combination vs. control

arm. Two other compounds are following the example of palbociclib; Ribociclib (LEE011), and Abemaciclib (LY2835219) are in active clinical testing in various settings. More studies are needed to identify mechanism of resistance to CDK 4/6 inhibitors and also to broaden current indication to other subtypes of breast cancer, as well as to find best combination partners.

PI3K/MTOR PATHWAY

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Dysregulation of PI3K/AKT/mTOR (PAM) pathway is frequently observed in breast cancer. PAM pathway hyperactivation has been associated with cancer pathogenesis, progression, and treatment resistance including hormone therapy resistance. mTOR, a serine/threonine kinase, is a downstream molecule of PI3K and AKT. It consists of two different complexes, mTORC1, and mTORC2. A close interaction between mTOR pathway and ER signaling has been reported. S6K1, a downstream molecule of mTORC1, can phosphorylate the activation function domain 1 of ER, which is responsible for ligand-independent receptor activation.

Many agents targeting PAM pathway have been developed and being tested in multiple clinical trials. Among these, only the mTOR inhibitor, everolimus, is currently approved for use in breast cancer in combination with exemestane in patients with ER+ HER2- breast cancer who have previously treated with non-steroidal aromatase inhibitors (AI).

Bolero 2 was a randomized phase 3 trials in advanced breast cancer evaluating everolimus and exemestane combination. It randomized 724 postmenopausal women with ER+ advanced breast cancer who had previously failed non-steroidal AI. The addition of everolimus to exemestane improved the PFS (10.6 months vs. 4.1 months, $p < 0.0001$). However, the adverse events such as stomatitis, non-infectious pneumonitis, and discontinuation of treatment were higher in patients receiving everolimus. Patients education, monitoring and timely management of adverse effects are critical to minimize toxicities and optimize efficacy.

Although clinical efficacy of everolimus has been shown in ER+ HER2- advanced breast cancer, the benefits may be more prominent in a selected subset of patients. Given the potential toxicity of mTOR inhibitors, it is especially important to identify reliable predictive markers to select the patients who are most likely to benefit from these combinations. Several studies have been performed to identify biomarker to predict the effect of mTOR inhibitors. However small sample size and inconsistent results suggest that further validation in larger studies need to be done before using the markers in routine clinical practice.

ESR1 MUTATIONS- A MECHANISM FOR ACQUIRED ENDOCRINE RESISTANCE IN BREAST CANCER

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Over two-thirds of breast cancers are positive for estrogen receptor (ER), therefore, patients with those cancers are treated with endocrine therapies. ER-positive tumors are primarily luminal subtypes and subclassified to either more differentiated and indolent luminal A subtype, or more aggressive and relatively endocrine-resistant luminal B subtype. Thus, endocrine sensitivity is primarily determined by level of ER expression. However, about 25% of primary breast cancers and most of the metastatic cancers finally develop endocrine resistance. Multiple mechanisms responsible for endocrine resistance have been proposed and include deregulation of various components of the ER pathway itself, alterations in cell cycle and cell signaling pathways, and the activation of escape pathways that can provide tumors proliferation and survival. In addition, recent advances in comprehensive clinical sequencing data identified activating mutations in ESR1 gene, encoding ERα.

Genomic alterations in ESR1 gene includes ESR1 amplifications, genomic rearrangements, and missense mutations, however, missense mutations were more recurrently discovered and reported so far. In the last few years, several studies revealed that mutations in ESR1 clustered in a hotspot within the ligand-binding domain (LBD) of the ER during endocrine treatment, such as tamoxifen and aromatase inhibitors. The mutations lead to constitutive ligand-independent activity of ER and promotion of tumor proliferation and metastatic capacity.

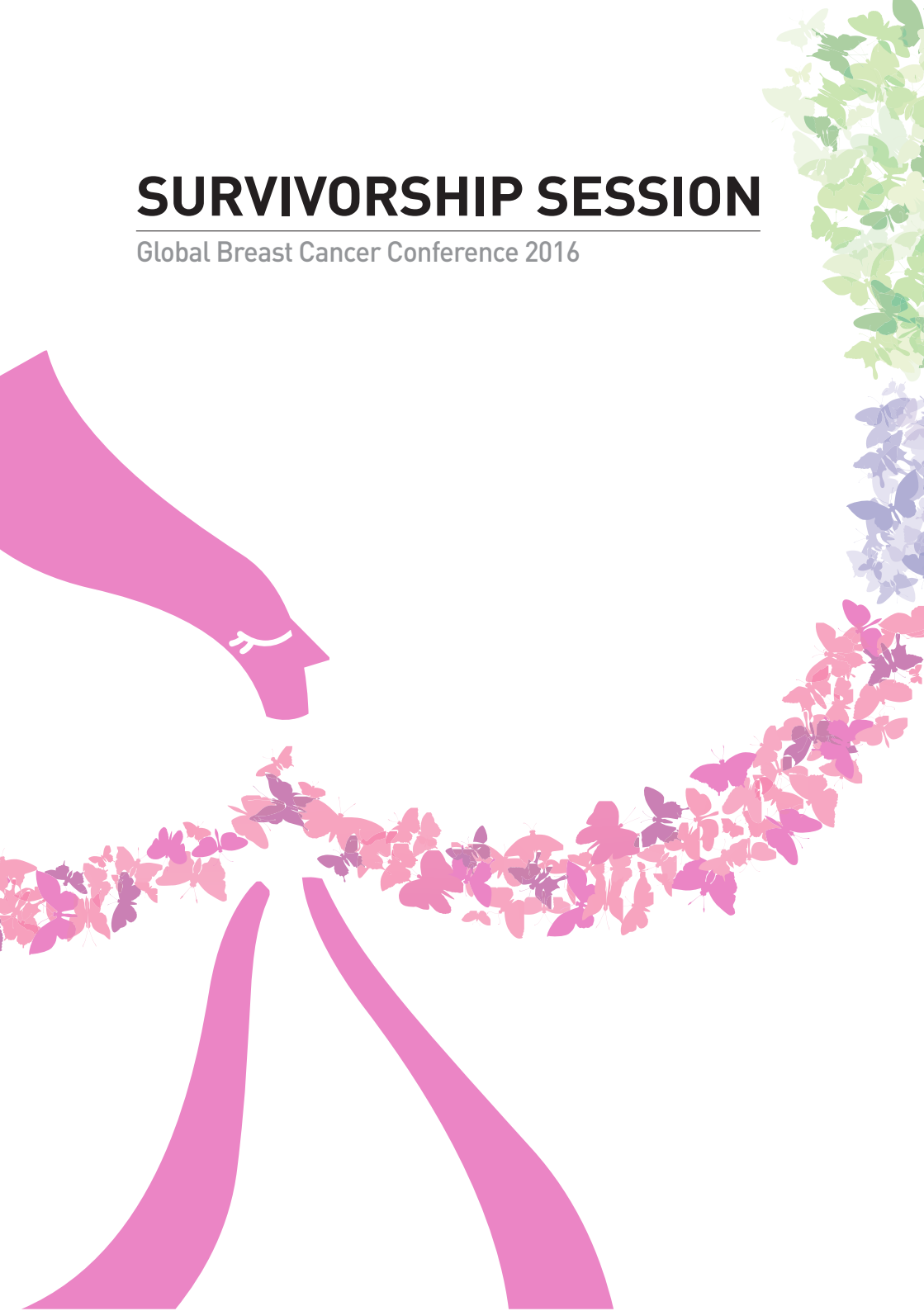
ESR1 mutations were first detected in metastatic diseases by whole genome sequencing in small number of patient samples. Next, targeted next-generation sequencing in 36 patients who had disease progression after hormonal treatment (MSKCC cohort), and 44 patients in BOLER0-2 trial showed 17.5% were found to harbor ER LBD mutations. The prevalence of the ER LBD mutations in different studies ranges 14-54% depending on the study population and treatment courses in the study. Notably, ESR1 mutations have been reported about 3% in primary tumors suggesting clonal evolution or selection during hormonal treatment.

Detection of ESR1 mutations might affect the clinical application of the new scientific knowledges. Massively parallel next-generation sequencing enabled the quantitation of cancer cells harboring mutations, but high error rate limits clinical application. Emerging promising newer technologies including ultrasensitive Duplex sequencing and digital droplet PCR might play a key role to detect rare mutations in small amount of genomic samples.

In conclusion, new discovery of recurrent ESR1 mutations in endocrine-resistant metastatic breast cancer will be the basis of understanding mechanism of treatment resistance. Parallel development of diagnostic and therapeutic strategies in this field will improve treatment outcome in those patients.

SURVIVORSHIP SESSION

Global Breast Cancer Conference 2016



COMMUNICATION AND UNMET NEEDS OF PATIENTS/FAMILIES/CAREGIVERS

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Considering the large number of women with breast cancer, researchers have begun to pay attention to the quality of life and the needs of these survivors. Studies show that most women with breast cancer, although free of disease, experience biomedical and psychosocial concerns such as body image, continued menopausal symptoms, fertility and pregnancy, fear of cancer recurrence, employment issues, and financial concerns.

Because of the threat posed by the cancer diagnosis, the uncertain outcome of treatment, and the physical and psychological hardships of cancer therapy, most patients require information about their disease and substantial emotional support. Even when they are motivated, patients often find it difficult to obtain timely information, and this leads to dissatisfaction, misinformation, and misunderstanding.

Good communication between patients with cancer, family caregivers, and the health care team helps improve patients well-being and quality of life. Communicating about concerns and decision making is important during all phases of treatment and supportive care for cancer. The goals of good communication in cancer care are to build a trusting relationship between the patient, family caregivers, and the health care team, to help the patient, family caregivers, and health care team share information with each other, and to help the patient and family talk about feelings and concerns.

The patientphysician interaction, a central component of the care delivery process, plays a significant role in the cancer setting. While the communication process between physicians and cancer patients shares most of the general features of standard patientphysician interactions, the stigma and fear associated with a cancer diagnosis, the complexity of medical information, and the uncertainty regarding the course of the disease and treatment benefits may add a greater emotional dimension to the interaction. Thus the manner in which physicians communicate with their cancer patients and their families can have a significant impact on patients quality of life. Studies indicate that women with breast cancer who are adequately informed about their illness

and treatment and who appropriately communicate with physicians are better able to reduce their feelings of distress. They are also more likely to maintain a sense of control and to cope with the uncertainty of the illness. On the other hand, poor communication is associated with increased patient stress, decreased satisfaction, decreased adherence, and elevated malpractice risk. Within this context, communication with family is important because families can help patients make better decisions about their cancer care. Patients and their family members can join together as partners to communicate with the doctor and health care team. Communication that includes the patient and family is called family-centered communication. Family-centered communication with the doctor helps the family understand its role in caregiving. Family caregivers who get specific and practical direction from the health care team are more confident about giving care. When caregivers receive this help, they can give the patient better care. Communication between family caregivers and the health care team should continue throughout cancer care.

After all, communication is important throughout cancer care, but especially when important decisions are to be made. These important decision times include: when the patient is first diagnosed, any time new decisions about treatment need to be made, after treatment - when discussing how well it worked, whenever the goal of care changes, when the patient makes his or her wishes known about advance directives, such as a living will. Yet, limited studies have been conducted regarding communication and unmet needs between breast cancer patients, families, and caregivers. This presentation aims to review current literature regarding communication and unmet needs between breast cancer patients, families, and caregiver focusing on survivorship stage.

PATIENT NAVIGATION SERVICES FOR BREAST CANCER SURVIVORS

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Patient navigation, which is defined as the logistic and emotional support and guidance, has emerged as a promising approach to reduce cancer disparities and address diverse barriers for vulnerable populations since its origin in Harlem, New York, in 1990. Although cancer patient navigation is being recognized as an essential service in cancer care for vulnerable populations in the U.S., however, patient navigation programs in Korea have not yet been developed. Given that health disparities in cancer care among the socio-economically poor in Korea exist, the adoption of the patient navigation program is necessary. Prior to the development of Korean patient navigation program, knowledge are needed of the range of specific barriers faced by Korean cancer patients, and their associations with patient navigation services that help Korean cancer patients through the cancer treatment and survivorship process. The current presentation will address 1) the patient navigation concept and models for breast cancer patients, 2) the application process for patient navigation program to Korean cancer patients, and 3) practical implications of patient navigation in underserved and vulnerable population coping with breast cancer.

M-HEALTH APPLICATION BEYOND QUALITY OF LIFE FOR BREAST CANCER SURVIVORS

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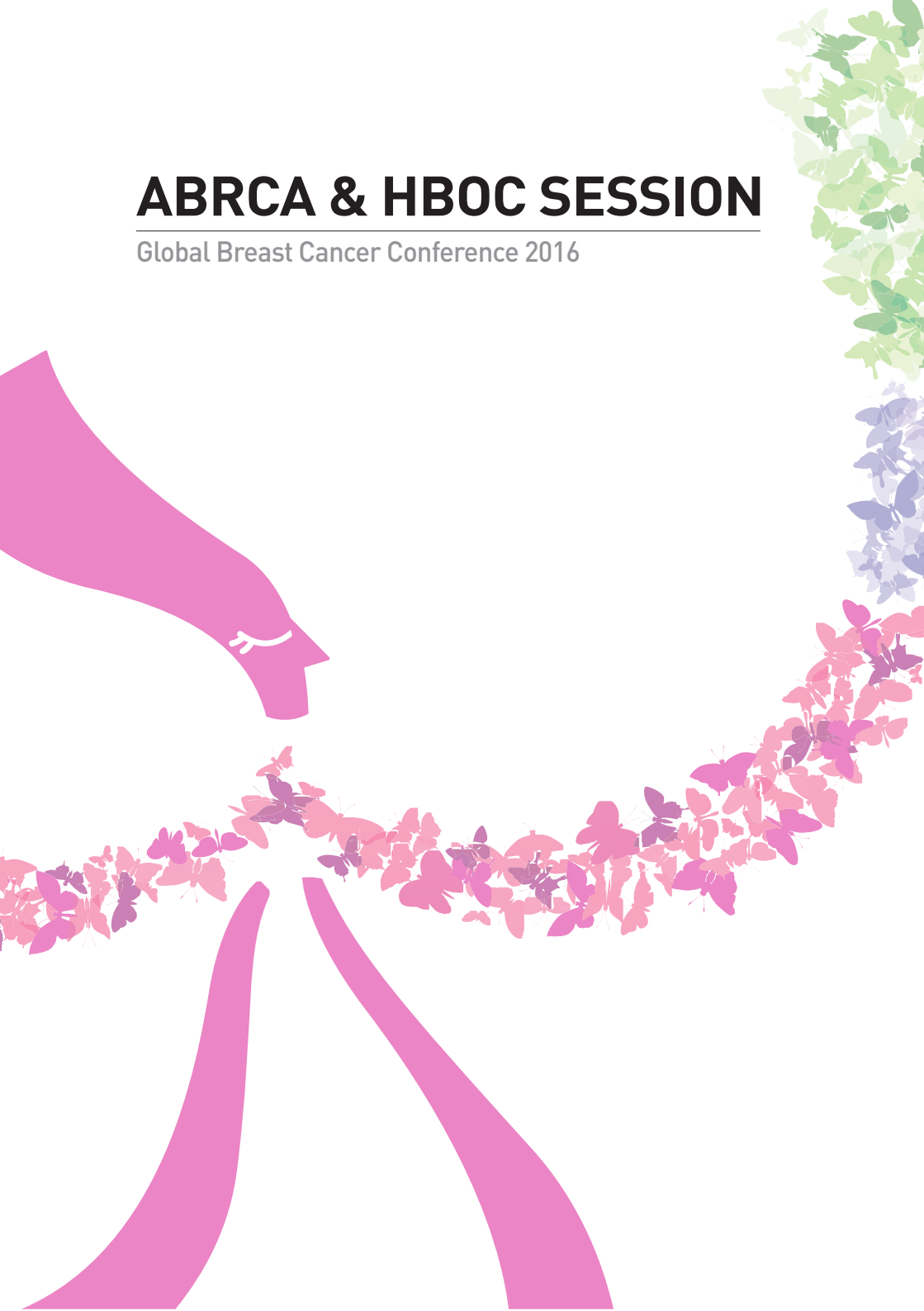
Electronic health (e-Health) can be defined as the practice of medicine and public health using information and communication technology (ICT) devices such as computers, mobile phones, and satellite communications. The term mobile health (m-Health) refers to a subsegment of eHealth and is now used when the practice involves wireless communications, especially mobile or smart phones. Among m-health applications in cancer survivorship care, two conceptual pathways could be focused by oncologists who meet survivors in the forefront; one is the easy, real-time access to patient-reported outcome (PRO) and the other is the potential aid of their lifestyle modification.

Distress is common and can occur at any time throughout the breast cancer course. It is associated with deleterious effects on not only the health-related quality of life but also survival. In terms of breast cancer survival outcomes, failure to identify distress in the early cancer course can result in reduced adherence to subsequent long term medication. Physical activity (PA) is also one of the most well established lifestyle factor associated with breast cancer outcomes. Among many underlying links between PA and survival outcomes, we are working on proving a hypothesis: Exercise can have positive effects on distress, and vice versa.

We will present our experience searching for an algorithm predicting distress in breast cancer patients, which is based on PRO of anxiety, emotion, and sleep. In addition, a trial for determining the association between PA and distress will be introduced, which uses ICT such as smart phone app and wearable devices.

ABRCA & HBOC SESSION

Global Breast Cancer Conference 2016



PRECISION MEDICINE FOR CANCER: THE BRCA1/2 PARADIGM

Timothy Rebbeck

Department of Epidemiology, Harvard TH Chan School of Public Health and Dana Farber Cancer Institute, U.S.A.

Inherited mutations in BRCA1or BRCA2 (BRCA1/2) may be necessary to explain the Mendelian pattern of breast cancer in some families, but are not sufficient to completely describe inter-individual variability in cancer risk. A number of studies suggest that modifier exposures or loci influence cancer penetrance among BRCA1/2 mutation carriers. BRCA1/2 mutation position or type also influence cancer risks. Therefore, the ability to predict and prevent cancer risk requires consideration of more than the presence or absence of the BRCA1/2 mutation. More complete models that consider individual risk factors and mutations can improve risk estimates. This information in turn can lead to improved risk assessment and decision making. The primary prevention strategies in BRCA1/2 mutation carriers involves surgical prophylaxis, which may confer non-trivial sequellae including impacts on childbearing, bone health, cardiovascular disease risk, and others. Therefore, application of these preventive interventions may be optimized by using a precision prevention approach.

MANAGEMENT OF HEREDITARY BREAST CANCER: ADVANCES AND CONTROVERSIES

Ava Kwong

Department of Surgery, The University of Hong Kong, Hong Kong

Women with a germline BRCA1 or BRCA2 mutation or other hereditary predisposition for breast and ovarian cancer have substantial increased risk of breast, ovarian and related cancer. Mutation carriers and families at risk benefit from individualized medical evaluation and risk management. Until recently, risk management has really been based on more intensive surveillance and screening programmes, prophylactic surgery and also chemoprevention. Standard Guidelines for testing and management options are available but practices may vary in different countries based on availability and resources. As we have more understanding of the mechanisms on carcinogensis of breast cancer, the identification of a mutation in susceptibility genes may also guide treatment decisionmaking by providing potential targets for biologic agents to help select treatment strategies. Hence genetic testing of hereditary breast and ovarian cancer syndromes (HBOC) has increasingly become the standard of care for high-risk patients and their family members. More advance diagnostic technologies such as Next- generation sequencing (NGS) in recent years have facilitated an unprecedented capability to gain a better understanding of the genetic complexity of many cancers including HBOC. Mutigene panels are increasingly being used but interpretation of the results in its application on clinical management maybe challenging. Hence, despite the advantages, new technologies may also created controversies and interpretation difficulties which may adversely affect clinical decisions. A review of supporting medical evidence of existing practice in management of these high risk individuals and the controversies which still exist will be discussed.

GENE-PANEL SEQUENCING IN THE CONTEXT OF THE PREDICTION OF BREAST-CANCER RISK IN ASIA

Soo-Hwang Teo

Cancer Research Malaysia, Malaysia

Although an association between protein-truncating variants and breast cancer risk has been established for 11 genes, only alterations in BRCA1, BRCA2, TP53 and PALB2 have been reported in Asian populations. Given that the age of onset of breast cancer is lower in Asians, it is estimated that inherited predisposition to breast cancer may be more significant. In my talk, I will review the status of our current knowledge of breast cancer predisposition genes in Asia and discuss the potential clinical utility of panel testing in Asian populations.

SATELLITE SYMPOSIUM

Global Breast Cancer Conference 2016

Reference 1. Campone M, et al. Eur J Cancer. 2013;49:2621-2632. **2.** 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.

아피니토정 2.5mg, 5mg, 10mg (에베로리무스)

[효능 • 효과] 1. 비스테로이드성 아로마타제 저해제에 불응성인, 에스트로겐 수용체 양성, HER-2 음성 국소 진행성 또는 전이성 유방암이 있는 폐경 후 여성에서 엑스메스탄과 병용투여 2. 췌장에서 기원한 진행성 신경내분비종양 (pNET) 3.VEGF (Vascular endothelial growth factor) 표적요법 (수니티닙 또는 소라페닙)의 치료에 실패한 진행성 신장세포암 4.치료적 중재가 필요하지만 근치적인 외과적 절제술을 받을 수 없는 결절성 경화증(TSC)과 관련된 뇌실막밑 거대세포 성상세포종 (SEGA) 5. 즉각적인 수술이 요구되지 않는, 결절성 경화증(TSC)과 관련된 신장 혈관근육지방종. [용법 • 용량] 이 약은 1일 1회 매일 일정한 시간에 복용하며, 계속해서 식사와 함께 복용하거나 또는 계속해서 공복시에 복용한다. 이 약은 물 한 컵과 함께 통째로 삼켜야 하며, 씹거나 부수지 말아야 한다. 약을 삼키기 어려운 경우, 이 약을 물(약 30mL)에 넣고 잘 저어 분산시킨 후 (약7분) 즉시 마신다. 마신 후, 컵에 같은 양의 물을 넣어 헹구고, 그 물을 다 마셔 약을 완전히 복용해야 한다. 이 약의 투여는 항암 요법에 대한 사용경험이 있는 의사에 의해 시작되어야 한다. 약의 투여는 임상적 유익성이 관찰되는 한, 또는 수용할 수 없는 독성이 나타나기 전까지 지속되어야 한다. 1.유방암, 신경내분비종양, 신장세포암 및 결절성경화증(TSC)과 관련된 신장 혈관근육지방종: 1일 1회 10mg 2.결절성 경화증(TSC)과 관련된 뇌실막밑 거대세포 성상세포종(SEGA): 용량은 Dubois계산식을 이용, 체표면적(body Surface Area; BSA, m2)에 근거하여 개인화된다(W:체중(kg), H:신장(cm)).[BSA=(W0.425 x H0.725) x 0.007184]. TSC와 관련된 SEGA환자 치료시 권장 시작용량은 4.5mg/m2이다.(가장 근접한 용량(n)정을 투여한다). 약은 이 약의 다른 용량과 혼합하여 총 투여 용량을 맞출 수 있다. 투약 시작 후 에베로리무스의 전체 최저 혈중 농도가 약 2주마다 평가되어야 한다. 최저 혈중 농도 5-15ng/mL에 도달하기 위해 용량은 적정되어야 한다. SEGA 부피를 이 약의 투여 시작 약 3개월 후에 평가하고, SEGA 부피의 변화, 상응하는 최저 혈중 농도 및 내약성을 고려하여 용량을 조정한다. 일단 안정된 용량이 얻어지면, 매 3개월에서 6개월 마다 바뀐 체표면적을 고려하여 최저혈중농도를 모니터링하거나, 치료하는 동안 안정적인 체표면적을 유지하는지 매 6개월에서 12개월마다 모니터링해야 한다. 3.용량조정: (1)중증 또는 견딜 수 없는 약물 이상반응이 나타날 경우, 일시적 용량감소나 투약중단이 필요할 수 있다. 용량 감량이 필요한 경우, 기존에 투여하던 용량의 약 50%의 용량이 권장된다. 이 약 한정의 최저 용량보다 낮은 용량으로 감량시, 2일마다 투여하는 것을 고려한다. (2)강력한 CYP3A4 저해제와 병용투여는 피해야한다. 중증도 CYP3A4 또는 PgP 저해제와 병용투여시 주의한다. 환자에게 이 약과 중증도 CYP3A4 또는 PgP 저해제의 병용투여가 필요한 경우, 이 약의 용량을 기존에 투여하던 용량의 약 50%로 감량한다. 약물 이상반응을 조절하기 위해 추가적인 감량이 요구될 수 있으며 가용한 이 약의 함량(2.5mg)보다 낮은 용량으로 감량시, 이틀에 한번 투여하는 것을 고려한다. 자몽, 자몽쥬스 및 CYP450이나 PgP의 활성을 저해하는 것으로 알려져 있는 다른 음식은 이 약의 노출을 증가시킬 수 있으므로 투약기간에는 피해야 한다. (3)유방암, 신경내분비종양, 신장세포암 및 결절성 경화증(TSC)과 관련된 신장혈관근육지방종 환자에게 강력한 CYP3A4 유도제의 병용투여가 필요한 경우, 이 약의 용량을 점진적으로 2배까지 증량하는 것을 고려해야 한다. 강력한 CYP3A4 유도제 투여를 중단할 경우, 이 약의 용량은 유도제를 투여하기 전의 용량으로 복구시키기 전에 적어도 3일에서 5일간의 wash out 기간(강력한 효소의 de induction 시간)을 고려해야한다. St. John's Wort는 이 약의 노출을 예측할 수 없게 감소시키므로 강력한 CYP3A4 유도제의 병용투여는 피해야 한다. 결절성 경화증(TSC)와 관련된 뇌실막밑 거대세포 성상세포종(SEGA)환자에게 강력한 CYP3A4 유도제를 병용투여시, 5-15ng/mL인 최저농도를 얻기 위해서 이 약을 증량한다. 이 약의 하루 용량을 두 배로 하고, 내약성을 평가하고, 2주 후에 에베로리무스의 최저농도를 평가한다. 5-15ng/mL을 유지하기 위해서 필요시 용량을 더 조정한다. 강력한 유도제를 중단하면, 이 약의 용량은 강력한 CYP3A4 유도제 투여 이전 용량으로 되돌려야하며, 에베로리무스 최저농도는 그 후로 약 2주 후에 다시 평가한다. 소아환자: 1.유방암, 신경내분비종양, 신장세포암 및 결절성경화증(TSC)과 관련된 신장 혈관근육지방종: 소아환자에서 이 약의 안전성 및 유효성은 확립되어있지 않다. 2.결절성 경화증(TSC)와 관련된 뇌실막밑 거대세포 성상세포종(SEGA): 1세 이상의 소아환자에서 이 약의 권장 용량은 성인 환자에서와 일치한다. 이 약은 1세 미만의 TSC와 관련된 SEGA 환자와 간장애가 있는 18세 미만의 TSC와 관련된 SEGA 환자에서 연구되지 않았으므로, 이 약의 사용은 권장되지 않는다. 간장애 환자: 1.유방암, 신경내분비종양, 신장세포암 및 결절성경화증(TSC)과 관련된 신장 혈관근육지방종: 경증 간장애(Child-Pugh A): 권장 용량은 1일 7.5mg 이다. 내약하지 못하는 경우, 5mg까지 감량할 수 있다. 중등도 간장애(Child-Pugh B): 권장 용량은 1일 5mg 이다. 내약하지 못하는 경우, 2.5mg까지 감량할 수 있다. 중증 간장애(Child-Pugh C): 투여가 권장되지 않는다. 치료상의 이익이 위험성을 상회할 경우에만 투여하되, 1일 2.5mg을 넘지 않도록 한다. 환자의 간 상태(Child-Pugh)가 치료 도중 변화하였을 경우 용량을 조절해야한다. 2.결절성 경화증 (TSC)과 관련된 뇌실막밑 거대세포 성상세포종 (SEGA) : 18세 미만 환자 : 이 약은 간장애를 보유한 18세 미만의 TSC와 관련된 SEGA환자에게 권장되지 않는다.; 18세 이상환자: 경증 간장애(Child-Pugh A) 권장용량은 BSA에 근거해 계산된 용량의 75%이다.; 중증도 간장애(Child-Pugh B) 권장 용량은 BSA에 근거해 계산된 용량의 50%이다. ; 중증 간장애(Child-Pugh C): 투여가 권장되지 않는다. 에베로리무스의 전체 혈중 최저 농도가 투약 시작 2주 후 또는 간상태(Child-Pugh)의 변화 후에 측정되어야 한다. 용량은 최저 농도 5-15ng/mL 도달을 위해 적정되어야 한다. 치료기간동안 환자의 간상태(Child-Pugh)가 변하면 용량을 조정해야 한다. [경고] 1)비 감염성 폐렴 2)감염 3)과민 반응 4)구강 궤양 5)신부전 6)실험실 검사 및 모니터링(신기능, 혈당, 혈액지질, 혈액학적 지표) 7)약물상호작용 8)간장애 9)예방접종 10)안지오텐신전환효소(ACE) 저해제의 병용으로 인한 혈관 부종 [금기] 이 약의 주성분, 다른 라파마이신 유도체 또는 이 약의 다른 성분들에 과민증이 있는 환자, 갈락토오스 불내성, Lapp 유당분해효소 결핍증 또는 포도당-갈락토오스 흡수장애 등의 유전적 문제가 있는 환자

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GETTING TARGETED THERAPY DEVELOPMENT UP-TO-DATE IN BREAST CANCER

Joohyuk Sohn

Yonsei Cancer Center, Korea

Hormone receptor positive tumors represent the most common form of breast cancer. Endocrine therapy remains the main initial therapeutic strategy for these patients and has been associated with significant clinical benefits in a majority of patients. However, most of the metastatic breast cancers progress ultimately to the endocrine therapies leading to death.

Recent developments in the understanding of molecular interactions of hormone signaling with other important pathways shed the light of improving treatment outcome by combining endocrine therapy with targeted therapies. The front line runner was mTOR inhibitor, everolimus combined with exemestane in non-steroidal aromatase inhibitor resistant breast cancer patients. Now, we have CDK4/6 inhibitor approved by FDA based on randomized phase II trial. Moreover, PIK3CA inhibitor, Buparlisib plus fulvestrant showed better survival outcome than fulvestrant alone in hormone receptor positive postmenopausal metastatic breast cancer.

Herein, we are going to discuss about current clinical trial outcomes with new targeted agents and future directions in terms of treatment of hormone positive breast cancer.

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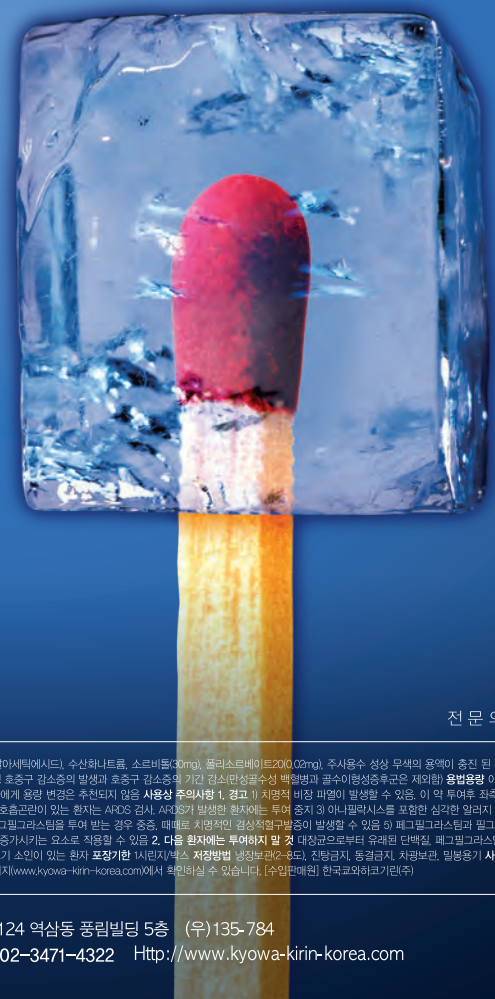

전 문 의 약 품

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 체험 *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) 경상적혈구질환 환자가 필그라스팀, 페그필그라스팀을 투여 받는 경우 중증, 때때로 치명적인 겸상적혈구발증이 발생할 수 있음 5) 폐그필그라스팀과 필그라스팀이 작용하는 G-CSF수용체가 암세포에서 발견됨. 폐그필그라스팀이 골수성 암과 골수이형성증을 포함한 암 종류를 증가시키는 요소로 직용할 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(2~8도), 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] 한국교와하코기린(주)

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PROPHYLAXIS OF FEBRILE NEUTROPENIA: EXPERIENCES WITH ADJUVANT TAC

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Febrile neutropenia (FN) is one of the life-threatening adverse events during breast cancer treatment. It is defined as grade 4 neutropenia with fever (single oral temperature >38.3C or temperature >38.0C over 1-2 hours). Old age, ECOG status, nutritional status, advanced stage, prior episode of FN, and dose intensity are factors increasing the risk of FN. Prolonged duration of FN could also cause dose reduction and treatment interruption of the chemotherapy, or frequent hospitalization that might raise burden of those patients. The administration of granulocyte colony-stimulating factor (G-CSF) is done from nine to fourteen times during single session of chemotherapy, and its use is related to bone pain, however, that can be managed with NSAIDs. The use of G-CSF is not considered to increase incidence of leukemia significantly during breast cancer chemotherapy. Primary prophylaxis is to use hematopoietic growth factors from the first and subsequent cycles, while the secondary prophylaxis is defined as addition of growth factors when neutropenic complication was seen from prior chemotherapeutic cycle. Two thirds of the breast cancer patients experience FN at the first cycle. Primary prophylaxis can effectively prevent febrile neutropenia, hospitalizations, and infection-related deaths. Therefore several guidelines support to use G-CSF as primary prophylaxis if the risk of FN is assessed more than 20% following chemotherapeutic regimen.

Pegfilgrstim is a pegylated form of G-CSF that has longer half life than filgrastim because of reduced renal clearance, so that it can be given once-per-cycle subcutaneously. Results from GEPARTRIO study, primary prophylaxis of pegfilgrastim (6 mg on day 2) showed significant lower incidence of febrile neutropenia than filgrastim(5 μg/kg/day from day 5 to day 10, primary prophylaxis). From a systematic review that compares pegfilgrastim prophylaxis with short-acting G-GSF showed decreased FN and related complications. A randomized study showed pegfilgrastim administration was more costly, however, the risk of FN was decreased in pegfilgrastim group (10% vs.38%). In FEC-D (Fluorouracil, epirubicin, and cyclophosphamide followed by docetaxel) regimen, it was cost-effective to use pegfilgrastim in primary prophylaxis during D admin-

istration. Pegfilstrastim discontinuation was related to infection (0% to 14%) in another study. Pegfilstrastim was also associated shorter hospitalization time in treatment of non-Hodgkins lymphoma, lung, breast, colon, and ovarian cancer. Pegfilgrastim should be administered after 24 hours followed by chemotherapy and should not be given 14 days before chemotherapy. Musculoskeletal pain is frequently reported during G-CSF treatment. Pegfilgrastim use is associated with higher incidence of bone pain compared to that of placebo. In a retrospective study, pegfilgrastim showed more severe bone pain than filgrastim. In a meta-analysis, there was no significant difference was shown in bone pain rates between pegfilgrastim and filgrastim.

Primary prophylaxis using pegfilgrastim is recently reimbursed in Korean National Health Insurance System, with adjuvant TAC(docetaxel, Adriamycin, and cyclophosphamide) and neoadjuvant dose-dense FEC(fluouracil, epirubicin, and cyclophosphamide) regimen. In BCIRG-005 trial that compared concurrent with sequential administration of docetaxel (TAC 6 cycles in every 3 weeks versus AC 4 cycles followed by docetaxel 4 cycles), there were no significant difference between two regimens in 10-year disease free survival (66.3% in TAC and 66.5% in AC-T, $p = 0.749$) and overall survival (78.9% in TAC and 79.9% AC-T, $p = 0.506$). The toxicity profile is different in both arms. From the results of Korean patients, TAC was associated with higher incidence of FN (without primary prophylaxis), but showed similar quality of life compared to AC-T treatment. Six cycles of TAC can provide shorter duration of treatment and especially with primary prophylaxis of pegfilgrastim, the quality of life during treatment could be improved. If the patients are consists with low risk from Multinational Association for Supportive Care in Cancer (MASCC) risk index score, therapeutic strategy with outpatient setting can be possible.

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원료약품의 분량 1mL중 주성분 풀베스트란트 (별규) 50mg **성상** 무색에서 노란색의 맑은 점성 액이 들어있는 프리필드시린지 **적응증 (효능 · 효과)** 에스트로겐 수용체 양성의 폐경기 이후 여성으로서 항에스트로겐 투여 후 질병이 재발된 국소 진행성 또는 전이성 유방암 **용법 · 용량** 성인 여성(노인 환자 포함): 한달 간격으로 500mg을 투여한다. 첫 투여 2주 후 500mg을 추가적으로 투여한다. 이 약은 각 둔부에 한 번, 천천히 근육 내 주사로 5mL를 두 번 연속적으로 투여한다. 소아 및 청소년:안전성과 유효성이 확립되지 않았으므로 투여하지 않는다. 신장애 환자:경증~중등도 신손상 환자(크레아티닌 소실율 30mL/min 이상)는 용량 조절이 필요하지 않다. 중증의 신손상 환자(크레아티닌 소실율 30mL/min 미만)에게서 안전성과 유효성이 평가되지 않았다. 간장애 환자:경증~중등도 간손상 환자의 치료시에는 주의하여 투여한다. 간손상 환자에서 안전성과 유효성이 평가되지 않았다. **주요 사용상의 주의사항** 1. 경고:벤질알코올은 미숙아에서 치명적인 가쁜 호흡증상과 연관이 있는 것으로 보고되었다. 2. 다음 환자에는 투여하지 말 것 1) 주성분이나 다른 성분에 과민반응을 보인 환자 2) 임산부 및 모유 수유부 3) 중증의 간장애 환자 4) 신생아, 미숙아(벤질알코올을 함유하고 있다.) 3. 다음 환자에는 신중히 투여할 것 1) 경증~중등도의 간장애 환자 2) 중증의 신장애 환자 3) 본제의 투여 경로 때문에, 출혈성 체질, 혈소판감소증, 항응고제 투여 환자 치료시에는, 신중히 투여한다. 4) 진행성 유방암 여성에서 혈색전증이 흔하게 나타나는 것으로 관찰되었다. 이런 위험이 있는 환자에게 처방할 때는 이를 고려하여야 한다. 5) 본제가 뼈에 미치는 영향에 대한 장기간의 자료는 없다. 작용기전을 고려할 때 골다공증의 위험이 있을 수 있다. 4. 주요 이상반응 1) 이상반응은 임상시험, 시판 후 조사 또는 자발적 보고에 근거한다. 가장 흔하게 보고된 이상반응은 주사 부위의 반응, 무력증, 오심과 간 효소(ALT, AST, ALP)치 상승이었다. 5.적용상의 주의 경고:사용 전 안전주사침(SafetyGlide)를 가압증기 멸균하지 않도록 한다. 사용 및 처분 시 손은 항상 손가락을 바늘 뒤에 위치하도록 한다. 두 개의 각 시린지에 대한 사용법은 다음과 같다:1) 트레이에서 유리 시린지 통을 꺼내어 손상 유무를 확인한다. 2) 부착된 고무 꼭지 뚜껑 덮개를 제거하기 위해 시린지 Luer connector의 흰색 플라스틱 덮개의 봉함을 개봉한다. 3) 안전 주사침(SafetyGlide)의 외부 포장을 개봉한다. 안전주사침을 Luer-Lok에 연결한다. 4) 완전히 장착될 때까지 돌린다. 5) 주사침을 Luer connector로 잠그기 위해 돌린다. 6) 바늘 끝의 손상을 막기 위하여 덮개를 곧게 당긴다. 7) 시린지를 투여부위로 옮긴다. 8) 주사침 덮개를 제거한다. 9) 투여 전 주사 용액에 이물이나 변색이 없는지 육안 검사한다. 10) 시린지의 과도한 가스를 제거한다. 11) 둔부에 천천히 근육내 주사로 투여한다(1-2분/투여). 사용자의 편의를 위하여 주사침의 경사진 부분은 레버방향으로 되어있다. 12) 투여 후, 주사침 보호장치를 활성화시키기 위하여 한 손가락으로 밀어 레버장치가 작동하도록 한다. 딸깍하는 소리를 듣고 바늘 끝이 완전히 덮였는지 확인한다. [문헌개정연월일 : 2014년 10월 15일]

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성상
백색 내지 미황색의 동결건조물이 충전된 무색 바이알의 주사제로서 용제를 넣었을 때 무색 내지 엷은 황색의 맑거나 또는 약간 혼탁한 액상

효능 • 효과
【 유방암 】
• 전이성 유방암

HER2 (Human Epidermal growth factor Receptor 2 protein) 양성 전이성 유방암환자 치료에 다음과 같이 투여한다.
1. 전이성 질환에 대해 1회 또는 그 이상의 화학요법 치료를 받은 적이 있는 환자에게는 단독투여
2. 전이성 질환에 대해 화학요법 치료를 받은 적이 없는 환자에게는 파클리탁셀 또는 도세탁셀과 병용투여
3. 이전에 트라스투주맙을 투여받은 적이 없는 호르몬 수용체 양성인 폐경기 이후 환자에게 아로마 타제 억제제와 병용투여

• 조기 유방암

HER2 양성 조기 유방암환자 치료에 다음과 같이 투여한다.
1. 수술 전 또는 후 화학요법(필요시 방사선요법)을 받은 후
2. 독소루비신 및 싸이클로포스파미드 보조화학요법 후 파클리탁셀 또는 도세탁셀과 병용투여
3. 도세탁셀 및 카보플라틴 보조 화학요법과 병용투여
4. 국소 진행성 (염증성 포함) 질환 또는 직경 >2cm인 종양에 대해 수술 전 보조요법(neoadjuvant)으로 이 약과 화학요법 병용투여 후 수술 후 보조요법(adjuvant)으로 이 약 단독 투여

【 전이성 위암 】
전이성 질환으로 이전에 항암치료를 받은 적이 없는 HER2 양성 전이성 위선암이나 위식도 접합부 선암환자에게 백금계 약물과 카페시타빈 또는 5-FU와 병용투여

용법 • 용량
투여 전 투여 전 투여하려는 제형(정맥 또는 피하주사)이 환자에 처방된 것이 맞는지 제품라벨을 확인하여야 한다. 이 약은 정맥주사용이다.

【 유방암 】
• 전이성 유방암

HER2 (Human Epidermal growth factor Receptor 2 protein) 양성 전이성 유방암환자 치료에 다음과 같이 투여한다.
이 약 단독요법 및 파클리탁셀, 도세탁셀, 아로마타제 억제제와의 병용요법시 이 약의 권장 용량은 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 매주 6mg/kg이며 초기부하용량 투여 3주일 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 투여 후 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 부하용량은 8mg/kg을 투여하고, 이후 매 3주마다 유지용량으로 6mg/kg을 투여한다.

▲ 1주 요법
안트라싸이클린과 싸이클로포스파미드 병용 화학요법실시 후, 초기 부하용량으로 4mg/kg을 투여 하고 이후 1주마다 2mg/kg을 유지용량으로 투여한다. 이때 파클리탁셀과 병용투여한다.

【 전이성 위암 】
▲ 3주 요법
초기부하용량으로 8mg/kg을 투여하고 이후 매 3주마다 유지용량으로 6mg/kg을 약 90분에 걸쳐 점적 주입한다. 초기부하용량에 내약성이 우수한 경우 유지용량은 30분에 걸쳐 주입할 수 있다.

【 유방암(조기 유방암 및 전이성 유방암) 및 전이성 위암 】
전이성 유방암이나 전이성 위암환자는 질병진행시까지 이 약을 투여한다. 조기 유방암의 경우는 1년 동안 또는 질병재발까지 이 약을 투여해야한다. 조기 유방암 치료를 1년 넘게 지속하는 것은 권장되지 않는다.

감량투여
임상시험 도중 감량투여가 이루어진 례는 없었다. 이 약에 의한 치료는 화학요법에 의해 유발된 가역성 골수억제기 동안 계속될 수 있으나 호중구 감소증의 합병증에 대해 주의 깊게 모니터해야 한다. 파클리탁셀, 도세탁셀 또는 아로마타제 억제제의 감량투여 또는 투여간격 연장에 대해서는 파클리탁셀, 도세탁셀 또는 아로마타제 억제제의 제품설명서를 참조한다.
좌심실박출률(LVEF)이 치료 전 수치에서 10 ejection point 이상, 50% 미만으로 떨어졌을 때, 이 약 투여를 중단하고 약 3주 이내에 LVEF를 다시 평가해야한다. LVEF가 개선되지 않거나, 더 감소하거나 증후성 울혈성심부전이 발생하는 경우에는, 치료상 유익성이 위험성을 상회하지 않는다면, 이 약의 투여 중단을 심각하게 고려해야 한다.

투약일이 지났을 경우
만약 환자가 계획된 투약일로부터 1주 이하가 지났을 경우, 계획된 주기까지 기다리지 말고 가능한 한 빨리 유지용량(1주요법: 2mg/kg, 3주요법:6mg/kg)으로 투여 받아야 한다. 이후부터는 이전 계획대로 유지용량(1주요법 : 2mg/kg, 3주요법 : 6mg/kg)을 투여한다. 만약 계획된 투약일로부터 1주를 초과하여 지났을 경우, 초기 부하용량(1주요법 : 4mg/kg, 3주요법 : 8mg/kg)을 약 90분에 걸쳐 재투여하여야 한다. 이후부터는 그 시점을 기준(1주 요법은 매주, 3주요법은 매3주마다)으로 유지용량(1주요법 : 2mg/kg, 3주요법 : 6mg/kg)을 투여한다.

주입방법
이 약은 90분에 걸쳐 정맥주입한다. 이 약은 급속정맥주입(intravenous push or bolus)으로 투여해서는 안된다. 초회 주입 시작 후 최소 6시간 및 유지용량 주입 시작 후 최소 2시간 동안 환자에서 발열 및 오한 또는 다른 주입관련증상 등이 나타나는지 관찰해야 한다. 주입중단이나 주입속도 감소로 이러한 증상 조절을 도울 수 있다.증상이 사라졌을 때 주입을 재개할 수 있다. 초기부하용량에 내약성이 우수한 경우 유지용량은 30분에 걸쳐 주입할 수 있다. 아나필락시스등에 대비하기위해 점적주입시 응급장비가 준비되어 있어야 한다.

사용상의 주의사항
1. 경고

1) 심기능 장애(Cardiac dysfunction) : 허셉틴 투여 시 울혈성 심부전[뉴욕심장학회(NYHA)등급 2-4등급] 또는 무증상 심기능 장애의 위험이 증가한다. 특히, 안트라싸이클린(독소루비신이나 에피루비신)을 포함한 화학요법 후, 허셉틴 단독 또는 파클리탁셀이나 도세탁셀과 병용투여 받은 환자에서 이러한 사례가 관찰되었다. 그 정도는 중등도-중증이었으며 사망과 관련이 있었다. 또한 심질환 위험성이 큰 환자(고혈압, 입증된 관상동맥질환, 울혈성 심부전, 이완기 장애, 55% 미만 LVEF, 고령자)에 투여 시 주의를 기울여야 한다. 허셉틴의 치료대상환자, 특히 이전에 안트라싸이클린 및 사이클로포스파미드를 투여 받은 환자는 치료개시 전에 병력 및 신체검사와 ECG, 심초음파도, MUGA scan 또는 MRI등의 심기능을 평가해야 한다. 허셉틴 투여를 결정하기 전에 주의 깊게 위험-유익성에 대한 평가를 내려야 한다. 트라스투주맙의 반감기는 약 28-38일이므로, 허셉틴 투여 중단 후 27주까지 트라스투주맙이 순환계에 존재할 수 있다. 허셉틴 투여 중단 후 안트라싸이클린을 투여 받은 환자에서 심기능 장애가 증가될 수 있다. 가능하다면 전문의는 허셉틴 투여 중단일로부터 27주까지 안트라싸이클린이 포함된 치료요법을 피하도록 해야 하며, 안트라싸이클린을 투여하는 경우 심장 기능을 주의 깊게 모니터해야 한다. 치료 전 검사 시 심혈관계 문제가 있는 환자의 경우 일반적인 심장 평가가 고려되어야 하며, 치료 중에는 심장 기능을 모니터해야 한다(예, 매 3개월마다). 모니터링을 통해 심기능 장애를 나타내는 환자를 발견할 수 있다. 무증후성 심기능 장애를 더 빈번한 모니터링을 통해 알아낼 수 있다(예, 매 6-8주마다). 좌심박출률(LVEF)이 지속적으로 감소된 환자가 계속 무증후성일 경우 허셉틴의 임상적 이점이 없다면 전문의는 허셉틴의 투여 중지를 고려해야 한다. 조기 유방암 환자에서 LVEF가 55% 이하인 경우 치료시 주의를 기울여야 한다. LVEF가 치료 전 수치에서 10 ejection point 및 50% 미만으로 떨어졌을 때, 허셉틴 투여를 중단하고 약 3주 이내에 LVEF를 다시 평가해야한다. LVEF가 개선되지 않거나 감소할 경우 또는 임상적으로 유의한 울혈성심부전이 발생할 경우, 치료상 유익성이 위험을 상회하지 않는 한 허셉틴의 투여 중단을 심각하게 고려해야 한다. 이러한 환자의 경우 심장 전문의에 진료를 의뢰해야 하며 계속 관리되어야 한다. 이 약 투여 중 증후성 심부전이 발생할 경우, 표준 요법으로 치료되어야 한다. 심기능 장애를 경험한 환자에서 허셉틴 투여의 지속 또는 재투여에 대한 안전성은 전향적으로 연구되지 않았다. 그러나 임상시험에서 심부전 또는 무증후성 심기능 장애가 발생한 대부분의 환자는 표준 요법으로 개선되었다. 표준요법은 ACE 억제제 또는 안지오텐신 수용체 차단제(ARB) 및 베타차단제를 포함하였다. 심장증상과 허셉틴 치료에 의한 임상적 유익성을 함께 나타낸 환자 중 대부분은 추가 심장 증상 없이 허셉틴 투여를 계속 실시하였다. - 전이성 유방암 : 허셉틴과 안트라싸이클린은 전이성 유방암에서 동시에 투여하지 않는다. 기존에 안트라싸이클린을 투여 받았던 전이성 유방암환자의 경우에도 허셉틴과 안트라싸이클린을 병용 투여 했을 때 보다는 그 위험도가 낮으나 허셉틴의 투여로 인한 심기능 장애의 위험이 있다. - 조기 유방암 : 조기 유방암 환자의 경우 치료 전, 치료 중 매 3개월마다, 치료 종료 후 매 6개월마다 24개월까지 심장평가를 실시해야 한다. 안트라싸이클린을 함유한 화학요법제를 투여 받는 환자는 추가적인 모니터링이 요구되고, 지속적인 LVEF 감소가 있는 경우 허셉틴의 치료 종료로부터 5년 이상 해마다 모니터링 해야 한다. 조기 유방암 환자를 대상으로 한 임상시험에서, 심근경색 병력이 있는 환자, 약물치료가 필요한 협심증환자, 울혈성 심부전(NYHA II-IV)이 있거나 병력이 있는 환자, 55%미만 LVEF, 기타 심근병증, 약물치료가 필요한 부정맥환자, 임상적으로 유의한 판막질환환자, 조절이 어려운 고혈압환자(단, 표준 약물 치료로 조절 가능할 경우 임상시험 참여 가능), 혈역학적 심낭삼출환자(Hemodynamic effective pericardial effusion)는 제외되었기 때문에 이 환자들에 대한 유익성/위험 비율에 대한 자료가 없다. 따라서 이러한 환자에 허셉틴 투여는 권장되지 않는다. - 보조요법 치료 : 허셉틴과 안트라싸이클린 약물은 보조요법 치료에서 동시에 투여하지 않는다. 조기 유방암 환자에서 도세탁셀과 카보플라틴의 비-안트라싸이클린 요법과 이 약 병용투여 시에 비해 안트라싸이클린 포함 요법 후 이 약 병용투여 시 증후성 및 무증후성 심장 이상반응의 발생률 증가가 관찰되었으며 이러한 증가는 탁산계 약물에 이어 순차적으로 투여시보다 탁산계 약물과 병용투여 시 더욱 현저했다. 사용된 요법에 상관없이, 대부분의 증후성 심장 이상반응은 첫 18개월 이내에 발생하였다. 중앙 추적조사기간이 5.5년이었던 3개 주요 임상시험 중 하나(BCIRG006)에서 증후성 심장 이상반응이나 LVEF 이상반응의 누적 발생율의 지속적인 증가가 나머지 두 대조군(안트라싸이클린+싸이클로포스파미드 투여 후 탁산 투여, 탁산+카보플라틴+허셉틴) 에서 약 1%에 비해 안트라싸이클린 투여 후 탁산과 허셉틴을 병용한 군에서 최대 2.37%로 관찰되었다. 보조요법에 관한 임상시험에서 확인된 심장 이상반응의 위험 요인은 고령(>50세), 허셉틴 투여 전 낮은 LVEF(<55%) 또는 LVEF의 감소(10-15 point), 파클리탁셀 투여 시작 전/후 낮은 LVEF(<55%), 허셉틴 투여, 항고혈압 약물 이전 투여 또는 병용투여였다. 보조요법이 끝난 후 허셉틴을 투여하는 환자에서, 허셉틴 투여 전 축적된 안트라싸이클린 및 체질량지수(BMI)가 25kg/m²을 넘는 경우 심기능 장애의 위험이 있었다. - 수술 전 보조요법/수술 후 보조요법 : 수술 전 보조요법/수술 후 보조요법 치료에 적합한 조기 유방암 환자에서, 허셉틴은 화학요법제 치료를 받지 않은 환자에 대해 저용량의 안트라싸이클린 요법과 동시 투여할 수 있다(최대 누적용량 : 독소루비신 180mg/m², 에피루비신 : 360mg/m²). 수술 전 보조요법 치료에서 저용량의 안트라싸이클린과 허셉틴을 동시에 투여 받은 환자는 수술 후에 추가적인 세포독성 화학요법제를 투여하지 않는다. 기타 상황에서 추가적인 세포독성 화학요법제의 필요성은 개개 요인에 따라 결정한다. 현재 저용량의 안트라싸이클린과 허셉틴을 동시에 투여한 경험은 제한적이다. 임상시험에서, 허셉틴은 수술전 보조요법으로 안트라싸이클린(독소루비신의 누적 용량 180mg/m² 또는 에피루비신 300mg/m²) 3-4주기 투여를 포함한 수술전 보조 화학요법제와 병용투여 하였다. 증후성의 심장 기능 장애는 허셉틴 투여 군에서 낮았다(115명 중 2명, 1.7%). 65세 이상 그룹의 임상 경험이 제한적이기 때문에 수술전/수술후 보조요법 치료에서 65세 이상인 환자에게는 권장하지 않는다.

2) 주입관련 반응, 알러지양 반응 및 과민반응 : 이 약 투여 시 주입관련반응이 발생하는 것으로 알려져 있다. 주입관련 반응의 발생 위험을 감소시키기 위해 전 처치를 할 수도 있다. 이 약 주입에 따라 보고된 중대한 이상반응으로 호흡곤란, 저혈압, 천명, 고혈압, 기관지연축, 심실위부정빈맥, 산소 포화도 감소, 아나필락시스, 호흡곤란증후군, 두드러기, 혈관부종이 있다. 이러한 이상반응의 대부분은 초회 주입 중 또는 초회 주입 시작으로부터 2.5시간 이내에 발생하였다. 주입관련 반응이 나타나면 허셉틴의 주입을 중단시키거나 주입속도를 감소시키고 증상이 소실될 때까지 환자를 모니터링 해야 한다. 대부분의 환자에서 증상이 소실되었고 이후 허셉틴의 주입을 재개하였다. 환자에 주입관련 반응이 나타나는지 관찰해야 하며, 메페리딘 또는 파라세타몰과 같은 진통/해열제나 디펜히드라민과 같은 항히스타민제로 이러한 증상을 치료할 수 있다. 중대한 이상반응은 산소, 베타작용제, 코르티코스테로이드와 같은 보조 치료를 통해 성공적으로 치료되었다. 드물게 이러한 반응은 치명적인 결과를 초래하는 임상 경과와 관련이 있었다. 진행성 종양의 합병증 및 동반질환으로 인해 안정 시 호흡곤란인 환자는 치명적인 주입관련 반응의 위험이 증가될 수 있으므로 이러한 환자들에게는 허셉틴을 투여하지 않는다. 초기 개선 후 임상적 악화 및 급격한 임상적 악화를 동반한 지연 반응이 보고되었다. 주입 후 수 시간에서 일주일 이내에 사망이 발생하기도 했다. 매우 드물게 허셉틴 주입 시작으로부터 6시간 이상 지난 후 주입반응 또는 폐 증상이 발생하기도 했다. 환자에게 이러한 지연성 반응의 가능성을 경고해야 하며 증상이 발생되었을 경우 전문의에게 연락하도록 해야 한다.

3) 폐이상반응 : 드물게 중증 폐이상반응이 이 약의 시판후조사에서 보고되었으며 이는 때때로 치명적일 수도 있다. 이러한 이상반응으로 폐침윤을 포함한 간질성 폐질환, 급성 호흡곤란 증후군, 폐렴, 간질성 폐렴, 흉막삼출, 호흡곤란, 급성 폐부종 및 호흡부전 등이 보고되었다. 간질성 폐질환과 연관된 위험 요소로는 탁산계약물, 젬시타빈, 비노렐빈, 방사선 요법과 같이 이러한 질환과 연관이 있는 것으로 알려진 여타의 항종양약물 요법을 이전에 투여 받았거나 동시에 투여하는 경우가 있다. 이는 주입관련 이상반응의 일부분이거나 지연형 이상반응과 함께 나타날 수 있다. 전이성 악성종양과 그에 따른 합병증의 발병으로 인해 안정 시 호흡곤란을 나타내는 환자는 폐질환의 위험성이 증가할 수 있다. 따라서 이러한 환자에 허셉틴을 투여하지 않는다. 폐렴환자, 특히 탁산계 약물을 병용 투여하는 경우 주의해야 한다.

4) 벤질알코올은 미숙아에게서 치명적인 가쁜 호흡증상과 연관이 있는 것으로 보고되었다. (허셉틴주 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 안정시 호흡곤란 또는 산소보충이 필요한 환자
3) 신생아, 미숙아 (벤질알코올을 함유하고 있다, 허셉틴주 440mg에 한함)

3. 다음 환자에는 신중히 투여할 것

1) 안트라싸이클린계 약물을 투여 중인 환자 또는 이전에 치료경험이 있는 환자
(심부전 등의 심장장애가 나타나기 쉽다)
2) 흉부로 방사능을 조사 중인 환자(심부전 등의 심장장애가 나타나기 쉽다)
3) 심부전증상이 있는 환자(증상이 악화될 우려가 있다)
4) 관상동맥질환(심근경색, 협심증 등)환자 또는 그 병력이 있는 환자
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MC20141015-005

RETHINKING NEOADJUVANT THERAPY: NEOADJUVANT THERAPY AS A PLATFORM FOR DRUG DEVELOPMENT IN HER2 POSITIVE BREAST CANCER

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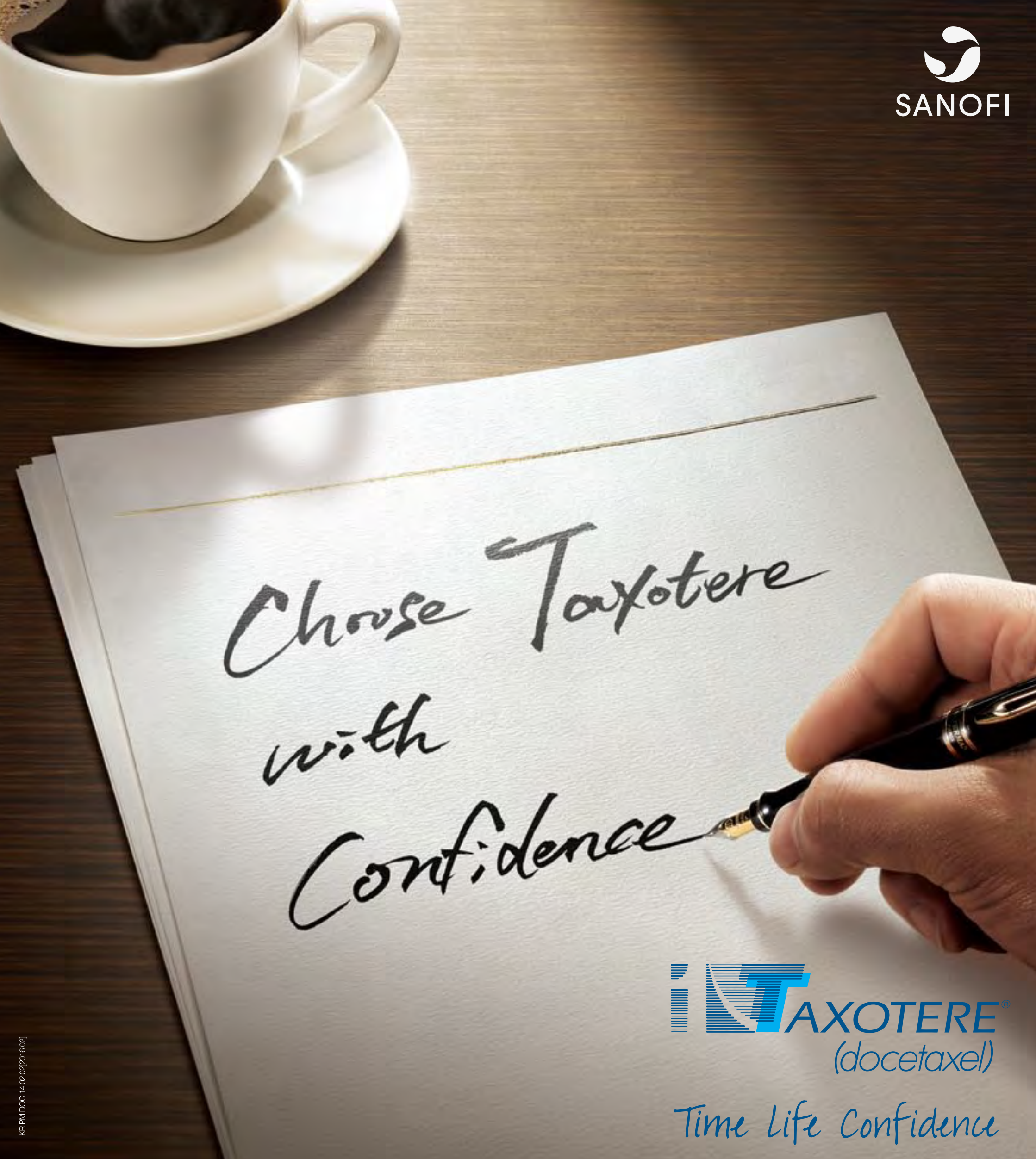
Since the results of NSABP B-18, which reported no difference in disease free and overall survival with neo-adjuvant and adjuvant chemotherapy in operable breast cancer, neoadjuvant chemotherapy is recommended as standard treatment in locally advanced, as well as operable breast cancer. Traditionally, neoadjuvant systemic treatment has theoretical advantage of increasing resectability, breast conservation, in-vivo test of chemosensitivity and eliminating micrometastases. In addition to its traditional role, numerous data suggests that pathological complete remission to neoadjuvant therapy may be a surrogate marker of improved disease-free survival and overall survival. Another important emerging role of neoadjuvant systemic treatment is as platform for new drug development. With improvement in breast cancer survival and dramatic decrease in the recurrence rate, number of patients needed in breast cancer adjuvant trials has increased to nearly 5,000-10,000. Greater expense and longer follow up periods has made adjuvant trials in breast cancer almost impossible to conduct. FDA has recently released guidance for industry, on the use of pathological complete response in neoadjuvant treatment of high-risk early stage breast cancer as an endpoint to support accelerated approval. Accelerated approval of neoadjuvant pertuzumab is the first example. Recent meta-analysis on association of pathologic complete response to neoadjuvant therapy in HER2 positive breast cancer with long term outcomes reported improvement in EFS for pCR vs. non-pCR in patient level; HR 0.37, and also in trial level, with R2 correlations between odds ratios for pCR and HRs reported as 0.63 for EFS and 0.29 for OS. In HER2 positive breast cancer, good response and high pCR rate to combination of chemotherapy plus anti-HER2 targeted therapy makes HER2 positive breast cancer an ideal indication for using neoadjuvant trials as platform for developing novel agents. Recent data on neoadjuvant systemic therapy in HER2 positive breast cancer will be summarized and role of neoadjuvant therapy in increasing breast conservation will also be addressed in the meeting.



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[Indication] 1 Breast Cancer • Metastatic and locally advanced breast cancer 1) 1st line treatment of patients with locally advanced or metastatic breast cancer in combination with doxorubicin. 2) In combination with trastuzumab, treatment of patients with HER2 overexpressed (IHC 3+ or FISH positive) and chemotherapy naive metastatic breast cancer which is overexpressed HER2 (IHC 3+ or FISH positive) and have not treated with chemotherapy. 3) Treatment of patients with locally advanced or metastatic breast cancer in whom previous chemotherapy has failed. 4) In combination with capecitabine, treatment of patients with locally advanced or metastatic breast cancer in whom previous chemotherapy has failed. Previous therapy should have included an anthracycline. • Adjuvant breast cancer 1) Adjuvant treatment in combination with doxorubicin and cyclophosphamide is indicated for the adjuvant treatment of patients with: -operable node-positive breast cancer - operable node-negative breast cancer with one or more high risk factors. (tumor size >2 cm, age <35 years, hormone receptor status negative, tumor grade 2 or 3) 2) Doxorubicin and cyclophosphamide followed by *TM* in combination with trastuzumab is indicated for the adjuvant treatment of patients with operable breast cancer whose tumors overexpress HER2.(AC TH regimen) 3) Taxotere in combination with trastuzumab, and carboplatin is indicated for the adjuvant treatment of patients with operable breast cancer whose tumors overexpress HER2.(TCH regimen) 4) Taxotere in combination with cyclophosphamide is indicated for the adjuvant treatment of patients with operable breast cancer (primary tumour of ≥1 cm and <7 cm) (TC regimen) **2 Non-Small Cell Lung Cancer :** Treatment of patients with locally advanced or metastatic non-small cell lung cancer, including those who have failed platinum-based chemotherapy. **3 Prostate Cancer :** Treatment of patients with androgen independent (hormone refractory) metastatic prostate cancer in combination with prednisolone. **4 Ovarian Cancer :** 1st line therapy for the treatment of patients with advanced or metastatic epithelial ovarian cancer in combination with carboplatin. **5 Head and Neck Cancer :** In combination with cisplatin and fluorouracil, induction treatment of patients with locally advanced squamous cell carcinoma of the head and neck. **6 Gastric cancer :** Advanced and metastatic or locally recurrent gastric cancer. **7 Esophageal cancer :** Advanced or recurrent squamous esophageal cancer. **[Dosage and Administration] 1 Breast Cancer •** Metastatic and locally advanced breast cancer 1) For the 1st line treatment of breast cancer, docetaxel 75mg /m^2 is given in combination therapy with doxorubicin (50mg/m^2) 2) In combination with trastuzumab for the treatment of HER2 overexpressed and chemotherapy naïve metastatic breast cancer, the recommended dose of docetaxel is 100 mg/m^2 as a 60-minute infusion every three weeks. Initial docetaxel infusion can be started the day following the first dose of trastuzumab. The docetaxel doses can be administered immediately after completion of the trastuzumab infusion, if the preceding dose of trastuzumab was well tolerated. * The recommended initial dose of trastuzumab is 4mg/kg as 90-minute intravenous infusion. The recommended weekly dose of Herceptin is 2 mg/kg, beginning one week after the initial dose. (Refer to the product information of trastuzumab.) 3) For the treatment of breast cancer in whom previous chemotherapy has failed, docetaxel 75-100 mg/m^2 is administered as a one-hour infusion every three weeks. 4) In combination with capecitabine, for the treatment of locally advanced or metastatic breast cancer in whom previous chemotherapy including anthracyclines has failed, the recommended dose of docetaxel is 75mg/m^2 every three weeks, combined with capecitabine at 1250 mg/m^2 twice daily (within 30 minutes after a meal) for 2 weeks followed by 1-week rest period. For capecitabine dose calculation according to body surface area, see capecitabine package insert. • Adjuvant breast cancer 1) In the adjuvant treatment of operable node-positive and node-negative breast cancer, the recommended dose of docetaxel is 75 mg /m^2 administered 1-hour after doxorubicin 50 mg/m^2 and cyclophospamide 500 mg/m^2 every 3 weeks for 6 cycles(TAC regimen). Prophylactic G-CSF may be used to mitigate the risk of hematological toxicities (See Dosage adjustments during treatment). 2) AC-TH regimen (1) AC (cycles 1-4): doxorubicin (A) 60 mg/m^2 followed by cyclophosphamide (C) 600 mg/m^2 administered every three weeks for 4 cycles. (2) TH (cycles 5-8): docetaxel (T) 100 mg/m^2 administered every three weeks for 4 cycles, and trastuzumab (H) administered weekly according the following schedule: - Cycle 5 (starting three weeks after the last cycle of AC):Day 1: trastuzumab 4 mg/kg (loading dose) Day 2: docetaxel 100 mg/m^2 Days 8 and 15: trastuzumab 2 mg/kg - Cycles 6-8: Day 1: docetaxel 100 mg/m^2 and trastuzumab 2 mg/kg Days 8 and 15: trastuzumab 2 mg/kg Three weeks after day 1 of cycle 8: trastuzumab 6 mg/kg is given every three weeks. (3) Trastuzumab is administered for a total duration of 1 year. 3) TCH regimen (1) Docetaxel (T) 75 mg/m^2 for 1 hour and carboplatin (C) at AUC of 6 mg/mL/min administration over 30 to 60 min every three weeks, Day 2 of cycle 1. Day 1 of cycle 2~6. (2)Trastuzumab (H) 4 mg/kg for 90 min in day 1 as loading dose, then weekly administered 2 mg/kg for 30 min as maintenance dose. (3) Trastuzumab 6 mg/kg for 30 min is given every three weeks after completion of adjuvant chemotherapy. Trastuzumab is administered for a total duration of 1 year. 4) TC regimen: TAXOTERE 75mg/m^2 over 1 hour and cyclophosphamide 600mg/m^2 as an intravenous administration over 30 to 60 minutes on day 1 of a 21 day cycle for a total of four cycles. Premedication with oral dexamethasone 8mg twice daily is administered commencing 1 day before administering TAXOTERE, and continuing for a total of five doses. **2 Non-Small Cell Lung Cancer :** The recommended dosage of Docetaxel is 75 mg/m^2 administered as a one-hour infusion every 3 week. Maximum dosage is 75mg/m^2 at platinum-combined chemotherapy. **3 Prostate Cancer :** The recommended dosage of docetaxel is 75 mg/m^2 administered as a one-hour infusion every 3 week. Prednisolone 5 mg orally twice daily is administered continuously. **4 Ovarian Cancer :** As the first line therapy for advanced or metastatic ovarian cancer, docetaxel is 75 mg/m^2 administered as a one-hour infusion every three week. Then carboplatin 6.0 mg/ml·min (AUC) is intravenously administered during 30~60 min. **5 Head and Neck Cancer :** 1) Induction chemotherapy followed by radiotherapy : For the induction treatment of inoperable locally advanced squamous cell carcinoma of the head neck (SCCHN), the recommended dose of docetaxel is 75 mg/m^2 as a 1 hour infusion followed by cisplatin 75 mg/m^2 over 1 hour, on day one, followed by fluorouracil as a continuous infusion at 750 mg/m^2 per day for five days. This regimen is administered every 3 weeks for 4 cycles. Following chemotherapy, patients should receive radiotherapy. 2) Induction chemotherapy followed by chemoradiotherapy : For the induction treatment of patients with locally advanced (technically unresectable, low probability of surgical cure, and aiming at organ preservation) squamous cell carcinoma of the head and neck (SCCHN), the recommended dose of docetaxel is 75 mg/m^2 as a 1 hour intravenous infusion on day 1, followed by cisplatin 100 mg/m^2 administered as a 30-minute to 3-hour infusion, followed by fluorouracil 1000 mg/m^2/day as a continuous infusion (from day 1 to day 4). This regimen is administered every 3 weeks for 3 cycles. Following chemotherapy, patients should receive chemoradiotherapy. **6 Gastric Cancer :** 1) As single agent, the recommended dosage of docetaxel is 75mg/m^2 administered as a one-hour infusion every three weeks. 2) The recommended dose of docetaxel is 75 mg/m^2 as a 1-hour infusion, followed by cisplatin 75 mg/m^2, as a 1- to 3-hour infusion (both on day 1 only), followed by fluorouracil 750 mg/m^2 per day given as a 24-hour continuous infusion for 5 days, starting at the end of the cisplatin infusion. Treatment is repeated every three weeks. Patients must receive premedication with antiemetics and appropriate hydration for cisplatin administration. Prophylactic G-CSF should be used to mitigate the risk of haematological toxicities. **7 Esophageal Cancer :** The recommended dosage of docetaxel is 70mg/m^2 administered as one-hour infusion every 3~4 weeks, and the dosage may be reduced or increased depending on the condition of patients **<Premedication Regimen>** All patients should be premedicated prior to TAXOTERE administration in order to minimize fluid retention and severe hypersensitivity reaction. Such premedication consisting of oral corticosteroids such as dexamethasone 16 mg per day (ex. 8mg bid) for 3 days starting one day prior to TAXOTERE administration, should be used unless it is contradiction. Prophylactic G-CSF may be used to mitigate the risk of hematological toxicities. **<Dosage adjustments during treatment>** Frequent monitoring of neutrophil counts should be performed during TAXOTERE therapy. Dosage should be adjusted if necessary depending on neutrophil count. **[Precautions] <Contraindications>** 1) Hypersensitivity reactions to TAXOTERE or Polysorbate 80. 2) Patients with baseline neutrophil count of <1,500 cells/mm^3. 3) Patients with severe liver impairment. 4) When combined with other medicinal products, contraindications for those products also apply (severe renal impairment, hypersensitivity to paraplatin, Pt-compounds and/or mannitol etc.) 5) Patients with complications of infections (infections could be worsened or fetal) 6) Patients who are suspected to have infectious fever (infections could be worsened or fetal) 7) Patients who have severe myelosuppression (severe infection could be occur or fetal) **<Special Precautions in Use>** 1) Patients with myelosuppression 2) Patients with liver impairment (See '5. General precautions') 3) Patients with renal impairment 4) Patients with pneumonia interstitialis or pulmonary fibrosis 5) Patients with edema 6) Patients with pregnant potential (both men and women)(Effective contraceptive measures must be taken during treatment, and for men at least 6 months after cessation of therapy.) ※ Please refer to package insert or homepage for the details. sanofi - aventis Korea Co., Ltd. 235, Banpo-daero, Seocho-gu, Seoul T.02-2136-9000 F.02-2136-9249 www.sanofi.co.kr

DETERMINING THE OPTIMAL ADJUVANT CHEMOTHERAPY FOR LOW OR INTERMEDIATE RISK OF BREAST CANCER - WHO SHOULD RECEIVE ADJUVANT CHEMOTHERAPY?

Kyoung Eun Lee

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Today, the breast cancer is regarded as a family of disease with different prognosis, biology and treatment. And much more patients have small and node negative tumors. Few adjuvant trials have addressed according to these risk groups including biologic subtypes. Since The National Institutes of Health recommends that adjuvant multiagent chemotherapy of 4-6 months be recommended to the majority of women with localized breast cancer regardless of lymph node, menopause, or hormone receptor status, anthracyclines and taxanes integrated into adjuvant chemotherapy regimens produce additional survival gains. Recommendations for the use of adjuvant therapy are based on the individual patients risk and the balance between absolute benefit and toxicity.

Factors considered in selecting patients for adjuvant therapy include tumor-specific factors and patient-specific factors. Tumor-specific factors include tumor size, metastatic nodes, tumor biology and patient-specific factors include age, comorbidities and patient preferences. Also multigene expression assays identify subsets of patients with ER-positive disease who derive greatest benefit from adjuvant chemotherapy.

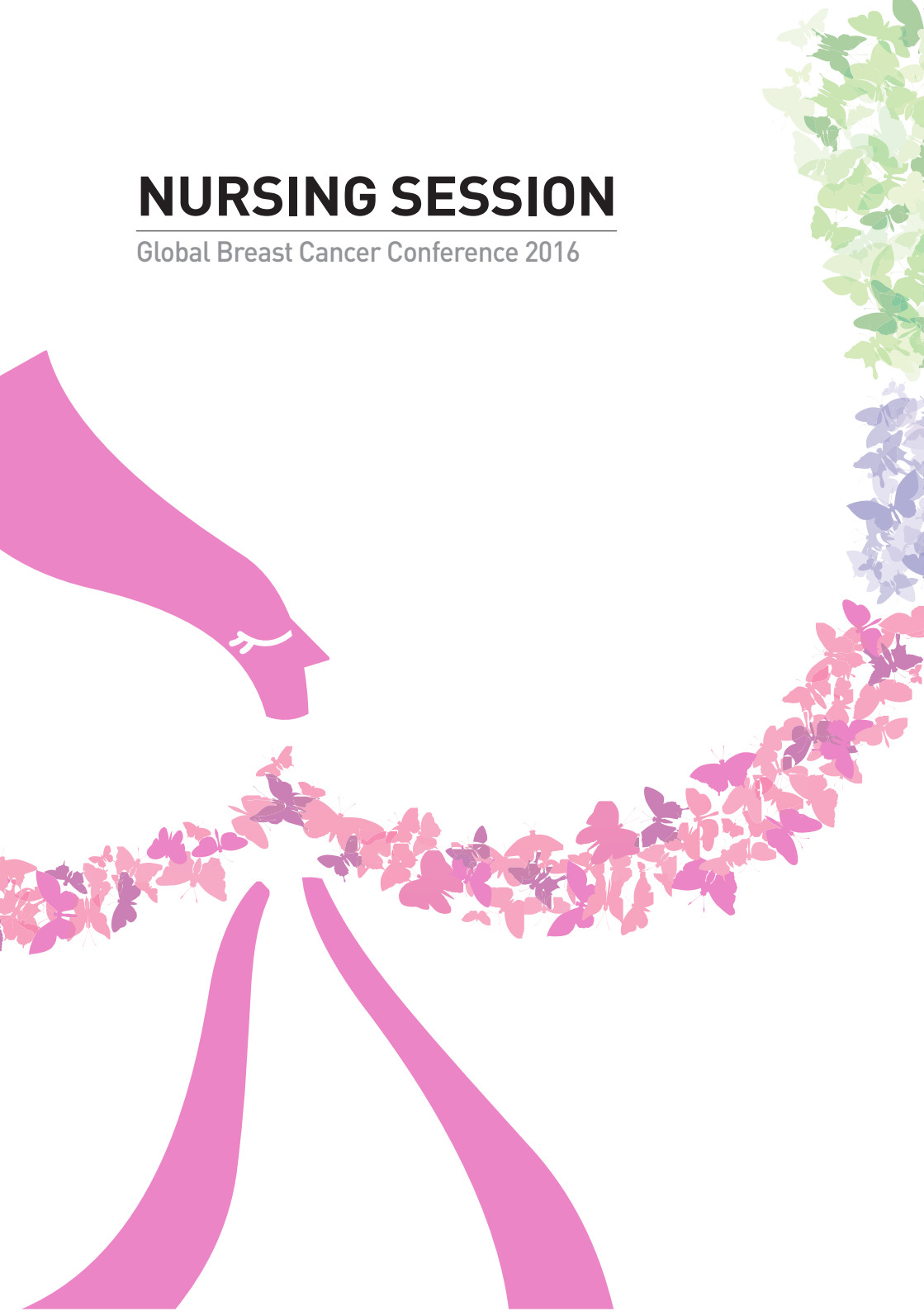
65% of women with invasive breast cancer have node-negative disease and NSABP B-14 and B-20 showed the benefit of endocrine therapy and chemotherapy in ER-positive and node-negative disease. To decide who will get benefit from adjuvant chemotherapy, the first thing is to identify low and intermediate risk patients. Beyond the conventional biomarkers, several multigene assays were introduced in the clinics such as Oncotype DX, EndoPredict, MammaPrint, Prosignia and more and more gene expression profile tests are used, the incidence of adjuvant chemotherapy is going down. And the results of several prospective trials with multigene assay are pending (MINDACT, TAILORx, PlanB). The second thing is to choose optimal chemotherapy regimen, de-escalating therapy without compromising efficacy. Anthracycline-based regimen is

preferred, but significant long-term toxicities are proved including cardiac toxicities and secondary MDS/AML. So the role of anthracyclines has come under close scrutiny, especially in those with low or intermediate risk of disease recurrence. Adding taxane is a standard in node-positive patients but no clear evidence for node-negative patients. Two randomized trials of taxane for node-negative patients showed better PFS. According to USO 9735, TC regimen as alternative to anthracycline-based adjuvant therapy is optimal treatment for low-risk breast cancer patients.

To determine the optimal adjuvant chemotherapy in low or intermediate risk breast cancer patients, we should consider the use of appropriate biomarkers to guide decisions on adjuvant systemic therapy and the avoidance of toxicities without benefit reduction.

NURSING SESSION

Global Breast Cancer Conference 2016



NURSING CARE IN ENDOCRINE THERAPY

Jung A Do

Cheil General Hospital & Women's Healthcare Center, Korea

By endocrine therapy the survival rate of breast cancer has been increased, but the side effects resulting in menopausal symptoms are getting also varied. Common problematic symptoms of menopause are hot flushes, urogenital atrophy and longer-term consequences osteoporosis. These side effects drop the quality of life of patients with breast cancer and affect the medication compliance of patients. Because of this, there is a study that 20% of breast cancer patients to stop taking the medication. Therefore, management of the menopause symptom caused by endocrine therapy is very important for medical provider and patients. The most effective hormone replacement therapy in Hot flash is usually contraindicated for breast cancer patients. So there have been treatments like non-hormonal pharmacological and complementary therapies. As a nurse, educating breast cancer patients in lifestyle changes which decrease the frequency and intensity of hot flush can offer significant help. Urogenital atrophy symptom occur Painful intercourse, vulval burning sensations, and recurrent urinary tract infections. Greater education about vaginal dryness and the range of available treatments is essential to encourage more women to seek help for this condition. Endocrine therapy for breast cancer can cause bone loss and associated fractures. Managements of osteoporosis are the assessment of risk factors for bone loss, the modifications of lifestyle, diet (calcium, vitamin D), and exercises. Above all, it should be noted that prior to the medical management of side effects in order to increase the adherence of patients to medication is that it is important that patient centered approach and improving patient-physician communication.

CHEMOTHERAPY-RELATED COGNITIVE FUNCTION IN PATIENTS WITH BREAST CANCER

Jin-Hee Park

Ajou University College of Nursing, Korea

Breast cancer has been reported as the second most commonly diagnosed cancer in Korea. Adjuvant chemotherapy increases the survival rate in breast cancer patients and with reduced mortality, morbidity related to cancer and its treatment has garnered increased attention, and issues surrounding quality of life have become ever more important. Women who receive chemotherapy for breast cancer often complain of changes in cognitive function. Chemotherapy-related cognitive impairment is a phenomenon of cognitive decline that some patients experience during and after chemotherapy. The prevalence of chemotherapy-related cognitive impairment in breast cancer range from 16% to 90%. A growing body of research has also shown that breast cancer patients perform poorer on objective tests of cognitive function relative to healthy age- and education-matched-controls. Cognitive changes can have a significant effect on cancer patients quality of life, and lack of information regarding the potential risk prevents patients from granting full informed consent prior to initiation of therapy. The purposes of this study were (1) to examine the prevalence of cognitive impairment and trajectory of cognitive function over time in women with breast cancer, who received adjuvant chemotherapy, (2) to evaluate the effect of Promoting Cognitive Health Program which is combined compensatory strategies and cognitive training for management of chemotherapy-related cognitive impairment among breast cancer.

CHEMOTHERAPY INDUCED PERIPHERAL NEUROPATHY IN BREAST CANCER PATINETS

Mi Sook Han

Inha University Hospital, Korea

Breast cancer is the second most common in Korean women, and 91% of women have breast cancer survive for at least five years in 2011 Korean data. Breast cancer survival has been attributed to advance in screening mammography and combination treatment with surgical techniques, focused radiation and more effective adjuvant chemotherapy. Taxan chemotherapy is often used for breast cancer causes a peripheral neuropathy. Chemotherapy induced peripheral neuropathy symptoms may last for several months or permanently even after quitting chemotherapy. Typically it is distributed bilaterally and started from the distal part of extremities and also is presented progressively in stocking and glove pattern. The prevention for chemotherapy induced peripheral neuropathy is not effective at present. The overall quality of a womans life has a breast cancer is affected by cancer treatment itself as well as chemotherapy induced peripheral neuropathy. Thus, the health care provider should notice issues of chemotherapy induced peripheral neuropathy symptoms. In addition to surveillance to monitor for recurrence, it is important to manage treatment-related adverse effects and enhance womens identities in patients with breast cancer. Appropriate counseling and evidence-supported surveillance strategy will impact patients satisfaction for cancer-related treatment and overall care.

NURSING CARE IN CARDIOTOXICITY

Onam Ok

Samsung Medical Center, Korea

The incidence of anthracycline-induced cardiotoxicity (AIC) varies depending on medication and cumulative dose: for doxorubicin from 4% to >36% in patient receiving 500-550 mg/m^2; epirubicin or idarubicin appears to have lower incidence of HF. However, it has been shown that the longer the follow-up, the higher the incidence of cardiac dysfunction. AIC has been categorized as acute (transient decline in myocardial contractility immediately after infusion, incidence <1%), early onset chronic progressive (within first year after treatment, incidence 1.6%-2.1%), late onset chronic progressive, presenting as dilated cardiomyopathy (CMP) from at least 1 year after completion of therapy, until 10-30 years from the first dose of treatment.

Risk factors for AIC, besides cumulative dose, are intravenous high single dose, time of drug infusion <30 minutes, history of prior irradiation, use of other concomitant agents such as cyclophosphamide, trastuzumab, paclitaxel, female gender, young or old age, underlying cardiovascular disease, increase in time elapsed since therapy administration. The incidence of trastuzumab-related HF is 2%-7%; it increases with age >50 years, borderline LVEF before treatment, history of CVD and prior treatment with anthracycline and it rises to 27% when trastuzumab is used concurrently with anthracycline plus cyclophosphamide. Unlike AIC, trastuzumab toxicity is not dose related, and it is frequently reversible.

The incidence of HF reported with cyclophosphamide therapy ranges from 7% to 28%; the risk of cardiotoxicity is dose related (>150 mg/kg and 1.5 g/m^2/day), occurs normally within 10 days after administration of the first dose, and it is also correlated to prior anthracycline or mitoxantrone therapy or mediastinal irradiation.

Although most cases of paclitaxel-induced cardiotoxicity are represented by subclinical sinus bradycardia (approximately 30%), paclitaxel may induce heart block with syncope, supraventricular or ventricular arrhythmias, and myocardial ischemia through unknown mechanisms. Furthermore, taxanes potentiate anthracycline-induced cardiotoxicity by increasing the plasma levels of doxorubicin, and by promoting the formation of the toxic alcoholic metabolite doxorubicinol in cardiomyocytes.

Docetaxel causes less cardiac toxicity than paclitaxel. Patients undergoing anticancer therapy should be encouraged to follow standard guidelines for reducing CV risk, such as blood pressure control, lipid level reduction, smoking cessation and lifestyle modifications.

- Periodic monitoring of cardiac function with Doppler echocardiogram (DEcho) is suggested especially for anthracyclines and their derivates, or monoclonal antibodies.

- Baseline clinical and ECG evaluation are recommended in all patients undergoing anthracycline therapy.

- Assessment of baseline systolic and diastolic cardiac function with DEcho should be conducted before treatment with monoclonal antibodies or anthracyclines and their derivates in patients aged > 60 years, or with cardiovascular risk factors such as hypertension, hypercholesterolaemia, diabetes, obesity or previous treatment with 5-hydroxytryptamine-2B agonists (in Parkinson or obese patients) potentially inducing cardiac valvulopathy, or documented cardiopathy or previous thoracic radiotherapy.

- Periodic monitoring (every 12 weeks) of cardiac function is also suggested for those patients receiving monoclonal antibodies, especially if previously treated with anthracycline.

- Assessment of cardiac function is recommended 4 and 10 years after anthracycline therapy in patients who were treated at < 15 years of age, or even at age > 15 years but with cumulative dose of doxorubicin of > 240 mg/m^2 or epirubicin > 360 mg/.

- LVEF reduction of ≥ 20% from baseline despite normal function or LVEF decline < 50% necessitate reassessment or discontinuation of therapy and further frequent clinical and echocardiographic checks.

Although anthracycline-induced LVD is frequently irreversible, a recent clinical study indicated that enalapril (ACE inhibitor) and carvedilol (beta-blocker; when possible) treatment resulted in a complete (42%) or partial (13%) recovery of LVEF, predominantly in patients in whom treatment was initiated at an early stage. Similarly, for trastuzumab-related cardiotoxicity, administering an ACE inhibitor is currently recommended when LVEF declines to less than 50%.

The American Society of Clinical Oncology endorses the use of dexrazoxane only for patients who have received a cumulative dose of doxorubicin 300 mg/m^2 or an equivalent dose of epirubicin for the treatment of metastatic disease. Given its potential detrimental impact on antitumor efficacy as well as on myelosuppression, dexrazoxane is not recommended for use in the adjuvant setting when the goal of therapy is cure.

NURSING MANAGEMENT FOR PATIENTS WITH ADVANCED BREAST CANCER WOUND

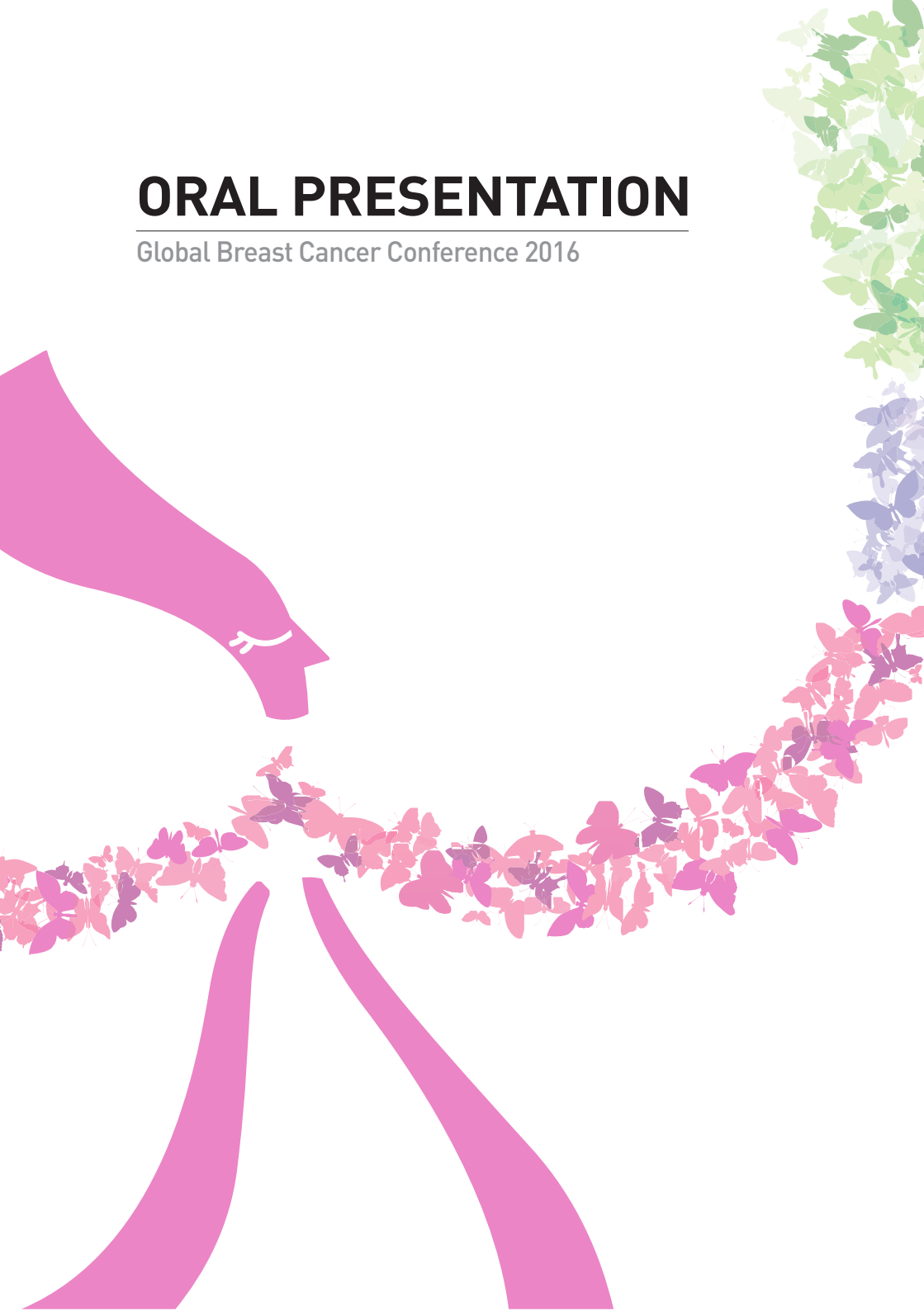
Hyun Seo

Ewha Womans University Mokdong Hospital, Korea

Advanced breast cancer wounds present a physical and emotional challenge to patients, families, and caregivers. Approximately 5% to 10% of patients with metastatic cancer will develop advanced cancer wound. Among them, more than 60% occur in the breast. Advanced breast cancer wounds are caused by the skin invasion of a local tumor and its supporting blood and lymph vessels or result of metastatic spread from a primary tumour. The purpose of advanced breast cancer wound treatment aims to improve the quality of life through maintaining current condition and controlling symptoms. The common symptoms of advanced breast cancer wound include pain, bleeding, odor and exudate. The quality of clinical practice would be the important factor to determine the patient quality of life. In addition, advanced breast cancer wounds can cause anxiety, depression and sense of psychological isolation to patients. Therefore, the quality improvement of holistic nursing care will help the patients deal with their difficult situations and functional limitation.

ORAL PRESENTATION

Global Breast Cancer Conference 2016



OP01-1

DETERMINATION OF ANTI-CANCER MECHANISMS OF GOSSYPETIN AND LUTEOLIN IN COMBINATION WITH CHEMOTHERAPEUTIC CYCLOPHOSPHOAMIDE ON MCF-7 HUMAN BREAST CANCER CELL LINES

Elif Candan, Zeynep Ulker akal, Lokman Alpsoy

Fatih University, Turkey

Background: Flavonoids, obtained from plants are agents that are used for the treatment of many diseases including cancer. Preventing the cancer cells without damaging normal cells, although molecules development work continues actively, still effective and harmless method of diagnosis and treatment couldn't be found The aim of this study is to assess the cytotoxic effects and the effect mechanism of Gossypetin, Luteolin (Lut) and Cyclophosphamide (CP) and to examine the effect of combination treatment of this three drug on breast cancer cell line.

Methods: We applied these compounds on breast cancer cell line, by using xCELLigence (real-time cell counter) for observe the viability of cells. MTT assay kit was employed to evaluate the effects of different concentration Gossypetin, Lut, CP and combination of this drugs with each other on MCF-7 cell line proliferation. Then, we performed Annexin V-Cy3 analyze the apoptotic rate of the cells. And finally, the inhibitory effects of these drugs on the expressions of Bcl-2 and Bax were detected by quantitative polymerase chain reaction (qPCR).

Result: As expected, combination of Lut+CP was most effective drug, inhibited the growth of MCF-7 cells by inhibiting cell proliferation and inducing cell apoptosis. qPCR demonstrate that Lut-CP inhibited the expression of Bcl-2 in MCF-7 cells with concentration dependent way.

Conclusions: We analyzed cell proliferation, cell death, apoptosis and changes the gene expression by cell survival assay, apoptosis assay and qPCR. The combination Treatment significantly decreased cancer cell viability, and had a grater efficiency in killing MCF-7 cells after 24 hr and 48 hr of treatment, compared to treatment with either agent alone.

OP01-2

DEVELOPMENT AND VALIDATION OF PERSONALIZED EX VIVO PLATFORM MIMICKING PATIENT HETEROGENEOUS TUMOR MICROENVIRONMENT TO ENABLE PERSONALIZED TREATMENT FOR BREAST CANCER

Govind Babu K[1], Pradip Majumder[2], Shiladitya , Sengupta[3], Peleg Horowitz[4], Mallikarjun Sundaram[2]

[1]*Kidwai Memorial Institute of Oncology, India*
[2]*Mitra Biotech, India*
[3]*Brigham and Women's Hospital, Harvard Medical School, U.S.A.*
[4]*The Broad Institute of the Massachusetts Institute of Technology and Harvard University, U.S.A.*

Oral Presentation

Background: Predicting clinical response to anticancer drugs remains a major challenge in the management of cancer. Recent advances show that tumor microenvironment (TME) and heterogeneity impact therapy outcomes; indicating the limitations of biomarker-guided strategies for personalizing therapy. There is a need for platforms that can predict treatment outcome with high fidelity by contextually integrating tumor heterogeneity and phenocopying the TME .

Methods: Tumor grade-matched matrix support and autologous sera from individual patients were used to engineer personalized Tumor Ecosystems (CANScript™) in head and neck, breast and colorectal cancers. We evaluated functional outcomes as a measure of response to a panel of anticancer drugs in this platform. In the training data set obtained from a cohort of patients. CANScript™ read-outs were integrated with their corresponding clinical outcomes for generation of a machine learning (M-score) algorithm to predict clinical response to these drugs. Algorithm was further validated in a test group of new patients.

Result: Histopathological and molecular characterization of the tumor slices cultured in CANScript™ revealed a close approximation to the parental tumor at baseline as confirmed by Ki-67 and critical phosphoproteomic status, global transcriptomic profiles and balance in active components of tumor and stromal phenotypes. The M-score algorithm when applied to the test cohort of more than 100 patient tumors assessed in

the functional CANScript™ achieved 100% sensitivity while keeping specificity in a desired high range for predicting short term clinical outcome.

Conclusions: The high specificity and sensitivity observed in predicting clinical outcomes using the CANScript™ supports the use of this novel platform for personalized cancer treatment (Part of the data is published in Nature Communications Feb-2015).

HI-PLEX FOR HIGH THROUGHPUT MUTATION SCREENING OF BRCA1, BRCA2, TP53, AND PALB2 IN BREAST AND OVARIAN CANCER PATIENTS

Wei Xiong Wen[1], Kah Nyin Lai[1], Daniel Jonathan Park[2], Tu Nguyen-dumont[2], Fleur Hammet[2], Melissa Southey[2], Yin Ling Woo[3], Cheng Har Yip[3], Nur Aishah Mohd taib[3], Soo Hwang Teo[1]

[1]*Cancer Research Malaysia, Malaysia*
[2]*University of Melbourne, Australia*
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Background: The advent of next generation sequencing (NGS) has enabled high-throughput sequencing at relatively low cost with shorter turnaround time. Here, we report the development of a high-plex (Hi-Plex) polymerase chain reaction (PCR) approach for massively parallel sequencing for breast and ovarian cancer predisposition genes BRCA1, BRCA2, TP53 and PALB2.

Methods: We evaluated the sensitivity and specificity of our 259-plex four-gene panel using 176 breast or ovarian cancer patients that had previously been screened using Sanger sequencing. From March to December 2015, we applied our method to determine the prevalence of BRCA1, BRCA2, TP53, and PALB2 in 319 high-risk breast cancer patients and 227 unselected ovarian cancer patients.

Result: Two-hundred and fifteen of 216 variants previously identified in these individuals were successfully detected (99.5% sensitivity). Twenty-three rare variants previously not reported by prior sequencing were detected by our method and later confirmed to be all true positive calls (100% specificity). In total, 9 (2.8%) BRCA1, 15 (4.7%) BRCA2, 2 (0.6%) TP53, and 2 (0.6%) PALB2 mutation carriers were identified among breast cancer patients whereas 16 (7.0%) BRCA1, 9 (4.0%) BRCA2, and 1 (0.4%) PALB2 mutation carriers were identified among ovarian cancer patients.

Conclusions: Here, we demonstrate Hi-Plex as a powerful approach for rapid, cost-effective and accurate high-throughput mutation screening for rare genetic mutations applicable in both research and clinical settings. We also provide additional information about the prevalence of BRCA1, BRCA2, TP53, and PALB2 in a multi-ethnic cohort of Malaysian women to enable risk assessment and management of breast and ovarian cancer patients attending clinical genetic services.

DEAD-BOX RNA HELICASE DP103 AS A BIOMARKER FOR THERAPEUTIC RESPONSE TO DOCETAXEL

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Background: Resistance to chemotherapy offers limitations to the treatment of breast cancer. This has generated an increased interest in identifying new biomarkers to better predict drug responses among patients.

Methods: Expression profile of DP103 in a retrospective phase II study that had 100 female breast cancer patients were measured at mRNA and immunohistochemistry. Cell based assays methods include cell viability, immunofluorescent, siRNA methodology, immunoprecipitation, western blot for protein quantification, mRNA measurements by taxman qPCR, and over expression methodology. Validation analysis were done using publicly available patient datasets with chemotherapy.

Result: Gene expression analysis and immuno-histochemistry profiling of patient samples, randomized to a combination of docetaxel and doxorubicin, revealed a chemotherapy induced decrease in DP103 expression among responders, and an increase among non-responders. These clinical findings were also validated in-vitro, using representative cell lines to mimic responders, and their corresponding drug resistant subtypes as non-responders. Upon stratification by the receptor status, the predictive value of DP103 was only observed in patient samples and cell lines with estrogen receptor α (ERα)-positive status and not with ERα-negative status. The observed changes in DP103 expression was well correlated to a similar drug induced change in the expression of ERα; raising a possibility of a cross-talk between DP103 and ERα.

Conclusions: These findings summarize a novel role of DP103 in acquired drug resistance; presenting a potential surrogate biomarker for predicting drug response in breast cancer. In addition, we have also uncovered a positive feed-forward loop between DP103 and ERα that could regulate the activity of the latter in ERα positive breast cancer.

OP01-5

THE BASIC FACTS OF KOREAN BREAST CANCER IN 2013 : RESULTS OF A NATIONWIDE SURVEY AND BREAST CANCER REGISTRY DATABASE

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Background: The Korean Breast Cancer Society (KBCS) has reported a nationwide breast cancer data through an online registration program and a nationwide survey since 1996. We present a comprehensive report on the facts and trends of breast cancer in Korea in 2013.

Methods: Data on the newly diagnosed patients in the year 2013 were collected from 99 hospital and clinics using nationwide questionnaire survey, and from the online registration database.

Result: A total of 19,316 patients were newly diagnosed with breast cancer in 2013. The crude incidence rate of female breast cancer including carcinoma in situ was 76.2 cases per 100,000 women (invasive ca : 63.3 cases, carcinoma in situ : 12.9 cases per 100,000 women). The median age at diagnosis was 50 years, and the proportions of postmenopausal women with breast cancer accounted for more than half of total patients. The proportion of stage 0 and stage I breast cancer increased consistently, and breast conserving surgery was most frequently performed. The total number of breast reconstruction increase markedly accelerated, 194.2% increase between 2002 and 2013. For invasive cancer, a continuous significant increase of the incidence was observed until 2010 with +8.5% annual percentile change (APC), and thereafter the incidence increase slowed with +2.0% APC. For DCIS, the incidence of DCIS consistently increased during observed period from the year 2002 to 2013. The proportion of patients with luminal type breast cancer was steadily increased.

Conclusions: Analysis of nationwide registry data will contribute to defining of the trends and characteristics of breast cancer in Korea.

Oral Presentation

OP01-6

IDENTIFICATION OF MOLECULES ASSOCIATED WITH TAMOXIFEN RESISTANCE THROUGH GENE EXPRESSION PROFILING OF TAMOXIFEN-RESISTANT BREAST CANCER CELLS

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Background: Treatment of estrogen receptor (ER)-positive breast cancers has primarily relied on the use of tamoxifen, a selective ER modulator that interferes with ER function. The major clinical hurdle in tamoxifen treatment is that a proportion of ER-positive patients do not respond to therapy at a later stage. However, the reasons for resistance to tamoxifen therapy are mainly unknown.

Methods: To elucidate the molecular mechanisms of tamoxifen resistance, we performed gene analyses and identified genes with altered expression in tamoxifen-resistant MCF7 cell line versus the parental cell line. To confirm the involvement of selected genes in tamoxifen resistance we adopted manipulations of gene expression by RNA interference and exogenous gene transfection in breast cancer cell lines.

Result: The tamoxifen-resistant MCF7 cells expressed higher protein levels of Lyn, BCAS1, HCAR1, and RagD than the parental cell line. Knockdown of Lyn in tamoxifen-resistant cells restored sensitivity to tamoxifen. Overexpression of BCAS1 suppressed tamoxifen-induced apoptosis in MCF7 cells by inhibition of c-Jun N-terminal kinase. Cell surface lactate receptor, HCAR1 exacerbated tamoxifen resistance of cells in conditions of low glucose supplemented with lactate. Tamoxifen-induced RagD expression led to mTOR activation, suggesting that the mTOR pathway may be a promising target for enhancing tamoxifen efficacy.

Conclusions: Our results indicate that the molecules identified here have an important role in tamoxifen resistance of ER-positive breast cancer cells, and those expressions in breast tumor may be an important novel biomarker of response to tamoxifen therapy in breast cancer.

Oral Presentation

OP01-7

INHERITED PREDISPOSITION FOR BREAST CANCER IN DIVERSE HEREDITARY CANCER SYNDROMES: STRATEGIES FOR SYNDROME SPECIFIC GENETIC TESTING AND RISK MANAGEMENT

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Background: Mendelian inheritance of breast cancer predisposition is seen in hereditary breast and ovarian cancer (HBOC) and in several other Mendelian syndromes like Li-Fraumeni syndrome (LFS), Peutz Jeghers (PJS), Cowden, Lynch and a few others. While BRCA1, BRCA2, TP53 and STK11 are the most commonly implicated genes in such families, several other genes with less certain penetrance are known. The burden and spectrum of inherited predisposition for breast cancer in diverse hereditary cancer syndromes has not been defined in the South Asian population.

Methods: During 2003-2015, we registered 3,300 families with inherited cancer predisposition in our cancer genetics clinic. The Mendelian cancer predisposition syndrome was ascertained, mutation probability for specific genes calculated, and appropriate genetic testing performed.

Result: In families with breast cancer affecting one or more members, HBOC was the most commonly identified syndrome, followed by LFS, PJS, Cowden, Lynch and NF1. Deleterious germline mutation were identified most frequently in the BRCA1/2 gene (345 carriers in 205 families), followed by TP53, mismatch repair (MMR) genes and a few other genes. Use of next generation sequencing (NGS) gene panel testing resulted in identification of several variants of uncertain significance (VUS) but very few pathogenic rare gene variants.

Conclusions: For common cancer like breast, which can present in its inherited form in a wide variety of syndromes, appropriate genetic testing and its interpretation is challenging. Accurate syndrome identification with detailed family history for clinical presentations, histology and IHC of cancers is the most reliable guide for single gene analysis and for correlation of rare gene variants identified on NGS panel testing. This allows individualized risk management plans for carriers.

Oral Presentation

OP01-8

EFFICACY AND SAFETY OF EVEROLIMUS AND EXEMESTANE IN PATIENTS WITH ADVANCED BREAST CANCER FROM ASIA AND AFRICA: ASIAN SUBSET RESULTS FROM THE PHASE 3B EVEREXES STUDY

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Oral Presentation

Background: In BOLERO-2, everolimus (EVE) plus exemestane (EXE) more than doubled the median progression-free survival (PFS) in patients with hormone receptor positive (HR+), human epidermal growth factor receptor 2-negative (HER2-) advanced breast cancer (ABC), recurring or progressing on/after prior non-steroidal aromatase inhibitors (NSAIs). EVEREXES, an expanded-access program, evaluated safety and efficacy of EVE+EXE in patients from Asia and Africa. Data from Asian subgroup of patients in EVEREXES is presented here.

Methods: EVEREXES is an open-label phase 3b, single-arm, multicenter, international trial (planned N = 400) in patients with HR+, HER2- ABC, progressing on/after prior NSAIs. Primary objectives were safety and tolerability of EVE+EXE. Secondary objectives included PFS, overall response rate (ORR) and clinical benefit rate (CBR) (RECIST 1.1).

Result: Out of 235 patients enrolled between March, 2013 and October, 2014, 191 patients were Asian. Median age was 58 years. Median follow-up was 50.9 weeks at data cut-off date (January 31, 2015). Most frequent any grade adverse events (AEs) were stomatitis (63.9%), rash (26.2%), and hyperglycemia (25.7%). Most frequent grade 3 or 4

AEs were stomatitis (11.5%) and hyperglycemia (6.3%). Treatment discontinuation due to AEs was observed in 15.7% of patients. Stomatitis (1.6%) was the most common AE leading to treatment discontinuation. Median PFS was 9.53 months (95% CI, 9.18-11.58), CBR was 42.4% (95% CI, 35.3-49.8), and best ORR was 17.3% (95% CI, 12.2-23.4).

Conclusions: Safety and efficacy results from the Asian subset of EVEREXES were consistent with BOLERO-2 data and support EVE+EXE regimen as a treatment option in Asian patients

OP02-1

INVESTIGATION OF CYTOTOXIC AND APOPTOTIC EFFECTS OF URTICA DIOICA AGGLUTININ ON MCF-7 AND L929 CELL LINES

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Background: There is significantly increasing interest in medical botanicals as part of complementary medicine in the world. Urtica dioica agglutinin (UDA) is the first lectin to be isolated from a member of Urticaceae family and differs definitely from all other known plant lectins with respect to its molecular structure. UDA is not only the smallest (8.5 kDa) lectin known at present, but also the first single chain lectin to be found in plants. Lectins are well known group of multivalent carbohydrate binding proteins that bind glycans of cell surface and mediate a variety of biological functions. Most of lectins contain two or more sugar binding sites and can agglutinate cells and/or precipitate complex carbohydrate conjugates. In this study, we investigated the cytotoxic and apoptotic effects of one of a good representative ingredients of UDA.

Methods: UDA, at different concentrations (5, 10, 20 μg/mL) on discrepant types of cancer cell lines which are human breast cancer (MCF-7) and also non-cancer mouse fibroblast (L929) cell lines by carrying out MTT (colorimetric assay for assessing cell viability), xCELLigence (real-time cell counter), TUNEL (apoptosis) assays, respectively.

Result: According to our results different concentrations of UDA have anti-proliferative and apoptotic effects on MCF-7 cell lines. The real-time cell analysis, MTT and TUNEL assays indicated that UDA in concentration, 20 M, has antiproliferative and apoptotic effects on MCF-7 cell lines after 24 hours.

Conclusions: Therefore, our current information regarding UDA confirms that UDA may be made use in cancer therapeutic strategies as a primary cure in the future.

OP02-2

SCREENING BY ABBREVIATED BREAST MAGNETIC RESONANCE IMAGING (MRI) IN WOMEN WITH A HISTORY OF BREAST CANCER OPERATION

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Background: To retrospectively investigated the outcomes of an abbreviated protocol, consisting of only pre- and one post-contrast acquisition and their derived images first post-contrast subtracted (FAST) and maximum-intensity projection (MIP) images, was suitable for breast magnetic resonance imaging (MRI) screening.

Methods: Between October 2014 and December 2015, 576 women (mean age, 56 years; age range, 26-84 years) were referred for screening in women with a history of breast cancer operation. In addition to mammography and high-frequency breast ultrasonography (US), patients underwent abbreviated breast MR imaging. Of the study population, 91.8% (529 of 576) patients underwent preoperative MR examinations. Cancer detection rate and characteristics of detected cancers were assessed. Three breast radiologists reviewed MIP and FAST images.

Result: 31 patients (5.4%) had a suspicious enhancing lesion depicted on MIP and FAST images (average size, 1cm; range, 0.4-2.9 cm). Five patients (0.86%) had malignant results as invasive ductal carcinoma (n = 3) and ductal carcinoma in situ (n = 2); only two patients (0.35%) had negative results on mammography and US and the size of enhancing lesion on MR were 1.1cm and 1.3 cm. Three patients had benign result as fibrocystic change, stromal fibrosis, fibroadipose tissue. 23 patients had no correlated lesion on US. 494 patients (85.8%) had negative or benign MR finding. 51 (8.9%) patients had probably benign MR finding.

Conclusions: Preliminary data suggest that abbreviated breast MRI (FAST with MIP) depicted 3.5 additional cancers per 1,000 women with a history of breast cancer operation.

Oral Presentation

OP02-3

ANALYSIS OF INTERVAL BREAST CANCER WITH A SINGLE CENTER DATASET

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Background: For early detection of breast cancer, a regular breast screening is recommended. However, an interval breast cancer may be detected during the follow-up period, which is a term given to cancers detected or presenting after a screening in which findings are considered normal. To reduce the incidence of interval breast cancer, the author investigated and analyzed the characteristics of interval breast cancers.

Methods: Between 1998 and 2015, a total of 1,564 patients with breast cancer were diagnosed in Lim,JaeYang clinic, Daegu, Republic of Korea. Among them, there were eighty-five cases of interval breast cancer (5.4%) who visited within 24 months.

Result: The interval breast cancers were classified as three groups as follows; true interval breast cancer (n = 56, 65.9%), false negative (n = 10, 11.8%) and missed cases (n = 16, 18.8%). And other three cases could not be classified clearly. Based on the interval of follow-up, the interval breast cancers were detected by 5 cases (5.9%) within ≤ 6 months, 14 cases (16.5%) between > 6months and ≤ 1 year, and 66 cases (77.6%) between > 1 year and ≤ 2 years. Twenty cases (23.5%) were ductal carcinoma in situ. And there were 52 cases (61.2%) of in situ and < 1 cm breast cancer, 22 cases (25.9%) of < 2 cm breast cancer (the stage I was confirmed in 74 cases (87.1%)). In interval breast cancers without axillary lymph node metastasis, tumor size was ≤ 1 cm (n = 32, 37.6%), > 1 cm to ≤ 2 cm (n = 22, 25.9%). About the number of metastatic lymph nodes, ≤ 2 and > 3 was confirmed in 6 cases (7.1%) and 5 cases (5.9%), respectively. There were 11 cases which showed unexpected worse results and an expired case after 9 months of treatment who were diagnosed at 8 months from last examination with 16 axillary lymph nodes metastasis.

Conclusions: Although more than 40-year old patients are receiving an annual follow-up surveillance regularly in my clinic and most of interval breast cancers showed an early stage of breast cancer, there were several cases which showed a worse prognosis. In conclusion, based on the analysis of interval breast cancers, following conditions should be evaluated with tissue confirmation for early detection of interval breast can-

Oral Presentation

cer; ① a new lesion appeared in age 40-50s, although previous result was BI-RADS category2, ② a suspicious microcalcification is detected, ③ a mild suspicious symptom or bloody discharge in age < 30s of unmarried female patients, because they generally are performed only ultrasonography and shows relatively worse prognosis when the breast cancer occurred. In conclusion, the interval breast cancer can be detected early with active surveillance and various approaches not to miss the suspicious lesion in ultrasonography.

ESTIMATING THE COST OF WORK LOSS OF CANCER SURVIVORS IN JAPAN

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Background: Cancer and its treatments largely affect socioeconomy of community. Support system for working cancer patients is urgently required in the world. In Japan, the prevalence of breast cancer by age is higher in younger women than in western countries. About half of breast cancer patients were diagnosed in 30-50s. Since they are considered most productive working force in society, it is urgent to investigate work loss by the disease and its treatment for cancer survivors and to develop interventions to minimize it.

Methods: We estimated the cost from all cancers resulting from Patients including in-patient, outpatient and non-treatment days. This was calculated with a new method, the product of the employment rate coefficient × productivity coefficient, making use of data published by the Japanese Ministries. Regarding breast cancer, we used the Survey on Cancer and Employment to estimate work loss on non-treatment days.

Result: The estimate on treatment days for all cancers was $1,820.21 million in men and $939.38 million in women. In terms of disease classification, lung cancer was the largest cause in men, whereas breast cancer was the largest in women. On non-treatment days, the work losses because of gastric, colon, and lung cancers were large in men, while breast cancer was the largest in women and in total. Regarding breast cancer, the total loss was estimated at $714.83 million.

Conclusions: Breast cancer was considered the leading cause, and the most influential cause when the product for breast cancer was assumed the same as the product for all other types of cancers.

OP02-5

THE RISK FACTORS OF PREGNANCY-ASSOCIATED BREAST CANCER IN KOREAN WOMEN

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Background: This study aimed to evaluate the risk factors of pregnancy associated breast cancer (PABC) compare with Non-PABC in Korea women.

Methods: From the Korea Breast Cancer Registry (KBCR) database, 344 patients with PABC were eligible between 1999 and 2013. PABC was defined as ductal carcinoma in situ, invasive ductal carcinoma, or invasive lobular carcinoma which was diagnosed during pregnancy or within 1 year after postpartum. Non-PABC patients were selected through 1:2 matching method from the KBCR database. The matching variables were operation period, age, and initial stage.

Result: Patients with PABC had higher histologic or nuclear grade, higher proportion of hormone receptor negative breast cancer than patients with non-PABC. In univariate analysis, PABC group was associated with high body mass index (BMI, ≥ 23kg/m2), early menarche (< 14 years), late first childbirth age (≥ 29 years), and family history. In multivariate analysis, the values significantly associated with PABC were early menarche (hazard ratio, 2.030, 95% CI, 1.468-2.806, $p < 0.001$) and late first childbirth age (hazard ratio, 1.680, 95% CI, 1.220-2.312, $p = 0.001$). And BMI had a tendency of associating with PABC (hazard ratio, 1.364, 95% CI, 0.990-1.878, $p = 0.058$).

Conclusions: PABC patients were associated with early menarche, late first childbirth age, and over BMI 23 in Korean women.

Oral Presentation

OP02-6

EFFICACY OF DOCETAXEL, TRASTUZUMAB AND PERTUZUMAB COMBINATION REGIMEN FOR HER2-POSITIVE METASTATIC BREAST CANCER

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Background: Anti-HER2 therapies achieve remarkable progress and post-recurrence survival prolongs drastically. The first-line treatment for metastatic breast cancer (MBC) patients by concurrent combination of docetaxel, trastuzumab and pertuzumab (DTP) showed 56.5 months overall survival in the CREOPATLA trial. It became the standard first-line regimen against metastatic breast cancer.

Methods: We surveyed efficacy of DTP combination regimen in our institution. Twenty-four HER2-positive MBC patients who received DTP chemotherapy in any treatment line between September 2013 and November 2015 and carried out at least one time of imaging evaluation were reviewed retrospectively based on medical records.

Result: The median age of the patients was 63 years old (range 35-78). Eleven patients had recurrence after surgery, eight had distant metastasis at the presentation and five were stage IIIC. Eight patients were estrogen receptor (ER)-positive and 16 were ER-negative. The median follow up period was 53weeks (range 16-105). The median administration period of docetaxel was 6 courses (range 1-8) and doses of docetaxel were reduced in half of them. They included 15 cases of first-line treatment, two of second-line and seven of further treatment lines. Two patients achieved complete response, 19 patients obtained partial response and three were stable disease. There was no progressive disease at the first evaluation. Time to treatment failure and overall survival did not reached 50% at the data cut off.

Conclusions: DTP regimen demonstrated considerable efficacy and long duration of treatment in daily practice as well as the results of existing trials.

Oral Presentation

INFLUENCE OF BODY MASS INDEX AT DIAGNOSIS IN RELATION TO HORMONE RECEPTOR, MENOPAUSAL AND NODAL STATUS ON BREAST CANCER PROGNOSIS

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Background: There is a controversy about the association between body mass index (BMI) and breast cancer outcome. The aim of this study was to access clinicopathologic characteristics which have an effect on the association between BMI and breast cancer prognosis.

Methods: We retrospectively analyzed the data of 15,956 non-metastatic invasive breast cancer patients from the Asan Medical Centers research database. The survival analysis was performed using the Kaplan-Meier method and Cox proportional hazard model.

Result: Only in premenopausal patients with node-positive, hormone receptor-positive breast cancer, obesity (BMI $\geq$ 30.0 kg/m^2) at diagnosis was associated with worse overall survival (OS) and breast cancer specific survival (BCSS) than normal weight patients. (hazard ratio [HR] = 2.46, 95% confidence interval [CI] = 1.39 to 4.37 and HR = 2.84, 95% CI = 1.60 to 5.08, respectively). Underweight (BMI < 18.50 kg/m^2) in node-positive, hormone receptor-negative breast cancer showed decreased OS (HR = 2.04, 95% CI = 1.02 to 4.06) and BCSS (HR = 2.26, 95% CI = 1.13 to 4.52).

Conclusions: Tumor burden, hormone receptor and menopausal status are clinicopathologic features which have an influence on the association between BMI and breast cancer outcome. BMI has a role as a prognostic factor of breast cancer mortality in the node-positive setting. Depending on the hormone receptor status, the role of BMI on breast cancer prognosis changes.

THE DISTRIBUTION OF PROBANDS AND BRCA CARRIERS FROM 4 ASIAN BREAST CANCER STUDIES (SINGAPORE, CHINA AND KOREA)

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Background: BRCA 1/2 mutation were associated with breast cancer and ovarian cancer. Most studies regarding these gene mutation and breast cancer were conducted in Western populations. We aimed to describe the distribution of probands and BRCA carriers in 4 Asian breast cancer studies.

Methods: We used data from 4 breast cancer studies in 3 Asian countries (Korea, Singapore and China). Korean Hereditary Breast cancer (KOHBRA) study, National University Hospital and National University of Singapore Breast cancer (NUHS BRCA) study, West China Hospital, Sichuan University Breast cancer (WCHBRCA) study and Zhejiang Cancer Hospital study collected 2,454, 57, 507, and 30 subjects respectively. Descriptive statistical methods were used for distribution of 4 Asian studies.

Result: Among 2,166, 56, 507, and 30 probands, 1,103 (45.0%), 56 (100%), 48 (9.5%), and 30 (100%) carriers were identified from KOHBRA, NUHS BRCA, WCHBRCA and Zhejiang Cancer Hospital study, respectively. The prevalence of BRCA 1/2 mutation in female probands were 44.0% and 14.6% were BRCA carriers from KOHBRA and WCHBRCA study. Distribution of affected subjects with breast cancer or ovarian cancer in female carriers were 967 (91.7%), 57 (100%), 48 (100%), and 30 (100%) from KOHBRA, NUHS BRCA, WCHBRCA and Zhejiang Cancer Hospital study. Distribution of 4 studies may be affected by selection bias from different study design.

Conclusions: We conducted descriptive study from 4 Asian breast cancer studies. This descriptive study could contribute to estimate penetrance of BRCA 1/2 mutation and basic information of other genetic studies.

OP03-1

SYNTHESIZATION, CHARACTERIZATION OF FOLIC ACID AND QUERCETIN FUNCTIONALIZED MAGNETIC NANOPARTICLES RESEARCH ON BREAST CANCER CELL LINE FOR HYPERTHERMIA AND TARGETED DRUG DELIVERY APPLICATIONS

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Background: Due to increase in cancer caused death, there are significant number of studies on nanoparticle (NP) based cancer drugs and that number going on. The purpose of this study was to synthesis and characterization of quercetin (CQ) and folic acid (FA) modified superparamagnetic nanoparticles (SPION) for determine its antiproliferative, hyperthermic and apoptotic activities on folic acid receptors (FR+) overexpressed (MCF-7) breast cancer cells and folic acid receptors none expressed (FR-) normal mouse fibroblast cells (L929).

Methods: The cellular uptake of SPION@APTES@FA-PEG@CQ were determined with prussian blue staining, cytotoxicity of SPION@APTES@FA-PEG and SPION@APTES@FA-PEG@CQ were studied by MTT and realtime cell analyzer (RTCA). Apoptosis induced by SPION@APTES@FA-PEG@CQ were analyzed by using TUNEL, Annexin V-Cy3 and Caspase 3/7 assays. Lastly, hyperthermic effects of SPIONs were investigated

Result: Results show that SPION@APTES@FA-PEG (0-200 μg/mL) was not cytotoxic whereas SPION@APTES@FA-PEG@CQ has decreased the cell viability only on MCF-7 cells. In vitro cellular uptakes of SPION@APTES@FA-PEG@CQ shows markedly higher internalization of SPION@APTES@FA-PEG@CQ by MCF-7 cells than L929 cells. SPION@APTES@FA-PEG@CQ caused higher apoptotic effects in 100 μg/mL concentration on MCF-7 cells. However on L929 cells induced apoptosis was not seen significantly. Hyperthermia combined with SPION@APTES@FA-PEG@CQ are considerably cytotoxic for the MCF-7 cells.

Conclusions: The findings suggested that newly synthesized nanoparticles had more effective on breast cancer cells due to its great medicinal properties for future in vivo targeted drug delivery.

Oral Presentation

BREAST CANCER RISK ASSOCIATIONS WITH DIGITAL MAMMOGRAPHIC DENSITY BY MAMMOGRAPHY DENSITY THRESHOLDS AND MAMMOGRAPHY SYSTEM

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Background: After adjusting for age and body mass index (BMI), mammographic density predicts breast cancer risk. We previously found that measuring mammographic density on digital mammography at a higher pixel intensity threshold than conventional better predicts breast cancer risk for Korean women. We conducted a validation study of this finding using two mammography systems.

Methods: This Korean Breast Cancer Study included 398 women diagnosed with invasive breast cancer and 737 matched controls by two mammography systems: GE and HOLOGIC. Mammographic density was measured using the semi-automated software at the conventional threshold (Cumulus) and at increasingly higher thresholds, called Altocumulus and Cirrocumulus. We used conditional logistic regression to estimate the change in Odds PER standard deviation Adjusted (OPERA) for each machine.

Result: For dense area measured by HOLOGIC, the OPERA were 1.56 (95%CI: 1.33-2.08, AUC = 0.69) for Cumulus; 2.15 (1.68-2.75, AUC = 0.76) for Altocumulus; and 3.48 (2.54-4.76, AUC = 0.89) for Cirrocumulus, respectively ($p < 0.001$). For dense area measured by GE, the OPERA were 1.35 (1.15-1.58, AUC = 0.60); 1.37 (1.17-1.60, AUC = 0.61) and 1.46 (1.25-1.70, AUC = 0.63) for Cumulus, Altocumulus and Cirrocumulus, respectively ($p < 0.001$). After fitting the Altocumulus measure or Cirrocumulus measure, addition of the Cumulus measure did not improve fit ($p > 0.4$). After fitting Cumulus, addition of Altocumulus or Cirrocumulus gave a better fit.

Conclusions: Cirrocumulus performed best in predicting breast cancer risk, especially when measured using the HOLOGIC system for which the risk gradient was greater

than would be achieved from knowing all genetic factors. Altocumulus performed better than Cumulus. This suggests that mammographically bright regions might be more aetiologically important for breast cancer, with implications for biological, molecular, genetic and epidemiological research and clinical translation.

TARGETING A NOVEL CHEMORESISTANCE GENE, ZBTB2, TO OVERCOME CISPLATIN-RESISTANCE IN TRIPLE-NEGATIVE BREAST CANCER

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Background: Zinc finger and BTB/POZ domain containing proteins (ZBTB) contributes to development, differentiation and carcinogenesis. We have previously identified ZBTB2 was upregulated in cisplatin-resistance cells and involved in drug resistance through ATP-binding cassette sub-family G member 2 (ABCG2) transporter. However, the molecular mechanism of ZBTB2 in drug resistance and breast cancer metastasis has not been studied.

Methods: A cisplatin-resistant triple-negative breast cancer (TNBC) cell line, MDA-MB-231/cis, was used to explore the drug resistance and drug transporter genes. Stem cell related genes were studied by RNA-sequencing. Characterization of ZBTB2 on cell proliferation, invasion and epithelial-mesenchymal transition (EMT) process were performed in ZBTB2 siRNA transfected cells. Stem like cells properties were validated using aldehyde dehydrogenase (ALDH) activity, tumorsphere formation ability and stem cell markers. Metastatic animal model was used to study the genetic changes during metastasis and associated with the findings in clinical samples.

Result: ZBTB2 was upregulated in MDA-MB-231/cis cells, as well as in primary breast tumor tissues when compared with non-tumor counterparts from TNBC patients. ZBTB2 siRNA significantly reduced cell proliferation, invasion and sensitized cells to cisplatin and induced apoptosis. RNA sequencing analysis showed that ABCG2, interleukin 6 signal transducer (IL6ST) and fibroblast growth factor receptor 1 (FBFR1) were upregulated in MDA-MB-231/cis cells and downregulated in ZBTB2 siRNA cells. In addition, higher expression of ZBTB2 was observed in metastatic tumors when compared with primary tumors from animal model. Silencing of ZBTB2 reduced ALDH activity and tumorsphere formation ability.

Conclusions: Silencing of ZBTB2 sensitize cancer cells to cisplatin through modulation of drug transporters and stem-like cell properties in TNBC. These findings suggest that targeting ZBTB2 offers therapeutic options for metastatic TNBC.

OP03-4

THE ROLE OF PREOPERATIVE BREAST MAGNETIC RESONANCE (MR) IMAGING FOR SURGICAL DECISION IN PATIENTS WITH TRIPLE-NEGATIVE BREAST CANCER

Jeeyeon Lee, Jin Hyang Jung, Wan Wook Kim, Seung Ook Hwang, Jin Ho Chung, Taek Ju Kwon, Ho Yong Park, Hye Jung Kim, Yee Soo Chae, Soo Jung Lee

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Background: Several reliable randomized studies do not recommend routine preoperative breast magnetic resonance (MR) imaging for patients with breast cancer. However, because the principle of MR imaging is based on the dynamics of contrast enhancement, a specific biologic subgroup of tumors should sensitively respond to the imaging process.

Methods: From 2008 to 2013, 918 eligible patients with breast cancer underwent breast surgery and were divided into two groups based on preoperative breast MR findings: patients in whom the surgical plan was changed and those in whom the surgical plan remained unchanged. We investigated the changing patterns of breast surgery based on routine mammography, ultrasound, and preoperative breast MR findings and analyzed the association between additional suspicious lesions on breast MR imaging and clinicopathologic factors.

Result: Additional suspicious breast lesions were detected on preoperative MR imaging in 104 cases (11.3%), and the surgical strategy was changed as the final decision in 97 cases (10.6%). There was no difference between oncologic results between two groups. However, the triple-negative breast cancer (TNBC) was significantly associated with changing of the surgical strategy based on breast MR findings ($p = 0.048$).

Conclusions: Additional preoperative breast MR imaging may be helpful in surgical decision for patients with TNBC.

OP03-5

CHANGES OF ABDOMINAL FAT DISTRIBUTION AFTER ENDOCRINE THERAPY IN BREAST CANCER PATIENTS

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Background: Abdominal fat distribution is closely related to steroid hormones and is thought to be a strong predictor of metabolic dysfunction. The purpose of this study was to evaluate changes of abdominal fat distribution (e.g., subcutaneous adipose tissue [SAT], visceral adipose tissue [VAT]) in breast cancer patients after endocrine therapy.

Methods: One hundred and Sixteen patients with breast cancer treated with adjuvant endocrine therapy were included. Patients were evaluated using computed tomography (CT) before and after at least 6 months of endocrine therapy. Total abdominal adipose tissue (TAAT) area was automatically calculated using a workstation. VAT was manually segmented and SAT area was obtained by subtracting VAT area from TAAT. Two groups (group A, who experienced an increase in TAAT, and group B, who experienced a decrease.) were created and compared changes of SAT, VAT, and VAT/SAT ratio in each endocrine therapy.

Result: Percentage of TAAT was increased by a mean of 8.5% from baseline after tamoxifen but decreased 0.7% after AI. Patients with tamoxifen, VAT/SAT ratio was significantly increased in both group A and B (18.5%, 15.1%). In addition, increase VAT/SAT ratio was observed in both groups of patient receiving aromatase inhibitor (20.4%, 17.4%).

Conclusions: Changes in abdominal fat distribution to relatively greater VAT/SAT ratio was observed in patients with endocrine therapy, regardless of whether they gained or lost weight after therapy. Since this pattern of fat distribution is associated with metabolic disorders, attention should be made to clinical manifestations in patients during follow-up management.

DEVELOPMENT OF SECOND PRIMARY CANCERS IN KOREAN BREAST CANCER SURVIVORS

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Background: Breast cancer survivors have slightly increased risk of second primary cancers. Importance of screening for second cancers has been raised due to increased survival in those populations. In this study, we assessed development of second primary cancers in breast cancer survivors.

Methods: Medical record of breast cancer patients was reviewed retrospectively in three medical institutions. Available data of ICD-9 code records after breast cancer diagnosis was evaluated. Diagnosis of second primary breast cancer was excluded in this evaluation. Cancer developed within two months from breast cancer diagnosis was considered as synchronous cancer. We used cancer incidence rates of primary cancer in general population for the calculation of standardized incidence ratios (SIR) of second primary cancers.

Result: From January 1989 to January 2014, available medical records were reviewed in breast cancer patients (N = 5,514) in three institutions. Cumulative incidence of overall second primary cancers was 1.8%. Among 99 second primary cancers, thyroid (48.48%) was the most common cancer, followed by stomach (10.10%) and endometrium (6.06%). The most common age group was 50s. Within 5 years after breast cancer diagnosis was the most frequent period of elapse time for second primary cancer. Overall SIR of second primary cancer was 1.66. Thyroid and endometrial cancer showed elevated SIR(2.47 and 8.36, available data from single institution).

Conclusions: Incidence of cancer in general population was reflected to development of second primary cancer in breast cancer survivors. Application of personalized cancer screening plan would be important in this patient group. A nationwide research is needed to make guidelines for second primary cancer screening

THE PRECISE QUANTIFICATION OF PROGESTERONE RECEPTOR COULD BE AN ALTERNATIVE TO THE RECURRENT SCORE IN HORMONE RECEPTOR-POSITIVE EARLY BREAST CANCER

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Background: Risk stratification based on results provided by the 21-gene assay in early breast cancer can help optimize hormone therapy and/or chemotherapy decisions. Proliferation and hormone receptor status are major factors to determine the 21-gene Recurrence Score (RS). We analyzed the correlation of factors evaluated in routine immunohistochemical staining of breast cancer and the 21-gene assay results.

Methods: This study included 458 patients with results of the 21-gene assay. The patients had estrogen receptor-positive, HER2-negative breast cancer with pN0 or pN1. The results of 21-gene assay including RS and progesterone receptor (PR) score, and the results of immunohistochemical staining including Allred scoring for PR and Ki-67 were analyzed using Pearsons correlation coefficient.

Result: Mean RS was 17.36 (range, 0-66). The RS was low in 276 cases, intermediate in 146 cases, and high in 36 cases. The Allred score for PR and Ki-67 had a weak correlation with the RS results (respectively, $r = -0.211$, $p < 0.001$ and $r = 0.306$, $p < 0.001$) and the PR score of 21-gene assay had a strong correlation with the RS results ($r = -0.601$, $p < 0.001$). The Allred score for PR had a moderate correlation with the PR score of 21-gene assay ($r = 0.494$, $p < 0.001$).

Conclusions: The PR score of 21-gene assay had a strong negative correlation with the RS results, while the Allred score for PR and Ki-67 had a weak correlation with the results of RS. The development of precise PR quantification methods could be an alternative to the multigene assay for decision of adjuvant treatment.

OP03-8

SIX-YEAR FOLLOW UP OF BREAST-CONSERVING SURGERY USING SUPINE MAGNETIC RESONANCE IMAGING IN BREAST CANCER PATIENTS RECEIVING PRIMARY SYSTEMIC THERAPY

Takafumi Sangai, Takeshi Nagashima, Masahiro Sakakibara, Junta Sakakibara, Toshiaki Iwase, Shoko Hayama, Emi Ishigami, Takahito Masuda, Ayako Nakagawa, Masaru Miyazaki

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Background: In 2005, we developed a new procedure of breast-conserving surgery (BCS) using magnetic resonance imaging (MRI) in surgical position. This procedure enables to recreate initial tumor image accurately onto the skin after primary systemic therapy (PST) at the time of surgery. Previously we showed that it was a reliable technique for breast conservation after PST with significant reductions in incision area and additional excision rate. We now report the 6-years findings in recurrence.

Methods: Between January 2006 and December 2011, 38 women with invasive breast tumors were underwent PST followed by MRI-guided surgery for breast conservation at Chiba University Hospital. All the patients received radiotherapy and patients who had luminal types of tumor received endocrine therapy at least 5-years after the surgery. The recurrence rate of the ipsilateral breast cancer and the survival outcome of patients who received PST followed MRI-guided surgery were compared with that of similar women who underwent PST or conventional BCS.

Result: The average of observation period was 83.6 months. The cumulative incidence of recurrent tumor in the ipsilateral breast was 10.5%. Time to recurrence was average 38.8 months. Three of these four cases relapsed in distant organs as well. Total eight cases (21.1%) developed distant metastasis, and the 6-year survival rate was 81.6%.

Conclusions: MRI-guided BCS after PST was equivalent in ipsilateral breast recurrence rates and survival outcome as compared to conventional methods. It is the simple procedure and can be performed safely, but we still need to give careful consideration to the indication for BCS after PST.

POSTER EXHIBITION

Global Breast Cancer Conference 2016

PO001

PREVALENCE OF MAMMOGRAPHICALLY DENSE BREASTS IN THE KOREAN WOMEN: RESULTS FROM A NATIONWIDE SURVEY

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Background: Mammographic breast density is an important risk factor for breast cancer. The current study was to examine the distribution of mammographic breast density by age of women undergoing mammography and estimate the prevalence of Korean women with dense breasts.

Methods: The current study used the National Cancer Screening Program (NCSP) data to 2009. We applied these breast density distributions to age-specific counts of the Korean women population derived to mid-year 2009 to estimate the number of Korean women with dense breasts.

Result: Overall, 63.3% (95% confidence interval [CI], 57.6% to 68.5%) of women 40 to 74 years of age had heterogeneously or extremely dense breasts, and this proportion was inversely associated with age. Based on the age distribution of Korean women, we estimated that 65.8 per 100,000 women (95% CI, 59.9% to 71.2 per 100,000) age 40-74 years in Korean have heterogeneously and extremely dense breasts. Women aged 40-54 years (N = 47.3 per 100,000) accounted for 71.9% of this group.

Conclusions: The prevalence of dense breasts among Korean women of breast cancer screening ages exceeds 50 per 100,000. Policymakers and healthcare provider should consider the large prevalence of dense breast women and provide strategic screening methods.

Poster Exhibition

A STUDY OF THE IMPACT OF THE 21-GENE BREAST CANCER ASSAY ON THE USE OF ADJUVANT CHEMOTHERAPY IN WOMEN WITH BREAST CANCER ; EARLY EXPERIENCE

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Background: The 21-gene (Oncotype DX) recurrence score (RS) assay is useful in predicting the benefits of adjuvant chemotherapy for early breast cancer patients and is widely used in Western countries. However, to date, it has not gained much popularity in East Asia. The aim of this study was to characterize the impact of the Oncotype DX assay on adjuvant therapy decision making.

Methods: The 21-gene assay was performed on 25 patients with estrogen receptor-positive early breast cancer in Dong-A University Hospital. Twenty-five patients with ER +, HER2 -, N0/N1-2 node-positive breast cancer from our hospital were eligible for the study. The primary endpoint was the overall change in treatment recommendations after receiving the assay.

Result: Among the 25 patients, 12 (48%) had a low RS of < 18, 10 (40%) had an intermediate RS of 18-30, and 3 (12%) had a high RS of ≥ 31. Histologic grade, presence of micrometastases, Ki-67, and presence of lymphatic invasion were statistically associated with the RS results. Treatment decisions were changed in 15 of 19 patients (76%) from chemotherapy plus hormone therapy to hormone therapy.

Conclusions: The 21-gene breast cancer assay proved to have a significant impact on treatment decision- making. The test reduces the overall use of chemotherapy in Korean estrogen receptor-positive, early breast cancer patients.

PO003

IPSILATERAL BREAST TUMOR RECURRENCE (IBTR) IN BRCA-POSITIVE BREAST CANCER MAY NOT ONLY RESULT FROM SURGICAL TECHNIQUES: A MULTICENTER ANALYSIS

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Background: The incidence of ipsilateral breast tumor recurrence (IBTR) in BRCA+ breast cancer was reported to be higher than sporadic breast cancer. However, the oncologic outcomes of BRCA+ cancer are different between short- and long-term follow up. This multicenter analysis study compared the oncologic outcomes of BRCA+ cancer in breast conserving surgery group, simple mastectomy group and mastectomy followed by immediate reconstruction group.

Methods: Thirty women with 34 BRCA 1/2+ cancers were treated with breast-conserving surgery (n = 17), simple mastectomy (n = 9) or mastectomy followed by immediate reconstruction (n = 8). The clinicopathologic factors and oncologic outcomes were compared among the three groups during a mean 3-year follow-up period.

Result: The mean age of patients with BRCA+ cancer was significantly low in the mastectomy group followed by the immediate reconstruction group. The performance of neoadjuvant chemotherapy, nodal stage and pathologic stage were significantly different between the breast-conserving and simple mastectomy groups. Although there was no locoregional recurrence or distant metastasis in the breast-conserving group during follow-up, there were several events in the other two groups.Oncologic analysis demonstrated that nodal stage was associated with locoregional recurrence in both groups and pathologic stage was associated with distant metastasis only in the simple mastectomy group.

Conclusions: There was no difference in oncologic outcomes between the three groups of BRCA+ breast cancer, even if the surgical scale and techniques were different. IBTR may not only result from surgical technique, but from the tumor stages.

Poster Exhibition

SOCIAL COGNITIVE INFLUENCES ON DIETARY BEHAVIORS IN BREAST CANCER SURVIVORS

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Dongyang University, Korea

Background: Cancer survivors have experienced a specific and unique situation. Diet plays an important role in cancer risk and it is important influences on health. However, few data are available about the relationship between social cognitive factors and dietary behaviors. Thus, the purpose of this study was to explore the impact of social cognitive constructs, which is defined in Social cognitive theory (Bandura, 1992), on dietary behaviors in breast cancer survivors.

Methods: A cross-sectional correlational design was used. Data collection took place from April to June 2015 in S. Korea. Social cognitive constructs included nutrition self-efficacy, outcome expectations for nutrition, negative impact, and social support (family and health care providers support).

Result: One hundred and fifty breast cancer survivors completed this study. The average ages were 52.9, ranging from 34 to 77 years. Dietary behaviors had a significant positive relationship with nutrition self-efficacy, negative impact, and family support. Multiple regression analyses revealed that 16.8% of the variance in nutritional health-promoting lifestyle was explained by the social cognitive variables. Nutrition self-efficacy, negative impact, and family support were significant predictors of dietary behaviors.

Conclusions: A lack of social cognitive understanding about cancer survivors could result in less than adequate care for their health due to inadequate advice on their lifestyle choices, which may impede their opportunity to live healthy lives after overcoming the cancer. The knowledge from this study will help guide the development of social cognitive interventions and may be of help in understanding various cancer groups.

METHOD TO DESIGN A HEREDITARY BREAST CANCER RISK PREDICTION FOR BRCA1/2 MUTATION CARRIERS

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Background: Since BRCA1 and BRCA2 mutations have very high penetrance, the method to calculate the breast cancer risk of BRCA1/2 mutation carriers could be different from the sporadic breast cancer risk prediction.

Methods: Survey data of 5,964 subjects from 142 BRCA1 mutation carriers pedigree and 216 BRCA2 mutation carriers pedigree enrolled in Korean hereditary breast cancer study (KOHBRA) was used to calculate the breast cancer risk of BRCA1/2 mutation carriers with BRCA1/2 mutation status and other risk factors such as family history.

Result: Customized time variant Cox regression was used to calculate the hereditary breast cancer risk. At first, we calculate the probability of BRCA1/2 mutations of each family member with the relationship between them and mutation carriers. After weighted by predicted penetrance, each family members disease status affects the risk of others. Affected family members increase the risk of other members since they developed breast cancer and not affected family members decrease the risk of other members until they develop breast cancer or are censored. The effect size of each family member to other members varies upon the relationship between each other.

Conclusions: Since this kind of process is very computationally demanding, it takes a long time to evaluate the all pedigrees. It will be possible to estimate more exact breast cancer risk for BRCA1/2 mutation carriers when evaluation of effect of family history on BRCA1/2 mutation carriers.

COMPARISON OF CHARACTERISTICS IN PATIENTS WITH BOTH THYROID AND BREAST CANCER: BASED ON ORDER OF INCIDENCE

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Yonsei University College of Medicine, Korea

Background: In this study we reviewed patients who were diagnosed of both thyroid and breast cancer during their lifetime and analyzed their clinicopathologic characteristics according to the order of incidence of the two cancers.

Methods: Between 1986 and 2014, we retrospectively reviewed all patients who underwent surgery for thyroid or breast cancer at Severance Hospital and identified 425 patients who had simultaneous thyroid and breast cancer. We classified these patients into 3 groups according to the order of incidence of the two cancers: simultaneous thyroid and breast cancer(S), thyroid cancer followed by breast cancer (TB), and breast cancer followed by thyroid cancer (BT). The clinicopathologic characteristics of the 3 groups were analyzed.

Result: There were 102 (24%) patients in group TB, 168 (39.5%) patients in group S, and 155 (36.5%) patients in group BT. Thyroid lobectomy was more frequently performed in group BT while bilateral total thyroidectomy (BTT) was more frequent in the other two groups. There was a significantly higher rate of postoperative radioactive iodine (RI) therapy in group TB compared to both group S and group BT.

Conclusions: There were no significant pathological differences in patients with both thyroid and breast cancer according to the order of incidence. However, in BT group, early detection of thyroid cancer during follow-up may have led to a higher rate of thyroid lobectomy rather than BTT. Additionally, the significantly higher rate of RI therapy in TB group may suggest a possible relation between postoperative RI therapy and the incidence of breast cancer.

PO007

MALIGNANT ADENOMYOEPITHELIOMA OF THE BREAST: A CASE REPORT

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Background: Malignant adenomyoepithelioma of the breast is a rare tumor characterized by malignant proliferation of dual differentiation into luminal cells and myoepithelial cells. These lesions are diagnostically challenging, because of the heterogeneity of adenomyoepitheliomas. Since first described by Hamperl, less than 50 cases were reported in the literature.

Methods: A 71 year-old woman presented with a palpable mass in the right breast. Mammography and breast ultrasonography showed 3 cm irregular microlobulated mass with linear and fine pleomorphic calcifications. Core biopsy result revealed stromal fibrosis and fibroelastosis with adenosis, distorted glands and calcifications, suspicious for comlex sclerosing lesion. Because of the discordance among clinical, imaging and pathologic results, a wide local excision was performed.

Result: A 3.4 cm sized well-defined ovoid firm mass was obtained, and final pathologic result was malignant adenomyoepithelioma. Resection margins were free of tumor, and results of the immunohistochemical study were CK7 positive, calponin positive, and p63 positive, and smooth muscle actin posistive. Further regional or distant metastasis was not identified on imaging studies including chest CT, bone scan, and PET/CT after surgery.

Conclusions: Malignant adenomyoepithelioma of the breast is a rare tumor which should be considered in the differential diagnosis of other solid breast lesions. Because a correct preoperative diagnosis is challenging, adequate sampling of the tumor is important to identify the features. A complete excision with appropriate margin is recommended to prevent local recurrence or potential metastasis.

Poster Exhibition

PO008

BREAST CANCER WITH CONTRALATERAL AXILLARY LYMPH NODE METASTASIS: A CASE REPORT

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Background: Metastatic involvement of a contralateral axillary lymph node is uncommon phenomenon. Traditionally, contralateral axillary lymph node metastasis (CAM) have been considered as stage IV disease. However, since the origin of CAM also could be occult primary cancer in the opposite breast, or metastasis from extra mammary site, it is dilemma for clinicians to make appropriate treatment plan.

Methods: We report a case of a 67-year-old female who had right breast cancer with synchronous contralateral breast cancer, CAM and skin metastasis. The excisional biopsy of primary right breast lesion showed invasive ductal carcinoma and estrogen receptor negative, progesterone receptor positive, HER2/neu positive. She has received Paclitaxel-Trastuzumab combined primary chemotherapy for 17-doses. Seeing the breast tumors, skin metastasis and CAM almost disappeared, we identified that clinically complete response status was made.

Result: For this patient, it is possible to postulate obstruction of normal lymphatic drainage by primary breast cancer cause CAM as regional spread. Positron-Emission-Tomography/Computed-Tomography didnt show any other extra mammary malignancy. This patient had concomitant skin metastasis, so she received primary systemic chemotherapy. Clinical response was so good, we are considering local therapy with surgery or radiation, because it will provide adequate disease control with the intent of possibly improving relapse free survival. After the local therapy, systemic therapy should be applied, since CAM is still considered stage IV disease.

Conclusions: The treatment of CAM cannot be standardized. We insist that treatment of CAM would be individualized and hope this case might be helpful to other clinicians to face with CAM.

PO009

PRACTICE PATTERN AND OUTCOME OF BREAST CANCER DEVELOPED IN CHRONIC KIDNEY DISEASE (CKD) PATIENTS

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Background: Having chronic kidney disease (CKD) can interfere diagnostic accuracy in mammographic screening and its poor life expectancy influence the decision making process during breast cancer treatment. Little is known about breast cancer in CKD have worse outcome. In this study, we reviewed the outcomes and practice pattern of treatment in those patients.

Methods: Among breast cancer patients who received primary treatment in single tertiary institution between January 2007 and September 2015, patients who have records of follow up visit within one year or patients who confirmed survival data were included in evaluation (N = 945). Patients who had CKD (n = 12) were identified and matched control of non-CKD patients were selected (n = 48) following the year at first diagnosis, age, stage, and hormone receptor status. Medical records were retrospectively reviewed.

Result: Mean eGFR level of the patients was 13.3 ± 12.3 mL/min in CKD group and 103.3 ± 14.1 mL/min in non-CKD group. Treatment disruption during chemotherapy were frequent in CKD group than non-CKD group (41.6% vs. 6.3%, $p = 0.006$). The main cause of treatment disruption in CKD group was development of leukopenia in low risk regimens. CKD patients showed nonsignificant increase of distant metastasis during follow up period (25% vs. 2.08%, $p = 0.023$).

Conclusions: Factors that can be related to poor outcome such as dose reduction or treatment disruption were frequent in breast cancer patients who have CKD. The limitation of this study is small number of patients. Either those factors can be connected worse outcome should be evaluated in large group study and more attention should be paid to those patients.

Poster Exhibition

PO010

CLINCOPATHOLOGIC FACTORS ASSOCIATED WITH RE-MAMMOTOME DURING FOLLOW UP AFTER 1ST TIME MAMMOTOME

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Background: We sometimes experienced the tumor regrowth in previous Mammotomesite or adjacent tissue. So we re-biopsied Recurrent breast tumor using Mammotome. We wanted to evaluate the factors that impact on remained or regrowth tumor at post Mammotome site or adjacent tissue. Especially our study focused on Atypical ducatl hyperplasia, Intraductal papilloma and phyllodes tumor influence in tumor regrowth.

Methods: From January 2010 to December 2015, we could analyze 511 cases because of follow up period. Median follow up period of the patients was 11 months. The patient age at initial diagnosis, the age of menarche, status of marriage, the number of babies, presence or absence of feeding Hx, status of menopause and presence or absence of family Hx were obtained from medical records. Tumor size, pathologic diagnosis, presence or absence of calcification were obtained from pathology reports. The chi-squared test was used to evaluate correlation between pathologic benign diseases and clinicopathologic parameters in all cases. A p-value of <0.05 was considered to indicate statistical significance.

Result: In our study Non proliferative breast diseases, proliferative diseases, Intraductal papilloma, Apocrine cell change, Atypical ductal hyperplasia and phyllodes were 69% (n = 353), 7.04% (n = 36), 13.8% (n = 71), 0.3% (n = 2), 7.6% (n = 39) and 0.5% (n = 3) respectively. Re Mammotome rate in Non proliferative breast disease was 18.6% (n = 66), in proliferative disesase was 16.6% (n = 6), in Intraductal papillomas was 23.9% (n = 17), in Atypical ductal hyperplasia was 43.6% (n = 17) and in benign phyllodes tumors was 33.3% (n = 1).

Conclusions: Previously diagnosed personal History as intraductal papilloma, atypical ductal hyperplasia, and benign phyllodes tumor in 1st time Mammotome were significantly associated with tumor regrowth.

PO011

DUCTAL CARCINOMA IN SITU ARISING IN MALIGNANT PHYLLODES TUMOR IN 44-YEAR OLD PATIENT: A CASE REPORT

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Background: Malignant phyllodes tumor of the breast is an uncommon neoplasm that can mimic fibroadenoma. Ductal carcinoma in situ in the epithelial component of malignant phyllodes is very rare.

Methods: A 44-year-old female patient presented to a palpable mass in the right breast (a firm, painless tumor). There was no palpable lymph node in the axillary or supraclavicular region. Mammography showed a high density lobulated shaped mass in the upper outer portion of the right breast. Ultrasonography evidenced a 3.3 cm × 2.3 cm lobulated hypoechoic solid mass without any calcification. US-guided core needle biopsy was performd on the breast lesion and the histopahtological examination of the biopsy specimen revealed fibroadenoma. This mass had rapidly increased in size during the five months. Ultrasonography revealed a 5.3 cm × 4.5 cm × 3.9 cm lobulated hypoechoic solid mass.

Result: Surgical excision was performed and the pathologic examination showed the tumor was biphasic; epithelial and stroma. The epithelial component shows ductal distension with florid proliferation of atypical ductal cells. The nuclei of the cells composed of monotonous rounded and polarized around secondary lumens which were cribriform in pattern, features definitive of low grade DCIS. The stromal component consists of elongated to spindle cells with stromal overgrowth and atypical cytologic features. There are areas with infiltrative boarders and high mitotic index (> 10/10HPF), features indicative of malignant phyllodes tumor of the breast.

Conclusions: We report a rare case of indetermediate grade DCIS arising in a malignant phyllodes tumor in a 44-year-old female patient.

PO012

DIETARY CHANGE AFTER BREAST CANCER DIAGNOSIS: ASSOCIATIONS WITH ANTHROPOMETRY, PHYSICAL ACTIVITY, AND HEALTH-RELATED QUALITY OF LIFE AMONG KOREAN BREAST CANCER SURVIVORS

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Background: Breast cancer survivors tend to change their diet after diagnosis, but there are limited studies that have examined lifestyle factors related to post-diagnostic dietary change.

Methods: A total of 155 women who had been diagnosed with stage I to III breast cancer and had breast cancer surgery at least six months before the interview were included. Participants provided information on dietary change after diagnosis, post-diagnosis diet, physical activity, anthropometric measures, and health-related quality of life (HRQoL) through face-to-face interview. We examined anthropometric features, physical activity and HRQoL for breast cancer survivors who changed their diet to healthy after diagnosis using generalized linear and logistic regression models.

Result: The 75% of participants reported that they have changed their diet to healthier diet after diagnosis. Breast cancer survivors who reported dietary change had higher intakes of vegetables and fruits and lower intakes of red and processed meats than those who did not. Also, they were more likely to engage in physical activity (top vs. bottom tertile: Odds Ratio [OR], 3.07; 95% confidence interval [95% CI], 1.10-8.52 for healthy change in diet) and have lower body mass index (BMI) (>25 vs. <23 kg/m^2: OR, 0.30; 95% CI, 0.11-0.82) compared to those who did not. We found that healthy change in diet was associated with higher scores of physical functioning ($p=0.02$) and lower scores of diarrhea ($p=0.003$) compared to those who did not.

Conclusions: Healthy changes in diet after breast cancer diagnosis may be associated with BMI, physical activity and HRQoL.

Poster Exhibition

PO013

THE ASSOCIATION BETWEEN PHYSICAL ACTIVITY AND HEALTH-RELATED QUALITY OF LIFE AMONG BREAST CANCER SURVIVORS

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Background: Quality of life of breast cancer survivors has become increasingly important because of their high survival rate and prolonged life expectancy. A few epidemiological studies mostly conducted in Western populations reported that physical activity improved breast cancer prognosis and health-related quality of life (HRQoL).

Methods: A total of 160 women aged 21-70 years who had been diagnosed with stage I to III breast cancer and had breast cancer surgery at least 6 months were included. We asked participants about their health-related quality of life and calculated leisure physical activity levels using MET scores. We examined the association between HRQoL levels and physical activity using the generalized linear model.

Result: Breast cancer survivors in the high physical activity (3rd tertile) were more likely to have lower scores of fatigue ($p = 0.03$) and higher sexual functioning ($p = 0.003$), compared with those in the low physical activity (1st tertile). When we stratified by stage, we found that these associations were more pronounced among those with stage II or III compared to those with stage I.

Conclusions: Engagement in physical activity was related to better quality of life among breast cancer survivors. Our findings may warrant further prospective and intervention studies to support the benefit of physical activity in improving quality of life and survival of Korean breast cancer survivors.

PO014

EFFECTS OF REPRODUCTIVE RISK FACTORS FOR DUCTAL CARCINOMA IN SITU, INVASIVE DUCTAL CARCINOMA, AND INVASIVE DUCTAL CARCINOMA WITH DUCTAL CARCINOMA IN SITU ON CLINICAL OUTCOMES

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Background: We aimed to determine whether reproductive risk factors are associated with survival by histologic types of breast cancer; invasive ductal carcinoma (IDC), ductal carcinoma in situ (DCIS), and invasive ductal carcinoma with ductal carcinoma (DCIS-IDC) patients.

Methods: Among 37,947 patients registered in the web-based breast cancer registration program of the Korean Breast Cancer Society (KBCS), parity, age at first birth (AFB), and breast feeding were analyzed via the multivariate Cox regression analysis into three categories: 1) pure DCIS group, 2) IDC with DCIS (DCIS-IDC) group, and 3) pure IDC group (≤ 2 cm, lymph node negative).

Result: Patients with high parity (≥ 4) tended to have a higher risk of death with hazard ratio (HR) (DCIS; HR, 1.52; 95% CI, 0.62-3.78; $p < 0.000$, IDC; HR, 1.43; 95% CI, 0.89-2.31; $p < 0.000$, and DCIS-IDC; HR, 1.44; 95% CI, 0.45-4.59; $p < 0.005$). Compared with nulliparous patients, any AFB tended to have a lower risk of death with HR in both DCIS group and IDC group. Patients with breast-feeding tended to have a higher risk of death with HRs of overall survival (OS) and breast cancer specific survival (BCSS) in the IDC group and DCIS group (HR of OS in IDC, 1.49;95% CI, 1.21-1.82; $p = 0.0001$ and HR of OS in DCIS, 2.02; 95% CI, 1.27-2.27 ; $p = 0.003$; and HR of BCSS in IDC, 1.47; 95% CI, 1.11-1.96 ; $p = 0.007$, HR of BCSS in DCIS, 3.36; 95% CI, 1.18-9.56; $p = 0.02$).

Conclusions: The breast feeding history and high parity show worse effects on either BCSS or OS found to be breast cancer risk factors that might be different from generally accepted trends.

Poster Exhibition

PROGNOSTIC AND PREDICTIVE VALUE OF TUMOR-INFILTRATING LYMPHOCYTES IN TRIPLE NEGATIVE BREAST CANCER

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Background: Previous preclinical and clinical data suggest that increased lymphocytic infiltration would be associated with good prognosis and benefit from immunogenic chemotherapy especially in triple negative breast cancer (TNBC). We investigated single-center experience of TNBC and relationship with lymphocytic infiltration.

Methods: From January 2004 to December 2012, at department of surgery, Kangbuk Samsung Hospital, Sungkyunkwan University, School of Medicine, we retrospectively reviewed 897 breast cancer patients-clinical outcomes, clinicopathological characteristics, breast cancer subtypes. And we reviewed lymphocytic infiltration of TNBC specimens by two pathologists. Statistical analysis of risk factors associated with recurrence was performed.

Result: A total of 897 patients, 76 were TNBC (8.47%). Mean age of TNBC patients were 50.95 (SD10.42) years, mean follow-up periods was 40.06 months. We reviewed 49 slides, and there were 8 recurrent breast cancer patients (16.32%), and 4 patients were expired (8.16%). There were 9 lymphocytic predominant breast cancers (LPBC) - carcinomas with either intratumoral lymphocytes in $>60\%$ of tumor cell nests. 1 patient of LPBC was recurred and 8 were not. In multivariate logistic regression, the odds ratio of lymphocytic infiltration was 0.59 ($p = 0.643$).

Conclusions: In a single-center experience of TNBC, the lymphocytic infiltration in tumor cell nest might be good trend on the prognosis but there was not statistically significant. Further study with more patients will be needed.

HIGH UPA EXPRESSION IS ASSOCIATED WITH LYMPH NODE METASTASIS IN INVASIVE DUCTAL CARCINOMA OF BREAST

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Background: The aim of the current study was to evaluate the levels of urokinase-type plasminogen activator (uPA) and plasminogen activator inhibitor-1 (PAI-1) by immunohistochemical staining to determine whether they are reliable prognostic markers for patients with breast cancer.

Methods: We analyzed the demographic and clinicopathological parameters of 214 patients with breast cancer, diagnosed and treated from 2006 to 2010. Tissue microarray was constructed and immunohistochemical stain was performed on each specimen.

Result: In univariate analyses, age at diagnosis, history of hormone replacement therapy, radiation therapy, skin/chest wall invasion, Paget disease, lymphovascular invasion, estrogen receptor (ER) positivity and triple negative subtype had statistically significant influences on patient prognoses ($p < 0.05$). Lymph node metastasis was more frequent in the group with high uPA levels, compared to the group with low uPA levels ($p = 0.001$).

Conclusions: There was a statistically significant correlation between uPA expression and lymph node metastasis.

THE EXPRESSION OF LYSYL OXIDASE AND FIBROTIC FOCUS IS RELATED TO INFLAMMATION IN BREAST CANCER

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Background: Lysyl oxidase (LOX) is an extracellular matrix enzyme that catalyzes the cross-linking of collagens or elastin. Our hypothesis is that LOX contributes to the formation of a fibrotic focus (FF), which is related to inflammation in breast carcinogenesis. In this study, we analyzed the association between the expression LOXs and FF, and investigated prognostic significance in breast cancer.

Methods: Tissue microarrarys were constructed from the specimens of 444 patients with primary invasive breast cancer. Immunohistochemical staining for LOX, LOX-like (LOXL)-, LOXL-2 and LOXL-3 was performed. The status of FF within the tumor was assessed. The number of CD4+ T cells, CD8+ T cells, CD68+ macrophages was counted, and intratumoral and peritumoral lymphocyte infiltration were evaluated. The clinicopathologic characteristics of the patients were analyzed.

Result: The percentage of positive FF was 39.2% and positive rate of LOX expression was 50% in primary breast cancer tissues. FF was found to be significantly associated with intratumoral and peritumoral inflammation, lymph node metastasis, high histologic grade, larger tumor size. LOX was associated with intratumoral and peritumoral inflammation, CD8+ T cells and menopausal status. LOXL-3 was significantly associated with positive expression of ER and PR, and molecular subtype.

Conclusions: FF and the expression of LOX were associated with inflammation in breast cancer in this study. Our results suggest that LOXs may contribute to the formation of a FF indirectly in relation with inflammation in breast cancer. Further studies are needed to clarify the role of LOXs, FF and inflammation in tumorigenesis and prognostic value of them in breast cancer.

PO018

ZERUMBONE SUPPRESSES THE MOTILITY AND TUMORIGENECITY OF TRIPLE NEGATIVE BREAST CANCER CELLS VIA THE INHIBITION OF TGF-β1 SIGNALING PATHWAY

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Background: Aberrant transforming growth factor-β (TGF-β) plays an important role in the development of cancer such as tumor metastasis and invasion. TGF-β-responsive gene signature is highly activated in chemotherapy-treated triple negative breast cancer (TNBC).

Methods: The levels of mRNA were analyzed by real-time PCR. The levels of protein were analyzed by ELISA, western blotting, and zymography, respectively. Cell invasion and migration were analyzed by boyden chamber assay and wound healing assay. Tumor growth and metastasis was studied by mouse orthotopic model.

Result: The level of TGF-β1 mRNA expression and cell invasiveness were higher in TNBC cells than in non-TNBC cells. On the other hand, the cell motility of TNBC cells was suppressed by LY2109761. In addition, FN and MMP-2 expression, which play an important role on cell motility in various cancer cells, were decreased by LY2109761. TGF-β1 increased FN, MMP-2 and MMP-9 expression in HCC1806 TNBC cells. TGF-β1-induced MMP-9 expression was decreased by both UO126 and SIS3. Induction of FN and MMP-2 by TGF-β1 was decreased by SIS3. Overexpression of smad3 increased FN, MMP-2, and MMP-9 expression. Interestingly, Zerumbone (ZER) suppressed TGF-β1-induced FN, MMP-2, and MMP-9 expression in HCC1806 cells. In addition, ZER decreased TGF-β1-induced the phosphorylation of smad3. Finally, ZER suppressed the tumorigenicity such as tumor volume, weight, Ki67 expression, and metastasis in TNBC cells xenograft models.

Conclusions: Conclusively, ZER suppresses TGF-β1-induced FN, MMP-2, and MMP-9 expression through the inactivation of smad3 and inhibits the tumorigenicity of TNBC cells. Therefore, we suggest that ZER may act as a promising drug for treatment of TNBC.

Poster Exhibition

ORGAN SPECIFIC METASTATIC PATTERN AND BIOLOGICAL CHARACTERISTICS OF RECURRENT BREAST CANCER

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Background: Our study aimed to analyze characteristics of recurrent breast cancer according to their molecular subtypes and to investigate organ specificity of metastasis according to biologic characteristics of initially diagnosed breast cancer.

Methods: We retrospectively collected clinic-pathologic data of patients of metastatic breast cancer between 1st January. 2000 and 31st. March. 2015, who underwent breast cancer treatments in the Department of Surgery, Sanggye paik hospital, Inje University. We analyzed data by age at diagnosis, TNM stage, estrogen receptor (ER), progesterone receptor (PR), human epidermal growth receptor-2 (HER2), bcl-2, Ki 67, and first recurred sites of breast cancer patients.

Result: Recurrence occurred in 140 patients and rate was 12.37%. Recurrence sites were bone 77 cases (55%), lung 44 (31.43%), liver 48 (34.29%), Lymph node (LN) 69 (49.29%), breast 54 (38.57%), axilla 34 (24.29%), brain 22 (15.71%), other visceral organs 10 (7.14%). Liver metastasis was most common in luminal B (45.0%) ($p = 0.008$), lung in TNBC (41.2%) ($p = 0.168$), brain in HER2 enriched (22.6%) ($p = 0.623$), LN in TNBC (64.7%) ($p = 0.088$), local recurrences in luminal A (36.0%) ($p = 0.104$), any other visceral in luminal A subtype (50%) ($p = 0.023$). In the endocrine responsive metastatic breast cancer, the proportion of loss or low PR expression was the higher in luminal B than luminal A subtype ($p = 0.0132$).

Conclusions: In the recurrent breast cancer, skeletal metastasis was most common among other organs and above all, luminal subtype was strongly related with initial skeletal metastasis. Liver metastasis was the most frequently occurred in luminal B subtype.

A NOVEL ROLE FOR FLOTILLIN-1 IN H-RAS-REGULATED BREAST CANCER AGGRESSIVENESS

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Background: Elevated expression and aberrant activation of Ras have been implicated in breast cancer aggressiveness. H-Ras, but not N-Ras, induces breast cell invasion. A crucial link between lipid rafts and H-Ras function has been suggested.The present study sought to identify the lipid raft protein(s) responsible for H-Ras-induced tumorigenicity and invasiveness of breast cancer.

Methods: We conducted a comparative proteomic analysis of lipid raft proteins from invasive MCF10A human breast epithelial cells engineered to express active H-Ras and non-invasive cells expressing active N-Ras.

Result: We identified a lipid raft protein flotillin-1 as an important regulator of H-Ras activation and breast cell invasion. Flotillin-1 was required for epidermal growth factor-induced activation of H-Ras, but not that of N-Ras, in MDA-MB-231 triple-negative breast cancer (TNBC) cells. Flotillin-1 knockdown inhibited the invasiveness of MDA-MB-231 and Hs578T TNBC cells in vitro and in vivo. In xenograft mouse tumor models of these TNBC cell lines, we showed that flotillin-1 played a critical role in tumor growth. Using human breast cancer samples, we provided clinical evidence for the metastatic potential of flotillin-1. Membrane staining of flotillin-1 was positively correlated with metastatic spread ($p = 0.013$) and inversely correlated with patient disease-free survival rates ($p = 0.005$). Expression of flotillin-1 was associated with H-Ras in breast cancer, especially in TNBC ($p < 0.001$).

Conclusions: Our findings provide insight into the molecular basis of Ras isoform-specific interplay with flotillin-, leading to tumorigenicity and aggressiveness of breast cancer.

MELANOMA INHIBITORY ACTIVITY (MIA) REGULATES CELL INVASION IN BREAST CANCER CELLS

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Background: Melanoma inhibitory activity (MIA) is highly expressed in melanoma cells and is related to cancer cell invasion, melanoma development and metastasis. However, its role in breast cancer remains unclear.

Methods: The mRNA analysis was performed using 14 breast cancer cell lines. Migration assay, adhesion assay and immunofluorescence were carried out in MDA-MB-231 or Hs578T cells after siRNA transfection against MIA. EMT and cytoskeleton related genes were also examined in MIA-silenced cells by PCR and qRT-PCR.

Result: MIA was upregulated in highly invasive breast cancer cell lines, MDA-MB-231 and Hs578T compared to other cell lines. After silencing of MIA, migration and adhesion was inhibited, invasive morphology of MIA-silenced cells was changed into more epithelial like state. E-cadherin was upregulated and its repressors were downregulated following MIA knockdown. In addition, cdc42, rac1 and rhoA, which play important roles in reorganization of cytoskeleton, were also downregulated in MIA K/D MDA-MB-231.

Conclusions: Tumor metastasis ability is usually determined by migration or adhesion ability of cancer cells and thus silencing of MIA can be regarded as a suppressor of metastasis of breast cancers. Therefore, MIA could be considered as a prognostic marker to determine tumor grade and stage although it is necessary to conduct additional studies.

PROGNOSTIC VALUE OF ERBB4 EXPRESSION IN PATIENTS WITH TRIPLE NEGATIVE BREAST CANCER

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Background: Triple-negative breast cancer (TNBC) is known for aggressive biologic features and poor prognosis. Epidermal growth factor receptor (EGFR) overexpression in TNBC indicates poor prognosis. However, there is no previous study of the relationship between expression of the entire human epidermal growth factor receptor (HER) family genes and patient prognosis in TNBC.

Methods: We used the nCounter expression assay to measure the expression of EGFR, erb-B2 receptor tyrosine kinase 2 (ERBB2), ERBB3 and ERBB4 genes using mRNA extracted from paraffin-embedded tumor tissues from 203 patients diagnosed with TNBC. Our data were validated using a separate cohort of 84 TNBC patients.

Result: A total of 203 TNBC patients who received adjuvant chemotherapy after curative surgery from 2000 to 2004 formed the training set. The 84 TNBC patients in the validation consort were selected from breast cancer patients who received curative surgery since 2005 to 2010. Analysis of the expression profiles of the HER family genes in TNBC tissue specimens revealed that increased expression of ERBB4 was associated with poor prognosis according to survival analysis (5-year disease relapse free survival [5Y DRFS], low vs. high expression [cut-off: median]: 90.1% vs. 80.2%; $p = 0.022$). This trend was also observed in the validation set of TNBC patients (5Y DRFS, low vs. high: 69.4% vs. 44.7%; $p = 0.053$). In a multivariate Cox regression model, ERBB4 expression was identified as a indicator of long-term prognosis in patients with TNBC.

Conclusions: The expression profile of ERBB4 might serve as a prognostic marker in patients with TNBC.

ASSOCIATION BETWEEN MUTATION AND EXPRESSION OF TP53 AS A POTENTIAL PROGNOSTIC MARKER OF TRIPLE-NEGATIVE BREAST CANCER

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Background: TP53, the most frequent mutated gene in breast cancer, are more frequently altered in HER2-enriched and basal-like breast cancer. However, no studies have clarified the role of TP53 status as a prognostic and predictive marker of triple-negative breast cancer (TNBC).

Methods: We performed p53 immunohistochemistry (IHC), nCounter mRNA expression assay, and DNA sequencing to determine the relationship between TP53 alteration and clinical outcomes of TNBC patients.

Result: Seventy-seven of 174 TNBC patients were found to harbor a TP53 mutation. Patients with missense mutations had high protein expression in contrast to patients with deletion mutations (positivity of IHC: wild type vs. missense vs. deletion mutation, 53.6% vs. 89.8% vs. 25.0% respectively, $p < 0.001$). TP53 mRNA expression was influenced by mutation status (mRNA expression (median): wild type vs. missense vs. deletion mutation, 207.36 ± 132.73 vs. 339.61 ± 143.21 vs. 99.53 ± 99.57 respectively, $p < 0.001$). According to survival analysis, neither class of mutation nor protein or mRNA expression status had any impact on patient prognosis. In subgroup analysis, low mRNA expression was associated with poor prognosis in patients with a TP53 missense mutation (5Y distant recurrence-free survival (DRFS), low vs. high: 50.0% vs. 87.8%, $p = 0.009$), while high mRNA expression with a TP53 deletion mutation indicated poor prognosis (5Y DRFS, low vs. high: 91.7% vs. 75.0%, $p = 0.316$).

Conclusions: Association between TP53 mutation and expression constitutes a potential prognostic marker of TNBC; hence both DNA sequencing and mRNA expression analysis may be required to predict the prognosis of TNBC patients.

EFFECT OF MARINE BROWN ALGA ON TWO HUMAN BREAST CANCER CELL LINES: APOPTOSIS AND CELL-CYCLE ARREST

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Background: Diekol and Seanol®, a phlorotannin compounds isolated from Ecklonia cava have been reported to several biologic properties, including anti-oxidant, anti-viral, anti-inflammatory, anti-cancer activities. The purpose of this study was to investigate the anti-cancer effects induced by these agents on human breast cancer cell lines.

Methods: In this study, cell viability assay induced by Dieckol and Seanol® was investigated using WST-1 assay on human breast cancer SK-BR-3, MCF-7 cell lines. Apoptosis and Cell-cycle analysis was assayed via Annexin V-flourescein isothiocyanate and propidium iodide staining followed by flow cytometric analysis. Immunoblotting analysis was also performed using BAX/Bcl-2, CDK2, CDK4, and cyclin D3.

Result: Dieckol and Seanol® reduced the number of viable cells and increased apoptotic cells in a dose-dependent manner. We analyzed the effect of Dieckol and Seanol® on the cell-cycle distribution using flow cytometry. In dieckol treated group, the percentage of cells at the G2/M phase significantly increased on MCF-7, SK-BR-3 cell lines. Immunoblotting analysis revealed that Dieckol and Seanol® increased the expression level of BAX/Bcl-2 and downregulated the expression of cyclin D3.

Conclusions: Dieckol and Seanol® were cytotoxic to SK-BR-3, and MCF-7 human breast cancer cells via induction of apoptosis and cell-cycle arrest. Therefore, we suggest that Dieckol and Seanol® may be a potential therapeutic agent for breast cancer treatment.

ONLY HISTOLOGICALLY EVALUATED LEVEL OF TUMOR-INFILTRATING LYMPHOCYTES (TILS) CAN BE PROGNOSTIC IN HER2 POSITIVE BREAST CANCERS

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Background: The prognostic significance of tumor-infiltrating lymphocytes (TILs) has been determined in breast cancers, especially in human epidermal growth factor receptor 2 (HER2) positive breast cancers and triple negative breast cancers (TNBCs). The TIL working group recommended to score all mononuclear cells including lymphocytes and plasma cells in intratumoral stroma, as a percentage of area occupied over total intratumoral stromal area and do not currently recommend to use immunohistochemistry to detect specific subpopulations outside of research setting.

Methods: Total 168 patients with HER2 positive breast cancer between 2011 and 2013 at Pusan National University Hospital were included. The full sections of H&E-stained slides were reviewed. Histopathologic factors include histologic grade, nuclear grade, necrosis, microcalcification, lymphovascular invasion, lymph node metastasis, TIL level, TLSs around DCIS and TLS around invasive component.

Result: The high level of TILs was significantly correlated with high histologic grade, absence of lymphovascular invasion, absence of lymph node metastasis, absence of HR expression, abundant TLSs around DCIS and abundant TLSs around invasive component ($p = 0.00$, $p = 0.007$, $p = 0.007$, $p < 0.00$, $p = 0.018$, and $p < 0.00$, respectively). High level of TILs was associated with better disease free survival, especially in HR-/HER2+ breast cancers ($p = 0.019$).

Conclusions: Only histologically evaluated TIL level can be prognostic, supporting the recommendation by an International TILs Working Group 2014 and providing additional evidence for clinical utility of TILs level as a prognostic factor in routine pathologic report.

Poster Exhibition

NUCLEAR RECEPTOR EXPRESSION IN A PANEL OF BREAST CANCER CELLS

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Background: Breast cancer is the leading cause of cancer related women death worldwide. Although several targeted drugs are clinically applicable to the breast cancer patients having the corresponding molecular targets (e.g., HER2, estrogen receptor, aromatase) of which are mostly hormonal receptors, triple-negative breast cancer (TNBC) patients still depend on conventional therapeutic approaches including radiation and/or non-selective chemotherapy after surgical removal of the tumors. The nuclear receptor (NR) superfamily consists of 48 individual nuclear receptors well-known druggable targets for many cancers, due to their ligand-controlled activity. In this study, our aim was to investigate if the NR superfamily as a whole or individually showed therapeutic potentials using both in vitro cell lines and in vivo xenografts.

Methods: Utilizing quantitative real-time PCR (QPCR), we profiled the mRNA expression of the entire NR superfamily in a panel of 35 breast cell lines, including 4 normal or immortalized human mammary epithelial cells with hTERt and/or cycline-dependent kinase 4, and 31 breast cancer cell lines.

Result: Comparative analysis revealed 12 cell lines showing mRNA expression of estrogen receptor alpha (ER), 6 cell lines with progesterone receptor (PR), and most cell lines with HER2 expression. Of particular interest, 5 cell lines showed extremely high expression of HER2 mRNA, suggesting that this particular subsets of cell lines would be treatable with Herceptin. In addition, the normal or immortalized cells showed no expression of ER, PR, and HER2.

Conclusions: Collectively, our study provides an insight of nuclear receptors as therapeutic targets into targeted therapy of breast cancer.

PO027

QUINACRINE-MEDIATED ANTI-PROLIFERATIVE EFFECT IS MEDIATED BY TARGETING AXL AND S-PHASE KINASE-ASSOCIATED PROTEIN 2 IN BREAST CANCER CELLS

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Background: Axl receptor tyrosine kinase (RTK) plays a critical role in cell growth, proliferation, and anti-apoptosis. Quinacrine is a small compound with multiple actions including antimalarial and anticancer activity.

Methods: The effect of quinacrine on cell proliferation and expression of Axl RTK, Skp2 and p21 was observed by cell viability test, clonogenic assay, promoter activity test, RT-PCR, and Western blot analysis.

Result: Quinacrine treatment of MDA-MB 231 cells was found to cause a dose dependent decline of Axl protein as well as mRNA levels. Axl promoter activity was also reduced by quinacrine, suggesting the transcriptional down-regulation of Axl expression by quinacrine. Moreover, Axl phosphorylation upon its ligand, Gas6, was inhibited by quinacrine, indicating that quinacrine also abrogates Gas6-induced Axl phosphorylation. Next, it was found that treatment of both MCF-7 and MDA-MB 231 cells with quinacrine decreased the cell viability and clonogenic ability in dose dependent manner. We further observed the synergistic anti-proliferative effect of quinacrine in cells transfected with Axl specific siRNA, while the reduction of its cytotoxic effect in Axl RTK overexpressing cells, confirming that quinacrine exerts its anticancer potential via interference of Axl expression. In addition, quinacrine was found to result in the increase of p2, a cyclin-dependent kinase inhibitor, as well as the decrease of S-phase kinase-associated protein 2 (Skp2), an oncogenic protein, in both MCF-7 and MDA-MB 231 cells.

Conclusions: Taken together, these data indicate that Axl RTK and Skp2 seem to be novel targets of quinacrine to exert its anti-proliferative effect in breast cancer cells.

PD-L1 PROTEIN EXPRESSION IN INVASIVE BREAST CANCER

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Background: The interaction of Programmed Death Receptor 1 (PD-1) and its ligand, Programmed Death Receptor Ligand 1 (PD-L1) negatively regulates immune responses. This study aims to clarify PD-L1 expression levels in breast cancers using immunohistochemistry (IHC) and correlate these findings with clinicopathologic variables, including prognostic significance.

Methods: IHC was performed on tissue microarrays of 465 invasive breast carcinomas. Associations between PD-L1 expression, clinicopathologic characteristics, and molecular subtype were retrospectively analyzed.

Result: High PD-L1 expression was demonstrated in 63 (13.5%) of 465 tumors. High PD-L1 expression significantly correlated with high histologic grade ($p < 0.001$), negative lymph node status ($p = 0.011$), early pathologic stage ($p = 0.025$), negative estrogen receptor status ($p < 0.001$), negative progesterone receptor status ($p = 0.002$), positive human epidermal growth factor receptor 2 (HER2) status ($p = 0.003$), high Ki-67 staining index ($p < 0.001$), positive cytokeratin 5/6 status ($p = 0.011$), positive epidermal growth factor receptor status ($p < 0.001$), and positive p53 status ($p < 0.001$). Based on molecular subtypes, high PD-L1 expression was significantly associated with HER2 type and triple-negative basal cancers ($p < 0.001$). In univariate analysis, there was a significant trend toward good disease free survival ($p = 0.041$) and overall survival ($p = 0.026$) for those with tumors having high PD-L1 expression compared to those with tumors having low PD-L1 expression.

Conclusions: PD-L1 expression was observed in the breast cancer patients. Further large prospective studies are required to determine the role of PD-L1 expression as a prognostic or predictive biomarker.

SERUM TOTAL 25(OH) VITAMIN D LEVEL DIFFERENCE BETWEEN NONINVASIVE EPITHELIAL BREAST TUMOR AND INVASIVE DUCTAL CARCINOMA

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Background: Serum total 25(OH) vitamin D level was known as deep correlation with breast cancer. So we check serum total vitamin D level in noninvasive epithelial breast tumor and invasive ductal carcinoma to find out whether serum total 25(OH) vitamin D level have influence on invasion of breast cancer or not.

Methods: Serum total 25(OH) vitamin D level was checked when breast cancer diagnosed by COBAS8000 from June 1 to December 31 2015. All patients had breast cancer operation.

Result: We had operated 131 breast cancer patients. 100 patients were invasive ductal carcinoma (IDC) and 31 patients were diagnosed with noninvasive epithelial breast tumor like ductal carcinoma in situ (DCIS). Mean vitamin level in IDC was 14.5 ng/mL and in DCIS was 17.6 ng/mL. Mean difference was 3.1 ng/mL. *p*-value was 0.065. Statistically analysis was done with student t test.

Conclusions: Although our study has not shown statistically meaning difference between noninvasive epithelial breast tumor and invasive ductal carcinoma with Serum total 25(OH) vitamin D level, mean difference was 3.1ng/mL with *p*-value 0.065. So we cant insist that serum total 25(OH) vitamin D level is related to the breast cancer invasion, but vitamin D and vitamin D receptor are regarded as cell differentiation and proliferation. Maybe too short research period has difficulty to adequate obtain end result. And furthermore study would be required. Therefore, pursuing vitamin D research when initial diagnosed breast cancer and following up vitamin d level after breast cancer surgery are necessary to understand and control breast cancer.

GINKGETIN INDUCES CELL DEATH IN BREAST CANCER CELLS THROUGH DOWN-REGULATION OF THE ESTROGEN RECEPTOR

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Background: Ginkgetin, a natural biflavonoid isolated from leaves of Ginkgo biloba L, has been reported to have anti-inflammatory activity and anti-tumor effects in prostate cancer. Although several reports state that it has also antitumor activity, the anti-proliferative effect of ginkgetin and the underlying mechanism in breast cancer cells have not been investigated.

Methods: In the present study, ginkgetin inhibited the cell viability of MCF-7 and T-47D cells dose-dependently and suppressed the expression of the estrogen receptor (ER) at both the mRNA and protein levels. Among the targets of the ER, 6-phospho-fructo-2-kinase/fructose-2,6-bisphosphatases 3 (PFKFB3), cyclin D, and survivin were also down-regulated by ginkgetin treatment. The anti-proliferative effects of ginkgetin were sufficient to suppress the growth by estradiol stimulation. And both the knock-down of the estrogen receptor and an inhibitor of PFKFB3 significantly sensitized MCF-7 and T-47D cells to ginkgetin

Result: The anti-proliferative effects of ginkgetin were sufficient to suppress the growth by estradiol stimulation. Maybe it can be reason which estrogen receptor down regulation by ginkgetin at estrogen receptor transcription. But ginkgetin did not significantly affect but nothing to sneez affect the viability of MDA-MB-231 cells and MCF 10A and BT-474, which are ER-negative cells and immotalized breast cancer cells and ER-HER2 positive cancer cells. Likewise this results can be considered that these cell undergo autophagy by ginkgetin.

Conclusions: These findings suggest that ginkgetin induces cell death in ER-positive breast cancer cells through the inhibition of ER expression and that it is a promising agent for breast cancer treatment.

BRCA1 MUTATION IS STRONGLY ASSOCIATED WITH A PHOSPHORYLATION OF S6 KINASE-1 IN BREAST CANCER PATIENTS

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Background: The breast cancer susceptibility gene (BRCA) plays a key role in both hereditary and sporadic breast cancer. Although the reason why BRCA leads to the tumorigenesis is not clearly understood, it might be related to the mTOR signaling pathway. In the present study, we investigated the relations between BRCA mutation and phosphorylated S6K1 (p-S6K1) expression, a downstream effector of mTOR pathway.

Methods: We retrospectively analyzed the data of 176 breast cancer patients who underwent BRCA1/2 genetic testing between February 2010 and September 2015. The p-S6K1 expression status of the primary tumor was assessed by immunohistochemistry, and +2 or more was regarded as positive.

Result: Of the 176 patients, positive p-S6K1 tumor expression was found in 74 patients (42%). BRCA1 and BRCA2 mutations were identified in 13 (7.4%) and 19 patients (10.8%), respectively. When stratified by BRCA mutation, p-S6K1 positivity was significantly correlated with BRCA1 mutation (10/13, 76.9%) compared with non-BRCA1 mutants (64/163, 39.3%) ($p = 0.008$). But there was no significant difference in expression of p-S6K1 between BRCA2-related (5/19, 26.3%) and non-BRCA2-related breast cancers (69/157, 43.9%) ($p = 0.141$).

Conclusions: Our findings here clearly demonstrate the upregulation of mTOR signaling pathway in BRCA1-mutated breast cancers and provide a rationale for the potential use of mTOR inhibitors as a therapeutic strategy for these tumor types.

PO032

BRAZILIN INDUCES HO-1/ MTOR- MEDIATED APOPTOSIS IN HUMAN BREAST CANCER CELLS

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Background: Brazilin, the major component of Caesalpinia sappan L., is a natural red pigment used for histological staining, and it was shown various biological activities. The aim of the study was to evaluate whether brazilin has an anticancer effect and investigate the mechanism of its regulation in human breast cancer cells.

Methods: Cell viability was measured via MTT assays. And signaling pathway and functional assay were explored by flow cytometry (FACS) and Western blotting.

Result: Brazilin showed dose- and time-dependent inhibition of cell viability, induction apoptosis, and reduction of heme oxygenase-1 (HO-1) expression in MCF-7 cells. Loss of cell viability by brazilin was prevented by hemin, a strong inducer of HO-1. Brazilin inhibited mTOR phosphorylation. The expression of HO-1 was reduced in torin1-treated cells. Loss of viability, reduction of HO-1 expression and mTOR phosphorylation were also observed in brazilin-treated MDA-MB-231 cells.

Conclusions: These results demonstrate that reduction of HO-1 expression by brazilin is mediated through mTOR, and this inhibition induced apoptosis in breast cancer cells.

DIFFERENTIAL EXPRESSION OF GLUCOCORTICOID RECEPTOR ACCORDING TO THE MOLECULAR SUBTYPES IN TRIPLE-NEGATIVE BREAST CANCER

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Background: Triple-negative breast cancer (TNBC) is the most heterogeneous among all breast cancer subtypes. For proper treatment, identifying a target for treatment is equally important as classifying the subtype. We aimed to examine the expression of glucocorticoid receptor (GR) by each subtype classified by Lehmann in order to investigate its potential as a treatment target.

Methods: Gene expressional profiling was performed using tumor-RNA from 100 TNBC samples. To identify the 6 molecular subtypes of TNBC, web-based subtyping tool and algorithm provided by the Vanderbilts group was applied. Tissue microarray was made and stained to identify GR expression. GR expression was evaluated by a semi-quantitative approach used to assign the intensity and proportion stained to tumor samples. The cut-off value for GR expression determined by combination of intensity grade 3 and proportion 30%.

Result: There was a likelihood of different distribution of GR expression among each TNBC subtype. GR showed higher expressions in Basal-like 2 and Luminal-androgen receptor type (LAR) (50.0% and 66.7%, respectively) than other subtypes. In clinicopathologic data, LAR type exhibited significantly lower histologic grade and lower Ki-67 expression compared to other subtypes.

Conclusions: In our data, we found that most TNBC samples showed GR expression; however, the expression of GR was higher in the LAR type compared to other subtypes. Through the status of GR expression, LAR type may be more clearly classified from other subtypes. Considering that GR expression was high in LAR type compared to other subtypes, further studies warrant in assessing the expression of GR as a potential therapeutic target.

PO034

REGULATION OF CELL SENSITIVITY TO DICHLOROACETATE (DCA) AND METFORMIN IS AN ESSENTIAL PREREQUISITE OF HIF1A SUPPRESSION

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Background: Cancer cells are known to have different metabolic properties than normal cells. Cancer cells are well documented to rewire cellular metabolism and energy production networks to demand rapid proliferation. Thus, targeting metabolic dependence might be an effective way of targeting cancers. Metformin, an oral drug widely used in the treatment of type 2 diabetes, is associated with a decreased risk of cancer in diabetic patients using this drug. Dichloroacetate (DCA) was shown to decrease glucose uptake and inhibit glycolysis.

Methods: Cell viability and cell death were assessed by MTT assay and Annexin V-FITC/PI staining, respectively. Small interfering RNA (siRNA) was used for suppressing gene expression. The protein levels were measured by western blot analysis. MCF-7 cells were treated with DCA (0-45 mM) in combination with metformin (0-50 mM) for 48 h and were examined for synergy by isobologram analysis.

Result: In the present study, combination of DCA and metformin markedly induced cell death, compared with each drug alone. Furthermore, the expression levels of glycolytic enzymes including HK2, LDHA and ENO1 were downregulated by two drugs. Interestingly, HIF-1α activation markedly suppressed DCA/metformin-induced cell death and recovered the expressions of glycolytic enzymes that were decreased by two drugs.

Conclusions: Based on these findings, we propose that targeting HIF-1α is necessary for cancer metabolism targeted therapy.

Poster Exhibition

PO035

TRAIL OVERCOMES THE HIF1A-INHIBITED CELL DEATH INDUCED BY COMBINATION OF DCA & METFORMIN

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Background: In a previous study, hypoxic conditions block MCF-7 cells from cell death induced by DCA and metformin. Thus, we strongly suggest that targeting hypoxia may be an essential prerequisite for cell sensitivity to drug combinations targeting cancer cell metabolism.

Methods: Cell viability and cell death were assessed by MTT assay and Annexin V-FITC/PI staining, respectively. Small interfering RNA (siRNA) was used for suppressing gene expression. The protein levels were measured by western blot analysis. Protein samples were separated by SDS-PAGE and transferred to NC membranes. The membranes were incubated with primary antibodies, followed by horseradish peroxidase-conjugated secondary antibodies.

Result: Combination treatment of DCA/Metformin increased expression of a death-associated mRNA and protein, such as DR5 and CHOP in normoxia condition. DCA/Metformin-induced cell death in MCF-7 cells decreased in hypoxia condition; up-regulated DR5 and CHOP expression was, however, maintained. Addition of tumor necrosis factor-related apoptosis-inducing ligand (TRAIL), a specific ligand of DR5, to DR5-upregulated cells was recovered the sensitivity to DCA/Metformin in hypoxia.

Conclusions: Based on these findings, we propose that combination with TRAIL overcomes the HIF1a-inhibited cell death induced by DCA/Metformin.

THE EFFECT OF NEOADJUVANT CHEMOTHERAPY ON TUMOR MARKER STATUS IN LOCALLY ADVANCED BREAST CANCER

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Background: Neoadjuvant chemotherapy (NAC) has become an acceptable option for patients with locally advanced breast cancer. There have been several reports that have demonstrated the changes of the histological and biological tumor markers after NAC. We also evaluated the effect of NAC on tumor marker in locally advanced breast cancer.

Methods: We retrospectively reviewed the pre- and post-NAC tumor marker (estrogen receptor (ER), progesterone receptor (PR), and HER2-neu) status of 52 patients, who underwent neoadjuvant chemotherapy for locally advanced breast cancer at our institute from January 2011 to December 2015. All the patients received 2 to 4 cycles of anthracycline-containing neoadjuvant chemotherapy. Pre- and post-NAC tumor markers were available for 42 of the 52 patients. Pre-NAC tumor specimens were taken by 14G core needle biopsy from multiple sites of a tumor, and the post-NAC specimens were taken at the time of the operation.

Result: The pathologic complete response (PCR) rate was 14.2% (6/42). Of those patients who did not achieve PCR (n = 36), ten patients (27.7%) revealed significant changes of more than one marker; 1 patient in ER status, 4 patients in PR status, 5 patients in HER2-neu status, and 1 patient in ER and HER2-neu status.

Conclusions: The specimens for the tumor markers should be taken before NAC because NAC can have effects on the expression of the tumor markers of locally advanced breast cancers, and this may influence predicting the prognosis and making the decision for adjuvant systemic treatment. And it is necessary to consider the post-NAC tumor marker status for proper adjuvant treatment plan.

PO037

PROGNOSTIC ROLE OF ADJUVANT CHEMOTHERAPY IN NODE-NEGATIVE, TRIPLE-NEGATIVE, MEDULLARY BREAST CANCER IN THE KOREAN POPULATION

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Background: Despite the favorable prognosis, the guidelines for the use of adjuvant chemotherapy for medullary breast cancer (MBC) have not been clearly established. This study investigated the prognostic role of adjuvant chemotherapy in Korean patients with node-negative (N0), triple-negative (TN) MBC patients.

Methods: We included data from 252 patients with N0 TN MBC and tumor sizes > 1 cm who were diagnosed between April 1997 and March 20, obtained from the Korean Breast Cancer Registry database. Patients were categorized as those who did not undergo adjuvant chemotherapy (group I) or those who did (group II). Breast cancer-specific survival (BCSS), and overall survival (OS) were compared between the groups. In addition, a subgroup analysis for survival based on tumor size was conducted.

Result: The median age was 44.95 years, and the median follow-up period was 93.94 months. Overall, the BCSS and OS in group II (97.3% and 97.3%, respectively) were significantly better compared with those in group I (89.2% and 86.2%, respectively). In the subgroup analysis, in patients with tumors > 2 cm in size, those in group II had significant better BCSS and OS (97.5% and 97.5%, respectively) compared with those in group I (78.3% and 73.9%, respectively). In contrast in those with tumors 1-2 cm in size, there were no significant differences in BCSS and OS between the groups. Multivariate analysis revealed that adjuvant chemotherapy significantly improved BCSS ($p = 0.009$) and OS ($p = 0.007$), but only for patients with larger tumors (> 2 cm).

Conclusions: In patients with N0 TN MBC, adjuvant chemotherapy had a significant clinical survival benefit, but only in those with tumors > 2 cm.

Poster Exhibition

PO038

ESTIMATION OF EFFICACY AND SAFETY OF GENEXOL-PM, A CREMOPHOR-FREE, POLYMERIC MICELLE FORMULATION OF PACLITAXEL, IN RECURRENT OR METASTATIC BREAST CANCER PATIENTS

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Background: Genexol®-PM is a Cremorphor EL (CrEL)-free polymeric micelle formulation of paclitaxel that allows higher-dose administration with less hypersensitivity. This study was conducted to evaluate the response and safety of Genexol®-PM monotherapy in patients with recurrent or metastatic breast cancer (MBC).

Methods: A total of forty-eight patients with recurrent or MBC, ECOG performance status ≤ 2 received Genexol-PM by intravenous infusion at 300 mg/m^2 over 3 h every 3 weeks. Response to therapy was assessed after every 3 cycles using the Response Evaluation Criteria in Solid tumors (RECIST) guideline (version 1.1) and adverse events were evaluated according to the NCI Common Terminology Criteria for Adverse events, Version 3.0.

Result: A total of 290 chemotherapy cycles were administered, with a median of 6 cycles per patient (range, 1–16). The overall response rate was 52.1% with 1 complete response (CR) and 24 partial responses (PR). Of 11 patients who received Genexol®-PM as a first-line therapy, there were 5 responses (45.5%). Disease control rate (CR + PR + stable disease) was 64.6% (first-line: 72.7%, second-line: 53.8%, respectively). The median time to progression (TTP) was 6.0 months (range, 2.0–36 months). The common grade 3/4 non-hematologic toxicities were peripheral neuropathy (n = 22, 45.8%) and myalgia (n = 5, 10.4%). Hematologic toxicities were grade 3 and 4 neutropenia (n = 15, 31.3% and n = 6, 12.5%, respectively), and grade 1 and 2 thrombocytopenia (n = 7, 14.6%). No febrile neutropenia was observed.

Conclusions: Genexol®-PM, a CrEL-free, polymeric micelle formulation of paclitaxel chemotherapy showed significant antitumor activity with relatively low incidence and

severity of toxicity in spite of a high paclitaxel dose in patients with MBC. Although further studies with larger sample size and different dosing schedules are warranted, this study suggests that Genexol®-PM monotherapy may be a candidate as a reasonable treatment for MBC patients.

PO039

PHYSICAL AND FUNCTIONAL ABILITY RECOVERY PATTERNS AND QUALITY OF LIFE AFTER IMMEDIATE AUTOLOGOUS LATISSIMUS DORSI BREAST RECONSTRUCTION

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Background: The authors evaluated arm and shoulder function and quality of life prospectively after breast reconstruction with the latissimus dorsi flap.

Methods: Muscle strength was checked by manual muscle test and range of mo- tion preoperatively and then at five postoperative time points: week 2, week 6, month 3, month 6, and month 12. Functional disability and quality of life were also measured by the Disabilities of the Arm, Shoulder and Hand questionnaire and the 36-Item Short-Form Health Survey. The assessments were performed preoperatively and then at three postoperative time-points (i.e., months 3, 6, and 12). Statistical analysis was performed by repeated-measures analysis of variance.

Result: Thirty-one patients were included for analysis. All manual muscle test and range-of-motion scale scores at postoperative week 2 decreased sig- nificantly compared with preoperative scores. After postoperative month 3, scores for both manual muscle test and range of motion nearly recovered to preoperative status. However, functional disability, according to the Disabilities of the Arm, Shoulder and Hand instrument, was increased considerably after latissimus dorsi flap surgery, and a substantial amount of disability remained 1 year postoperatively. The mental component of the 36-Item Short-Form Health Survey improved consistently for 1 year postoperatively, whereas the physical component decreased significantly until the sixth month postoperative- tively and was still lower than the preoperative score at postoperative month 12.

Conclusions: One year after latissimus dorsi flap surgery, shoulder strength and range of motion returned to baseline. However, functional disability and deteriorated physical aspects of quality of life persisted.

PO040

ONCOLOGIC OUTCOMES OF VOLUME REPLACEMENT TECHNIQUE AFTER PARTIAL MASTECTOMY FOR BREAST CANCER: A SINGLE CENTER ANALYSIS

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Background: Volume replacement technique is a good option for Asian women with small to moderate-sized breasts undergoing partial mastectomy for breast cancer. We analyzed the oncologic outcomes of this procedure in a single center

Methods: Seventy-two patients with breast cancer underwent partial mastectomy with volume replacement technique in this prospective study. Volume replacement techniques were tailored individually according to the volume of excised breast and tumor location. The mean duration of follow-up was 40.9 months. We analyzed association between various clinicopathologic factors and locoregional recurrence, distant metastasis and assessed cosmetic outcomes.

Result: The incidences of locoregional recurrence and distant metastasis were 2.8% and 5.6%, respectively. According to univariate analysis, locoregional recurrence was associated with a history of contralateral breast cancer, having received adjuvant radiotherapy, chronic postoperative complication (fat necrosis), and pathologic tumor size, whereas distant metastasis was associated with occurrence of the postoperative complication of fat necrosis, pathologic tumor size and stage, and positivity of c-erbB2 protein. According to multivariate analysis, history of contralateral breast cancer and fat necrosis significantly associated with incidence of locoregional recurrence and pathologic tumor size and stage significantly influenced the incidence of distant metastasis.

Conclusions: From an oncologic perspective, volume replacement procedures after partial mastectomy are an appropriate form of surgical management of breast cancer.

PO041

CLINICOPATHOLOGICAL CHARACTERISTICS AND IMAGING FEATURES OF BREAST CANCER IN KOREAN WOMEN UNDER 40 YEARS OLD

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Background: To evaluate the clinicopathological characteristics and imaging features of mammography, ultrasonography, and magnetic resonance imaging (MRI) for breast cancer in Korean women under 40 years old.

Methods: We included 176 consecutive women younger than 40 years old who had been diagnosed with breast cancer between January 2012 and November 2014 in this study. Patients' clinical records and pathologic characteristics were available as electronic medical records. Pre-operative imaging studies were performed for all women; 177 mammographies, 183 ultrasonographies, and 178 MRIs were available. Retrospective reviews of clinicopathological characteristics and imaging features of each modality were performed.

Result: Masses were the most common initial presentation. Eighty-six percent (158/183) of lesions were symptomatic while 14% (25/183) were diagnosed without symptoms. Luminal A subtype was the most common tumor type (n = 79, 43%), followed by triple negative (TN) (n = 43, 24%), luminal B (n = 42, 23%), and human epidermal growth factor receptor 2 (HER2)-enriched subtypes (n = 19, 10%). Luminal and HER2-enriched subtypes showed indistinct margins on mammography ($p = 0.006$). TN subtype tumors commonly depicted posterior enhancement on ultrasonography ($p < 0.001$) and rim enhancement pattern on MRI ($p < 0.001$).

Conclusions: Young women with breast cancer in Korea are more likely to present with a mass that is luminal A subtype. In our study, imaging characteristics and pathologic features of breast cancer in younger women were similar to those previously reported for older patients. Some imaging features showed statistically significant correlations with immunohistochemical subtypes.

PO042

PREOPERATIVE CLIPPING OF AXILLARY LYMPH NODES IN PATIENTS WITH BREAST CANCER BEFORE NEOADJUVANT CHEMOTHERAPY: A FEASIBILITY STUDY

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Background: The aim of this study is to determine the feasibility of image-guided clipping of axillary lymph nodes positive for disease at initial presentation in combination with sentinel lymph node biopsy and assess this procedure as a reliable method to axillary staging after neoadjuvant chemotherapy.

Methods: A ligaclip was placed at axillary lymph nodes under ultrasonography guidance before initiation of neoadjuvant chemotherapy. The localized lymph nodes were removed with sentinel lymph nodes and used radiography of the specimen to confirm removal of the clip.

Result: Image-guided localization was performed successfully with clip in 14 patients. The localized lymph node was detected and removed selectively after neoadjuvant chemotherapy. Of the 14 patients who underwent additional sentinel lymph node dissection, 1 had residual metastasis after chemotherapy; which was identified in non-clip containing lymph node. The pathological response to chemotherapy in the marked lymph node was not indicative of the overall response in other removed lymph nodes.

Conclusions: Image-guided clipping of axillary lymph nodes positive for disease at initial presentation before neoadjuvant chemotherapy and removing them with sentinel lymph node biopsy should be further investigated.

A NOMOGRAM FOR PREDICTING THE ONCOTYPE DX RECURRENCE SCORE IN WOMEN WITH T1-3N0-1MIM0 HORMONE RECEPTOR-POSITIVE, HUMAN EPIDERMAL GROWTH FACTOR-2 (HER2)-NEGATIVE BREAST CANCER

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Background: The aims of this preliminary study were to evaluate the association between the Oncotype DX (ODX) recurrence scores and traditional prognostic factors and to develop a nomogram that predict a subgroup of patients with low ODX recurrence scores (≤ 25), in whom addition of chemotherapy can be avoided.

Methods: Clinicopathological and immunohistochemical variables from a series of 265 T1-3N0-1miM0 hormone receptor-positive, human epidermal growth factor-2 (HER2)-negative breast cancer patients with available ODX test results at Asan Medical Center from 2010 to 2014 were retrospectively retrieved and analyzed. Seventy three (28%) had positive axillary lymph node micrometastases, and 218 (82%) had ODX recurrence scores of ≤ 25. Logistic regression was performed to build a nomogram for predicting a low-risk subgroup of the ODX assay. The cutoff value of ODX recurrence scores for the low-risk subgroup was set at 25, which is used in the ongoing Oncotype DX phase 3 TAILORx trial.

Result: Multivariate analysis revealed that estrogen receptor (ER) score, progesterone receptor (PR) score, histologic grade, and Ki-67 had statistically significant association with the low-risk subgroup (all p values < 0.001). With these variables, we developed a nomogram to predict the low-risk subgroup with the ODX recurrence scores of ≤ 25. The area under the ROC curve was 0.90 (95% CI, 0.85-0.96).

Conclusions: Low ODX recurrence score subgroup can be predicted by a nomogram incorporating four traditional prognostic factors: ER, PR, histologic grade, and Ki-67. An independent prospective validation for the present nomogram is underway to confirm its accuracy.

Poster Exhibition

USEFULNESS OF RAPIPLUG IN NIPPLE RECONSTRUCTION TO IMPROVE NIPPLE PROJECTION

Jung Dug Yang, Joon Seok Lee, Gyu Sik Jung, Jae Bong Kim, Jeong Woo Lee, Jeeyeon Lee, Wan Wook Kim, Jin Hyang Jung, Ho Yong Park

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Background: Nipple reconstruction is the last stage of breast reconstruction. Immediately the reconstructed nipple with a fi-ne projection becomes smaller over time and in severe cases, it becomes flat. In this study, therefore, a Rapiplug graft made of type 1 collagen was applied to the central core of the nipple reconstruction and a long-term observation was carried out to demonstrate the usefulness of the authors technique.

Methods: The nipple reconstruction technique was applied using the Hammond flap and this study targeted 26 patients of a control group from February 2008 to March 2012 and 15 patients of an experiment group from January 2014 to June 2014. This technique was applied to the patients, who had a nipple areolar complex reconstructed using the extended latissimus dorsi (LD) flap, among those whose nipple areolar complex was excised dur-ing mastectomy. For nipple reconstruction, the hat-shaped Rapiplug was grafted onto the Hammond flap and nipple projection was measured through one, six and twelve-month follow-up.

Result: After a year, the nipple loss rate of the control group and the experiment group was 43.7% and 41.2% respec-tively and nipple projection stayed fine during the long-term follow-up (twelve-month). No infection caused by complications was found in this study and congestion occurred in one case.

Conclusions: It was revealed that when the hat-shaped Rapiplug graft was applied to nipple reconstruction, nipple projec-tion of the experiment group kept better than the control group. It is thought that the authors method is safe, can be easily applied and is useful as a reproducible technique.

PO045

COMPLETE HORMONAL BLOCK COMPARED TO CHEMOTHERAPY FOLLOWED BY TAMOXIFEN IN PREMENOPAUSAL PATIENTS WITH LUMINAL A, LOW KI-67, AND T1N0 BREAST CANCER

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Background: We aimed to study the difference in the oncologic outcomes of complete hormonal block (CHB) compared to adjuvant chemotherapy followed by tamoxifen (CTT) in premenopausal with luminal A, Ki-67 < 25%, and T1N0 breast cancer.

Methods: From 2008 to 2013, retrospective review for the data of premenopausal patients who underwent surgery for the tumor < 2 cm, node negative, estrogen and progesterone receptors strongly positive, HER-2 negative and Ki-67% less than 25%. Then, we divided patient population into two groups; those who underwent adjuvant CHB using luteinizing hormone releasing hormone (Goserelin) plus Tamoxifen, and the other group was those who underwent adjuvant CTT.

Result: We found 235 patients underwent CHB and 171 patients underwent CTT. Median follow up duration was 50.9 (12-285) months. Significant number of patients in CHB group were younger than 40 year old (32% CHB vs. 22% CTT, $p = 0.0314$). Mean tumor size was significantly smaller in CHB group (1.19 cm vs. 1.48 cm, $p < 0.0001$). There was no mortality in both groups. There was no significant difference in 5-year disease free survival (DFS) between two groups (CHB = 98.9% vs. CTT = 95.73%, $p = 0.2485$). After univariate analysis considering age, tumor size, nuclear grade and P53%, we could not find any statistical significant difference in DFS in both groups.

Conclusions: There is no significant difference in the DFS between CHB and CTT groups. CHB can be considered as alternative treatment option for carefully selected patients, which can offer good disease control and avoid exposing the patients to the adverse effect of cytotoxic medications in this low risk population.

PO046

THE EFFECTIVITY OF INTRAOPERATIVE FROZEN SECTION ANALYSIS IN DCIS

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Background: Many studies show the intraoperative frozen section margin is useful for breast conserving treatment in early breast cancer patients. DCIS does not easily check that size. So if the intraoperative frozen section margin is checked, it can be helpful for deciding the resection range. This study is performed to evaluate the sensitivity and specificity of intraoperative frozen section analysis in DCIS patients.

Methods: With forty-six patients from 2006 until 2015, the current progress of the operation of the DCIS patients for surgery in my hospital compares the sensitivity and specificity between the frozen section results and final results.

Result: Twenty-five patients (54.3%) had the DCIS with Breast-conserving surgery. 5 patients show microcalcification, and 20 patients show mass lesions. The re-resection during surgery resulting in intraoperative frozen section analysis were found to be 1 case (20%) for microcalcification, and 2 cases (10%) for mass lesions. The sensitivity and specificity of Frozen section analysis were 60% and 95.8%. Individualized sensitivity and specificity were 100% and 100% for microcalcification, and 33.3% and 94.7% for mass lesion.

Conclusions: This study is limited because there is not enough data to draw any conclusions; however, it seems that there is a means to determine range in surgery to determine the margin but does not look into mass DCIS to determine the intra-operative frozen section analysis.

PO047

ADULT ONSET STILL'S DISEASE IN PATIENT WITH SILICONE BREAST IMPLANT: A CASE REPORT

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Background: Adult onset Still`s disease (AOSD) is a rare multi-systemic inflammatory disorder characterized by the classical triad of spiking fevers, arthralgias, and rash. We report a case of 54 years old female with AOSD after explantation of the silicone breast implant.

Methods: A 54 years old woman was hospitalized for the evaluation of spiking fever. She had a skin sparing mastectomy with silicone implant because of right breast cancer, nine months ago and one week prior to admission, underwent uneventful silicone explantation surgery because of recurrent cellulitis, fever and myalgia.

Result: Initially, her spiking fevers were simply considered as a postoperative infection however, all the inflammatory parameters including cultures were normal. All autoantibody tests were negative results. Although antibiotic therapy was broadened and changed multiple times, her symptoms did not improve and skin rash and severe polyarthralgias were noted. On the hospital day fourteen, she complained of shortness of breath. Chest CT showed the enlarged lymph nodes in multiple sites. Besides, interstitial pulmonary edema with both pleural effusions was revealed. She was diagnosed with AOSD based on the Yamaguchi criteria and treated with NSAIDS, anti-histamines, diuretics and low dose oral steroid. Four weeks later, her clinical and laboratory data returned to normal. The patient discharged and has been monitored after discharge regularly up to six months. The patient remained asymptomatic.

Conclusions: AOSD is a rare inflammatory disorder, while silicone breast implant is common cosmetic procedure. Physicians should be considered the possibility of AOSD when encountered the silicone implant patient with uncontrolled fevers.

PO048

PREDICTIVE FACTORS FOR UPGRADING PATIENTS WITH BENIGN BREAST PAPILLARY LESIONS USING A CORE NEEDLE BIOPSY

Young Ran Hong, Byung Joo Song, Sang Seol Jung, Bong Joo Kang, Sung Hun Kim, Byung Joo Chae

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Background: Intraductal papilloma (IDP) is a benign breast disease with malignant potential, for which complete surgical excision is usually recommended. The present study was to investigate predictive factors for upgrading patients with benign papillary lesion (BPL) using a core needle biopsy (CNB).

Methods: This study is an observational study using a prospectively collected cohort. In total, 13,049 patients who underwent a CNB for a breast lesion between January 2009 and May 2015 were enrolled. All patients had pathologically confirmed BPL from a CNB and were surgically treated.

Result: Surgical treatment was performed for 349 lesions out of 587 lesions. According to the pathological differences, the lowest upgrade rate was shown in IDP without atypia (without atypia: 7.6%, with atypia: 28.6%, papillary neoplasm: 31.6%, $p < 0.001$). In IDP without atypia, the age of diagnosis, size of BPL on ultrasonography, density of mammography, and synchronous breast cancer were associated with an upgrade by a univariate analysis. A multivariate analysis revealed that an age of older than 54 years and size greater than 1 cm were significantly associated with an upgrade to malignancy (OR 4.365, $p = 0.005$; OR 3.39, $p = 0.022$, respectively).

Conclusions: The indication for a surgical treatment can be defined as elderly patients with large sized mass (> 1 cm), even though IDP without atypia, including IDP with atypia or papillary neoplasm in the CNB results. Therefore, we suggest that a closed observation without surgery will be sufficient in younger women with a small IDP without atypia.

PO049

NO NEGATIVE EFFECT OF SHORT-TERM DELAYS IN SURGERY ON TUMOR PROGRESSION AND SURVIVAL OUTCOMES IN INVASIVE BREAST CANCER

Jonguk Lee, Saebyul Lee, Jong-Won Lee, Beom-Seok Ko, Hee-Jeong Kim, Jisun Kim, Il-Yong Chung, Guiyun Sohn, Sei-Hyun Ahn, Byung-Ho Son

ASAN Medical Center, Korea

Background: The impact of treatment delay on survival in breast cancer is still uncertain, but it is being an important issue to patients and clinicians. The purposes of this study were 1) to determine the impact of the delay from cancer diagnosis to potentially curative surgery on survival and 2) to determine the correlation between the prolongation of these delay interval and tumor progression such as tumor size and lymph node metastasis.

Methods: Among, 219 patients who received breast cancer surgery at Asan Medical Center between January 2008 and December 2008, patents who satisfy to inclusion and exclusion criteria were, 074. Patients were divided into 2 groups based on interval to treatment: ≤ 30 days (Group 1) and > 30 days (Group 2). We analyzed clinical characteristics, change of tumor size and axillary lymph node status, overall and disease-free survival.

Result: Between Group 1 and Group 2, there was no differences in clinical characteristics, tumor size changes between ultrasonography at diagnosis and pathologic result after surgery ($p = 0.134$). Also, tumor size change and lymph node status between USG result at AMC and pathologic result showed no differences ($p = 0.249$, $p = 0.233$, respectively). Additionally, there was no significant differences on disease-free survival ($p = 0.395$) and overall survival ($p = 0.813$).

Conclusions: Our study showed that short-term delays (within 2 months) from diagnosis to surgery of breast cancer do not effect negatively to cancer progression and on survival rate.

PO050

ONCOLOGICAL SAFETY OF ONCOPLASTIC BREAST CONSERVING SURGERY-COMPARE WITH CONVENTIONAL BREAST CONSERVING SURGERY AND TOTAL MASTECTOMY

Yumi Kim[1], Eunshin Lee[2], Young Joon Kang[1], Han-Byoel Lee[1], Jai Hong Han[1], Tae-Kyung Yoo[1], Hyeong-Gon Moon[1], Wonshik Han[1], Dong-Young Noh[1]

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Background: In recent decades, the surgical management of breast cancer has steadily and considerably improved. A satisfactory cosmetic result could be difficult to obtain due to high tumor to breast size ratio, unfavorable location, close to the nipple and contralateral ptosis. Oncoplastic techniques allows the performance of wide excision, conserving an excellent breast shape, may be helpful in many cases. This study was aimed to evaluate the oncological safety of oncoplastic surgery for primary breast cancer.

Methods: We compared 1,320 consecutive patients who underwent surgery between August 2011 and December 2014 for breast cancer at Seoul National University Hospital by one experienced surgeon. Retrospectively medical chart review was done and patients divided into three groups. Among them 42.65% underwent oncoplastic surgery (OPS), 49.70% underwent conventional breast conserving surgery and 7.65% underwent total mastectomy. Among the OPS group, level I technique was excluded. Finally 418 patents data of OPS group was analysed.

Result: 1,175 patients data were analysed (OPS: n = 418, conventional BCS: n = 656, TM: n = 101). Tumor size, resected area and volume in OPS group were significantly bigger than conventional BCS group. Distance to nipple in OPS group was closer than conventional BCS group. Also margin safety in OPS group was better than conventional BCS group.

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

PO051

DERMOGLANDULAR ROTATION FLAP WITH SUBAXILLARY SPREADING FLAP AS AN ONCOPLASTIC TECHNIQUE FOR BREAST CANCER

Seokwon Lee, Younglae Jung, Youngtae Bae

Pusan National University Hospital, Korea

Background: We propose a novel oncoplastic surgical technique, dermoglandular rotation flap with subaxillary spreading flap, as a feasible one-stage operation.

Methods: Breast conserving surgery, incorporating the dermoglandular rotation flap with subaxillary spreading flap, was performed in 49 female patients with breast cancer, between January and December 2015. After a full-thickness fibroglandular resection including the tumor, an inferior- or a superior-based rotation flap was performed according to the location of the defect. The subaxillary flap consisted of skin, dermis and subcutaneous fat tissue and was mobilized from the chest wall musculature. Since subaxillary skin has greater redundancy, it can be easily moved to reach the lateral aspect of the breast. Approximation of the subaxillary flap to the lateral side of rotated dermoglandular flap served to relieve skin tension and avoid displacement of the nipple-areola complex (NAC). Consequently, there was wider dermoglandular tissue rotation and efficient filling of defect without any significant postoperative deformity.

Result: Mean tumor size, on pathology, was 2.1 cm (range, 0.4-6.0). Mean excised breast tissue weight was 78.4 g (range, 28.6-195.0). More than half of the patients (51%) studied had excised breast tissue weighing more than 80 g. None of the included patients had positive surgical margins in final pathologic reports. Most patients answered excellent or good for self-estimated cosmetic outcomes including symmetry of the breast and NAC, breast shape, scarring, and overall satisfaction.

Conclusions: A modified dermoglandular rotation flap technique along with subaxillary spreading flap, is a feasible and effective oncoplastic technique for breast cancers.

PO052

THE CLINICAL SIGNIFICANCE OF ANTI-MULLERIAN HORMONE EVALUATION IN BREAST CANCER PATIENTS WHO ARE TAKING TAMOXIFEN

Cheol Min Kang, Beom Seok Ko, Eunhae Um, Jinsung Kim, Sungchan Gwark, Hee Jeong Kim, Il Yong Chung, Jong Won Lee, Byung Ho Son, Sei Hyun Ahn

ASAN Medical Center, Korea

Background: According to several guidelines, it is recommended for premenopausal breast cancer patients, after taking tamoxifen for five years, to either continue with tamoxifen or change to the aromatase inhibiter, depending on their menopausal status. Menopause is defined as having no menstrual periods for 12 consecutive months. The elevated serum follicle-stimulating hormone (FSH) levels may be helpful in confirming menopause. However, it is known that patients administered with tamoxifen usually show low FSH levels. Anti-Mullerian Hormone (AMH) levels provide a more accurate indicator of menopausal status than FSH levels.

Methods: Out-patient subjects who visited the survivorship clinic at Asan medical center between December.2014 and January. 2015 were reviewed and included. The patients FHS and AMH levels were measured and they were asked the date of their last periods. Patients are said to be in menopause if more than one year has passed since their last period or if their FSH levels are over 30 and their AMH levels are below 0.08.

Result: AMH and FSH levels were measured from a total of 48 breast cancer patients. The average age was 52. Statistically, menopause compared to FSH levels has a *p* value: 0.582, indicating there is no significant relationship between them. Menopause compared with AHM levels has a *p* value: 0.030, indicating a significant relationship.

Conclusions: This research shows that serum AMH levels are indicator of menopause. However, it is considered that a long term follow up after discontinued tamoxifen. à This research shows that serum AMH levels are indicator of menopause. However, it is considered that a long term follow up after discontinued tamoxifen is needed.

PO053

INTRAPLEURAL PACLITAXEL CHEMOTHERAPY FOR MALIGNANT PLEURAL EFFUSION IN BREAST CANCER

Jung Eun Choi, Jeong Yeong Park, Su Hwan Kang, Soo Jung Lee

Yeungnam University College of Medicine, Korea

Background: The treatment response rate of malignant pleural effusion is very low and uncontrolled pleural effusion causes severe pain and discomfort to the patients.

Methods: We investigated the efficacy and safety of paclitaxel, as an intrapleural chemotherapeutic agent. From January 2006 to June 2015, total 35 times of intrapleural chemothepapy were performed in 26 breast cancer patients who had developed malignant pleural effusion. They were infused 120 mg/m^2 of paclitaxel through a chest tube, which was clamped for 48 hours. The chest tube was maintained until drainage was reduced to less than 50-100 mL/day.

Result: Mean follow up period after intrapleural chemotherapy was 11 months. The average time of indwelling with a chest tube after intrapleural chemotherapy was 9.7 days. Mean progression free survival was 7.8 months. During the follow-up period, 5 patients had no progression of pleural effusion and two of them were free from progression for more than 36 months. In 26 attempts, intrapleural chemotherapy was effective and chest tube could be removed, but, in other 9 attempts, there was no improvement. There were 3 severe adverse effects related death caused by respiratory failure with or without G4 neutropenia.

Conclusions: Intrapleural paclitaxel chemotherapy is helpful for some patients with uncontrolled pleural effusion because it could reduce the duration of hospital stay and improve quality of life. But it needs to be determined carefully, considering the side effects and response rate of treatment.

PO054

USAGE OF ESTIMATED SURGICAL PLAN IN MASTECTOMY FOR BREAST CANCER TO DECREASE DEAD SPACE

Heeseung Park, Taewoo Kang

Pusan National University Hospital, Korea

Background: Dead space has been considered as one of the important factors in seroma formation. In this study, we compared conventional mastectomy design and modified design based on estimation which minimize dead space primarily and reviewed on seroma formation and other beneficial effects.

Methods: 138 Consecutive patients undergoing mastectomy for breast cancer (total 146 cases) during 2011.10.01-2015.8.18 in Pusan National University Hospital were reviewed in this retrospective observational study. 107 Patients (113 case) who received conventional mastectomy design (61 case) or estimated design using pytagorian method (52 case) for incision plan were compared. Two group of patients were subsequently seperated along its axillary procedure. Estimated skin length, operation time, seroma drainage duration, perioperative complications and recurrence rate were reviewed.

Result: Estimated skin length from two method showed statistically meaningful difference (5.27 vs. 7.10, *p*-value 0.034). Operation time benefit of new incision group was not meaningful (148.38 vs. 141.39, *p*-value = 0.345). Wound seroma was significantly decreased in axillary dissection group of estimation manner than that of classic manner (10.61 vs. 6.75, *p*-value 0.041). However, in other groups, there were no significant difference along design manner (7.52 vs. 6.20 *p*-value 0.410). Perioperative complications were four case in classic manner.

Conclusions: We could observe some clinical benefits as well decreased seroma formation by decreasing dead space, without the cost of perioperative complicatio. This new manner could be used as a proper, non biased communicable way in mastectomy for breast cancer patient.

PO055

ADJUVANT ENDOCRINE THERAPY ALONE IN PATIENTS WITH NODE-POSITIVE, LUMINAL A TYPE BREAST CANCER

Sungmin Park, Hyun-June Paik, Jai Min Ryu, Ha Woo Yi, Soo Youn Bae, Jong Han Yu, Se Kyung Lee, Jeong Eon Lee, Seok Won Kim, Seok Jin Nam

Samsung Medical Center, Samsung Seoul Hospital, Korea

Background: Hormone receptor (HR)-positive and HER2-negative (luminal A) breast cancer generally shows favorable prognosis. Luminal A with node positive patients is typically treated with cytotoxic chemotherapy but recent studies have shown that adjuvant chemotherapy provides little benefit. The purpose of this study was to identify the feasibility of adjuvant endocrine therapy without systemic chemotherapy in node positive, luminal A breast cancer.

Methods: This was a retrospective study of 870 patients who were surgically treated for invasive breast cancer at Samsung Medical Center between 2005 and 2013. Luminal A subtype was defined as ER & PR+, HER2- and Ki-67 < 14%. We compared AC based (AC: doxorubicin or epirubicin, plus cyclophosphamide) adjuvant chemotherapy versus endocrine therapy without chemotherapy in node-positive, luminal A breast cancer.

Result: We performed 1: n matching, with a maximum n of 8. The median age of the patients was 58.26 ± 9.49 years in chemotherapy group and 58.68 ± 11.73 in endocrine therapy only group. The median follow up time was 51.9 months (range, 1-125 months). In a multivariable analysis, axillary lymph node metastasis revealed significantly different between the two groups in disease-free survival (DFS). Survival analysis showed no difference in overall survival and DFS between two groups ($p = 0.125$; $p = 0.348$).

Conclusions: Chemotherapy could provide little benefit to patients with luminal A, node positive breast cancer and may help reduce the morbidity by avoiding chemotherapy in some patients. And future studies with a large number of patients and longer follow-up time would be necessary to support omission of chemotherapy in this patient population.

PO056

A MULTI-CENTER PHASE II TRIAL TO EVALUATE THE EFFICACY AND SAFETY OF NEOADJUVANT

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Background: This multi-center phase II study was investigated to evaluate the efficacy and safety of the combination of docetaxel and gemcitabine into neoadjuvant therapy in 98 stage II, III breast cancer.

Methods: Operable female breast cancer patients were enrolled. The primary endpoint was pathological complete response (pCR) rate of invasive cancer. Secondary end point included clinical response rate (RR), rate of breast-conserving surgery, toxicity, and disease-free survival (DFS).

Result: A pCR in breast and axillary lymph node was observed in 7 of 98 patients (7.1%; 95% CI, 2.05%-12.15%). The overall clinical response rate (RR) was 65.3% (64 of 98; 95% CI, 55.8%-74.8%). Breast-conserving surgery was performed for 75 of 98 (76.5%) assessable patients. The neutropenia was frequent and observed in 92 of 98 patients (93.9%), including grade 3 in 24 patients (24.5%) and grade 4 in 63 patients (64.3%). Dose reductions were required in 30 (32.6%) of 92 patients. Second dose reduction was required only one patient. After median follow-up of 24 months, disease-free survival (DFS) was 86.7%. At the time of analysis, 13 patients (13.3%) had relapsed. The relapses were local only in 3 patients, distant only in 6 patients and both local and distant in 4 patients.

Conclusions: Combination of docetaxel and gemcitabine has promising effective and manageable toxicity as neoadjuvant chemotherapy for stage II, III breast cancer.

PO057

THE EFFECT OF QUILTING IN THE PREVENTION OF SEROMA AFTER LATISSIMUS DORSI FLAP DONOR SITE

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Pusan National University Hospital, Korea

Background: Latissimus dorsi myocutaneous flap (LDMCF) is a commonly used technique for breast reconstruction following breast conserving surgery. And seroma is the common complication in the donor site. In this study, the effect of quilting at donor site and the need for drainage was evaluated.

Methods: From May of 2014 to December of 2015, retrospective review of 136 patients who underwent LDMCF was performed. Patients were divided into 3 groups : Group A, in which half quilting at donor site and drain was used, Group B, in which total quilting at donor site and drain was used, and Group C, in which only a total quilting was done at donor site and drain was not inserted. The outcome measures were age, BMI, mastectomy volume, LD volume, duration of drain, total drain volume, length of hospital stay, total aspiration volume and incidence of postoperative aspiration.

Result: There were no statistically significant difference in age, BMI or mastectomy volume among three subgroups. In group B and C, duration of drain ($p < 0.0001$), total drain volume ($p < 0.0001$), length of hospital stay ($p < 0.0001$), total aspiration volume ($p = 0.002$) and incidence of postoperative aspiration ($p = 0.003$) were reduced than group A.

Conclusions: Total quilting at donor site reduces seroma and may not need closed suction drain.

PO058

EFFECT OF PRIMARY TUMOR RESECTION ON OVERALL SURVIVAL IN PATIENTS WITH STAGE IV BREAST CANCER

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Yonsei University College of Medicine, Korea

Background: The clinical role of primary tumor resection for breast cancer patients with distant metastasis is not certain; currently it is used mostly as palliative care, but there are some indications that it may improve oncological outcomes.

Methods: In total, 284 breast cancer patients presenting with breast cancer at stage IV at initial diagnosis, between 2001 and 2014, were enrolled in the study. Patients were divided into two groups based on surgical resection of the primary tumor. Overall survival (OS) between the two groups was analyzed.

Result: Patients in the surgery group (n = 92) had smaller tumors than those in the no-surgery group (n = 192, T0-1: 17.7% vs. 34.8%, $p < 0.001$). The surgery group more often had negative nodal status (5.7% vs. 33.7%, $p < 0.001$). Multiple metastatic organ sites were more common in the no-surgery group than in the surgery group (55.7% vs. 15.2%, $p < 0.001$). The surgery group showed a better OS than the no-surgery group ($p = 0.01$). Multivariate analysis showed that surgical resection of primary tumors tended to be associated with improved OS (HR = 0.67, $p = 0.055$). T stage, ER, HER2, and metastatic organ sites were independent prognostic factors for OS in multivariate analysis.

Conclusions: Surgical resection of the primary tumor may be a treatment option for patients with stage IV disease in terms of improving overall survival.

PO059

THE CHARACTERISTICS OF GYNECOMASTIA ACCORDING TO AGES

Seongbae Hwang, Byungseo Choi, Geonyoung Byun, Bumhwan Koo, Sungryul Lee

Damsoyu Hospital, Korea

Background: The clinical role of primary tumor resection for breast cancer patients with distant metastasis is not certain; currently it is used mostly as palliative care, but there are some indications that it may improve oncological outcomes.

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Conclusions: Surgical resection of the primary tumor may be a treatment option for patients with stage IV disease in terms of improving overall survival.

PO060

CLINICAL EXPERIENCES OF 1,206 ACCESSORY BREAST EXCISIONS IN A SINGLE CENTER

Seongbae Hwang, Byungseo Choi, Geonyoung Byun, Bumhwan Koo, Sungryul Lee

Damsoyu Hospital, Korea

Background: Accessory breast has received little attention in the surgical field, although it is common occurring in 2-6% women. Its convexity and cyclic pain make women embarrassed, so they often have desires for improvement of cosmesis and pain by surgical excision. This study is to investigate clinical experiences of 1,206 accessory breast excisions in a single center.

Methods: 1,206 patients who have been treated with an excision of accessory breast tissue from September 2012 to December 2015 at the Damsoyu Hospital were analyzed for clinical factors retrospectively.

Result: All patients were female. Unmarried patients were 641 (53.2%), and married patients were 565 (46.8%). In operation method, accessory breast excision without skin removal using more than 3 cm incision was performed in 58 patients (4.8%), accessory breast excision with skin removal and liposuction using more than 3Cm incision in 181 patients (15.0%), accessory breast excision with liposuction using minimal incision (Magic accessory breast surgery) in 967 patients (80.2%). Mean operation time was 58 minutes. Postoperative complications developed in 63 patients and ugly contuor after operation was the most common (2.48%). After reoperation, 6 patients were revealed with remnant breast tissue. In our study, 96.7% of patients enjoyed cosmetically satisfying outcomes.

Conclusions: In conclusion, from our experience, the treatment of choice is surgical removal, which makes women comfortable in clinical manifestation and satisfied with their cosmetic axillar line. Complete accessory breast excision, liposuction, and minimal incision for a little scarring are the most important factors in the operation of accessory breast excision.

PO061

CHEMOTHERAPY FOR NODE-NEGATIVE, HORMONE RECEPTOR-POSITIVE MUCINOUS CARCINOMA OF BREAST

Sung Chan Gwark, Jong Won Lee, Sae Byul Lee, Guiyun Sohn, Jisun Kim, Il Yong Chung, Hee Jeong Kim, Beom Seok Ko, Byung Ho Son, Sei Hyun Ahn

ASAN Medical Center, Korea

Background: Some patients with node negative, hormone receptor positive mucinous carcinoma (MC) have been treated with chemotherapy against the NCCN guideline. The aim of this study was to compare clinicopathologic characteristics and prognosis between two groups of node negative, hormone receptor positive MC categorized by adjuvant chemotherapy or not.

Methods: A total of 196 node negative, hormone receptor positive MC cases from 1989 to 2008 were categorized into two groups: Chemotherapy group (Group 1, n = 72) and no chemotherapy group (Group 2, n = 124).

Result: Group1 showed a tendency to have younger age at diagnosis, higher T stage, and more frequent overexpression of HER2, compared with group2 (43.7 years vs. 48.7 years, $p = 0.006$; T1/T2/T3 = 26.4%/66.7%/6.9% vs. 69.4%/30.6%/0%, $p < 0.01$; IHC 3+ = 11.8% vs. 8.4%, $p = 0.465$) The 5- and 10-year CSS for each group was 97.2% vs. 100%, 95.7% vs. 91.0% respectively, without statistically significant difference ($p = 0.95$).

Conclusions: Chemotherapy for node-negative, hormone receptor positive MC, the decision of which might be caused by factors such as younger age and larger tumor size, is inappropriate.

PO062

POSITIVE SUPERFICIAL AND/OR DEEP MARGINS AND LOCAL RECURRENCE IN INVASIVE BREAST CANCER WITH BREAST-CONSERVING THERAPY

Jin Sung Kim, Sei Hyun Ahn, Byung Ho Son, Jong Won Lee, Beom Seok Ko, Hee Jeong Kim, Jisun Kim, Il Yong Chung, Guiyun Sohn, Tae In Yoon

ASAN Medical Center, Korea

Background: There have been few reports evaluating the effect of positive superficial and/or deep margins on local failure in breast cancer patients with breast-conserving therapy (BCT).

Methods: A retrospective analysis was performed on 3,399 stage I and II invasive breast cancer patients with breast conserving surgery followed by radiotherapy at Asan Medical Center from January 2000 to December 2008. The patients were divided into three groups: Group 1 (n = 3,195), clear resection margins for all sections; Group 2 (n = 121), positive margins on superficial and/or deep sections; and group3 (n = 83), positive conventional margins regardless of superficial and/or deep margin involvement. Ipsilateral breast tumor recurrence (IBTR) were evaluated between the three groups.

Result: The three groups did not differ significantly with respect to age, tumor size, nodal status, histology, grade, lymphovascular invasion, and Her2 status. The Group 3 had greater proportions of positive extensive intraductal component (EIC), positive hormone receptor, and without chemotherapy, compared with group 1 and 2. Five year IBTR rates of group, 2, and 3 were 1.9%, 0%, and 7.7%, respectively ($p < 0.001$). On Cox proportional hazard model, positive superficial and/or deep margins (group2) had no significance as predictor of IBTR (HR 0.704, 95% CI 0.172-2.584).

Conclusions: Superficial and/or deep margin involvement following breast conserving therapy does not affect local recurrence.

PO063

BREAST VOLUME REPLACEMENT USING HUMAN ACELLULAR DERMAL MATRIX (MEGADERM) AFTER PARTIAL MASTECTOMY FOR BREAST CANCER

Junghyun Youm, Jaepak Yi, Sangah Han, Jungkyu Ryu, Jeongyoon Song, Sun Young Min

Kyung Hee University School of Medicine, Korea

Background: There are various oncoplastic techniques developed for breast cancer patients. Breast volume replacement technique is a good option for Asian women with small to moderate-sized breasts undergoing partial mastectomy or total mastectomy for breast cancer. In the case of incidental extensive resection during breast surgery, an autologous tissue flap cannot be immediately applied in the absence of an expert surgeon. Silicone implants are also not an optimal option due to its increased rate of capsular contracture after adjuvant radiation therapy (RT). Usage of a Vicryl mesh or Interceed volume replacement is easily applicable for volume replacement surgery but increases the risk of infection.

Methods: Megaderm is a human acellular dermal matrix, which can be used as for soft tissue replacement. It is especially useful as a tissue expander or in implant-based primary breast reconstruction after partial or total mastectomy.

Result: This case is of a 45 year old female patient with small-sized breasts who had a large amount of breast volume removed during partial mastectomy because of a multifocal breast cancer. We used Megaderm for breast reconstruction and reinforcement of soft tissue.

Conclusions: We are reporting this case to demonstrate how a similar breast volume can be obtained postoperatively using Megaderm with imaging findings before and after radiation and also introduce its application techniques.

PO064

LYMPHOVASCULAR INVOLVEMENT CAN PREDICT PROGNOSIS IN BREAST CANCER PATIENTS TREATING NEOADJUVANT CHEMOTHERAPY

Young Jae Ryu, Dong Hoon Cho, Jung Han Yoon, Min Ho Park

Chonnam National University Hwasun Hospital, Korea

Background: The molecular subtype of breast cancer has been correlated with disease-free survival (DFS) and overall survival (OS). Neoadjuvant chemotherapy (NAC) had become the standard treatment in patients with locally advanced breast cancers. The purposes of this study was to evaluate prognosis according to molecular subtype and factors in patients with locally advanced breast cancer treating NAC.

Methods: We analyzed medical records of 91 patients with breast cancer who received NAC followed by operation between January 2005 and January 2010 retrospectively. The patients were classified into four molecular subtype groups (luminal A, luminal B, Her 2 overexpression, triple negative).

Result: 35 patients were luminal A breast cancer; 13 patients luminal B; 22 patients Her2 overexpression; 21 patients triple negative(TN). TN patients have tendency of more than 50 age and higher histologic grade. There were significance of ypNstage (ypN0 vs. ypN1-3; $p = 0.019$, 5 year DFS; $p = 0.005$, 5 year OS) and lymphovascular invasion (LVI) ($p = 0.003$, 5 year DFS; $p = 0.005$, 5 year OS) in the univariate analysis. In the multivariate analysis, LVI was a significant factor in 5 year DFS (OR 2.145, 95% confidence interval 1.064-4.324, $p = 0.033$). There was no significance among molecular subtype in 5 year DFS ($p = 0.161$) and 5 year OS ($p = 0.084$).

Conclusions: LVI was associated with DFS in patients with locally advanced breast cancer treating NAC and operation.

PO065

CLINICAL IMPLICATION OF INTERNAL MAMMARY LYMPH NODE BIOPSY DURING IMMEDIATE BREAST RECONSTRUCTION USING AUTOLOGOUS TISSUE FREE FLAPS IN BREAST CANCER SURGERY

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Background: This study is aimed to explore clinicopathologic factors associated with IMLN metastasis, and discuss the clinical value of opportunistic biopsy during immediate breast reconstruction using autologous tissue free flap.

Methods: We retrospectively reviewed the records of 277 patients who underwent total mastectomy and immediate reconstruction using transverse rectus abdominis musculocutaneous free flap from May 2012 to April 2015. Suspicious IMLN encountered during dissection of recipient vessels were biopsied. Clinicopathologic characteristics were evaluated.

Result: Suspicious lymph nodes were biopsied in 53 patients (19.1%, 53/277). Eleven had a final diagnosis of in situ carcinoma with no IMLN metastasis. Of the 42 patients with invasive carcinoma (15.2%, 42/277), IMLN was positive in 12 patients (28.6%, 12/42). Five patients with positive IMLN had no axillary lymph node metastasis and two were upstaged due to IMLN metastasis. Larger invasive tumor size ($p = 0.001$) and the presence of lymphatic tumor emboli ($p = 0.025$) were significantly associated with IMLN metastasis on univariate analysis. Invasive tumor size ≥ 2 cm was the only factor associated with IMLN metastasis on multivariate analysis (OR 7.875, 95% CI 1.330-46.628, $p = 0.023$). Ten of 23 patients with preoperative diagnosis of in situ carcinoma had a final diagnosis of invasive carcinoma and two had IMLN metastasis.

Conclusions: Opportunistic biopsy of suspicious IMLN during immediate breast reconstruction using a free flap should be considered in patients with tumor size ≥ 2 cm. Selective IMLN biopsy may provide a more accurate staging of the disease, which could lead to appropriate additional treatment that would not have been given without the biopsy.

PO066

EVALUATION OF SURGICAL GUIDES USING A 3D PRINTER IN BREAST CANCER PATIENTS WHO RECEIVED NEOADJUVANT CHEMOTHERAPY

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Background: Many studies have shown that MRI is the most accurate technique for evaluating residual disease after neoadjuvant chemotherapy. However, it is difficult to directly marking a range of tumors in MRI image to the breasts. The objective of this study is to evaluate the use of 3D printing surgery guides in breast cancer patients undergoing breast-conservation therapy after neoadjuvant chemotherapy.

Methods: This prospective pilot study was performed on breast cancer patients who received neoadjuvant chemotherapy and planned to receive breast conserving surgery. Breasts and tumors were modelled in 3D using the pretreatment MRI images. We made a surgical guide that can mark the primary tumor using the 3D printer. After surgery, the distances to the margins from tumor were measured.

Result: Five patients enrolled from December 2015 to January 2016. Median age was 46.5 years. All patients had clear resection margins. The median distance from the tumor to the margins was 1.2 cm.

Conclusions: The breast surgical guide using a 3D printer is expected to enable more appropriate conserving surgery for patients who received neoadjuvant chemotherapy by accurately marking the extent of the primary tumor based on pretreatment MRI imaging. This procedure is a non-invasive method that does not use an H-wire.

PO067

COMPARISON OF PATHOLOGIC COMPLETE REMISSION RATE AFTER NEOADJUVANT CHEMOTHERAPY WITH TRASTUZUMAB VERSUS NEOADJUVANT CHEMOTHERAPY ALONE IN PATIENTS WITH LOCALLY ADVANCED BREAST CANCER

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Background: Neoadjuvant systemic therapy is now being used to increase the tumor control and for rapid assessment of drug efficacy. And pathologic complete remission has been proposed as a surrogate end point for prediction of long-term clinical benefits, such as disease-free survival and overall survival. The purpose of this study was to predict the complete remission (CR) rate of the locally advanced breast cancer after neoadjuvant chemotherapy by comparing the clinicopathological characteristics between treatment groups.

Methods: From May of 2012 to January of 2016, we retrospectively reviewed the medical records of 31 female patients who were diagnosed with locally advanced breast cancer and received neoadjuvant chemotherapy. 15 patients received Doxorubicin combined with cyclophosphamide followed by Paclitaxel combined with trastuzumab (ACTH). 16 patients received epirubicin combined with docetaxol (ET). We compared age, clinical T stage, clinical N stage, type of surgery, pathological stage, HER2 receptor status, hormone receptor status, histological grade, nuclear grade, lymphovascular emboli, CA15-3 between two groups.

Result: 7 out of 31 patients achieved pathological CR after neoadjuvant chemotherapy. 6 were in group of ACTH and 1 was in ET group. CR rate was significantly higher in ACTH group than ET group ($p = 0.005$). Clinical T, Nstage, type of surgery, hormone receptor status, histological grade, nuclear grade, present of lymphovascular emboli, CA15-3 did not have statistical significance in two groups. HER2 receptor status showed statistical difference in the two groups ($p = 0.005$).

Conclusions: In comparison with ACTH group to ET group, CR rate is meaningfully higher in ACTH group. This result maybe contributed by development of HER2 target therapy.

PO068

THE INCIDENCE OF LYMPHEDEMA IN STAGE I/II BREAST CANCER AFTER MINIMAL AXILLARY OPERATION

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Background: The incidence of lymphedema was 3.8% to 32% in the stage I/II breast cancer patients in previous studies. The number of dissected axillary lymph nodes (N-ALNs) is the main risk factor of lymphedema. In this study, we investigated the impact of the N-ALNs on the occurrence of lymphedema in the Era of minimal axillary operation.

Methods: Among 829 patients who underwent primary breast cancer surgery in National Cancer Center in 2013, we analyzed 372 stage I/II patients with harvested node number six or fewer. Patients were grouped according to the N-ALNs (≤ 3, group one vs. > 3, group two). The lymphedema status was evaluated preopratively and postoperatively.

Result: The patients number of group one was 290 and group two was 82. The mean node number was 1.82 ± 0.77 in group one and 4.71 ± 0.84 in group two. Lymphedema occurred in 5 (1.7%) and 4 (4.9%) patients in group one and two, respectively. The incidence of lymphedema was not significantly different between two groups ($p = 0.644$). Lymph node metastasis was the only independent risk factor for lymphedema [hazard ratio (HR), 5.34; $p = 0.023$].

Conclusions: Although the comparison between two groups (≤ 3, group one vs. > 3, group two) was statistically not significant, the lymphedema incidence showed a rising tendency when the number of dissected axillary lymph nodes increased. Considering node metastasis was an independent risk factor for lymphedema, meticulous axillary operation could be emphasized especially in the patients without node metastasis.

PO069

METAPLASTIC BREAST CARCINOMA: CLINICAL PRESENTATION, TREATMENT AND PROGNOSIS WITH RADIOLOGIC FINDINGS

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Background: Metaplastic carcinoma is a rare subtype of breast cancer that is histologically diverse group of malignancies. Metaplastic carcinoma tends to have an aggressive clinical presentation. Although many clinical and pathologic finding have been reported, to our knowledge, there are few reports of imaging findings for this type of tumor.

Methods: Data of 5 patients with histopathologically proven metaplastic breast carcinoma were reviewed retrospectively. Mammography, ultrasonography, MRI, and PET CT were recorded retrospectively using BI-RADS lexicon. In this review, clinical presentation, other pathologic characteristics, prognosis, treatment as well as potential future research directions will be also discussed.

Result: The patients ages ranges from 46 to 55 years. Two patients had axillary nodal metastases at the time of diagnosis. Estrogen and progesterone receptors were negative in all tumor. Adjuvant chemotherapy was administered to three patients, and radiotherapy to two patients after operation. One patient received preoperative chemotherapy.

Conclusions: Metaplastic carcinomas tend to show more benign imaging features such as round or oval shape with circumscribed margins than IDC. High signal intensity on T2-weighted MRI may also be useful for diagnosis of metaplastic carcinoma. Metaplastic carcinoma should be included in the differential diagnosis, especially in rapidly growing palpable mass. It tends to have a high metastatic potential, more chances of local recurrence and poor prognosis compared to intraductal carcinoma. This can be explained by its greater size, pathological heterogenicity, higher proliferation index, poorer differentiation and suboptimal response to systemic chemotherapy or hormonal therapy. So, further study is needed for novel targeted therapeutic options for this aggressive tumor.

CORRELATION OF HYPOXIA INDUCIBLE TRANSCRIPTION FACTOR IN BREAST CANCER AND SUVMAX OF F-18 FDG PET/CT

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Background: Tumor hypoxia induces the expression of several genes via the hypoxia-inducible transcription factors alpha (HIF-1α), which is associated with the prognosis of several cancers. We studied the immunohistochemical expression of HIF-1α in patients with invasive ductal breast cancer (IDC) and the possible correlation with SUVmax of the primary tumor (pSUVmax) as well as other biological parameters. Prognostic significance of pSUVmax for the prediction of progression-free survival (PFS) was also assessed.

Methods: Two-hundred seven 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 (LN) metastasis, stage and HIF-1α. The prognostic value of pSUVmax for PFS was assessed using the Kaplan-Meier method.

Result: The pSUVmax was significantly higher in patients with HIF-1α ≥ 2 compared to patients with HIF-1α < 2 (5.2 ± 4.5 vs. 3.7 ± 3.1, $p = 0.008$). pSUVmax was also significantly higher in higher stage ($p < 0.000001$), ER-negative tumors ($p < 0.0001$), PR-negative tumors ($p = 0.0011$) and positive LN metastasis ($p = 0.0013$). pSUVmax was significantly higher in patients with progression compared to patients who were disease-free (6.8 ± 4.4 vs. 4.1 ± 3.7, $p = 0.0005$). A receiver-operating characteristic curve demonstrated a pSUVmax of 6.51 to be the optimal cutoff for predicting PFS (sensitivity; 53.6%, specificity; 86.0%, $p < 0.0001$).

Conclusions: The pSUVmax on pretreatment F-18 FDG PET/ CT reflects expression of HIF-1α 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 presence of glucose metabolism and hypoxia in breast cancer cell.

INCREASED BRAHMA-RELATED GENE 1 EXPRESSION PREDICTS DISTANT METASTASIS AND SHORTER SURVIVAL IN PATIENTS WITH INVASIVE DUCTAL CARCINOMA OF THE BREAST

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Background: Previous studies have demonstrated aberrant expression of Brahma-related gene 1 (BRG1) in various tumor types. Increased expression levels of BRG1 have recently been shown to correlate with aggressive oncogenic behavior in many different types of human cancers. However, the role of BRG1 in breast cancer development and progression is not fully understood.

Methods: We evaluated BRG1 expression in 224 patients with invasive ductal carcinoma (IDC) of the breast using tissue microarray technique and immunohistochemistry. We also investigated whether BRG1 expression status is associated with clinicopathological characteristics and outcomes of IDC patients.

Result: Among the 224 patients with IDC, 37.5% (84/224) exhibited high BRG1 expression. IDC exhibited significantly higher BRG1 expression levels compared with ductal carcinoma in situ ($p = 0.009$) and normal breast tissue ($p = 0.005$). High BRG1 expression in IDC significantly correlated with higher histologic grade ($p = 0.035$) and presence of distant metastasis ($p = 0.002$), and was an independent factor for predicting distant metastasis (relative risk = 4.079; $p = 0.007$). Furthermore, high BRG1 expression predicted both shorter overall survival ($p = 0.011$) and recurrence-free survival ($p = 0.003$) in patients with IDC. In particular, BRG1 had significant prognostic value regarding recurrence-free survival for IDC patients with lymph node metastasis or stage III disease.

Conclusions: Our findings suggest that BRG1 is involved in the progression and metastasis of breast cancer and can serve as a novel predictive biomarker for distant metastasis and patient outcome

FOREIGN MATERIALS OF BREAST: CLINICAL AND IN VIVO, IN VITRO RADIOLOGIC CORRELATION

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Background: Foreign body in breast is very rare, but it happens infrequently. Patients with foreign body visited hospital for symptoms, or abnormal image. Not only there were various imaging findings, but also some of them showed specific radiologic findings depend on materials. And it had similar appearance of in vivo and in vitro radiologic finding. Therefore, we could know composition of material by not invasive modality.

Methods: We would like to present radiologic findings of foreign body in mammography, USG, CT, and MRI. Also, we correlate them with clinical symptom result of removed material in reoperation, and in vitro radiologic finding for incomplete removed surgical material.

Result: First, accidentally incomplete removal of surgical materials such as suture thread, silastic drain and penrose drain can be remnant. Most of them are incidentally found in follow up. Second, direct injection and leakage of implant could happen such as polyacrylamide gel, paraffin and plastic silicon or saline implant bag. Occasionally there are typical radiologic finding. Third, parasite can be found in breast like sparganosis. Lastly, foreign material can be inserted in breast such as golden puncture needle.

Conclusions: Awareness of foreign body in breast is very important because it can be associated with clinical symptom or underdiagnosis of other entities. In some cases, where postoperative care of the wound is not performed by the surgeon, the staff may not always be aware of the presence of the drain. Therefore, close follow up care and imaging are extremely important.

PREOPERATIVE BREAST MRI FOR THE ASSESSMENT OF THE SIZE OF DUCTAL CARCINOMA IN SITU

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Background: To determine whether magnetic resonance imaging (MRI) can assess the size of ductal carcinoma in situ (DCIS) more accurately than mammography and ultrasonography using the histopathological dimension of the surgical specimen as the reference measurement.

Methods: This is a retrospective review study from a Samsung Medical Center (SMC) database of breast cancer. Preoperative contrast-enhanced MRI, mammography and ultrasonography were performed to detect and assess the size of DCIS in 131 patients. The greatest dimensions of DCIS determined by the imaging modalities were compared with the histopathological dimensions of the surgical specimen. Intra-class coefficients were calculated to check the agreement among the MRI, mammography and ultrasonography measurements. The Wilcoxon signed-rank test was used to evaluate the statistical significance of the differences in size between MRI, mammography or ultrasonography and histopathology.

Result: Of the 131 patients, 126 (96.18%) underwent MRI, 103 (78.63%) underwent mammography, and 121 (92.37%) underwent ultrasonography. The mean lesion size was 3.882 cm on histopathology, 3.595 cm on MRI, 2.879 cm on mammography and 2.327 cm on ultrasonography, and the difference among modalities was statistically significant. The correlation coefficient between histopathological measurement and MRI was 0.837, versus 0.461 between histopathology and mammography and 0.284 between histopathology and ultrasonography. The lesion size was correctly estimated (± 5 mm), under-estimated (< 5 mm), or over-estimated (> 5 mm), respectively, by MRI in 60%, 19% and 21% of cases, by mammography in 38%, 31% and 31% of cases and by ultrasonography in 24.43%, 62.6% and 12.98% of cases, respectively.

Conclusions: MRI was more accurate for the detection and assessment of the size of DCIS than mammography and ultrasonography.

PO074

THE USEFULNESS OF PETCT FOR PREOPERATIVE EVALUATION OF DUCTAL CARCINOMA IN SITU

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Background: PETCT is useful in preoperative evaluation of invasive breast cancer (IBC) to predict axillary metastasis and staging workup. The usefulness is unclear in the case of ductal carcinoma in situ (DCIS) diagnosed on biopsy before surgery which sometimes is upgraded to IBC after definitive surgery.The aim of this study is to find out the usefulness of PETCT on DCIS as preoperative evaluation tool.

Methods: We investigated 102 cases of preoperatively diagnosed as DCIS who subsequently underwent definitive surgery between 2010 and 2015. We analyzed maximum standardized uptake value (SUVmax) of each patients with clinicopathologic variables.

Result: 15 cases out of 102 cases (14.7%) were upgraded to IBC after surgery. SUVmax was higher in the patients upgraded to IBC (mean 2.56 vs. 1.36), ($p = 0.0072$). SUVmax was significantly higher in the patient who have symptoms, palpable mass ($p = 0.0013$, $p = 0.0003$), the lesion over 2cm in size, BI-RAD category 5 ($p = 0.049$). There were no significant SUVmax difference regarding as nuclear grade, hormone receptor, comedonecrosis. SUV max 2.65 was theoretical cut off value in ROC curve analysis to predict underestimation of IBC. Underestimation rate was significantly higher in the patients with SUVmax > 2.65 ($p = 0.0001$). 10 patients (38.5%) were underestimated in 26 patients with the value of SUVmax > 2.65 and 5 patients (6.6%) were underestimated in 76 patients of SUVmax < 2.65. The sensitivity and specificity of prediction for underestimation in this cut off value were 66.7% and 82.8% respectively.

Conclusions: PETCT can be used as complementary evaluation tool to predict the underestimation of DCIS combined with the lesion size, palpable mass, symptomatic lesion, BI-RAD category.

USEFULNESS OF BREAST TC 99M-METHOXYISOBUTYL-ISONITRILE (MIBI) SCINTIMAMMONGRAPHY FOR BI-RAD CATEGORY 4 OR HIGHER LESIONS

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Background: In general diagnostic modalities, such as mammography and ultrasound, BI-RAD category 4 or higher lesions have been performed core-needle biopsy for confirmation rather than observation. In advancement of molecular breast imaging techniques on diagnosis of breast cancer, usefulness of Technetium-99m methoxyisobutyl isonitrile scintimammongraphy (MIBI scan) has been reported in a few studies. Thus, we aimed to evaluate usefulness breast MIBI scan, which would reveal potential diagnostic alternatives.

Methods: 301 patients with 801 lesions have enrolled in this study with general diagnostic modalities with breast MIBI scan. Data have been categorized by all lesions with biopsy confirmed along with MIBI scan results. All data were analyzed by McNemar and Kappa test for statically significance.

Result: Mean age was 49.2 9.37 years old (range from 26 to 85 years old). Detection results of Breast MIBI scan were divided into three categories: 236 positive intensity (29.5%), 565 negative intensity (70.5%), and 67 suspicious abnormal intensity (8.4%). Pathologic reports were also allocated into four subgroups: 122 invasive cancers (15.2%), 44 non-invasive cancers (5.5%), 194 proliferative benign lesions (24.2%), and 441 non-proliferative benign lesions (55.1%). Diagnostic sensitivity, specificity, positive predictive value, and negative predictive value were 83.5%, 55.6%, 59.1%, and 95.2%, respectively ($p < 0.001$). Specificity of MIBI scan plus general diagnostic modalities was dramatically increasing up to 85.2% comparing to general modalities (6.8%) ($p < 0.001$).

Conclusions: MIBI scan may offer an alternative diagnostic tool for invasive biopsy procedures, because its specificity and negative predictive value provided confident results on non-proliferative benign lesions in this study.

KIKUCHI-FUJIMOTO DISEASE: CASE REPORT

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Background: Kikuchi-Fujimoto disease (KFD) or histiocytic necrotizing lymphadenitis is a rare, benign and idiopathic, self-limiting disorder and predominantly affects young women. The most common presentation is cervical lymphadenopathy, though the etiology of the disease is still controversial. Clinical findings, histological diagnosis and immunohistochemistry help in diagnosis. Once diagnosed, steroids have been found to alleviate symptoms in patients with systemic manifestations.

Methods: We report a 18-year-old female who presented with right axillary lymphadenopathy and pain. She had multiple enlarged axillary nodes. Examination of other systems was normal. Lymph node biopsy was performed, and the histological features, and immunohistochemistry confirmed the diagnosis. The patient was treated symptomatically with analgesics and the symptoms slowly improved.

Result: The patient was treated symptomatically with analgesics and the symptoms slowly improved.

Conclusions: KFD is typically self-limiting, resolving within 1 to 4 months, though a possible recurrence rate of 3 to 4% has been reported. Analgesics, antipyretics and non-steroidal anti-inflammatory drugs may be used to alleviate lymph node tenderness and fever. The use of corticosteroids has been recommended in severe extra nodal or generalized KFD but is of uncertain efficacy. In case of severe and persistent symptoms in addition to high doses of glucocorticoids, intravenous immunogloubulins should be prescribed.

PO077

SURGICAL IMPORTANCE OF RECOGNITION FOR THE FRAGMENTED SPARGANOSIS LOCATED IN THE BREAST: CASE REPORT

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Background: Sparganosis is a rare infection disease caused by sparganum, a plerocercoid tapeworm larva of genus Spirometra. In humans, Sparganosis is accidentally acquired by ingestion of larvae are commonly or by eating raw snakes and frogs.Sparganosis of the breast is an uncommon disease, but should be considered in the differential diagnosis of unusual and suspicious breast masses. breast sparganosis can mimic malignancy. Here, we report a case of the fragmented sparganosis of the breast following core needle biopsy of worms from the left breast.

Methods: A 50-year-old female patient visited our hospital with a chief complaint of a palpable left breast mass from one month prior. She had no history to eat either frogs or snakes, but had the history of drinking impure water. Core needle biopsy was performed in local clinic. The pathologic reporting demonstrated granulomatous inflammation or Sparganosis.

Result: Sonography revealed a poorly defined irregularly dumbel shaped hyperechoic lesion with an internal serpiginous hypoechoic tubular structure in breast subcutaneous fat layer (depth 2.7 mm). The surgically removed specimen included 4 pieces of irregularly shaped fat tissue and a 6-7 cm length of fragmented white worm.

Conclusions: Generally, the most of suspicious or indeterminate breast lesions undergo core needle biopsy. However, preoperative biopsy procedures may result in fragmenting the worms, thus incomplete surgical removal may lead to recurrences. In this respect, Surgeons should be investigated without exception the surrounding tissue to eliminate the fragmenting the larvae, which at the same time as removing the main mass completely remains.

PO078

EXPERIENCES OF ULTRASONOGRAPHY-GUIDED SURGICAL CLIP PLACEMENT FOR LOCALIZATION IN PATIENTS WITH BREAST LESIONS

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Background: The placement of radiopaque markers is essential for patients with preoperative chemotherapy and breast conserving surgery (BCS) because radiopaque marker is the only way that can allow the surgeon to accurately locate and excise any residual cancerous tissue in a patient with dramatic pCR. NCCN guideline recommend pre-treatment localization of tumor bed for future surgical management in patients with desire breast preservation. But, none of these markers had been legally allowed for use in South Korea. So, we tried various ways using dye, charcoal or hook-shaped thread for localization. However, the results were not satisfactory. Last year there was a journal dealing with localization using surgical clip (J Breast Cancer 2015 March; 18(1): 44-49). We report our experiences of ultrasonography-guided surgical clip placement for localization.

Methods: A short skin incision was made using local anesthesia under aseptic conditions. A14/16-gauge coaxial guiding needle was inserted into the center of the malignancy, and the inner stylet was removed under US guidance. One surgical clip was passed through the inserted introducer, and the inner stylet was reinserted to complete the clip placement. The location of the clip was confirmed by US immediately after clip insertion. Postprocedural mammography was performed to confirm objectively the appropriate location.

Result: We performed pre-treatment localization for not only in patients with preoperative chemotherapy but also with suspicious malignant calcification patients detectable by US. The results were satisfactory, especially in patients with pCR.

Conclusions: Ultrasonography-guided surgical clip placement for localization in patients with breast lesions is safe, feasible and cost-effective method.

EFFECTS OF CIRCUIT EXERCISE ON AUTONOMIC NERVE SYSTEM OF SURVIVORS AFTER SURGERY OF BREAST CANCER

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Background: Breast cancer survivors are in various stressful conditions. They could be in worsening of Autonomic Nerve System (ANS). This study was designed to show effects of circuit exercise on ANS of survivors after surgery of breast cancer through Heart Rate Variability (HRV).

Methods: 25 participants whose pathologic stage was Ductal Carcinoma in Situ (DCIS) or I-III were randomly assigned into exercise group (EG) and control group (CG) using control group pre-and post-test design. 12 weeks of moderate intensity circuit exercise training according to exercise guideline of cancer patients of American College of Sports Medicine (ACSM2010) was applied to EG for an average of 50 minutes per day, 3 times a week. HRV was measured in both groups before and after 8 weeks.

Result: Two patients in EG and one patient in CG dropped out and were not included in the analysis. In the remaining 22 patients (EG = 12 and CG = 10), significant changes were found between groups on HRV indexes (i.e. After 8 weeks LF (ms2) EG 5.67 ± 0.66 and CG 4.61 ± 1.01 $p = 0.008$, HF (ms2) EG 6.00 ± 0.92 and CG 4.5 ± 1.63 $p = 0.014$, SDNN (ms) EG 45.14 ± 12.62 and CG 30.68 ± 16.22 $p = 0.029$, RMSSD(ms) EG 46.54 ± 24.45 and CG 24.73 ± 22.18 $p = 0.042$). But There was no significant difference in LF/HF (EG 0.95 ± 0.73 and CG 1.58 ± 1.81 $p = 0.324$).

Conclusions: HRV indexes were raised significantly after eight weeks circuit exercise on breast cancer survivors. It could be also mentioned that there was positive effects on ANS.

PO080

EFFECT OF ACUPUNCTURE FOR IMPROVING CANCER-RELATED FATIGUE IN BREAST CANCER PATIENTS: A RANDOMIZED SINGLE BLIND CONTROLLED PILOT STUDY

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Background: Cancer-related fatigue (CRF) affects the functional status and quality of life of patients with breast cancer. The purpose of this study was to assess the feasibility and safety of acupuncture for improving CRF in patients with breast cancer.

Methods: Twenty breast cancer patients presenting with CRF were enrolled. We randomly assigned 10 patients to acupuncture group and 10 patients to control group. In acupuncture group, acupuncture was administered 2 times a week for 6 consecutive weeks. In control group, sham acupuncture was administered. The outcomes were measured using Multidimensional Fatigue Inventory (MFI), Hospital Anxiety and Depression Scale (HADS), EORTC quality of life questionnaire -core questionnaire (EORTC QLQ-C30) and breast cancer module (EORTC QLQ-BR23) assessed by a self-administered questionnaire.

Result: The outcome measure using MFI tended to decrease of general fatigue, physical fatigue and mental fatigue, but without statistical significance. Acupuncture significantly reduced the severity of anxiety, as assessed by HADS, and the scores of global health status, functional scales and symptom scales as assessed by EORTC QLQ-C30 significantly improved following acupuncture, however there was no significant difference between acupuncture and control group

Conclusions: Acupuncture may be an effective intervention for managing the symptom of CRF and improving quality of life in patients with breast cancer. However, the pure effect of acupuncture is unclear, because sham acupuncture also showed improvement of symptoms of CRF in this study. Overall, the results of this study are insufficient to draw meaningful conclusions. Further randomized controlled studies with a larger sample size are required.

DETECTING DEPRESSION WITH DAILY MENTAL HEALTH LOGS FROM A SMARTPHONE APPLICATION FOR BREAST CANCER PATIENTS

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Background: Mobile mental-health trackers are smartphone applications that gather self-reported mental logs from users, and they have recently received attention from clinicians as a tool for screening depression in individual patients. However, these mental-health trackers ask only a few simple questions using face emoticons, and no reported study has examined the validity of their screening performance. This study evaluated the potential of a mobile mental-health tracker with three daily mental logs as a good indicator for detecting depression, and tested the impact of adherence to reporting using the mobile mental-health tracker on its accuracy in screening depression.

Methods: This study used the data in 5,792 sets of daily mental-health logs collected from 78 breast cancer patients over a 48-week period. We employed random logistic panel regression and receiver operating characteristic analysis to evaluate the screening performance of the mobile mental-health tracker. The Patient Health Questionnaire-9 test was used to measure the true depression status. In addition, we classified patients into subgroups (higher adherence and lower adherence) using a k-means clustering algorithm, and compared the screening accuracies in these two groups.

Result: The area under the ROC curve (AUC) for the mobile mental-health tracker was 0.8012. The AUC was significantly higher ($p < 0.01$) for the higher adherence group (0.8524) than for the lower adherence group (0.7234).

Conclusions: The results support the potential of mobile mental-health trackers for detecting depression in breast cancer patients. Furthermore, empirical evidence was obtained for the critical role of adherence to self-reporting, which represents crucial information for both doctors and patients.

SCREENING FOR PSYCHOLOGICAL DISTRESS IN BREAST CANCER PATIENTS AND PSYCHIATRIC REFERRAL ACCEPTANCE AMONG SCREEN POSITIVE PATIENTS

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Background: This study aims to identify the clinical characteristics of breast cancer patients with high levels of distress and the patients who accept the offered referrals for psychiatric consultation in screen detected patients.

Methods: From November 2011 through October 2013, 1,681 breast cancer patients at Asan medical center were screened for distress using the Center for Epidemiologic Studies-Depression Scale (CES-D). High risk patients who scored ≥ 19 were offered referrals for stress clinic at Asan Cancer Center. The characteristics of patients who were screened positive and accepted referrals were analyzed based on clinical characteristics.

Result: Using 19 as a cut point for referral, 771 out of 1,681 patients were screened positive and offered referrals for stress clinic. The patients who were screened positive tend to be smokers ($p = 0.033$), with previous history of psychotropic medication ($p = 0.045$), mastectomy ($p < 0.0001$) and recur cases ($p = 0.041$). Among 771 patients, 182 patients accepted referrals and visited stress clinic. Mean CES-D score of referral accepters group was 28.7 (SD = 8.27), statistically higher when compared to non-accepters group (26.9; SD = 6.79; $p = 0.006$). Other than CES-D scores, there was no difference in age, primary or recurrence, family history of breast cancer, operation type or stage between two groups.

Conclusions: Based on CES-D questionnaire, 45.8% of patients were screened positive for psychological distress, and smoking, a family history of breast cancer, previous history of psychotropic medication and mastectomy might be clinical predictor for high level of distress. Only 23.6% of patients accepted referrals and there is no significant clinical predictor for referral acceptance.

DIFFERENTIALLY EXPRESSED GENES IN PAIRED NORMAL, CANCER, AND LYMPH NODE METASTATIC TISSUES FROM BREAST CANCER PATIENTS CAN PREDICT CLINICAL OUTCOMES

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Background: Genome-wide screening of transcriptome dysregulation among normal, cancer, and metastatic tissues would provide insights into the molecular basis of breast cancer metastasis.

Methods: We profiled mRNA expression in matched normal, cancer, and lymph node metastatic tissues of seven patients with estrogen receptor-positive, HER2-negative breast carcinoma by using massive parallel sequencing of RNA transcripts (RNA-seq).

Result: We identified 1,522 and 664 differentially expressed genes (DEGs) between the normal and cancer tissues and between the cancer and nodal metastatic tissues, respectively. We identified 461 upregulated and 203 downregulated genes in nodal metastatic tissues compared with the corresponding cancer tissues. The DEGs from the comparisons of normal vs. cancer tissues and cancer vs. nodal metastatic tissues were significantly clustered in one and eight KEGG pathways, respectively. The chemokine signaling pathway was the most significant pathway in the cancer to nodal metastasis transition. Several candidate DEGs were subsequently verified to be able to serve as prognostic biomarkers for patients with breast cancer using BreastMark. Interestingly, lower IKZF1 and INPP5D expression was associated with significantly worse survival in patients with breast cancer. These genes have not been previously associated with an aggressive phenotype in breast cancer.

Conclusions: Using RNA-seq analysis in breast cancer and their matching normal and lymph node metastatic tissues, we are able to identify DEGs associated with the metastatic progression of breast cancer. The DEGs identified in this study can be used as new biomarkers for predicting the prognosis of patients with breast cancer.

WHAT IS THE SIGNIFICANT PREDICTORS FOR LOCAL RECURRENCE OF PHYLLODES TUMOR WITH EXPOSED OR CLOSED RESECTION MARGIN?

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Background: We aimed to determine the clinicopathologic factors influencing clinical outcome in patients of phyllodes tumor (PT) and their utility as prognostic predictors.

Methods: We retrospectively collected PTs from Kosin University, Gospel Hospital and Dong-A University Medical center, Busan, Korea. All slides were reviewed and graded by 2012 WHO classification. Immunostains for EGFR, CD34, SMA, p53 and Ki67 were performed and semiquantatively assessed for proportion and intensity. We analyzed the clinicopathologic factors to influence subsequent recurrence and recurrence free-survival (RFS) stratified by grade, surgical margin status and previous history for PT.

Result: Total 190 PTs (94 benign, 84 borderline and 12 malignant) were enrolled and they had 29 subsequent recurrences, 2 metastases and 2 deaths. Their surgical margins were frequently exposed (62.1%) or had narrow rim of normal breast in almost remainder. Although subsequent recurrence had no significant association with clinicopathologic and immunohistochemical findings, when stratified by several viewpoint, age ($p=0.032$) in malignant PT, EGFR immunoreactivity ($p=0.010$) in borderline PT, cytologic atypia ($p=0.048$) and CD34 immunoreactivity ($p=0.032$) in PT with exposed resection margin status, and operation type ($p=0.020$) in recurrent PT were significant factor. By multivariate Cox regression analysis, RFS had significant association with EGFR immunoreactivity ($p=0.03$) in borderline PT, CD34 immunoreactivity ($p=0.015$) for PT with exposed resection margin.

Conclusions: In present study, the outcome of PT, particularly subsequent recurrence were unpredictable just by clinicopathologic findings and immunohistochemical staining. However, we suggest the utility of EGFR and CD34 immunostain as significant prognostic factors in PT of particular clinical settings.

PREDICTIVE FACTORS FOR PATHOLOGIC COMPLETE RESPONSE AFTER PREOPERATIVE CHEMOTHERAPY IN TRIPLE-NEGATIVE BREAST CANCER

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Background: The purpose of this study was to identify the predictive factors of pathologic complete response (pCR) to neoadjuvant chemotherapy (NAC) in triple-negative breast cancer (TNBC).

Methods: Eighty seven TNBC patients who received NAC during 2004-2012 were included in this study, and we analyzed the relationship between clinicopathological factors including age, menstrual status, histology type, prechemotherapy stage, histological grade, chemotherapeutic regimen, molecular biomarkers (Ki-67, p53 and EGFR) and neutrophil/lymphocyte ratio (NLR), and response to NAC. Furthermore, we analyzed the relationship between the response to NAC and disease-free survival (DFS).

Result: Pathologic complete response was observed in 25 (28.7%) patients among 87 patients. Among variables, high expression of Ki-67 and low NLR were significantly associated with pCR in patients with TNBC ($p = 0.002$ and 0.007, respectively); tumors with high expression of Ki-67 ($\geq 15\%$) showed a higher pCR rate than those with low expression of Ki-67 (35.7% vs. 0%), and patients with low NLR (≤ 1.7) had a higher pCR rate to NAC, compared to those with high NLR (42.1% vs. 18.4%). Low NLR remained the only predictive factor for pCR in multivariate analysis (odds ratio = 4.274, $p = 0.008$). On survival analysis, as expected, DFS differed significantly between pCR and non-pCR groups (5-year DFS rate 90% vs. 67.5%, $p = 0.012$).

Conclusions: The NLR of patients with TNBC shows significant association with pCR to NAC, suggesting the association between tumors response to chemotherapy and patients inflammation status.

EVALUATION OF THE CHANGES IN SERUM CHOLESTROL LEVEL DURING FOLLOW UP PERIODS IN BREAST CANCER PATIENTS: CORRELATION WITH CLINICOPATHOLOGICAL PARAMETERS AND SURVIVAL RATE

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Background: The aims of our study were to assess the correlation between serum Cholesterole and clinicopathologic factors and to assess the effect of the changes in serum Cholesterole levels on survival rate.

Methods: The study subjects, 447 women with breast cancer, were a subset of patients operated at Kosin University hospital from January 2000 to December 2010. We used a cutoff of 250 mg/dL to distinguish between high and low serum Cholesterol levels. We also evaluated the changes in serum Cholesterol levels between measures. Clinicopathologic factors were compared with 3 categories of serum Cholesterol level changes. Serum Cholesterol levels changes were divided into 3 groups (up sign, no change, and down sign groups). Clinicopathologic factors were compared with 3 categories of Cholesterol level.

Result: The number of patients with up sign (continuous increased Serum Cholesterol levels), down sign (continous decreased serum Cholesterole levels), and no change groups was 156 (34.8%), 284 (63.5%) and 7 (1.5%) respectively. The univariate analysis for prognostic factors associated with Disease Free Survival rate (DFS) revealed that the type of operation methods, AJCC T-stage, AJCC N-stage, the type of breast cancer, the mutation of p53, the regimens of adjuvant chemotherapy, adjuvant radiatioin therapy, and adjuvant hormonal therapy were statistically significant ($p = 0.0067$, 0.0001, 0.001, 0.0407, 0.0230, 0.0001, 0.0001, and 0.0003 respectively).

Conclusions: According to our study, the upward changes in serum Cholesterol levels were not associated with 5-year DFS.

SYNCHRONOUS OR METACHRONOUS DOUBLE PRIMARY CANCER IN PATIENTS WITH BREAST CANCER

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Background: Double or multiple malignancies in patients with breast cancer are not uncommon. However, the characteristics of synchronous or metachronous breast cancer, which are important for the management of the disease, are not fully understood. This study is designed to compare the characteristics of synchronous or metachronous double primary cancer in patients with breast cancer to those of single primary breast cancer.

Methods: Between January 2005 and May 2013, 335 patients with breast cancer were retrospectively collected from Uijeongbu St. Mary's Hospital. All patients underwent surgery for breast cancer in the same institution. Cases of metastatic breast cancer at diagnosis were excluded. Patients with metachronous cancer were defined as those with a disease-free interval of six months or more at the diagnosis of breast cancer. Second primary cancer was confirmed by histological diagnosis.

Result: Among the 335 patients with breast cancer, 21 (6.26%) patients were diagnosed with double primary cancer. The mean age of patients with double primary cancer was 54.28 ± 12.52 years, which was older than those with single primary cancer. Synchronous and metachronous double primary cancer was discovered in 5 (23.8%) and 16 (76%) patients, respectively. The most common cancer was thyroid cancer. This was followed by colon cancer and gynecologic cancer. Compared with breast cancer alone, subtype and TNM stage were not significantly different. Of the 21 patients with double primary cancer, 5 (23.8%) died. No significant difference in OS was noted between groups.

Conclusions: In this study, synchronous or metachronous double primary cancer was found in 21 of 335 breast cancer patients (6.26%), most commonly in the thyroid gland. Because of the limited sample size, it is difficult to obtain meaningful results. There is no difference in the clinicopathologic features of double primary cancer compared with breast cancer alone.

THE RELATIONSHIP OF SERIAL SERUM HUMAN EPIDERMAL GROWTH FACTOR RECEPTOR-2 (HER2) MEASUREMENT AND DISEASE RECURRENCE IN PRIMARY HER2 NEGATIVE BREAST CANCER PATIENTS

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Background: This study aimed to investigate the relationship between the serial serum human epidermal growth factor receptor-2 (HER2) level and breast cancer recurrence/recurrence aggravation in each patient with primary HER2 negative breast cancer after curative surgery.

Methods: Patients with primary HER2 negative breast cancer underwent curative surgery from 2008 to 2012 were included for this analysis. Of these patients, disease recurrence has been detected in 94 patients during routine follow-up period. Disease recurrence was confirmed by biopsy of the metastatic site or by imaging methods. Serial serum HER2 has been examined from diagnosis to disease recurrence in 39 patients among the patients with disease recurrence.

Result: Serum HER2 level was increased over 15.0 ng/mL at the same time of disease recurrence in five (12.8%) patients who showed normal serum HER2 level at the time of diagnosis. In 8 patients, the level of serum HER2 was serially measured after disease recurrence. In these patients, serum HER2 level has positive linear relationship with tumor burden which was examined by computed tomography (correlation coefficient = 0.522, $p = 0.006$).

Conclusions: Serum HER2 was elevated at the time of disease recurrence during regular follow-up period after curative treatment, and the recurred tumor burden was positively associated with the serum HER2 level in some patients with primary HER2 negative breast cancer.

PREDICTIVE FACTORS OF STABLE OR PROGRESSIVE DISEASE DURING ANTHRACYCLINE WITH/ WITHOUT TAXANE-BASED NEOADJUVANT CHEMOTHERAPY IN BREAST CANCER

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Background: Neoadjuvant chemotherapy (NAC) has been shown to effectively downstage of locally advanced breast cancer, but clinically no response or progression of tumor could be occurs in some cases. Predictive factors of no response or progression are unknown compared to predictive factors of response. We investigated of predictive factors of stable (SD) or progressive disease (PD) during anthracycline with/without taxane based NAC.

Methods: From January 2012 to December 2015, data were collected retrospectively by reviewing medical records of patients who received NAC. Statistical analysis was performed to compare patients with partial response and complete remission with patients with SD or PD after anthracycline or taxane based chemotherapy.

Result: 242 patients received NAC with anthracycline based regimen and 159 patients received anthracycline followed by taxane. 41 (17%) patients had SD or PD after anthracycline, and 50 (31%) patients had SD or PD after taxane. Factors predictive of SD or PD after anthracycline included clinical stage ($p=0.002$), lymphovascular invasion (LVI) ($p=0.011$) and after taxane included clinical T stage ($p=0.001$), clinical N stage ($p=0.042$), LVI ($p=0.001$). SD or PD after taxane was a negative predictor of disease-free survival. And SD or PD after anthracycline or taxane was a negative predictor of overall survival.

Conclusions: Clinical stage, LVI were predictive factors of SD or PD after anthracycline with/without taxane based NAC. We need a combination of predictive factors of clinical data and novel molecular marker to identify patients who reveal no response to standard NAC regimen.

THE ASSOCIATION BETWEEN PATIENT COMORBIDITY AND BREAST CANCER SURVIVAL

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Background: In breast cancer, patient comorbidity can influence the oncologic outcome by affecting the decisions regarding adjuvant treatments. In this study, we examined the long term oncologic outcome in breast cancer patients who underwent curative surgery according to the comorbid conditions.

Methods: The medical records of 2,502 patients who underwent surgery for primary breast cancer from June 2006 to June 2010 were retrospectively reviewed. The patients were classified into three groups (ASA I, II, III) according to preoperative ASA status. Clinico-pathologic characteristics of the patients were compared among the groups by chi-square test. Recurrence free survival and overall survival were analyzed by performing Kaplan-Meier analysis and Cox regression.

Result: The median follow-up period was 71 months. There were 1,792 (71.6%), 666 (26.6%), and 44 (1.8%) patients in ASA I. II, and III. Total 96 (3.8%) deaths and 269 (10.8%) recurrences occurred in follow-up period. With regard to the mortality, patients with high comorbidity showed significantly higher rate of death 51 (2.8%), 38 (5.7%), 6 (13.6%) deaths in ASA I, II and III group, respectively, $p < 0.001$). The ASA III patients also showed significantly higher rate of breast cancer recurrence when compared to other groups (179 (66.5%), 81 (30.1%) and 9 (3.3%) in ASA I, II and III, respectively, $p = 0.034$). Cox multivariate analysis demonstrated that high ASA score was an independent prognostic factor in DFS and OS (95% confidence interval [CI], 1.067-1.839; $p = 0.015$ and 1.250-2.787; $p = 0.002$).

Conclusions: In this study, high comorbidity was related to higher rates of mortality and recurrence in breast cancer patients.

MICRORNAS RELATED WITH RECURRENCE IN DUCTAL CARCINOMA IN SITU AND THEIR CLINICAL SIGNIFICANCE

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Background: Ductal carcinoma in situ (DCIS) is a precursor to invasive cancer and local recurrence rate for women with DCIS is about 15% at 10 years. Clinicopathologic factors such as young age, larger lesion size, high nuclear grade, positive margin status have been associated with an increased risk of local recurrence or progression to invasive cancer. We attempted to find microRNA aberration that may associated with DCIS recurrence.

Methods: We performed miRNA expression profiles via miRNA microarray with paraffin-embedded tissue blocks of 10 DCIS patients with local recurrence and 10 patients without recurrence, along with immunohistochemical staining of ER, PR, HER2, Ki-67.

Result: The miRNA microarray revealed 73 miRNAs were up-regulated and 3 miRNAs were down-regulated by > 1.5-fold in the recurrent DCIS compared with no-recurrent DCIS. Among these altered miRNA, miR-106b cluster (miR-106b-5p, miR-93-5p, miR-25-3p) and miR-17 cluster (miR-17-5p, miR-20a-5p) were all up regulated. These miR-106b and miR-17 clusters are suggested as a key modulators of TGF-beta signaling in many tumors, interfering with cell cycle arrest and apoptosis and leading to tumor cell proliferation. Immunohistochemical staining result of Ki-67 showed higher proliferation labeling index in recurrent DCIS group.

Conclusions: MiR-106b and miR-17 clusters may play a significant role in DCIS recurrence or progression to invasive cancer.

AN OBJECTIVE NODAL STAGING SYSTEM FOR BREAST CANCER PATIENTS UNDERGOING NEOADJUVANT SYSTEMIC TREATMENT

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Background: In this study, we aimed to develop an objective staging system to determine the degree of nodal metastasis in breast cancer patients undergoing neoadjuvant systemic treatment (NST).

Methods: We reviewed the pre-treatment computed tomography (CT) images of 393 breast cancer patients who received NST. The association between the patterns of the enlarged regional lymph nodes and treatment outcome were analyzed.

Result: In the development cohort of 261 patients, the number of lymph nodes larger than 1cm was most significantly associated with the tumor recurrence. The accuracy of the CT-based nodal staging system was validated in an independent cohort of 132 patients. The presence of the enlarged supraclavicular nodes was associated with worse outcome, but the effect seemed to originate from the accompanied extensive axillary nodal burden. The prognostic effect of the objectively measured axillary nodal metastasis was more pronounced in hormone receptor negative tumors.

Conclusions: We have developed and validated an objective method of nodal staging in breast cancer patients who undergo NST based on the number of the enlarged axillary lymph nodes. Our system can improve the current subjective approach using physical examination alone.

EXTREMELY LOW AXILLARY LYMPH NODE COUNT IN AXILLARY DISSECTION IS RELATED TO POOR SURVIVAL IN BREAST CANCER TREATED WITH NEOADJUVANT CHEMOTHERAPY

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Background: Axillary lymph node (ALN) count is known to be lower after neoadjuvant chemotherapy (NAC) compared to primary surgery patients. In this study, we have investigated the clinical significance of ALN count after ALN node dissection in breast cancer patients treated with NAC.

Methods: A total of 427 patients who were treated with NAC between 2006 and 2011 were retrospectively reviewed. All patients were treated with anthracycline and/or taxane-based chemotherapy regimens with a median of 3 cycles and underwent breast surgery along with ALN dissection. The association between ALN count and treatment outcome was analyzed.

Result: The median follow-up duration was 62 months. The median of dissected ALN count was 15 (range 0-52). Patient survival did not differ when dichotomized by median of ALN count. However an ALN count of 5 or lower was significantly associated with a lower disease-free survival (hazard ratio 2.316, $p = 0.008$). This extremely low ALN count (≤ 5) was also an independent prognostic factor when adjusted for clinical stage, grade, subtype, Ki67, yp stage and response to NAC (hazard ratio 2.761, $p = 0.003$).

Conclusions: An extremely low ALN count of 5 or lower is an independent prognostic factor in breast cancer patients treated with NAC, despite of number of involved ALNs and response to NAC. Aggressive adjuvant treatment can be considered in this small group of patients.

THE PROGNOSTIC VALUE OF KI-67 IN BREAST CANCER WITH AXILLARY LYMPH NODE METASTASIS

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Background: The Ki-67 protein, well known cellular marker for proliferation, is closely associated with the growth and invasion of breast cancer without axillary lymph node metastasis. We evaluate prognostic difference according to KI-67 expression in invasive breast cancer with axillary lymph node metastasis.

Methods: Of 307 female patients with positive axillary lymph node who underwent curative surgery followed by standard adjuvant therapies in Hallym Sacred Heart Hospital from 2003 to 2011. We compared disease free survival (DFS) and overall survival (OS) of Ki-67 > 25% group (n = 183) with those of Ki-67 < 25% group (n = 124) using Kaplan-Meier survival curve.

Result: The mean age of all patients was 50.14 (range, 2,385) years and the median follow-up period was 61 months (range 7-137). In the clinicopathological factors between the two groups, patient in Ki-67 > 25% group had more poor-prognostic factors such as histologic grade (96.2% vs. 79.0%), nuclear grade (94.5% vs. 81.5%), hormone receptor (HR) negative (39.9% vs. 26.6%), and p53 positive (67.8% vs. 46.8%). In survival analysis for all patients, there was no significant prognostic difference according to Ki-67, statistically. In subgroup analysis by HR status, however, Ki-67 < 25% group had significant DFS benefit (5-year DFS 93.9% vs. 80.8%). Of 106 HR negative patients, recurrence was related to Ki-67 was only statistically significant factor that was related recurrence in univariate and multivariate analysis.

Conclusions: In this study, Ki-67 was independent prognostic factor for DFS in HR negative group. Therefore, we suggested that Ki-67 might be adequate biomarker to predict prognosis in hormonal receptor negative breast cancer with axillary lymph node metastasis.

PROGNOSTIC FACTOR FOR PARTIAL RESPONDER AND PREDICTIVE VALUE OF LYMPH NODE RATIO IN NEOADJUVANT CHEMOTHERAPY PATIENT

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Background: Neoadjuvant chemotherapy (NAC) results in an improvement in disease free survival and overall survival (OS) similar to that obtained with adjuvant chemotherapy. Pathologic complete response (pCR) has been shown to predict improved survival. However, achieving pCR is a relatively uncommon and, there is no known predictive factor to evaluate OS of patients with partial response, yet. We evaluated the prognostic factor for partial responder. And we also assessed the axillary lymph node ratio (the ratio of the number of positive nodes to the total number of excised nodes, LNR) because LNR has been reported as an independent prognostic factor in adjuvant setting.

Methods: 215 patient who underwent neoadjuvant chemotherapy at Korea University Hospital, Seoul, Korea were eligible for this study. Operation method, histologic type, clinical and pathologic stage, hormone receptor status, HER-2 receptor status, tumor grade, presence of lymphovascular invasion (LVI) and margin status were evaluated as a prognostic factor for survival after NAC. The cut-off range of LNR were divided to low (≤ 0.20, n = 45), intermediate ($2 <$, ≤ 0.65, n = 25) and high (< 0.65, n = 6).

Result: Clinical N stage ($p = 0.02$), overall stage ($p = 0.04$), pathologic N stage ($p = 0.03$), hormone receptor status ($p = 0.01$) and LVI ($p = 0.02$) were significantly associated with the OS. Especially lower cut-off limit 0.20 of LNR, were significant risk factor for disease free survival ($p = 0.01$).

Conclusions: Clinicopathologic factors are still valuable to predict OS. We proved that nodal ratio could be a candidate as prognostic factor in neoadjuvant setting and 0.20 is acceptable lower cut-off value of LNR.

EN1 OVEREXPRESSION AS A POTENTIAL PROGNOSTIC MARKER IN QUINTUPLE-NEGATIVE BREAST CANCER

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Background: Triple-negative breast cancer (TNBC) is down-classified as basal-like breast cancer (BLBC, ER/PR/HER2/CK5/6+ or EGFR+) and quintuple-negative breast cancer (QNBC, ER/PR/HER2/CK5/6/EGFR). TNBC is associated with poorer prognostic outcome than the other subtypes, luminal A and luminal B or HER2 breast cancers, and moreover, no targeted therapy is recently available for TNBC. Therefore, TNBC is a challenging subtype for which identification of prognostic markers and targetable molecules is urgently needed. Interestingly, a recent study has suggested that Engrailed 1, one of neural specific transcription factors, is exclusively overexpressed in BLBC tumors and its overexpression might activate survival pathways. However, the clinical and functional significance of the overexpression of EN1 in breast cancer, and more specifically, in TNBC, is not yet known. Here, we investigated whether EN1 might play specific roles in TNBC by analyzing relationship between EN1 overexpression and patient survival and characterizing functions of EN1 overexpression in TNBC cell lines.

Methods: EN1 protein expression was examined in 843 breast cancer paraffin-embedded tissue samples by immunohistochemistry. EN1 mRNA expression was analyzed using 394 TNBC samples public dataset. The importance of EN1 expression to TNBC viability and migration was evaluated by using TNBC cell lines.

Result: In multivariate analysis, EN1 overexpression was associated with poor disease free survival (DFS) only in QNBC ($p = 0.036$). In QNBC cells, EN1 enhanced cell proliferation and migration. Using microarray analysis, we identified ZIC3 and UPT11L as candidates of EN1 transcription target.

Conclusions: Our findings suggest that EN1 overexpression is a useful prognostic marker and a potential target for therapy in QNBC.

PROGNOSTIC IMPACT OF DEL-1 EXPRESSION IN EARLY BREAST CANCER

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Background: Del-1 on circulating extracellular vesicles was revealed as a promising diagnostic marker for breast cancer in our previous study. In the current study, we examined the prognostic impact of Del-1 expression in tumor cells on prognosis in patients with early breast cancer (EBC).

Methods: We compared Del-1 mRNA levels from breast epithelial cell line (MCF10A) and breast cancer cell lines (MDA-MB-231, MCF7, SK-BR3 and T-47D) performed by real-time PCR. Then, Del-1 expression in breast cancer cells was investigated on the basis of the immunohistochemistry (IHC) of tissue microarray specimens from 417 EBC patients who underwent surgery between 2003 and 2008. We scored staining intensity (0 through 3) and analyzed association of del-1 expression with clinical/pathological characteristics and outcomes in patients with EBC.

Result: Del-1 mRNA was highly expressed in all breast cancer cell lines in particular MDA-MB-231 compared with MCF10A (Fig. 1). A total of 329 (78.9%) patients were identified as del-1 positive, and in particular higher expression rate of del-1 was observed in HER2-positive EBC among TMA specimens (86.9% for HER2-overexpressed vs. 78.6% and 75.6% for hormone responsive and triple negative EBC, respectively; $p = 0.016$). However, no statistical difference in tumor characteristics and clinical outcomes including relapse and death were observed according to tumor expression of Del-1.

Conclusions: Del-1 expression in breast cancer does not seem a prognostic marker for survival in patients with early breast cancer. However, higher expression rate of del-1 in breast cancer cell identified in the current study compared with that of CEA or mammaglobin in previous studies suggests a new diagnostic marker for differential diagnosis of breast cancer involvement.

STUDY OF PREDICTING FACTORS FOR NEOADJUVANT ANTI-HER2 THERAPY RESPONSE IN LOCALLY ADVANCED HER2 POSITIVE BREAST CANCER PATIENTS

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Background: HER2 targeting receptor tyrosine kinase (RTK) inhibitors show clinical efficacy in HER2 positive breast cancer, its use was expanded to neoadjuvant therapy. To lower the treatment failure rate, predicting drug response became more important in each patient. This study aims at identifying new potential biomarker genes and druggable signal pathways with different response to neoadjuvant anti-HER2 therapy.

Methods: We identified 64 women with locally advanced HER2-positive breast cancer who underwent surgical resection after neoadjuvant anti-HER2 systemic therapy at our instituition between July 2005 and January 2014. Genechip microarray was performed with 5 samples collected from NCC Frozen tissue bank. Gene expression data was analyzed using David Bio-informatics Resource Tool and Ingenuity Pathway Analysis (IPA).

Result: Total 732 genes were selected with HER2-positve breast cancer specific related genes. In the pathway analysis results, the function of most commonly and strongly showed 10 pathways were related with cell cycle, mitotic role and cell signaling. We could find the different gene expression levels in PCR and electrophoresis experiments within each group (complete response, partial response and drug resistance).

Conclusions: In our study, our now-established subpathway identification approach is highly effective for accurate pathologic biomarker and pathway discovery. The pathways related cell cycle or cell activity are strongly related with drug response to anti-HER2 therapy.

THE UTILITY OF SCALP COOLING SYSTEM FOR PREVENTION OF HAIR LOSS AND SCALP FOLLICULITIS IN BREAST CANCER PATIENTS RECEIVING CHEMOTHERAPY: A PROSPECTIVE COHORT STUDY

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Background: Hair loss is one of the most common and emotionally distressing side-effects of chemotherapy. Scalp hypothermia to prevent hair loss in breast cancer patients who are treated by chemotherapy is debatable.

Methods: One hundred nine breast cancer patients received chemotherapy were enrolled from February 2013 to October 2015. Photo documentation and patient assessment of discomfort were recorded. The efficacy was assessed as the success in hair preservation, defined as WHO criteria for alopecia grade < 2. The system providing scalp cooling consists of a compact refrigeration unit containing a coolant that is circulated through specially designed cooling caps. As coolant passes through the cap to extract heat from the patients scalp, inline temperature sensors ensure the cap maintains the scalp at a constant temperature.

Result: For adjuvant treatment, 88 patients were treated with anthracycline and cyclophosphamide, 4 patients with docetaxel and cyclophosphamide, and 9 patients with cyclophosphamide, methotrexate and fluorouracil, and for palliative treatment, 12 patients were treated with various regimens. Sixty nine patients (63.3%) stopped using the system before completion of their chemotherapy. Prevention rate of hair loss was 8/25 in AC-treated patients, 1/1 in TC-treated patients, and 6/6 in CMF-treated patients. Incidence of folliculitis of scalp was 2.5%.

Conclusions: Scalp-cooling system was effective and safe to preserve hair loss and prevent folliculitis of scalp in breast cancer patients treated by chemotherapy even though it was not as useful as in western countries. Long term follow-up for scalp metastases and comparison of dermatologic toxicities on scalp between cooling group and reference group are needed.

PO100

EFFECT OF MIND AND BEAUTY EDUCATION ON BODY IMAGE AMONG YOUNG BREAST CANCER PATIENTS: A RANDOMIZED CONTROLLED TRIAL

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Background: Young breast cancer (YBC) patients are more likely to suffer from altered appearance due to cancer treatment. This study is evaluated to the effect of education program on body image among YBC patients.

Methods: We were recruited and randomly assigned to intervention and control group from July 2014 and April 2015 at samsung medical center.Intervention group received a structured 8 hours education (2 hours for 4 weeks, 1 hour for mind control and 1 hour for altered appearance management) and control group had education after outcome evaluation. Body image as primary outcome was assessed using both EORTC QLQ-BR23 and body image scale.Outcomes were evaluated before the intervention, right after the interventionand 3 and 6 months after the intervention. T-test and intention-to-treat analysis performed to compare the outcomes of the two groups.

Result: A total of 54 and 55 patients were assigned to intervention and control group respectively with block randomization. They were 53 (48.6%), 32 (29.3%), 23 (21.1%) stage I, II, and III.While there was no difference with the body image at baseline between intervention (57.69 ± 20.57) and control group (53.09 ± 26.98) ($p = 0.327$),intervention group reported significantly improved body image than control group (EORTC QLQ-BR23 - Intervention; 71.69 ± 20.27 and Control; 55.97 ± 23.07, $p < 0.001$).

Conclusions: This study provided evidence supporting that mind & beauty education program would be beneficial to YBC patients who would suffer from low body image. Active education program and psychosocial support related to altered appearance would help YBC patients to make a smooth transit when they return to usual life.

Poster Exhibition

BODY SIZE AND BREAST CANCER IN CHINESE NORTHERN HAN WOMEN: A CASE-CONTROL STUDY

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Background: Even obesity has been accused to predispose to breast cancer, there are still some inconsistencies regarding the association between obesity and breast cancer.

Methods: To better understand the characteristics and risk factors for breast cancer in Chinese Northern Han women, we conducted a case-control study of 2,800 Chinese Han female participants and analyzed association between ascending BMI ranges and breast cancer risk in different status.

Result: Factors related to body size was confirmed to be associated with an increased risk for breast cancer, resulting in a phased association. Women with breast cancer, especially premenopausal ones, manifested higher body mass index (BMI), longer waist and hip circumference. However, these body size factors were identified not associated with postmenopausal breast cancer. Meanwhile, high level BMI were identified related to breast cancer among both overall and premenopausal individuals, but not in postmenopausal group. In multivariate conditional logistic regression, we found waist circumference, number of births and positive family history, but not BMI significantly associated with female breast cancer in Chinese Han individuals. However, the inconsistent between our finding among Chinese Northern Han women and other population previously reported might be resulted from the substantial environmental and genetic difference between ethnic and regions.

Conclusions: In summary, it is important to realize that the body weight control and avoiding abdominal obesity should be considered as one of the most effective methods to reduce the breast cancer susceptibility.

EXPERIENCE OF BREAST CANCER AWARENESS IN RURAL POPULATION IN NON ACADEMIC TERTIARY CARE CENTRE IN RURAL INDIA

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Background: Breast cancer is potentially curable disease if detected early. The rural population is certainly less targeted and deprived of facilities. The rural population still have social stigma regarding breast cancer. Kailash Cancer Hospital is nonprofit trust organization in rural INDIA providing higher end care to rural populations. Most of the breast cancer patients were advanced stage disease. We planned to make them aware with different methods and assess the results.

Methods: Patients diagnosed with breast cancer (except stage IV) are included in this review from January 2013 to December 2015. They were divided in stage at the time of diagnosis, treatment given & regularity in follow up to see the effect of awareness started in January 2013.

Result: Total 416 new patients of non metastatic breast cancer identified in the duration. In 2013, 2014, 2015 patients identified with breast cancer were 98, 114, 204. stage I , II, III in 2013 were 7%, 25%, 69%, In 2014 15%, 38%, 68%. In 2015 33%, 39%, 28%. Breast conservation increased from 2% to 7% to 23% in consecutive years. Regularity in follow up- 30% to 53% to 78%.

Conclusions: Rural population really requires awareness of breast cancer and facility in nearby area. Being in rural area this institute serves to rural population. By educating rural population, there is drastic improvement in early stage diagnosis, more patients are offered advanced treatments like breast conservation and reconstruction. Patients become more regular in follow up. All these leads to better survival in same population.

BASELINE KNOWLEDGE AND ATTITUDES TOWARDS GENETIC TESTING AMONG HONG KONG CHINESE FEMALES UNDERTAKING GENETIC COUNSELLING AND TESTING FOR HEREDITARY BREAST AND OVARIAN CANCERS

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Background: Genetic testing of hereditary breast and ovarian cancer syndromes (HBOC) has become standard of care for high-risk patients and their family members. It facilitates more precise risk estimations, guide surveillance regimes, and prophylactic procedures. This study focused on the baseline knowledge and attitudes affecting decisions on undertaking genetic counselling and testing of HBOC among Southern Chinese females residing in Hong Kong.

Methods: Eligible at-risk Hong Kong Chinese females were offered genetic counselling and testing service sponsored by Hong Kong Hereditary Breast Cancer Family Registry. They were surveyed by a face-to-face interview at a multi-disciplinary breast clinic right before their pre-testing genetic counselling consultation. Socio-demographic information, medical history, pre-testing knowledge, and attitudes towards HBOC were acquired.

Result: 142 females (88.7% with cancer history) were recruited. Better pre-testing baseline knowledge on HBOC was significantly associated with higher educational level ($p < 0.001$) and younger age ($p < 0.001$). Before going through genetic counselling process, the majority (69.7%) could not identify the specific genes related to HBOC. Over half of them (55.7%) were either unsure of or misunderstood that one's gender and physical appearance resemblance to the gene-carrier would increase the chance of inheritance of the mutated gene.

Conclusions: Results showed that high risk Hong Kong Chinese females with cancer history, higher educational level, and younger age had better pre-testing baseline knowledge of HBOC. Proper genetic counselling is a crucial process to improve knowledge and clarify concepts especially for older and less well-educated at risk females. Public educational programmes will help to improve the awareness and knowledge of HBOC.

IDENTIFICATION OF A NEW GERMLINE MUTATION, RECQL, IN HEREDITARY CHINESE BREAST CANCER PATIENTS

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Background: BRCA mutations attributed to only 20-25% of hereditary breast cancer, implicated other gene mutations are yet to be determined. With the advances in sequencing technology, other penetrance genes (TP53, PTEN, CDH1, ATM, CHEK2, PALB2, RAD50) have also been identified to be associated with breast cancer and the prevalence of these mutations varies across ethnicity. RECQL, associated with genomic stability, has been recently been identified as a new breast cancer susceptibility gene. However, the genetic changes in Chinese population are still unknown.

Methods: High-risk breast cancer patients who were underwent genetic test for BRCA1 and BRCA2, TP53 and PTEN were selected from the Hong Kong Hereditary Breast Cancer Family Registry. In the study, 1,114 patients who tested negative and 88 population-matched controls were performed RECQL full gene sequencing using targeted next generation sequencing by Miseq platform. All detected mutations were further validated by bi-directional DNA sequencing. The analysis of sequencing data were carried out by our in-house developed bioinformatics pipeline including BWA-MEM and variant callers, SAMtools and GATK.

Result: One of the mutations, RECQL c.796C>T was identified in two unrelated families. 3 out of 6 mutations (50%) affect the splice donor consensus sequence and RECQL c.974_977delAAGA is a small deletion. Overall, the prevalence of RECQL is 0.5% in Chinese population.

Conclusions: Among the mutation negative cases, 0.5% of the cases were RECQL carriers, which is comparable to the detection rate of TP53 in the same cohort. Further validation in larger cohort is warranted to examine the prevalence and penetrance of RECQL in Chinese population.

PO105

CLINICAL ANALYSIS OF BRCA1/BRCA2 FOR JAPANESE BREAST CANCER PATIENTS: THE JAPANESE FOUNDER MUTATION OF BRCA1 THE L63X

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Background: Founder mutations of Hereditary breast and ovarian cancer syndrome (HBOC) have been reported in each country. However, there are few reports of founder mutation of HBOC on breast cancer in the Japanese population. In this study, we report the breast cancer clinical characteristics of L63X, which is one of the founder mutations in BRCA1 in the Japanese population.

Methods: Data on 304 affected breast cancer patients (36 BRCA1 carriers, 26 BRCA2 carriers, 15 variants of uncertain and 227 non-carriers) were collected at Showa University in Tokyo from September 2010 to December 2015. In 21 independent mutations of BRCA1, the L63X mutation was detected in ten patients. Data regarding the age of breast cancer onset, pathological features, clinical features, and family history of cancer (breast, ovary, pancreas, prostate, gastric, colon) were collected.

Result: There was no significant difference in the age of breast cancer onset, pathological features, clinical features, and family history of cancer, except that L63X carriers had a higher tendency to have a family history of breast cancers than did the carriers of the other BRCA1 mutations .

Conclusions: L63X mutations have been reported to originate in the Eastern part of Japan. The breast cancer clinical characteristics of L63X might be considered no different from those seen in other types of BRCA1 mutations, except for a family history of breast cancer. L63X mutation is located in the breast cancer cluster region in BRCA1. Further investigation is necessary for appropriate validation and accumulation of data.

PO106

IDENTIFICATION OF GERMLINE ALTERATIONS IN BREAST CANCER PREDISPOSITION GENES AMONG MALAYSIAN BREAST CANCER PATIENTS USING PANEL TESTING

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Background: Although an association between protein-truncating variants and breast cancer risk has been established for 11 genes, only alterations in BRCA1, BRCA2, TP53 and PALB2 have been reported in Asian populations. Given that the age of onset of breast cancer is lower in Asians, it is estimated that inherited predisposition to breast cancer may be more significant. To determine the potential utility of panel testing for the identification of women with inherited predisposition to breast cancer in Asian women from Malaysia, we investigated the prevalence of germline alterations in 11 established and 4 likely breast cancer genes in a cross-sectional hospital based cohort of breast cancer patients.

Methods: 108 moderate to high risk breast cancer patients were included in this study and germline DNA was sequenced to identify mutations using targeted next generation sequencing.

Result: Twenty patients (19%) were identified to carry deleterious mutations, of whom thirteen (12%) were in the BRCA1 or BRCA2, six (6%) were in 5 other known breast cancer predisposition genes and one patient had a mutation in both BRCA2 and BARD1. Notably, the majority of the deleterious mutation carriers have family history of breast cancer within their families.

Conclusions: Our study shows that BRCA1 and BRCA2 account for the majority of genetic predisposition to breast cancer in our cohort of Asian women. Although mutations in other known breast cancer genes are found, the functional significance and breast cancer risk have not yet been determined, thus limiting the clinical utility of panel testing in Asian populations.

BARRIERS AND MOTIVATORS FOR THE COMMUNICATION OF GENETIC INFORMATION BY BRCA CARRIERS TO THEIR RELATIVES IN MALAYSIA

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Background: BRCA carriers are encouraged to disclose their BRCA status and of the availability of genetic testing to their relatives to ensure that the appropriate risk management strategies are taken. In this study, we looked at communication patterns among families with known BRCA mutations and addressed barriers and motivators which may influence genetic testing uptake among these families.

Methods: A total of 38 BRCA carriers were recruited into the study and had undergone genetic counselling and results disclosure. A survey was administered to gather information about whom the BRCA carriers disclosed their test results to and their reasons for disclosing or not.

Result: Around 94.7% of those surveyed diclosed results to at least one at-risk relative. Disclosure to first degree relatives were higher (72.0%) compared to both second (16.1%) and third degree relatives (16.4%). Genetic testing uptake rates were highest in first degree female relatives (39.8%) compared to first degree male relatives (14.1%) or second and third degree relatives (30.6% and 12.3% respectively). Main motivator for results disclosure were the belief that the information may benefit relatives regarding their cancer risk (84.2%) whereas main barrier encountered were mainly due to poor relationship with relatives (47.4%).

Conclusions: Our study shows that there is a high rate of disclosure among first degree relatives but it is low among second and third degree relatives. Furthermore, genetic testing uptake was higher in female relatives compared to males. More research is necessary to aid in the communication of genetic information to relatives in order to increase genetic testing uptake.

PREVALENCE AND PROGNOSIS OF MUTATIONS OF BRCA AND GENES OF HOMOLOGOUS RECOMBINATION IN PATIENTS WITH TRIPLE-NEGATIVE BREAST CANCER

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Background: Mutational prevalence of BRCA and other genes of homologous recombination (HR) among Asian women with triple-negative breast cancer (TNBC) is not clear, and the prognostic value of these mutations needs to be determined.

Methods: Patients diagnosed as stage I-III TNBC between 2001 and 2013 were enrolled. DNA was extracted from tumor specimen and HR genes were sequenced by next-generation sequencing.

Result: A total of 105 patients were analyzed and 17 (16.2%) were found to carry somatic mutations of HR genes, including 6 in BRCA1, 4 in BRCA2, 1 in BRAD1, 1 in FANCA, 2 in FANCB, 1 in PALB2 and 2 in RAD51D. Among the 17 patients, clinical characteristics of age, family breast cancer history, tumor grade and stage were not associated with mutation status. However, 10 patients with BRCA mutation have a significant family history (Wt vs. Mut, 16.8% vs. 60.0%, $p = 0.001$) and early stage ($p = 0.026$). At a median follow-up of 46 months, the recurrence-free survival (RFS) of these 17 patients or the 10 BRCA mutation cases was similar to non-mutation patients. Adjusting for age, tumor grade and stage, mutation of HR genes (hazard ratio: 0.527, 95% CI 0.151-1.833) and BRCA (hazard ratio: 0.347, 95% CI 0.072-1.672) were not an independent predictor of RFS.

Conclusions: Mutational prevalence of HR genes in TNBC was 16.2% and these patients have a similar RFS to those without mutation. Women with BRCA or HR-mutation-related breast cancer may benefit from DNA-damaging therapies and further study is needed.

ESTIMATED NUMBER OF KOREAN WOMEN WHO COULD BENEFIT FROM TAMOXIFEN OR RALOXIFENE FOR BREAST CANCER CHEMOPREVENTION: DATA FROM THE KOREA NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY

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Background: According to the NSABP-P1 and P2 studies, tamoxifen and raloxifene can protect about 50% of breast cancer. These chemopreventive agents were approved for women with a 5-year breast cancer risk of 1.67% or higher. However, they were associated with adverse events, and not all eligible women have a positive risk-benefit index. So we estimated the numbers of Korean women who could benefit from tamoxifen or raloxifene using the data from the Korea National Health and Nutrition Examination Survey (K-NHANES).

Methods: We used data of third K-NHANES conducted in 2005. We collected the risk factors of breast cancer and calculated 5-year breast cancer risk of individuals using Korean breast cancer risk assessment model. We calculated an expected number of breast cancer by each individuals sample weights. The numbers of Korean women who have a 5-year risk of 1.67% or higher and who have a positive risk-benefit index with tamoxifen or raloxifene chemoprevention.

Result: Of the 11,821,465 women aged 35-79 years, only 447,174 women (3.8%) had 5-year risk of 1.67% or higher. Most of them were premenopausal women under the age of 50. 2,605,457 women (22.0%) would have a positive risk-benefit index for tamoxifen chemoprevention and 184,670 women (1.6%) would have a positive risk-benefit index for raloxifene chemoprevention.

Conclusions: A small percentage of Korean women would be eligible for chemoprevention according to criteria of 1.67% because of relatively low risks of breast cancer for Koreans. A substantial percentage would have an estimated net benefit by tamoxifen chemoprevention but rarely by raloxifene chemoprevention.

DETECTION RATE, PREVALENCE RATE AND SOJOURN TIME OF MAMMOGRAPHY FOR BREAST CANCER IN THAI WOMEN

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Background: A recent guideline by the American Cancer Society recommended that mammography (MMGs) should be done for women in their 40s. In Thailand, information on the opportunistic mammography screening is limited. The incidence of breast cancer was also lacking. The purpose of the study was to estimate the breast cancer detection rate, prevalence rate and mean sojourn time among Thai women.

Methods: We prospectively enrolled normal women age of 30-80 years that underwent opportunistic mammography screening between 2001 and 2010. All women were followed until 2012. The detection rate and prevalence were calculated. Markov models method was used to calculate mean sojourn time.

Result: Of the 47,430 women, there were 152,091 mammography or approximately 3.2 occasions per person (range 1-10). An average duration of the interval between each subsequence visit was 1.8 years. Overall, breast cancer was detected in 543 women, with a detection rate of 11.83 per 1,000 persons. The prevalence of breast cancer at the first visit was 5.78 per 1,000 persons. The incidence or new cases detected at any follow-up visits was 10.36 per 1,000 persons. The mean sojourn time is 4.50 years, 5.46 years and 8.03 years in age between 40 to 49 years, 50 to 59 years and 60 to 69 years, respectively.

Conclusions: Opportunistic mammography screening in Thailand detected a case of breast cancer from every a hundred women. Apart from sojourn time, interval cancer time and sensitivity should be considered for decision on how often screening mammogram should be done.

AUDIT SCREENING BREAST IMAGING EXAMINATIONS IN A SINGLE DEDICATED BREAST CENTRE: WHAT DOES THE MEDICAL AUDIT CONTRIBUTE?

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Background: Breast cancer is the most common cancer in Thai women with incidence rate of 28.5/100,000 in 2012. Modern cancer care demands quality assurance (QA), statistic information and collaboration. Medical audit or auditing breast imaging examinations is the key of QA for breast cancer screening and collaboration. Our centre has done the medical audit regularly every 2-3 years since 2001, we found that it contribute not only performance indicators, but answer many questions.

Methods: We performed the medical audit of screening breast imaging examinations 52,839 out of 68,645 and 47,758 out of 57,587 exams (mammogram with/without breast ultrasound) during 2008-2010 and 2010-2012 (2 phases). Performance indicators including the percentage of DCIS, minimal cancer, false negative rate, true interval cancer were analysed.

Result: During 2008-10 and 2011-12, the detected cancers were 192 and 227 cases respectively. The performance indicators were; CDR = 3.6 and 3.8, PPV2 = 15.7 and 20.6, sensitivity = 75.9 and 79.7, specificity = 98.0 and 98.5 respectively. The percentage of DCIS were 26.7, 30.1 and minimal cancer were 49.0, 46.5 respectively. These key indicators and detected-cancer histopathology by age group will also be shown. The false negative rates were 24.1% and 19.9% respectively. Among false negative cases, the true interval cancers were 49.5% and 44.4% respectively. The analysis of histopathology of true interval cancer by age group will be discussed.

Conclusions: Regular medical audit contributes information to fight against breast cancer. Knowing of performance indicators of each facility will provide information for local and national knowledge.

PO112

GENOME-WIDE ASSOCIATION STUDY OF BREAST CANCER IN MALAYSIAN AND SINGAPOREAN WOMEN

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Background: Identifying the underlying genetic risk factors of breast cancer may unveil the relevant mechanisms responsible for risk and enable risk stratification. To date, approximately 94 breast cancer susceptibility loci have been identified. A large fraction of these have been through genome-wide association studies (GWAS) in predominantly women of European ancestry. We sought to validate previously identified genetic variants in Chinese, Malay and Indian women living in Malaysia and Singapore.

Methods: As part of the Breast Cancer Association Consortium (BCAC), a total of 1,303 cases and 1,104 controls were genotyped using the iCOGS array with ~220,000 SNPs while 1,740 cases and 1,962 controls were genotyped on the OncoArray with ~600,000 SNPs. We used logistic regression models to investigate the association between SNPs and breast cancer risk. We will also perform a meta-analysis of the iCOGS and OncoArray GWA results using METAL.

Result: We compared our findings with known breast cancer susceptibility variants and found significant associations ($p < 5 \times 10^{-6}$) for two out of 72 SNPs that could be evaluated from the iCOGS data. Both SNPs, rs2046210 and rs3803662, were first identified as risk loci in East Asian women and were subsequently replicated in European women. Results from the OncoArray data and meta-analysis will also be presented.

Poster Exhibition

Conclusions: We confirmed the association of variants in ESR1 and TOX3/CASC16 with breast cancer risk for Asian women. The tagging SNPs of causal variants may be different across different populations. Therefore, additional GWAS in Asian women would be necessary to identify other genetic factors associated with breast cancer risk.

PO113

QUALITY INDICATORS AVAILABLE FOR QUALITY ASSURANCE OF BREAST CANCER CARE BASED ON NATIONAL CLINICAL DATABASE BREAST CANCER REGISTRY IN JAPAN

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Background: Clinical practice guidelines were published by the Japanese Breast Cancer Society (JBCS) in Japan. It is necessary to develop indicators for evaluating the quality of medical care and to measure disparities in breast cancer care following the clinical practice guidelines.

Methods: Development of Quality Indicators (QIs) The experts of JBCS have developed the QIs with grade A recommendations in the JBCS guideline published in 2010. For each of them, it has been identified: definition and calculation formula from the database. We performed feasibility study among 7 panel breast care facilities to evaluate validity of these QIs based on National Clinical Database Breast Cancer Registry (NCD-BCR). NCD-BCR in Japan was developed by JBCS. More than 50 items on the demographic, clinical and pathological factors of newly-diagnosed primary breast cancer patients were voluntarily registered to the JBCS through the Web-based system. More than 70,000 cases per year were registered to NCD-BCR.

Result: In overall 15 main QIs have been identified, respectively, 3 on diagnosis, 6 on surgery and loco-regional treatment, 4 on systemic treatment and 2 on staging or counselling. As a results of feasibility study, the implementation rate were considered almost satisfactory.

Conclusions: We are planning to feed back the implementation rate of each QI timely to registration facilities through the Web-based system, it is expected that each facilities's quality improvement will be accomplished in the future.

PO114

IMMUNOGLOBULIN G4-RELATED DISEASE

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Immunoglobulin G4-related disease (IgG4-RD) is a recently recognized disease entity characterized histopathologically by an IgG4-positive lymphoplasmacytic tissue infiltrate, storiform fibrosis, and, often but not always, elevated serum IgG4 concentrations. The pathogenesis of IgG4-RD is still uncertain, raising the possibility of it being autoimmune or allergic. It involves multiorgan and is rarely seen in the breast. We report here on a case of Ig G4-RD in the breast, along with a review of the literature.

PO115

A CASE OF BREAST SPARGANOSIS

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Background: Sparganosis is an uncommon parasitic infection caused by the plerocercoid larva of tapeworms belonging to the genus Spirometra. The common site of infection in humans was abdomen wall and viscera, urogenital organs, extremities, central nervous system, chest, orbital region, neck and oral cavity. Breast is a rare site of infection, less than 2% of all case. We report a case of sparganosis that were confirmed by the surgical removal of worms from the right breast

Methods: Our patient presented with a palpable right breast lump before 4-5 months. There was vague discomfort in her right breast, no nipple discharge and no systemic symptoms. Recently, she described an itching sensation at the site.

Result: Mammography and ultrasonography imaging findings for our patient were characteristic of sparganosis. She underwent wide excision of the entire mass. During the dissection, 4 tapeworms were visually identified. Microscopic pathology confirmed a diagnosis of sparganosis with foreign body reaction including granulomatous inflammation with multinucleated giant cells.

Conclusions: We report a 1 case of breast sparganosis that were confirmed by complete surgical excision. Sparganosis of the breast is an uncommon parasitic infection. When examining the migrating palpable breast mass, we should be considered in the possibility of breast sparganosis. Complete surgical excision is the treatment of choice and confirmative diagnosis. Sparganum can undergo migration in anywhere in the body such as abdominal wall, lung, and extremity. A thorough inspection should be required to find the possibility of simultaneous involvement of other site.

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PO116

A PROSPECTIVE RANDOMIZED CONTROLLED TRIAL OF EVONAIL SOLUTION FOR PREVENTION OR TREATMENT OF ONYCHOLYSIS IN BREAST CANCER PATIENTS WHO RECEIVED NEOADJUVANT/ADJUVANT DOCETAXEL CHEMOTHERAPY

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Background: Onycholysis and other nail toxicities occur in approximately 20-30% of breast cancer patients receiving docetaxel chemotherapy. Onycholysis, the separation of the nail plate from nail bed, is also often associated with painful paronychia decreasing patients' quality of life.

Methods: We aimed to determine the efficacy and safety of a hydrating nail solution, EVONAIL (Evaux Laboratories, France) for the prevention and treatment of docetaxel-induced onycholysis and nail toxicities.

Result: This study is a prospective randomized controlled study of EVONAIL solution for prevention or treatment of onycholysis in patients with breast cancer receiving docetaxel chemotherapy. Breast cancer patients treated with 3-weekly docetaxel in adjuvant or neoadjuvant setting could be included. We randomly assigned patients in a 1:1 ratio to receive EVONAIL solution or not. In experimental arm, each patient painted EVONAIL solution on nails and periungual areas once a day till developing onycholysis grade 2 or more. After Gr 2 onycholysis development, patients painted EVONAIL solution twice a day regardless of treatment arms. The primary endpoint is the incidence of onycholysis Gr 2 or more and the secondary endpoints include: the incidence of all grade onycholysis; duration from first docetaxel treatment until onycholysis symptom appearance; degree of pain from nail toxicities; the incidence of other nail toxicities. According to previous research, 15% of patients treated with docetaxel underwent onycholysis Gr2 or more.

Conclusions: Based on the assumption that EVONAIL solution reduces onycholysis by 7%, a 10% two-sided significance level, and 80% power, 100 subjects will be required. Patient enrollment started in August 2015, and is currently ongoing (ClinicalTrials.gov number,NCT02670603).

PO117

FIBROADENOMA OF ECTOPIC UPPER ARM BREAST TISSUE RESEMBLING EPIDERMAL CYST

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Background: Accessory breasts are remnant of embryonic mammary tissue and are usually found within the milk line, but may occur in the sternum, infraclavicular or epigastric areas as ectopic breast tissue. The full spectrum of extra parts, from nipples to fully formed breasts, is wide-ranging. The axilla is the most common site, accounting for approximately 60-70% of accessory breasts. Because of a fibroadenoma of ectopic breast tissue is quiet rare, I report a case of fibroadenoma in axillary breast tissue.

Methods: A 42-year-old married woman with no remarkable medical history arrived at our institution with left axillary tender nodule one day ago (1st time). She had no risk factors for breast cancer and family history of cancer. Physical examination revealed a hard, well-capsulated and oval shape skin nodule that looks like an epidermal cyst. The nodule located on not axillary area but medial side of upper arm. Mammogram showed accessory breast tissue on right axillary area but, no specific finding on left axillary area. Sonography revealed a solitary, well circumscribed, 1.1 cm size hypoechoic mass on proximal humeral area and axillary portion is normal.

Result: Excisional biopsy performed on left arm nodule. The pathological diagnosis was a fibroadenoma arising in accessory breast ($1.5 \times 1.2 \times 1.0$ cm).

Conclusions: Fibroadenoma of ectopic breast tissue is quiet rare, but should always be kept in mind for differential diagnosis of a milk line mass. Also, Breast surgeons should do their best for accurate should do our best for accurate radiologic study without prejudice.

PO118

GOING WITH MINORITY: 1 CASE OF ABNORMAL LUMINAL A BREAST CANCER

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Background: Generally speaking, Luminal A breast cancer is not sensitive to chemotherapy, it is more likely sensitive to endocrine therapy. Here we report a case of abnormal Luminal A breast cancer.

Methods: In July 12, 2012, a 48-year old woman was diagnosed with breast cancer, T3N0M0, ER (++80%), PR (++65%), Ki67 (5%), Her-2 (-). Neoadjuvant chemotherapy regimen TAC 4 cycles later , the outcome of therapeutic efficiency was SD, then regimen NP 4 cycles later, the outcome of therapeutic efficiency was CR .then modified radical mastectomy, radiotherapy and endocrine therapy (TAM) was given in senquence. In September 7, 2013, the patient came back because of 4 nodules on chest wall, breast cancer recurrence was confirmed by biopsy of one of the nodules. IHC result: ER (++80%), PR (++70%), Ki67 (10%), Her-2 (-). Letrzole was given, three months later, the outcome of therapeutic efficiency was PD, then regimen NP 4 cycles later, the nodules disappeared. Exemstane was given, three months later, the outcome of therapeutic efficiency was PD, then regimen NP 4 cycles later, the nodules disappeared again.

Result: Since Fulvestrant 500 mg was given. up to now, it has been 25 months, the chest wall is clear.

Conclusions: We should follow the treatment guideline, but we do not have to stick to it. For Luminal A breast cancer, it may not be sensitive to TAC chemotherapy, it may be sensitive to NP chemotherapy; it is may not be sensitive to TAM or AIs, it may be sensitive to Fulvestrant. More patience of doctor, more chance for patient.

PLACE OF DEATH IN FEMALE BREAST CANCER DECEDENTS IN KOREA, 2001-2013: A SHIFT FROM HOUSE TO HOSPITAL

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Background: Proportion of death by places of occurrence is one of the key performance indicators for end-of-life care. This study aimed to describe patterns in places of death and evaluate associated factors in female breast cancer decedents in Korea during 2001-2013.

Methods: Data was obtained from death registration database collected by Korean National Statistical Office and extracted decedents who died of breast cancer (ICD-10 code C50). Time trends in proportions of places of death (House and Hospital) were analyzed. Logistic regression was used to evaluate factors associated with decedents place of death (hospital vs. house deaths). Covariates included are age, residential area, education level and marital status.

Result: 21,706 breast cancer deaths were included. Hospital was the most common place of death (84.26%), followed by house (11.49%). Deaths in social welfare facilities were rare (1.02%). There was an increase in hospital deaths (70.25% in 2001 to 92.04% in 2013, $p < 0.001$), with a subsequent decrease in house deaths (24.62% in 2001 to 6.07% in 2013, $p < 0.001$). Hospital deaths were more likely for younger patients (OR 2.24, 2.05-2.44), living in more affluent area (OR of capital area 2.31, 2.00-2.67) or with higher education level (OR of university/college 3.94, 3.36-4.63). However, impacts of associated factors on the probability of dying in hospital had a tendency to decline throughout the period.

Conclusions: The trend towards increasing hospital deaths has been consecutive over the period. Considering this pattern, as well as the aging population in Korea, support for end-of-life care in hospital for breast cancer patients is more essential.

PO120

INCIDENCE AND PROGNOSIS OF TRIPLE NEGATIVE BREAST CANCER (TNBC) AMONG DIFFERENT RACES IN SINGAPORE

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Background: This study aims to determine the incidence of triple negative breast cancer (TNBC) in Singapore, to compare TNBC among the different races and to determine its associated risk factors for prognosis.

Methods: Patients with invasive breast cancer were obtained from the database of KK Womens and Childrens Hospital from 2005 to 2013 and were divided into subtypes. Demographic and clinical information were obtained and analyzed. Log-rank test, univariate and multivariate Cox proportional hazard regression models were used to find associated risk factors related with overall survival (OS) and recurrence-free survival (RFS).

Result: Among 1,227 patients, 129 (10.5%), 822 (67.0%), 160 (13.0%), and 116 (9.5%) were triple negative, luminal A, luminal B and Her2 positive respectively. There were 963 (78.5%) Chinese, 117 (9.5%) Malay and 73 (5.9%) Indian patients. Kaplan-Meier graphs indicate that TNBC patients have the worst OS (p-value 0.0005) and RFS (p-value 0.0042). Malays have the worst RFS (p-value 0.0132) and OS (p-value 0.0389). However, race does not affect OS (p-value 0.8029) or RFS (p-value 0.9048) in patients with TNBC. Multivariate and univariate analysis of TNBC patients shows that increasing tumor size, T3 tumor stage, N3 nodal stage, ductal histology, presence of Paget's disease, and presence of lymphovascular invasion are associated risk factors for worse RFS. Ductal histology, larger tumor size, presence of lymphovascular invasion, and N2 or N3 nodal stages were associated with worse OS while patients who had chemotherapy had better OS.

Conclusions: Overall, OS and RFS differ between races in breast cancer patients however race does not affect prognosis in TNBC.

Poster Exhibition

PO121

SCREENING UPTAKE DIFFERENCES NOT IMPLICATED IN POORER BREAST CANCER OUTCOMES AMONGST SINGAPOREAN MALAYS

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Background: Breast cancer is the most common cancer amongst Singaporean women. We want to determine if screening accounts for differences in outcomes.

Methods: 7,379 patients treated at the National Cancer Centre Singapore 1976 to 2014 were analysed.

Result: Median age at diagnosis for Malays is 49 years, Chinese 51 and Indian 52 years ($p < 0.001$). Malays had higher staged and higher grade tumours. More Chinese and Indians presented with screening mammograms than Malays. For OS, compared to the Chinese, the hazard ratio (HR) for Malays is 1.44 (95% CI 1.16 1.79) and for Indians 1.01 (95% CI 0.73-1.39). For DFS, the HR for Malays is 1.17 (95% CI 0.97-1.42) and for Indians 0.80 (95% CI 0.59-1.09). For CSS, the HR for Malays is 1.49 (95% CI 1.15-1.95) and Indians 1.06 (95% CI 0.71-1.58). Using a multivariate model incorporating ethnicity, age, T-stage, number of positive nodes, hormone sensitivity and differentiation, ethnicity remains significant. Among subjects who presented with mammograms, compared to the Chinese, the OS HR for Malay is 5.78 (95% CI 2.64-12.64) for radiological presentation, the Indians HR was not significantly different. For DFS, the HR for Malays is 2.18 (95% CI 1.19-3.99) and Indians 2.07 (95% CI 1.06-4.03). For CSS, the HR for Malays is 5.93 (95% CI 2-15-16.39) and Indians 1.87 (95% CI 0.51-6.86).

Conclusions: After accounting for age, stage and histology subtypes, and breast screening uptake differences, ethnicity remains significant for survival outcomes.

PO122

CLINICAL AND PATHOLOGICAL LANDSCAPE OF ELDERLY BREAST CANCER PATIENTS IN SINGAPORE AND CORRESPONDING TREATMENT PATTERNS

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Background: The number of elderly breast cancer patients is rapidly increasing with aging population in Singapore. Limited age-related breast cancer characteristics and controversy in treatment options for this subgroup promotes this investigation.

Methods: Retrospective review of 863 patients female elderly breast cancer patients with age over 70 years old treated in Singapore General Hospital and National Cancer Center Singapore between 1996 to 2015 with three subgroups with 70-74 (n = 460), 75-79 (n = 240) and over 80 (n = 163) years old are established. Comparisons were performed using Fisher exact tests.

Result: The number of elderly breast cancer cases in 2014 is ten times more than 2000 in Singapore (118 vs. 18, $p < 0.001$). Compared to patients in other subgroups, patients over 80 years old present with larger tumor size ($p = 0.002$) with better differentiated tumor type ($p = 0.028$). TNM stage among three subgroups were not significantly different ($p = 0.848$). The ratio of patients over 80 years old without surgery is significantly higher than other subgroups ($p < 0.001$). For DCIS, patient over 80 years old more frequently underwent breast-conserving surgery than mastectomy ($p = 0.002$). For IDC, patient with 75-79 and over 80 years old were more likely to choose mastectomy and underwent less aggressive following adjuvant therapies, 47% breast cancer patients over 80 years old received surgery only ($p = 0.009$).

Conclusions: Patients over 80 years presents with larger tumor size and received less aggressive treatments compared to the younger population in Singapore. Active surveillance and age-specific treatments should be considered.

CLINICAL PATHOLOGIC CHARACTERISTICS OF MUCINOUS BREAST CANCER: A RETROSPECTIVE ANALYSIS OF 10-YEAR STUDY

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Background: Mucinous breast carcinoma (MC) is a special type of breast cancer comprising approximately 4% of all invasive breast cancers. In this study, we aimed to report the last 10-year experience of the Zhejiang Cancer Hospital in China regarding mucinous breast carcinoma with its clinical data, histological and immunohisto-chemical particularities.

Methods: All patients were divided into three groups: patial mixed mucinous breast carcinoma (pMMC) was defined as less than 50% mucinous component; main mixed mucinous breast carcinoma (mMMC) was defined as mucinous component accounted from 50% to 90%; Pure Mucinous Breast Carcinoma (PMC) was defined as mucinous component accounted more than 90%. We evaluated the clinical characteristics of breast cancer patients using t-tests and chi-square tests.

Result: We identified 48 cases diagnosed PMC, 58 cases with pMMC and 19 cases with mMMC). The tumor size was larger in mMMC than PMC (44.84 mm vs. 30.06 mm, $p = 0.031$). The pMMC group had more III-IV stages patients than the other groups ($p = 0.005$). The LN+ was more frequent in pMMC either than mMMC and PMC (50% vs. 31.58% and 18.75%, $p = 0.003$). PMC had much less P53 expression than other two groups (27.08% vs. 55.17% and 57.89%, $p = 0.007$).

Conclusions: Based on this study, we can conclude that LN+, higher clinical stages, P53 mutations were presented more often in Mixed Mucinous Breast Carcinoma (MMC) patients than in PMC patients. The amount of mucinous component in MMC patients should be considered in diagnosis.

PO124

TUMOR SUPPRESSIVE ROLE OF MIR-199A-5P IN TRIPLE-NEGATIVE BREAST CANCER

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Background: Triple-negative breast cancer (TNBC) is defined by lack of expression in estrogen, progesterone receptors and human epidermal growth factor receptor 2. TNBC exhibited a more aggressive phenotype than other subtypes. Our previous study identified miR-199a-5p as TNBC-specific circulating marker, so we further investigated its role in breast cancer.

Methods: MTT, migration/invasion assay, cell cycle analysis, single-cell clonogenic assay and aldehyde dehydrogenase (ALDH) activity were performed in TNBC cell line MDA-MB-231 transfected with miR-199a-5p mimic. Gene expression level was investigated by real-time PCR.

Result: Overexpression of miR-199a-5p significantly inhibited cell proliferation, migration and invasion leading to G0/G1 phase arrest, early apoptosis and alteration in epithelial-mesenchymal transition-related genes in MDA-MB-231. Also, miR-199a-5p correlated with stemness characteristics by inhibiting single cell colony formation and decreasing CD24-/CD44+ subpopulation and ALDH activity. ALDH1A3 had a higher expression in breast cancer plasma especially in TNBC when compared to normal individuals. Furthermore, luciferase assay identified that PIK3CD is the potential downstream target of miR-199a-5p.

Conclusions: Our data implicated that miR-199a-5p confers tumor suppressive role in TNBC, which inhibited stemness characteristics. These findings may help the development of novel therapeutic strategies towards this highly malignant disease.

PO125

CD44 POSITIVE CELLS WERE ENRICHED IN LYMPH NODE METASTASIS

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Background: CD44 expression level was associated with malignant activity. High levels expression of CD44 in tumor have an unfavorable prognosis. The metastatic lymph node (LN) could be influenced by tumor cells becomes a site of immune suppression. Although LN metastasis is the most important prognostic factors in many solid tumors, the studies about CD44 expression in metastatic LN is quite limited.

Methods: Tumor specimens from breast cancer patients were obtained through Kaohsiung Medical University Chung-Ho Memorial Hospital under the Institutional Review Board-approved protocol. Immunohistochemical staining for CD44 were performed with the fully automated Bond-Max system (Leica Microsystems, Wetzlar, Germany). The differences between groups were estimated by χ^2 test or Fishers exact test appropriately. Disease-free survival curve for study population was visualized using Kaplan-Meier survival curve and analyzed by two-sided log-rank test.

Result: Total 116 primary breast tumors and 77 paired metastatic lymph nodes were enrolled in this study. According to the study result, high CD44 expression in primary tumor was significantly correlated with LN involvement and hormonal receptors expression levels, high expression levels in metastatic lymph node only correlated with high tumor grade. CD44-knockdown breast cancer cells showed repressed migration, invasion, stem-like and chemoresistant abilities. Low CD44 expression in primary tumor ($p < 0.001$) an LN ($p = 0.025$) show significant disease-free survival benefit, but resisted in high CD44 expression.

Conclusions: Our study results show that the LN metastasis could enrich CD44 expression in breast cancer. In addition, CD44 overexpression, especially in metastatic LN could induce treatment resistance and served as a predictive marker clinically.

Poster Exhibition

IDENTIFY TRIPLE-NEGATIVE BREAST CANCER SUBTYPES USING REVERSE PHASE PROTEIN ARRAYS (RPPAS)

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Background: Gene expression analyses have identified molecular subtypes of triple-negative breast cancer (TNBC), such as the Lehmanns seven molecular subtypes, and the Bursteins four subtypes that are refining our understanding of breast cancer biology. However, these subtypes are not well defined enough to enable development of targeted therapy or new treatment strategy. In this study, we classified TNBC subtypes using reverse phase protein arrays (RPPAs) that allows classification of TNBC at the protein level, then investigated the biological features using pathway analysis.

Methods: We used 80 TNBC RPPAs obtained from patients at The MD Anderson Cancer Center. RPPA analysis showed 154 breast cancer related proteins, including both total and phosphorylated proteins. We classified the TNBC samples using 2 types of clustering analysis, k-means and hierarchical. To assess the biological features of each TNBC subtype, we mapped antibody names from the RPPA dataset to HUGO Gene Nomenclature Committee (HGNC) gene symbols and fit a Gene Set Enrichment Analysis.

Result: Results of both clustering showed that the optimal number of subtypes in the TNBC RPPA dataset was 2-3. Clusters of k = 2 from the k-means and hierarchical clustering methods showed the same, indicating that these 2 clusters were stable and sufficiently different. The top canonical pathways, which were associated with 2 clusters, were the immune response and adipocytokine signaling pathways (cluster 1) and the DNA repair and replication pathway (cluster 2). As previously suggested, even in TNBC, Estrogen Receptor (ER) and Androgen Receptor (AR) showed high expression in cluster 1.

Conclusions: We identified 2 stable TNBC subtypes. Their biological features were similar with mesenchymal-luminal a ndrogen and basal subtype.

HIGHER LGR5 EXPRESSION IS ASSOCIATED WITH POOR PROGNOSIS IN BREAST CANCER PATIENTS IN TAIWAN

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Background: Wnt signaling is required for normal mammary development as well as mammary oncogenesis. Leucine-rich repeat-containing G protein-coupled receptor 5 (LGR5) is a Wnt-regulated target gene that has been identified as a stem cell marker. Recent studies showed that LGR5 plays a vital role in tumor progression and correlates with poor outcome. This study is to investigate the role of LGR5 in human breast cancer.

Methods: 121 breast cancer tissue blocks were sampled for tissue microarray (TMA). Follow-up information, histopathological and clinical data including age, tumor size, ER, PR, HER2 overexpression, tumor grade, stage, and survival were obtained from the cancer registry and medical charts. The breast TMA was evaluated for LGR5 expression using immunohistochemical staining and scores.

Result: 55 patients (45.5%) showed negative/low LGR5 expression while 66 (54.5%) showed high LGR5 expression. There was a statistically significant difference between the two groups with respect to grade ($p = 0.004$), tumor size ($p < 0.001$), lymph node involvement ($p = 0.020$), stage ($p < 0.001$), ER positivity ($p = 0.039$), and Her2 overexpression ($p = 0.050$).

Conclusions: Our results showed that LGR5 expression is statistically related to many important clinicopathological parameters. Therefore, it can be concluded that LGR5 is an oncoprotein. Unfortunately, limited by a small patient size, a statistically significant correlation cannot be established between LGR5 expression and OS. We plan to increase the number of our samples in the coming months.

NADPH OXIDASE REGULATE TPA-INDUCED MMP-9 EXPRESSION AND INVASION IN MCF-7 BREAST CANCER CELLS

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Background: The The NADPH oxidases (NOXs) are proteins that transfer electrons across biological membranes. In general, NOXs have been thought to generate superoxide at the plasma membrane and release it into the extracellular space where it is converted into hydrogen peroxide. The biological function of NOXs is the generation of Reactive oxygen species (ROS). Recent studies reported that protein kinase (PKC) mediates the phosphorylation of NOXs. However, NOXs activation via PKC in the invasion of breast cancers is still unclear.

Methods: MCF-7 breast carcinoma cells were investigated using Western blot analysis, Quantitative real-time PCR, Quantification of intracellular ROS, Invasion assay, NOX activity assay and RNA interference.

Result: GF109203x (GF; a broad inhibitor of PKC isoforms) treatment of cells blocked the up-regulation of phorbol ester (TPA)-induced matrix metalloproteinase (MMP-9) protein expression. TPA-induced increases in ROS levels were significantly reduced by treatment with the three PKC inhibitors. Incubation of cells with TPA resulted in an increase in NOX activity. However, treatment with GF diminished. NOX inhibitors treatment of cells blocked the up-regulation of TPA-induced MMP-9 protein expression, RNA levels and Matrigel invasion assay. Transfection of cells with NOX-4 siRNA knocked down NOX-4 mRNA expression and attenuated TPA-induced MMP-9 expression and cell invasion.

Conclusions: In conclusion, this study revealed that NOX-4 inhibits TPA-induced invasion by reducing MMP-9 activation mainly through blocking the generation of ROS. This is the first study showing that TPA-induced PKC dependent-MCF-7 cell invasion is suppressed by NOX-4 via the inhibition of MMP-9 expression through suppression of ROS generation. This is also the first characterization of the molecular mechanisms responsible for this inhibitory effect.

UNDERSTANDING THE THERAPEUTIC EFFECT AND MOLECULAR MECHANISM OF GNRH AGONIST FOR TNBC, USING PATIENT DERIVED XENOGRAFT MODEL

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Background: Recently, gonadotropin releasing hormone (GnRH) agonist treatment concurrent with chemotherapy showed effective fertility preservation during chemotherapy and increased survival in breast cancer. In this study we purposed to establish triple negative breast cancer (TNBC) patient derived xenograft (PDX) model and use this for studying the therapeutic effect and molecular mechanism of GnRH agonist.

Methods: we utilized 10 TNBC PDX model, and measured the expression level of GnRH receptor from tumor tissues. We chose 3 samples whose GnRH receptor expression level was relatively high, middle, and low (marked as GnRHR-H, GnRHR-M and GnRHR-L, respectively).

Result: When the GnRH agonist (Zoladex) was introduced, the tumor volume of GnRHR-H was remarkably reduced compared to the GnRHR-L. We also found that apoptosis was increased in GnRHR-H tumor, by performing Annexin v/PI staining. Western blot analysis of several protein was conducted to reveal the molecular mechanism of GnRH agonist, which showed that the level of B-Raf, p-ERK and CREB level was decreased by the GnRH agonist treatment.

Conclusions: Our research can provide the mechanism of antitumor effect of the GnRH agonist in the molecular level via GnRH receptor and suggest an effective therapeutic strategy for triple negative breast cancer.

PHOSPHORYLATION STATUS OF HER2 AND HER3 DETERMINE SENSITIVITY TO PIPERLONGUMINE

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Background: Piperlongumine (PL) is a biologically active component from long pepper, which has been reported to induce apoptosis in cancer cells via reactive oxygen species (ROS) accumulation.

Methods: Cell viability and apoptosis were analyzed by the MTT assay and annexin V and propidium iodide staining, respectively. Small interfering RNA (siRNA) was used for suppressing gene expression. The mRNA and protein expression were analyzed by RT-PCR and Western blot analysis, respectively

Result: PL reduced HER-3 phosphorylation levels. Protein and mRNA of these three receptors were also reduced in breast cancer cells with PL. Pretreatment with N-acetylcysteine, a ROS scavenger, restores the downregulation of these receptor by PL, suggesting that downregulation of HER family members by PL are due to the accumulation of ROS. During PL treatment, MCF7 cells with low levels of these receptors had less impact on cell viability than BT474 and SkBr3 cells with high levels of these receptors. Increased HER2 and HER3 phospholylations were observed in MCF7/HER2 cells. Sensitivity to PL was higher in MCF7/HER2 cells than MCF7. These data suggest that increased HER2 and HER3 phosphorylation can render breast cancer cells sensitive to PL.

Conclusions: Taken together, phospholylation status of HER2 and HER3 determined sensitivity to PL in breast cancer cells.

THE EXPRESSION OF UBE2C AND BRCA1 IN BREAST CANCER CELL MDA-MB-231 AND THE MECHANISM OF UBE2C IN DOXORUBINCIN CHEMORESISITANCE

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Background: UBE2C, the cancer-related E2 ubiquitin-conjugating enzyme, is involved in cell cycle, mitosis. The abnormal expression of UBE2C participates in the process of occurrence, development and metastasis of breast cancer. BRCA1 expression can be almost detected in sporadic breast cancer, its mutation are more likely to be resistant to drugs such as doxorubicin. Recently studies have indicated that the interactions between BRCA1 and ubiquitin proteasome system are involved in the sensitivity of tumor cells to chemotherapeutic drugs. Few reports about the correlation between UBE2C and BRCA1.

Methods: Analysis of UBE2C gene associated with the distribution in types of breast cancer, pathological grade of breast tumors, overall survival and metastasis-free survival of breast cancer patients in TCGA database. Knockdown UBE2C and BRCA1 in MDA-MB-231 by siRNA techniques,cells cultured in different concentrations of Doxqubincin. Compare protein expression of UBE2C and BRCA1 by Western Blot, mRNA expression levels of MRP1, BCRP, and P-gp were detected by Quantitative Real-time PCR, cell proliferation were detected by CCK-8 assay.

Result: Basal-like breast cancers (BBC) showed the highest expression level of UBE2C ($p < 0.01$). The higher expression of UBE2C was strongly associated with higher histologic grade in breast cancer ($p < 0.0001$).Higher UBE2C expression levels were strongly associated with earlier metastasis ($p < 0.001$, HR = 0.282) and increased mortality ($p < 0.05$, HR > 2). Western blot: UBE2C expression increased in BRCA1-siRNA cells ,while BRCA1 was unchanged in UBE2C-siRNA cells. Doxorubincin under 1ug/ml promotes UBE2C expression. CCK8:the cell viability of BRCA1-siRNA cells enhanced significantly ($p < 0.02$). Quantitative Real-time PCR:MRP1, BCRP, and P-gp inhibited in UBE2C-siRNA cells.

Conclusions: High UBE2C expression seems to be a unique phenomenon for TNBC and may be a molecular marker for breast cancer recurrence and metastasis. BRCA1 may regulate UBE2C gene directly or indirectly through uncertain signaling pathway. UBE2C may be a therapeutic target for drug resistance of TNBC.

INCREASED IGF2BP1 ASSOCIATED WITH DOWNREGULATION OF PROGESTERONE RECEPTOR IN ER-POSITIVE BREAST CANCER BASED ON GENE MICROARRAY DATA

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Background: Recent reports provide a large body of evidence that low expression of progesterone receptor has a negative prognostic value in estrogen receptor (ER)-positive breast cancer. However, it is not clear which genetic markers contribute to loss of progesterone receptor (PR) and increasing glucose metabolism in ER-positive breast cancer. Thus, we tried to discover key factors associated with PR-loss in ER-positive/HER2-negative cancer using gene-expression profiling data, particularly focusing IGF pathway.

Methods: In 72 patients with ER-positive/HER2-negative patients,total RNA more than 500 ng was extracted from frozen tumors. Microarray images were scanned by Agilent DNA microarray Scanner (Agilent Technology, USA) and the data quantification was performed using Agilent Feature Extraction software 9.3.2.1 (Agilent Technology, USA). PR expression was determined by modified Allred score (high PR: 2+, 3+ vs. low RT: 0, 1+).

Result: Fifty five (76.4%) had high PR tumors, while 17 (23.6%) had low PR tumors. Among genes belong to IGF pathway, mRNA expression of IGF2BP1 was significantly higher in low PR tumor than in high PR tumors ($p = 0.013$). When mRNA expression levels of PR and IGF2BP1 was compared as continuous variables, an inverse correlation was noted ($p = 0.037$, $R^2 = -0.247$).

Conclusions: Our findings suggest that the expression of IGF2BP1 was increased in low PR cancer among ER-positive/HER2-negative tumors. Further study warrants in searching a mechanistic interaction between PR and IGF2BP1 in ER-positive breast cancer.

PO133

ENDOSCOPIC ASSISTED MASTECTOMY FOR BREAST CANCER PATIENTS-TAIWAN EXPERIENCE

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Background: Endoscopic assisted breast surgery (EABS), performed via minimal peri-areolar and/or axillary incisions, offer an additional choice for the surgical treatment in breast cancer.

Methods: In this study, we report our preliminary results of EABS in the National Cheng-Kung University Hospital (NCKUH), Taipei Medical University Hospital (TMUH) and Changhua Christian Hospital (CCH). Patients with breast cancer managed by EABS were search from 3 medical centers database. The patients' clinicopathologic characteristics, type of surgery, method of breast reconstruction, complication and recurrence were recorded (IRB Nr 121229). A total of 250 patients with breast cancer undergone EABS from the above three endoscopic breast surgery centers in Taiwan. All of them were female, and the mean age at diagnosis was 49.5 ± 10.1 years old (range 26 to 80 year). Among these 250 patients, 40 (16%) underwent endoscopic assisted partial mastectomy (EAPM), and 210 received endoscopic assisted total mastectomy (EATM). In the 210 EATM patients, 52 (24.76%) received endoscopic assisted skin sparing mastectomy (E-SSM), and 158 (75.24%) underwent endoscopic assisted nipple sparing mastectomy (E-NSM).

Result: The mean pathologic tumor size of these 250 patients was 2.3 ± 1.2 cm (0.1 to 8.5 cm). Lymph node metastasis was found in 40 (16%) patients, 27 patients with 1-3 positive lymph nodes, and 13 patients with 4-9 lymph nodes metastasis. The postoperative stage distribution were 88 (35.2%) ductal carcinoma in situ (DCIS), 85 (34%) stage 1, 40 (16%) stage 2a, 26 (10.4%) stage 2b, and 11 (4.4%) stage 3a. Among the 210 EATM patients, 168 (80%) received immediate breast reconstruction. Most (62.5%) of them received Gel implant reconstruction, and 37.5% received breast reconstruction with autologous pedicled transverse abdominal myocutaneous (TRAM) flap. Complications (9%) follow EABS were all minor, and most of them were wound related. The cosmetic result

was satisfactory in most cases. In the oncologcial safety analysis, only two (1%) patients were found to have positive surgical margin, which occurred in case with DCIS and underwent EAPM. No local recurrence was observed during the mean 27.4 months (range 3 to 72) of follow-up. However, one 34 year old female with bilateral triple negative breast cancer, pT2N1, stage IIB, was found to have multiple brain metastasis 9 months post operation. She died 5 months after brain metastasis.

Conclusions: Endoscopic assisted breast surgery provides an alternative for the management of selected breast cancer patients.

PO134

ONCOLOGIC AND AESTHETIC OUTCOMES USING PERIAREOLAR INCISION FOR NIPPLE-SPARING MASTECTOMY

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Background: Nipple-sparing mastectomy (NSM) with immediate reconstruction is gaining wide acceptance as a surgical option for the treatment of breast cancer. NSM provides the best aesthetic outcome without compromising oncologic safety. We evaluated our own experience in NSM via a periareolar incision.

Methods: From 2009 to 2015, patients who underwent NSM via periareolar incision were identified, data were gathered and oncologic as well as aesthetic outcomes were examined.

Result: 36 NSM using periareolar incision were performed in 32 patients. Mean age of patients was 46 years. The absolute contraindication was gross and histologic involvement of the nipple-areolar complex (NAC). 32 (88.9%) NSMs were done mainly for therapeutic indication while the rest 4 (11.1%) were prophylactic procedures. The median breast weight was 335 g (range 175-900 g). Periareolar incision alone was done for 12 patients (33.3%) while 24 (66.7%) required with lateral extension up to 3 cm. 2 (5.6%) patients had total nipple loss. One patient had an avascular NAC intra-operatively while the other had full thickness necrosis 3 weeks post-operatively, both requiring surgical resection. Superficial nipple loss was observed in 3 (8.3%) patients who were managed conservatively. One patient (2.7%) had poor cosmetic outcome as described by the attending surgeons. One (2.7%) ipsilateral chest wall recurrence was diagnosed at 6 years.

Conclusions: Our study showed that despite the limited visualization and access of the surgical field afforded by periareolar incision during NSM, excellent oncologic and aesthetic outcome can be achieved.

PO135

THE PREDICTIVE VALUE OF TRADITIONAL CHINESE MEDICINE SUBTYPE COMBINED WITH MOLECULAR SUBTYPE IN NEOADJUVANT CHEMOTHERAPY IN BREAST CANCER

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Background: In order to predict the effect of neoadjuvant chemotherapy accurately, we combined traditional Chinese medicine subtype with molecular subtype to have a prospective case study.

Methods: In this study, every breast cancer patient must get molecular subtype through immunohistochemistry test and traditional Chinese medicine subtype (stagnation of liver-qi and phlegm, deficiencies of healthy qi and exuberance of toxin, incoordination between the Chong and Ren Meridians) identified by rich experienced traditional Chinese physicians. Through 4-cycle standard neoadjuvant chemotherapy regimens, anthracycline combined with taxanes, we compared the pathological complete response (pCR) among those subtypes.

Result: The study brought in 128 cases. The Luminal A/stagnation of liver-qi and phlegm patients accounted for 24.22%, more than the others. The Luminal B/deficiencies of healthy qi and exuberance of toxin accounted for only 0.78%. Luminal A and Luminal B patients tended to be the type of incoordination between the Chong and Ren Meridians, while triple negative patients were likely to be the type of deficiencies of healthy qi and exuberance of toxin. In Luminal A patients, the type of deficiencies of healthy qi and exuberance of toxin had higher pCR comparing with other traditional Chinese medicine subtype. The same result also was found in HER2 overexpression patients, the type of stagnation of liver-qi and phlegm had more pCR than other traditional Chinese medicine subtype.

Conclusions: Traditional Chinese medicine subtype combined with molecular subtype have important predictive value on the effect of neoadjuvant chemotherapy in breast cancer.

PO136

AXILLARY AND INTERNAL MAMMARY SENTINEL LYMPH NODE BIOPSY IN BREAST CANCER AFTER NEOADJUVANT CHEMOTHERAPY

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Background: The definition of pathological complete response (pCR) is eradication of tumor from both the breast and axillary lymph nodes (ALN) without the internal mammary lymph node (IMLN). The IMLN metastasis has similar prognostic importance as that of ALN. This study was to evaluate roles of axillary sentinel lymph node biopsy (ASLNB) and internal mammary sentinel lymph node biopsy (IM-SLNB) after neoadjuvant chemotherapy (NAC).

Methods: From January 2012 to October 2015, seventy-four patients underwent NAC were enrolled into the study. IM-SLNB was performed for all patients with radioactive internal mammary sentinel lymph node (IM-SLN). Patients (n = 8) with cN0 and ycN0 received ASLNB, and ALND in cases of positive axillary sentinel lymph node (ASLN). Patients (n = 48) with cN+ but ycN0 received ASLNB and ALND. Patients (n = 18) with ycN+ received ALND without ASLNB.

Result: The success rate of ASLNB was 100% (56/56). The false negative rate (FNR) of ASLNB was 17.2% (5/29). The FNRs in patients with 1, 2, and ≥3 ASLNs examined were 27.3% (3/11), 20.0% (2/10), and 0% (0/8). ALN were found residual tumor in all patients with ycN+ except one. The visualization rate of IM-SLN was 56.8% (42/74). The success rate of IM-SLNB was 97.6% (41/42). The metastasis rate of IM-SLN was 7.3% (3/41) and all of the three combined with positive ALNs.

Conclusions: ASLNB should be performed on selected patients after NAC. IM-SLNB should be performed routinely in patients after NAC in case of under-stage and under-/over-treatment, and complete the definition of pCR.

PO137

REVIEW OF CLINICAL OUTCOMES AND PROGNOSIS OF PHYLLODES TUMOUR OF THE BREAST IN HONG KONG

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Background: Phyllodes tumour (PT) is an uncommon fibroepithelial tumour of the breast. It has a spectrum of aggressiveness in biological behaviour, and is prone to local recurrence, and more uncommonly, metastasis. We looked at the risk factors for local recurrence and distant metastasis.

Methods: A 15 year retrospective review from a multicentre database in Hong Kong was performed.

Result: Between 1998 and 2014, the clinicopathological records of 465 patients with 469 PT were reviewed. Median age of occurrence was 44 years (range 12-86 years). Two hundred and eighty one (59.9%) PT were benign, 124 (26.4%) were borderline and 64 (13.6%) were malignant. About half of all PT (239, 51.5%) were between 2 to 5 cm while another 186 (40.1%) were more than 5cm in size. Breast conserving surgery was feasible in 384 (82%) patients whereas 84 (18%) patients had mastectomy. There was no difference in the risk of local recurrence between the grade of PT ($p = 0.221$). However, the risk of distant metastasis occurred solely in malignant PT (8 patients, 89%) or PT with malignant transformation (1 patient, 11%). Univariate analysis for the risk of local recurrence was tumour size and surgical margin. Multivariate analysis for the risk of local recurrence was malignant PT grade and surgical margin. The prognosis for benign or borderline PT was excellent.

Conclusions: Local recurrence of PT occurs irrespective of the tumour grades. Surgical margin is the only amendable factor to reduce the rate of recurrence. Distant metastasis occurs only in malignant PT.

PO138

PARTIAL BREAST IRRADIATION USING MULTICATHETER BRACHYTHERAPY FOR BREAST-CONSERVING THERAPY: EFFICACY EVALUATION OF 301 CASES AND LONG-TERM COSMETIC OUTCOMES

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Background: Partial breast irradiation (PBI) is an alternative to whole breast irradiation (WBI) for breast-conserving therapy. Recently, a randomized phase 3 trial by GEC-ESTRO demonstrated that PBI using multicatheter brachytherapy (MCB) showed an equivalent efficacy to WBI after breast-conserving surgery (BCS). However, limited data are available on MCB-PBI for Asian patients. Further, long-term cosmetic outcomes are considered to be an important issue.

Methods: Patients aged ≥ 40 years, with a maximum tumor diameter of ≤ 3.0 cm, and with sentinel nodes negative for metastases underwent MCB-PBI, which was performed in an accelerated manner with a dose of 32 Gy in 8 fractions over 5-6 days. Patients who had a minimum follow-up period of 5 years were extracted to evaluate cosmetic outcomes using the Breast Cancer Conservative Treatment Aesthetic Results (BCCT.core) software tool.

Result: Between October 2008 and December 2015, 301 consecutive patients underwent BCS followed by MCB-PBI. The mean age was 56.5 years, and the median follow-up time was 45.9 months. Ipsilateral breast tumor recurrence (IBTR) was observed in 5 (true: 3, elsewhere: 2) patients, and the IBTR rate was 1.7% (95% CI: 0.2%-3.1%). Cosmetic results could be assessed in 62 of 71 patients with > 5 years of follow up, and excellent or good outcomes were observed in 51 patients (82.3%).

Conclusions: Although there was a relatively small number of patients and a short follow-up period in this study, MCB-PBI had an adequate clinical efficacy for local control and acceptable long-term cosmetic outcomes in Asian patients.

PO139

RETROSPECTIVE ANALYSIS OF PRIMARY PROPHYLAXIS WITH A HALF-DOSE PEGFILGRASTIM RECEIVING DOSE-DENCE DOXORUBICIN AND CYCLOPHOSPHAMIDE IN JAPANESE BREAST CANCER PATIENTS

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Background: In many countries, the recommended dosage of pegfilgrastim is 6 mg once per chemotherapy cycle. However, it was approved for the use of 3.6 mg pegfilgrastim in Japan on the basis of the results of internal clinical trials. In those trials, triweekly based regimens (TAC and TC) have been used, but dose-dense chemotherapy has not yet been performed. Therefore we evaluate primary prophylaxis with a half-dose pegfilgrastim on maintaining relative dose intensity (RDI) in early breast cancer patients receiving dose-dence chemotherapy.

Methods: Since 6 mg pegfilgrastim has not been approved in Japan, we performed comparisons between dose-dense AC (ddAC) with 3.6 mg pegfilgrastim support and EC regimen. A retrospective analysis was performed for patients who received 3.6 mg pegfilgrastim after each ddAC (doxorubicin 60 and cyclophosphamide 600 mg/m^2, respectively; every 14 days for 4 cycles) and for those who received EC (epirubicin 90 and cyclophosphamide 600 mg/m^2, respectively, every 21 days for 4 cycles). RDI and the patient incidence of dose reduction and dose delay were summarized.

Result: From Janualy 2014 to Janualy 2016, 81 patients were enrolled. 30 patients in the ddAC group and 51 patients in the EC group. Median age was 53.4 and 49.9, respectively. Mean RDI was 97% and 95%, respectively ($p = 0.50$). The incidence of dose reduction was 3.3% (1/30) and 15.7% (8/51), respectively ($p = 0.04$). The incidence of dose delay was 6.7% (2/30) and 15.7% (8/51), respectively ($p = 0.24$).

Conclusions: Use of a half-dose pegfilgrastim primary prophylaxis maintained RDI in Japanese breast cancer patients receiving dose-dence chemotherapy.

Poster Exhibition

PO140

INTENSIFYING TAXANE-CARBOPLATIN-CONTAINING NEOADJUVANT CHEMOTHERAPY (NAC) INCREASED RESPONSE IN LOCALLY ADVANCED HER2-POSITIVE BREAST CANCER PATIENTS WITH HORMONE RECEPTION (HR) EXPRESSION

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Background: Trastuzumab combined with docetaxel-carboplatin (DC) is an established anthracyline-sparing NAC for HER2+ breast cancer. Intensified regimens by shortening the dosing interval have been postulated to improve tumor control in adjuvant setting. This retrospective study analysed the efficacy of 3 different taxane-carboplatin schedules in locally advanced HER2+ breast cancer patients.

Methods: Patients received trastuzumab combined with one of 3 regimens: DC every 3 weeks for 6 cycles (DCH), dose-dense paclitaxel-carboplatin every 2 weeks for 6 cycles (DD-TCH), or weekly paclitaxol-carboplatin for 18 weeks (Wkly-TCH). Primary endpoint was pathologic complete response (pCR).

Result: A total of 104 pt were identified between years 2007-2015 (DCH - 50 pt; DD-TCH - 34 pt; Wkly-TCH - 20 pt). Baseline characteristics were similar among 3 groups. Median follow-up was 3.79 years. Majority of pt completed all scheduled treatment with no severe adverse events. There was a trend in increase of overall pCR rate with shortened dosing interval (DCH -18%; DD-TCH - 26%, Wkly-TCH - 40%). Subgroup analysis by HR status showed the pCR rate was not affected by the dosing interval in HR-negative pt. In HR-positive pt, there was significant increase in pCR rate with the intensified schedules (DCH 6%; DD-TCH 20%; Wkly-TCH 40%; $p = 0.02$ by Fishers exact test). Median disease-free survival was not reached. A longer follow up is required for conclusive survival result.

Conclusions: Trastuzumab combined with taxane-carboplatin are effective NAC strategies for HER2+ breast cancer. DD-TCH and Wkly-TCH are practical and tolerable alternatives to DCH. Wkly-TCH may enhance pCR rate in HER2+/HR-positive pt.

Poster Exhibition

PO141

MAMMA BALANCE: A NOVEL SOFTWARE TO ANALYZE THE SYMMETRY OF NIPPLE POSITION IN BREAST RECONSTRUCTION

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Background: Symmetrical nipple position is key components of aesthetic outcomes of breast reconstruction. New software named Mamma Balance (MB) was sold to analyze the symmetry of nipple position. The aim of this study is to investigate the reliability and validity of this novel software.

Methods: The subjects were 27 breast cancer patients undergoing nipple-sparing mastectomy followed by tissue expander reconstruction between August 2009 and August 2014. Three observers measured the degree of nipple position symmetry using patients photographs of frontal views both pre- and post-operative period respectively by two methods: one way was a 0 to 4 point scale (grading method: GM) and the other was MB. Inter- and intra- observe reliabilities were assessed with intraclass correlation coefficient (ICC), and validity was tested using Spearman correlation coefficient. $p < 0.01$ was considered statistically significant.

Result: Intra- and inter-observer reliability of MB were the following: ICC was 0.8 to 0.95 and was 0.78 respectively. Intra-observer reliability of GM was acceptable (ICC = 0.90). The correlation coefficient between both methods was moderate-to-high (r = 0.65-0.95). The result of MB tended to show variability widely in the cases with 0 score in GM.

Conclusions: MB has high reliability and validity. However, correlation between both methods showed lower relatively, which was occurred by floor effect of GM. Because MB has some advantages that are free from floor effect, easy to apply, and has reasonable price, it is useful software for examination of the degree of nipple position symmetry.

Poster Exhibition

PO142

THE ROLE OF POSTMASTECTOMY RADIATION THERAPY IN PATIENTS WITH CLINICAL STAGE II-III BREAST CANCER AFTER NEOADJUVANT CHEMOTHERAPY

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Background: The purpose of this study was to investigate the role of postmastectomy radiation therapy (PMRT) in patients with clinical stage II-III breast cancer and with pathologic N0 or N1 after neoadjuvant chemotherapy (NAC).

Methods: We retrospectively analyzed 144 patients with clinical stage II-III breast cancer and who received NAC and mastectomy between 2005 and 2012. Locoregional recurrence-free survival (LRRFS) and disease-free survival (DFS) were calculated . The effect of PMRT on LRRFS and DFS was evaluated.

Result: Of the 144 patients, 127 (88%) received PMRT. At a median follow-up of 69 months (rang: 10-111 months), 9 patients (6.3%) developed LRR and 18 patients (12.5%) developed distant metastasis. 40 patients (27.8%) achieved pathologic complete response (pCR) and 91 patients (63.2%) achieved pathologic N0. The LRRFS rates were significantly increased with PMRT, with a 5-year LRRFS of 95% vs. 72.7% ($p=0.012$). The 5-year DFS was significantly improved in patients who received PMRT (91% vs. 61.6%, $p=0.002$). By univariate analysis, PMRT was the only significantly factor for LRRFS, while PMRT, pathologic T stage, pCR, molecular subtype and adjuvant chemotherapy significantly effecting DFS. By multivariate analysis, PMRT was the only significant prognostic factors affecting LRRFS (hazard ratio [HR] 6.647, 95% confidence interval [CI] 1.45-30.39, $p=0.015$) and DFS (HR 3.457, 95% CI 1.3-9.21, $p=0.013$). In the subgroup of patients who achieved pCR, PMRT still significantly improved LRRFS and DFS (both $p<0.05$).

Conclusions: In patients with clinical stage II-III breast cancer and pathologic N0-1 at surgery, PMRT could significantly improved LRRFS and DFS after NAC, even when patients achieved pCR.

PO143

BREAST CANCER AFTER BILATERAL SUBCUTANEOUS MASTECTOMY IN FEMALE TO MALE TRANSSEXUAL: CASE REPORT IN OKAYAMA UNIVERSITY HOSPITAL

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Background: In Okayama University Hospital we report a case of breast cancer that developed in after receiving a sex reassignment surgery in female to male transsexual.

Methods: A case is 41 years old. He received a sex reassignment surgery at diagnosis in 2005 to gender identity disorder, and then changed the family register from female to male. He had been received continuous administration of methyl testosterone after surgery. He felt left chest mass, visited nearby hospital and recognized 2 cm tumor on the left chest, and diagnosed of breast cancer by fine needle aspiration cytology (FNAC). We recognized 2 cm tumor on the left breast. Preoperative diagnosis was left breast carcinoma. T2N0M0 cStage IIA.

Result: Partial mastectomy + sentinel lymph node biopsy was performed. Histological diagnosis was carcinoma with neuroendocrine features: nuclear grade 2, ER positive, PgR positive, HER2 (Score0) Ki-67 20% and Androgen receptor (+). He received aromatase inhibitor for the adjuvant therapy.

Conclusions: This case is a very rare case as a breast cancer that developed in men after gender reassignment surgery. Due to his family register was changed to men, there is no chance of breast cancer screening examination, so we have to pay enough attention. In addition, in the case of breast cancer that occurred under methyl testosterone administration, as in this case of the androgen receptor-positive breast cancer, it is necessary to pay attention to the future of methyl testosterone administration. In the adaptation of postoperative hormone therapy, there is a need for the accumulation of further cases.

PO144

IMPLICATION OF BENEFICIAL ROLE OF POSTMASTECTOMY RADIATION THERAPY IN BREAST CANCER PATIENTS WITH T1-2 AND ONE TO THREE POSITIVE AXILLARY LYMPH NODES

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Background: The role of postmastectomy radiation therapy (PMRT) for patients with T1-2 and one to three lymph nodes was still controversial. This study aimed to investigate the effect of PMRT for the risk of locoregional recurrence (LRR).

Methods: Between 1994 and 2011, a total of 409 patients who received curative surgery at our institution were divided into three groups by treatment modality: breast conserving surgery plus radiation therapy (Group 1, n = 213), mastectomy alone (Group 2, n = 175) and postmastectomy radiation therapy (Group 3, n = 22).

Result: During the median follow-up of 81 months, 37 patients (9.0%) experienced LRR as the first failure; 13 patients (6.1%) in Group 1, 24 patients in Group 2 (13.7%) and none (0%) in Group 3. The 10-year cumulative incidence rate of LRR was 8.4% for Group 1, 19.3% for Group 2 and 0% for Group 3 ($p = 0.022$). In the analysis of subgroup who received taxane-based adjuvant chemotherapy (n = 293), the 10-year cumulative incidence rate of LRR was 5.4% for Group 1, 15.0% for Group 2 and 0% for Group 3 ($p = 0.036$). In competing risk regression, histologic grade 3 ($p = 0.000$) and 3 positive axillary lymph nodes ($p = 0.046$) were independent factors for increased risk of LRR in Group 2 patients.

Conclusions: PMRT improved the risk of LRR compared to patients with mastectomy alone and the risk was comparable to those with breast conserving surgery plus radiation therapy. Further study is required to validate our results.

PO145

IS CHEMOTHERAPY NECESSARY FOR PREMENOPAUSAL WOMEN WITH ENDOCRINE RESPONSIVE EARLY BREAST CANCER?

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Background: The optimal adjuvant endocrine therapy in premenopausal women with early stage breast cancer continues to evolve. Ovarian function suppression plus tamoxifen was endorsed as a standard treatment option for premenopausal patients with hormone-sensitive breast cancer. Whereas the benefit of adding chemotherapy to combined endocrine treatment with ovarian function suppression and tamoxifen remains unclear.

Methods: From January 2008 to December 2012, 371 premenopausal patients with hormone receptor positive tumors (T1 -3) and N0-1 were treated with endocrine therapy alone or endocrine therapy plus chemotherapy. Endocrine therapy included ovarian suppression plus tamoxifen to 5 years. The method of ovarian function suppression was either bilateral surgical oophorectomy, or GnRH analogue 3.6 mg every 28 days continuing for 2 years or whichever longer. Patients received chemotherapy four courses of anthracycline-based or six courses of CMF. The primary endpoint was disease-free survival (DFS).

Result: Patients had Luminal A or HER2 negative Luminal B subtype and also had HER2 positive tumor in each group, and median age was 47. After 5.6 years median follow up, there remains no difference between the two treatment groups for disease-free (HR = 1.09 [0.48-1.67]; $p = 0.79$) or overall survival (HR = 0.88 [0.42-2.78]; $p = 0.67$).

Conclusions: This study, although retrospective, small sample size, offers no evidence that chemotherapy provides additional disease control for premenopausal patients with endocrine-responsive early breast cancer who receive adequate adjuvant endocrine therapy. A large prospective trial is needed to determine whether chemotherapy adds benefit to endocrine therapy for this population. Additional risk scoring assessment (Oncotype Dx or Endopredict, etc.) could help for providing more information.

PO146

MALE BREAST CANCER: A CLINICOPATHOLOGICAL STUDY OF EGYPTIAN POPULATION (ALEXANDRIA EXPERIENCE)

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Background: The purpose of this retrospective study is to evaluate the clinicopathological features and treatment results of male breast cancer presented to our center.

Methods: Between January 1998 and December 2005, a total of 39 men with breast cancer treated at Clinical Oncology department, Alexandria Main University Hospital and their medical records were reviewed.

Result: The median age of patients was 59 years. Only 3 (7.7%) patients had positive family history. All patients presented by breast swellings that were associated with axillary mass in about one third of them. Around 80% had hormone receptor positive. Two third of patients had advanced T-stage (T3 and T4). Left sided breast cancer occurred in 51.3%. Infiltrating ductal carcinoma was the most common type of histology encountered. Modified radical mastectomy was the most common (87.2%) type of surgery done followed by chemotherapy for 32 patients and loco-regional radiotherapy for 20 patients. Tamoxifen was administered in 31 patients. Distant relapse occurred in 7 patients (17.9%) and local recurrence occurred in 2 patients (5.1%). The 5-year disease-free survival (DFS) was 82% and the 5-year overall survival (OS) rate was 84%. Only axillary lymph node negative and hormone receptor positive were significantly associated with favorable DFS and OS. T-stage, grade of tumor and type of chemotherapy given had no statistically significant impact on either DFS or OS.

Conclusions: Male breast cancer is very similar to female breast cancer but has certain unique features, which should be further explored in future research. Management should be based on female breast cancer guidelines.

PO147

PREDICTION OF FALSE-NEGATIVE OF SENTINEL LYMPH NODE BIOPSY WITH PREOPERATIVE IMAGING AFTER NEOADJUVANT CHEMOTHERAPY

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Background: Sentinel lymph node biopsy (SLNB) is being considered in patients with initially node-positive but clinically node-negative disease after neoadjuvant chemotherapy (NAC). We evaluated the predictive role of preoperative imaging studies before and after NAC for false-negative rate (FNR) of SLNB.

Methods: We retrospectively reviewed patients with breast cancer who received NAC at Gangnam Severance hospital from 2005 to 2015. We included 128 patients who underwent breast cancer surgery with axillary lymph node (ALN) dissection after SLNB. We evaluated FNR of SLNB in patients with negatively converted ALN in imaging studies.

Result: After NAC, FNR of SLNB was 18.1%. In patients with only 1 or 2 sentinel lymph nodes retrieved, FNR was 23.8% compared to 6.9% when 3 or more sentinel lymph nodes were retrieved. In patients with negatively converted ALNs after NAC in imaging studies, FNR of SLNB was 20%, 13.6%, and 21.4% for US, MRI, and PET/CT, respectively. When ALNs were persistently suspicious, FNR of SLNB was 21.6%, 26.9%, and 15.8%, respectively.

Conclusions: In patients with suspicious ALN metastasis in imaging studies before NAC, FNR of SLNB was high irrespective of negative conversion after NAC in imaging studies. In patients with 3 or more SLNs retrieved, FNR was 6.9%. Thus, even if imaging studies after NAC show non-suspicious for ALN metastasis, SLNB can be performed only when 3 or more SLNs were retrieved.

PO148

FEASIBILITY OF SENTINEL LYMPH NODE BIOPSY IN BREAST CANCER PATIENTS WITH NEGATIVE AXILLARY CONVERSION AFTER NEOADJUVANT CHEMOTHERAPY

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Background: An increasing proportion of patients with node-positive breast cancer will obtain an axillary complete clinical remission after neoadjuvant chemotherapy (NAC). But the use of sentinel lymph node biopsy (SLNB) after NAC has been the subject of some controversy. This study was conducted to evaluate the SLNB guided decision with negative axillary conversion after NAC.

Methods: A total of 1,813 patients aged over 18 years with operable breast cancer who achieved negative axillary conversion after NAC from five hospitals in Korea from 2005 to 2012 were reviewed. Patients underwent axilla operation by SLNB guided decision (arm A). If patients with complete axillary dissection was done regardless of SLNB who were grouped others (arm B). The primary endpoint was node recurrence free survival. Secondary endpoints included comparison of distant metastasis and overall survival.

Result: Of 1,813 patients enrolled, 509 had SLNB guided surgery attempted, 1,304 underwent ALND. Node recurrence analysis using Kaplan-Meier method showed that the two groups had no significant difference in recurrence-free survival ($p=0.113$). Distant recurrence free survival was also no difference between arm A and B ($p=0.744$). The overall survival of sentinel guided surgery group was better but not significant ($p=0.074$). Axilla recurrence in 19 (3.7%) of 507 patients in arm A, 34 (2.6%) of 1,301 patients in arm B and axilla recurrence did not differ by axilla surgery method ($p=0.199$).

Conclusions: In node-positive breast cancer patients who obtain a clinically negative node conversion following NAC, SLNB guided surgery is a reliable operative method.

Poster Exhibition

PO149

LYMPH NODE RATIO: AS A PROGNOSTIC FACTOR IN PN1 BREAST CANCER

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Background: To evaluate the prognostic value of the lymph node ratio (LNR, defined as the proportion of involved nodes in dissected nodes) in pN1 breast cancer.

Methods: We retrospectively analyzed clinical data of patients with pN1 breast cancer patients (N = 149) from 2001 to 2010 at Keimyung university Dongsan medical center. The range of age was from 27 to 66 (median 47). One hundred thirty patients had LNR from 0.01 to 0.15 (Low-LNR) and 19 patients had LNR over than 0.15 (High-LNR). According to AJCC TNM 7th edition, there were 70 patients (47.0%) with T1, 74 patients (49.7%) with T2, and 5 patients (3.4%) with T3. Eighty five patients (57.0%) undergone total mastectomy (TM), and 64 patients (43.0%) undergone partial mastectomy (PM). Regional RT was given in 15 patients (10.1%). Median follow up duration was 77 months.

Result: The 5-year and 10-year disease free survival (DFS) were 93.0% and 82.6%. On univariate analysis for factors related to DFS, high-LNR ($p = 0.013$), younger age ($p = 0.008$), TM ($p = 0.005$), T2 & 3 stage ($p = 0.008$), HER2 negative ($p = 0.036$) were unfavorable factors. In no regional RT group, high-LNR showed significantly worse DFS ($p = 0.004$), but not in regional RT group ($p = 0.371$). On multivariate analysis, younger age ($p = 0.001$), TM ($p = 0.043$) and high-LNR ($p = 0.001$) were related to DFS.

Conclusions: High-LNR was an independent prognostic factor in pN1 breast cancer patients. And it could be one of the indications for adjuvant RT in pN1 breast cancer patients.

Poster Exhibition

PO150

AXILLARY DISSECTION VERSUS NO AXILLARY DISSECTION IN BREAST-CONSERVING SURGERY FOR ELDERLY PATIENTS WITH CT1-2N0M0 BREAST CANCER: A RETROSPECTIVE STUDY

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Background: Treatment strategies for elderly patients with breast cancer are controversial. Our study aimed to evaluate the long-term safety of breast-conserving surgery (BCS) without axillary lymph node dissection (ALND) in elderly patients with early breast cancer.

Methods: Patients admitted to our institute from January 1995 and December 2011 who met the following inclusion criteria were recruited in the study: (1) Age ≥65 years, (2) diagnosed with primary breast cancer with cT1-2N0M0 stage, (3) treated with breast-conserving surgery. The end point were disease free survival (DFS) and overall survival (OS).

Result: We enrolled 146 patients. 78 of them had BCS with ALND, and 68 patients were treated without ALND. The median follow up was 61 months. At the time of data collection 5-year DFS (86.8% vs. 82.1%, $p=0.406$) or 5-year OS (94.1% vs. 91.0%, $p=0.490$) between two groups showed no significant difference. The radiotherapy after conserving surgery did not either affect the outcomes of elderly patients with early-stage breast cancer (DFS, 85.5% vs. 83.1%, $p=0.590$; OS, 94.2% vs. 90.9%, $p=0.382$). Multivariate analyses indicated that pathological tumor size was an independent risk factor for DFS (HR = 2.413, $p=0.036$) and OS (HR = 3.731, $p=0.030$).

Conclusions: Our results implied that elderly patients with cT1-2N0M0 primary breast cancer may not benefit in terms of DFS and OS from immediate axillary dissection. Evidences about the necessary of axillary dissection in elderly patients are still controversial, however each case deserves a thoroughly consideration before the best treatment option was chosen.

EFFICACY AND TOXICITY OF PEMETREXED PLUS PLATINUM REGIMENS IN REFRACTORY TRIPLE NEGATIVE BREAST CANCER

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Background: To assess the efficacy of pemetrexed plus platinum regimens in refractory triple negative breast cancer.

Methods: Clinical data of 26 patients diagnosed and treated for mTNBC between 2010 and 2015 at the Tianjin Cancer Hospital were retrospectively analyzed. All patients were pretreated with anthracyclines and taxane and vinorelbine, etc. for mTNBC.Patients should be having at least one measurable metastatic lesion. Totally, 26 patients were included in this study, of which 7 cases received third-line chemotherapy and 19 cases received more than third-line chemotherapy. All patients were treated with pemetrexed plus platinum.

Result: After 20 months follow-up, in the total group of patients, median age of 49 years, patients received treatment for a median of four cycles. The objective response rate was 18.4%, clinical benefit rate was 36.8%, median progression free survival (PFS) was 3.4-1.0-18.0 months and median overall survival (OS) was 19.5-2.0-30.0 months. In addition, the ORR was significantly better in the premenopausal breast cancer arm (23.8% vs. 15.7%, $p=0.029$) as well as PFS was statistically improved in the premenopausal breast cancer arm (5.3 m vs. 3.0 m, $p=0.023$). Similar trend was observed in the OS, although the difference was not statistically significant (23.7 m vs. 18.8 m, $p=0.077$). In all, the most frequently reported adverse events were G1/2 gastrointestinal toxicity (56.8%).

Conclusions: pemetrexed plus platinum combination chemotherapy demonstrates moderate efficacy in refractory triple negative breast cancer with manageable toxicity. pemetrexed plus platinum regimen should be further verified in randomized phase III clinical trial in larger cohort.

PO152

CLINICAL APPLICATION OF INDOCYANINE GREEN COMBINE WITH METHYLENE BLUE TRACER IN THE EARLY BREAST CANCER'S SENTINEL LYMPH NODE BIOPSY

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Background: Research the feasibility of indocyanine green combine with methylene blue tracer in the early breast cancer's sentinel lymph node biopsy and forecast the axillary lymph node status. Compare the sentinel lymph node detection rate and false negative rate of both methods, then analyze the reason.

Methods: Choose 276 patients who were performed both sentinel lymph node biopsy and axillary lymph node dissection from January 1, 2015 to December 31, 2015 in the Affiliated Tumor Hospital of Xinjiang Medical University, 131 cases were traced by indocyanine green combind with methylene blue, other 145 cases were traced only by methylene blue. All cases were diagnosed as breast cancer by core needle biopsy or intraoperative rapid frozen pathological examination. The patients agreed to SLNB, and the axillary lymph nodes dissection were performed regardless of SLN was negative or positive.

Result: The detection rate of combination group was 96.9%, the average detection SLN is 3.0, and the false negative rate was 7.3%, the methylene blue group's detection rate was 89.7%, 2.1 SLNs were detected on average, its false negative rate was 10.5%. Both detection rate and average number of sentinel lymph nodes in combination group were higher than the other group. The false negative rate was not statistically significant ($p = 0.916$).

Conclusions: Indocyanine green and methylene blue tracer in sentinel lymph node biopsy can accurately predict axillary lymph node status, and it is a safe and feasible, simple and convenient method. Age factors have significant effect on the fluorescence development of sentinel lymph node, so the patients over 60 years should be detected by combined method.

PO153

COBIMETINIB (COBI) + PACLITAXEL (PTX) AS FIRST-LINE TREATMENT IN PATIENTS (PTS) WITH ADVANCED TRIPLE-NEGATIVE BREAST CANCER (TNBC): INTERIM SAFETY REVIEW OF THE ONGOING PHASE 2 COLET STUDY

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Poster Exhibition

Background: Since most TNBC pts develop resistance to taxanes and TNBC tumors harbor genetic alterations in the MAPK pathway, the combination of a taxane and COBI, a potent MEK inhibitor may be beneficial.

Methods: COLET (EudraCT number, 2014-002230-32) study includes a safety run-in stage of approximately 12 pts, followed by a randomized stage in which approximately 100 pts will be randomized (1:1) to receive PTX + COBI or placebo.

Result: The median age of 16 pts in the safety run-in stage was 55 years. At data cutoff (Jun 25, 2015), 12 pts had completed at least 1 cycle; all 16 pts received at least 1 dose of

study treatment. Median time on treatment was 47 days (range, 1-85). Most pts tolerated COBI + PTX. The most common (≥ 20%) AEs of any grade were diarrhea (63%), rash (44%), nausea (38%), and alopecia, pyrexia, stomatitis, vomiting, and abdominal pain (all 25%). 7 pts (44%) had grade 3 AEs; there were no grade 4-5 AEs. Ocular toxicity has been reported with MEK inhibitors; in this study, 1 pt had a grade 1 AE of increased macular drusens. Preliminary efficacy results were unconfirmed partial response (n = 7), stable disease (n = 4), and progressive disease (n = 2); 3 pts had not completed a tumor assessment.

Conclusions: The safety profile of COBI + PTX was consistent with known safety profiles of each drug, with no exacerbation of anticipated COBI or PTX toxicities and no new safety signals. Results support further evaluation, and enrollment to the randomized stage was opened.

PO154

BRCA1 AND BRCA2 LARGE GENOMIC REARRANGEMENTS SCREENING IN THAI FAMILIAL BREAST CANCER PATIENTS BY MULTIPLEX LIGATION-DEPENDENT PROBE AMPLIFICATION (MLPA)

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Background: Breast Cancer has now become the most frequently diagnosed cancer and the leading cause of cancer death in females. BRCA1 and BRCA2 inherited mutations account for 5%-10% of all female breast cancers. However, prevalence of BRCA genes mutation is vary in between difference populations. In Thailand, there are no previous studies of BRCA1 and BRCA2 large genomics rearrangement (LGRs) have been reported.

Methods: In this study, we screened the high-risk group consisted of 100 individuals who met clinical criteria for genetic examination of BRCA1/2 using Multiplex Ligation-dependent Probe Amplification (MLPA).

Result: Among a total of 100 selected cases, one duplication of BRCA1 exon 15 was determined but none of any LGRs were found in BRCA2.

Conclusions: Similar to the other studies in Asian population, the prevalence of LGRs in Thailand likely to be low. The information of BRCA1 and BRCA2 LGRs from this study will be as a nationwide of Thai database which will be useful for further study of the familial breast cancer.

Poster Exhibition

PO156

A NEW B LYMPHOCYTE-TARGETED TRACER FOR SENTINEL LYMPH NODE IN BREAST CANCER: INDOCYANINE GREEN-RITUXIMAB

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Background: The aim of the study is to produce a new B lymphocyte-targeted tracer for sentinel lymph node (SLN), to identify the appropriate combination ratio of the tracer, and to test the biological property and safety limitation of the tracer. The localization ability of the new tracer for SLN was evaluated.

Methods: Rituximab is an antibody targeting CD20 antigen on B-cell surface. It was combined directly with the fluorescence tracer (Indocyanine green, ICG) in five different combination ratios. The new tracer was analyzed for labeled rate by instant thin-layer chromatography-silica gel, molecular integrity by sodium dodecyl sulfate-polyacrylamide gel electrophoresis and molecular immune activity by ELLAS. The acute toxicity and the local toxicity were tested in mice. The localization ability of the tracer for SLN was tested and compared with the standard radiotracer in mice.

Result: The new tracer was intact and kept the immune activity of rituximab. The ICG labeled rate of rituximab was 100%. The new tracer was pyogen free, and was no toxicity to mice with local injection. The appropriate combination ratio of rituximab and ICG was 4:1, which had a stable and clear imaging of SLN for 20-24 hours with 10 μL injection dose. The location of SLN identified by the new tracer was accorded with the standard radiotracer.

Conclusions: The produce method of the B lymphocyte-targeted tracer for SLN is simple and no radioactive burden. The new tracer was safe with local injection. It could make only SLN imaging with appropriate injection dose.

PO157

PREOPERATIVE AXILLARY LYMPH NODE EVALUATION IN BREAST CANCER PATIENTS BY BREAST MAGNETIC RESONANCE IMAGING (MRI): CAN BREAST MRI EXCLUDE ADVANCED NODAL DISEASE?

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Background: To evaluate the diagnostic performance of breast magnetic resonance imaging (MRI) in preoperative evaluation of axillary lymph node metastasis (ALNM) in breast cancer patients and to assess whether breast MRI can be used to exclude advanced nodal disease.

Methods: A total of 425 patients were included in this study and breast MRI findings were retrospectively reviewed. The diagnostic performance of breast MRI for diagnosis of ALNM was evaluated in all patients, patients with neoadjuvant chemotherapy (NAC), and those without NAC (no-NAC). We evaluated whether negative MRI findings (cN0) can exclude advanced nodal disease (pN2-pN3) using the negative predictive value (NPV) in each group.

Result: The sensitivity and NPV of breast MRI in evaluation of ALNM was 51.3% (60/117) and 83.3% (284/341) respectively. For cN0 cases on MRI, pN2-pN3 manifested in 1.8% (6/341) of the overall patients, 0.4% (1/257) of the no-NAC group, and 6% (5/84) of the NAC group, respectively. The NPV of negative MRI findings for exclusion of pN2-pN3 was higher for the no-NAC group than for the NAC group (99.6% vs. 94.0%, $p = 0.039$).

Conclusions: Negative MRI findings (cN0) can exclude the presence of advanced nodal disease with an NPV of 99.6% in the no-NAC group.

PO158

USEFULNESS OF CONTRAST-ENHANCED ULTRASOUND WITH SONAZOID FOR EVALUATION OF RESIDUAL TUMOR AFTER NEOADJUVANT CHEMOTHERAPY FOR BREAST CANCER PATIENTS

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Background: Contrast-enhanced magnetic resonance imaging (CEMRI) has been reported to be useful to evaluate breast tumors. But it is difficult to perform CEMRI for patients with allergy of contrast agent, renal dysfunction and asthma. Contrast-enhanced ultrasonography (CEUS) is more reasonable, less time of examination, and simpler methods than CEMRI, and we can use safely Sonazoid contrast agent for patients with renal dysfunction. CEUS has been reported to have more accuracy of diagnosis for breast tumor than CEMRI. We compared the diagnostic ability of CEUS and CEMRI for residual tumor after neoadjuvant chemotherapy (NAC) of breast cancer.

Methods: Nine patients who underwent NAC for invasive breast cancer were enrolled between October 2014 and October 2015. All patients were female. CEUS and CEMRI after NAC were performed before surgical treatment. Pathological response of NAC was diagnosed as complete response or nearly complete response. We used LogiqE9 (GE) for CEUS. We acquired images of CEUS for about 1 minute after intravenous injection of Sonazoid. We compared between these images and the results of CEMRI.

Result: In 8 patients (89%) no enhanced lesion were indicated by CEUS, and in 1 patient (11%) lesion showed light and homogenous enhancement. All result of CEUS showed benign pattern of enhancement. In 4 patients (44%) no enhanced lesion were detected by CEMRI, and in 5 patients (56%) CEMRI showed micro enhanced nodules or malignant pattern of enhancement.

Conclusions: It was suggested that CEUS was more useful for the evaluation of residual cancer in breast cancer patients with high response of NAC than CEMRI.

PO159

USEFULNESS OF 3-DIMENSIONAL LOCALIZATION WITH DIGITAL BREAST TOMOSYNTHESIS BEFORE PERFORMING STEREOTACTIC BIOPSY

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Background: To assess the usefulness of 3-dimensional (3D) digital breast tomosynthesis (DBT) for exact determining the lesion's location before performing stereotactic biopsy.

Methods: A total of 80 patients with abnormal findings only on mammography were enrolled this study. And, they were scheduled to undergo stereotactic biopsy. Before performing stereotactic biopsy, all of these patients underwent unilateral DBT. According to DBT information, we defined exact depth of the lesion and calculated the shortest distance from the lesion to skin.

Result: In 6 cases of 80 patients, the lesions were too close to skin or pectoralis muscle, stereotactic biopsy could not be done. In other 74 patients determined to do stereotactic biopsy, we also calculated the shortest distance from the lesion to skin. It was helpful to define how to approach, lateral or supine. We performed stereotactic biopsy in 59 patients with upright sitting position and 15 patients with lateral recumbent position

Conclusions: DBT detects very small breast cancer and suspicious BI-RADS 4 and BI-RADS 5 lesions not visualized on other study. Stereotactic biopsy on the DBT system has become an integral part of the work-up of patients with suspicious breast lesions, only visible on mammography. But, the possibility of stereotactic biopsy is depending on the location of lesions. Therefore to define the accurate location of lesion is important. The 3D localization in the breast is possible with DBT, it enables the breast radiologists to determine with accurate depth, safety margin for the biopsy, and to define the approach (lateral and supine).

CAN MORPHOLOGICAL ANALYSIS OF PHYLLODES TUMOUR PREDICT THE LIKELIHOOD OF MALIGNANCY IN BREAST MRI?

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Background: To evaluate the multimodality imaging findings of phyllodes tumour of the breast and correlate its imaging findings with histologic grade and suggest radiologic clues to distinguish malignant from benign.

Methods: Radiologic images and clinical histories of 59 patients with histologically verified phyllodes tumours were retrospectively studied. All patients were female and between the ages of 15 and 68 years (mean age, 44.6 years). Mammography (n = 52), breast ultrasonography (US) (n = 59), breast computed tomography (CT) (n = 6) and breast magnetic resonance (MR) imaging (n = 26) were performed. The diagnosis of phyllodes tumours of the breast was pathologically confirmed by means of examination of the specimens obtained at surgical biopsy. We correlated radiologic findings with pathologic results.

Result: 33 masses were benign, 12 masses were borderline, and 14 masses were malignant. The mean size was 5.5 cm for the benign phyllodes tumours, 4.2 cm for the borderline tumours, and 12.6 cm for the malignant tumours. Internal haemorrhage and cystic change with irregularly enhancing wall were significantly associated with malignant histologic grade ($p < 0.001$). However, the size, tumour shape, margin and internal enhancement pattern did not correlate with histologic grade.

Conclusions: A phyllodes tumour greater than 6 cm in diameter suggests a higher likelihood of malignancy; however, the radiologic characteristics of benign and malignant tumours overlapped substantially. Internal haemorrhage and cystic change with irregularly enhancing wall are suggestive of malignant phyllodes tumour of the breast.

USEFULNESS OF TUMOUR MARKERS AND POSITRON EMISSION TOMOGRAPHY (PET) ON POST-OPERATIVE SURVEILLANCE OF BREAST CANCER

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Background: The role of tumour markers in postoperative breast cancer surveillance was defined by the American Society of Clinical Oncology in 2007. Currently there is still limited biomarker discovery for monitoring metastasis. With the advances in imaging modalities, we revisited the use of tumour markers in early detection of breast cancer recurrences by correlating its trend with positron emission tomography (PET) scan tumour load detection.

Methods: The clinicopathological data of patients undergoing regular postoperative surveillance by tumour markers and PET scan between January 2005 and December 2010 were reviewed. CEA < 5 ng/mL and Ca 15-3 < 23 U/mL were used as cut-off values. Correlation between tumour markers and PET scan findings were defined by Chi-square test.

Result: 250 patients included. Median CEA and Ca 15-3 levels were 2.2 ng/mL (0.2, 1,763 ng/mL) and 16 U/mL (3.9, 558 U/mL) respectively. Mean clinical tumour size was 30 mm (0-150 mm) and 55 patients had palpable axillary lymph node (22.2%). When CEA was ≥ 5 ng/mL, recurrence was detected in 61.8% patients on PET scan ($p = 0.004$) and when Ca 15-3 was ≥ 23 U/mL, 64.1% patients had positive PET ($p < 0.001$). The positive predictive values of CEA and CA15-3 were 61.8% and 64.1% respectively.

Conclusions: Both CEA and Ca 15-3 had high sensitivity in detecting metastasis when used with PET scan. The efficacy of these tumour markers as first-line of tools for postoperative surveillance can be re-evaluated. Nonetheless, clinicians should remain vigilant for tumour recurrence in patients with normal tumour marker levels due to its low specificity.

PO162

A CASE SERIES OF METASTASIS OF PRIMARY LUNG CARCINOMA TO BREAST: AN UNUSUAL PRESENTATION

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Background: Breast cancer is the most commonly diagnosed malignancy in adult women worldwide. Around 1 in every 8 women will be diagnosed with breast cancer in their lifetime. However, breast malignancy can sometimes present as metastasis. It is rare, occurring only in about 0.4% to 1.3% of all breast malignancies. A variety of malignancies have been reported to metastasis to the breast. Common primary tumors are melanoma, lung carcinoma or hematological malignancies. Despite its rarity, metastatic breast disease is a significant diagnostic clinical dilemma as breast metastasis from other primary malignancy can mimic triple negative breast carcinoma and can be difficult to identify despite immunohistochemistry analysis.

Methods: Hereby we report two cases of female patients who presented with breast lumps with an initial preliminary diagnosis of primary breast carcinoma. They were subsequently diagnosed with lung carcinoma with breast metastasis.

Result: Radiological imaging of the two cases was evaluated and discriminative ultrasonic and mammographic imaging characteristics of extra mammary metastasis were described.

Conclusions: In conclusion, metastatic disease to the breast though rarity should be considered in the differential diagnosis in patients presenting with a breast abnormality as the prognosis and treatment differ significantly. There are many features both clinically and radiologically to help differentiate between breast adenocarcinoma and metastatic disease. Consequently, clinical correlation is crucial to prevent unnecessary surgery in the setting of metastatic disease and assuring that appropriate treatment for the patient is administered if their primary disease is a lung carcinoma that is first diagnosed via breast biopsies.

THE INSIGHT OF TRANSITION BETWEEN NGS PLATFORMS

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Background: There is a huge demand for applying next generation sequencing (NGS) in both germline and somatic mutation screening for breast cancer patients. The coverage of the gene panel is crucial to cope with the needs of novel targeted therapy. However, the specificity and sensitivity of the test are rarely mentioned.

Methods: A feasible option for the clinical laboratory is the adoption of commercially available amplicon based strategy coupled with the MiSeq sequencer which has a medium output that suits the clinical setting.

Result: A pilot study of 5 tumours from the patients with BRCA1/BRCA2 germline mutation (variant allelic frequency [VAF] 40-60% in 454-Junior) by MiSeq indicated the fluctuation of VAF from < 10% to > 50% with standard bioinformatic tools. We conclude that the throughput of MiSeq is approximately 25 times higher but compromised with the shorter read length. The overall quality of the reads with Q30 drops below 80% beyond the 200th nucleotide for the first-read and 150th nucleotide for the second-read. The imperfection of primer trimming contributes to the deviation of the VAF. Short amplicons strategy adopted by the commercial kit implied that more primers are required. The most obvious downside is the present of Single Nucleotide Polymorphism (SNP) or the mutation fall in the primer binding regions. The combination of both short reads and a large number of primers further increase the difficulty of calling complex indels.

Conclusions: Germline and somatic mutation screening could be transferred to new NGS platform, but tuning and validation of bioinformatic pipeline are essential to improve the specificity and sensitivity.

PO164

DIFFERENTIAL DIAGNOSIS OF BREAST CANCER IN THE PRE-MENOPAUSAL KOREAN POPULATION USING DIFFUSE OPTICAL SPECTROSCOPIC IMAGING (DOSI)

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Background: The incidence of breast cancer in Korea has drastically increased over the past 20 years. The positive biopsy rate for breast cancer, poor in the general population, worsens considerably in young patients with dense breasts (~1 in 7). In this work, we investigate the benefit of using a functional and metabolic imaging technique, Diffuse Optical Spectroscopic Imaging (DOSI), to help improve the accuracy of current standard of care imaging tools to distinguish benign from malignant lesions in premenopausal Korean women. In the long-term, DOSI could potentially help reduce the number of unnecessary biopsies.

Methods: DOSI uses near-infrared light to measure breast tissue composition and metabolism by quantifying tissue concentrations of water (ctH2O), bulk lipid (ctLipid), deoxygenated (ctHHb) and oxygenated (ctHbO2) hemoglobin. Lesion to normal ratio of tissue components were statistically compared between the benign and malignant lesions. Univariate logistic regression was performed to determine the ability of DOSI to predict a malignant finding.

Result: Nineteen premenopausal subjects (average age 41 ± 9) with 21 lesions (11 benign and 10 malignant) were measured using DOSI. Elevated ctH2O, ctHHb, ctHbO2, total hemoglobin (ctHHb+ ctHbO2) were observed in the malignant compared to benign lesions. These differences were all statistically significant (p-values < 0.02). Lesion to normal tissue total hemoglobin was the best single predictor of malignancy with 90% sensitivity and 100% specificity.

Conclusions: Malignant lesions showed significantly higher metabolism and perfusion than benign lesions. DOSI showed high predictive power for identifying malignant from a mixed cohort of lesions in the Korean dense breasts.

Poster Exhibition

PO165

CLINICO-PATHOLOGIC ANALYSIS OF VACUUM ASSISTED BREAST BIOPSY (MAMMOTOME) FOR BREAST DISEASE - 11,221 CASES EXPERIENCE IN A SINGLE INSTITUTE

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Background: The aim of this study is to evaluate the clinical and histopathological profile, usefulness and safety of the Mammotome (MMT) breast biopsy for the purposes of diagnosis and treatment of breast disease.

Methods: A retrospective study was conducted, based on medical records and histopathological findings of 11,221 cases of 8,748 patients who underwent MMT breast biopsy at Department of Surgery, Kangnam CHA Hospital from January 2003 to December 2015.

Result: Among the 11,221 cases of MMT biopsy, 993 lesions were ≤ 0.5 cm in diameter (8.8%), with the majority (4,443 cases) between 0.6 and 1.0 cm (39.5%) and 3,141 cases (27.9%) between 1.1 and 1.5 cm, 1,368 cases between 1.6-2.0 cm (12.1%), 921 cases between 2.1 and 2.9 cm (8.2%) and 355 cases ≥ 3.0 cm (3.1%). Histologically, the most common lesions (4,813 cases, 42.8%) were fibroadenoma, 2,732 cases (24.3%) were fibrocystic disease, 403 cases (3.5%) were intraductal papilloma, 93 cases (0.8%) were phyllodes tumor, 260 cases (2.3%) were atypical ductal hyperplasia and 1,810 cases (17.0%) were other benign lesions. 414 cases (3.6%) were invasive ductal carcinoma or other malignant cases where additional breast cancer operations were performed. There was no conversion to incision due to bleeding and there was no case of histologic underestimation or specific complication. No residual lesion was confirmed in 7,060 (94.3%) in 7,480 cases where follow-up USG was possible 3 to 6 months later.

Conclusions: The study suggests MMT breast biopsy can completely replace ultrasound-guided core biopsy and excisional biopsy procedures for the diagnostic and therapeutic management of benign breast lesions.

PO166

METHYLATION STATUS OF BRCA1 IN TRIPLE-NEGATIVE BREAST CANCER ACCORDING TO SUBTYPE

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Background: Triple-negative breast cancer (TNBC) is one of the molecular subtype of breast cancer and recently has been further classified into different subgroups. BRCA1-related breast cancers share phenotypic characteristics with TNBC and epigenetic changes of *BRCA1* has been shown to be related to its expression. We aimed to examine the *BRCA1* promoter methylation status of TNBC in each subtype classified by Lehmann et al.

Methods: Using gene expression data of 100 TNBC samples, we classified them into subtypes according to a web-based subtyping tool (http://cbc.mc.vanderbilt.edu/tnbc) developed by Lehmann et al. Methylation status of samples were evaluated by pyrosequencing method and we used a cutoff of 20% to call a sample methylated. We assessed the association between TNBC subtype and methylation status of *BRCA1*.

Result: Patients samples were classified into 6 subtypes. Methylation status of *BRCA1* was evaluated in 87 samples and hypermethylation of *BRCA1* was detected in 25.3% of patients. Methylation status was different according to each TNBC subtype. Hypermethylation of *BRCA1* was significantly associated with basal-like 1 subtype (57.1%, $p < 0.001$). In basal, immunomodulatory, luminal androgen receptor, esenchymal, and mesenchymal stem-like subtype hypermethylation of *BRCA1* showed 25%, 0%, 0%, 26.3%, and 0%, respectively.

Conclusions: Methylation status of *BRCA1* was different among TNBC subtypes. Basal-like 1 subtype showed significantly higher methylation status compared to other subtypes. Our results show that methylation status of *BRCA1* could be used to characterize and classify TNBC into specific subtypes.

Poster Exhibition

PO167

DELAYED DIAGNOSIS OF MUCINOUS CARCINOMA OF THE BREAST WITH RADIOLOGICALLY BENIGN FEATURES

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Background: Mucinous breast carcinomas mimic benign lesions on imaging studies, leading to delay in diagnosis. In this study, we attempt to determine the frequency and factors leading to delayed diagnosis in such cancers.

Methods: Patients with histologically proven invasive mucinous breast cancer treated at Singapore General Hospital and National Cancer Centre, Singapore between March 2000 and July 2014 were identified. Patient demographics, imaging data and histopathological features were collected. Univariate and multivariate analysis were done on factors influencing the decision to obtain histological diagnosis despite benign imaging studies.

Result: A total of 197 patients were identified. 152 (77.2%) were scored as either Breast Imaging Reporting And Data System (BIRADS) 4 or 5 on initial imaging studies and 45 (22.8%) were scored BIRADS 3 or lower. In those with BIRADS 3 and below, 1 (2.2%) was scored as BIRADS 1, 14 (31.1%) as BIRADS 2, and 30 (66.7%) as BIRADS 3. 41 (91.1%) were symptomatic on presentation while 4 (8.9%) were asymptomatic cases. Among the symptomatic patients, 26 (63.4%) underwent biopsy after the initial imaging assessment. There was a delay in diagnosis in 15 (36.6%) of the symptomatic cases. The median delay was 21 months (2 to 42 months). On univariate analysis, 88.2% of patients with a family history of breast or ovarian cancers underwent biopsy after initial imaging, compared to 57.1% of the patients without ($p = 0.036$).

Conclusions: Our study shows that 1 in 5 mucinous breast cancer did not have suspicious imaging features on initial assessment, leading to delayed diagnosis in 36.6% of symptomatic patients.

FALSE-POSITIVE LESIONS MIMICKING BREAST CANCER ON MAMMOGRAM, US, MRI, CT AND F-18 FDG PET/CT IMAGING STUDIES

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Background: The various benign conditions such as inflammation, physiologic lactation, benign breast masses including silicone granuloma, fat necrosis, fibroadenoma, and postsurgical changes, may be confused with malignant lesions on imaging studies.

Methods: A 35-year-old woman had no known current health problems and no family history of breast cancer. One week ago, she had a normal screening mammogram. A left breast malignancy and ipsilateral axillary lymphadenopathy were diagnosed. Subsequent additional imaging studies and biopsy were performed to confirm histologically proven breast malignancy and for initial staging.

Result: On MR imaging, there was a mass compatible with left breast malignancy and ipsilateral axillary lymphadenopathy (level I). On both CT and US studies, left breast malignancy was highly suggested, however, ipsilateral axillary lymphadenopathy was indeterminate. On F-18 FDG PET/CT scan, the left breast malignancy was correlated, however, any metastatic disease was not observed. US-guided biopsy result was proved a extensive granulomatous inflammation centered in lobules with numerous lymphocytes, plasma cells, epithelioid histiocytes and multinucleated giant cells.

Conclusions: False-positive breast malignancy on all performed imaging studies and false-positive ipsilateral metastatic axillary lymphadenopathy on both mammogram and MRI were observed in patient with granulomatous inflammation. However, US, CT and PET/CT show indeterminate and negative metastatic axillary lymphadenopathy. Our findings suggest that careful attention to these benign condition is required for more accurate image interpretation.

COMPARATIVE ACCURACY OF PREOPERATIVE TUMOR SIZE ASSESSMENT ON ULTRASONOGRAPHY AND MRI

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Background: Ultrasonography (US) is a traditional modality for preoperative estimation of breast cancer size; magnetic resonance imaging (MRI) is more recent but not as well studied. We compared US and MRI for preoperative imaging of primary breast cancer presenting as a mass in patients treated at our center.

Methods: Records from patients who underwent breast cancer operation in 2013 and in whom tumor was seen on all two imaging modalities were retrospectively reviewed for maximum tumor size measurements. Patients with positive tumor margins and those who had undergone neoadjuvant chemotherapy were excluded. Tumor size measurements obtained on the two imaging modalities were compared for accuracy with those obtained during the final pathologic examination.

Result: A total of 120 breast cancer patients were included in this study. Of the 120 breast cancers with all two imaging modalities performed, 106 were infiltrating ductal carcinoma, 4 were infiltrating lobular carcinoma, 10 were other histologic type. The mean (±SEM) tumor size measured on MRI was significantly greater than that measured on pathology, whereas the sizes measured on US was not statistically significantly different from that measured on pathology. Tumor size measured on MRI was greater than that measured on US.

Conclusions: Preoperative MRI overestimated tumor size. Measurements obtained on US was more accurate in measuring tumor size than MRI.

BREAST IMAGING IN ONCOPLASTIC BREAST-CONSERVING SURGERY

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Background: Oncoplastic breast-conserving surgery (oBCS) is increasingly performed by breast surgeons to achieve good cosmesis while maintaining optimal oncologic resection. Depending on tumour and breast characteristics and patients' desires, such surgery may take the form of parenchymal displacement for breast remodeling or replacement of breast volume by either fasciocutaneous or musculocutaneous autologous flaps. Breast imaging after such procedures differ from the standard breast conserving surgery.

Methods: Breast imaging of patients who had oBCS performed were reviewed. These included patients who underwent volume displacement with Benellli mastopexies, Wise pattern or vertical scar mammoplasties and other modified procedures; as well as patients who had volume displacement procedures utilizing fasciocutaneous flaps from the chest wall or the LD miniflap.

Result: A representative selection of these breast imaging studies are presented with descriptions and illustrations of the surgery performed. The issues that may affect post treatment imaging surveillance of breast cancer recurrence are also discussed.

Conclusions: As oncoplastic BCS gains more grounds, radiologists and clinicians will need to be more familiar with the expected findings on breast imaging for clinical decision making. Many breast imaging findings are reflective of the surgical procedures performed. This pictorial study describes the typical changes based on the various types of oncoplastic breast surgery performed.

PO171

CHANGES BODY AND INTIMACY AFTER TREATMENT AMONG WOMEN WITH BREAST CANCER

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Background: The purposes of this study were to explore the lived experiences and the changes in sexuality for Korean women after breast cancer treatment. Utilize qualitative approach which most appropriate in examining patients perceptions of a disease and the effect of treatment within a given social-cultural context and particularly with a sensitive and personal subject.

Methods: A qualitative descriptive study using focus group discussion was used to address the research question: what are the changes in sexuality after treatments among women with breast cancer in South Korea? Three group discussion were conducted with three groups of between three to four participants each to collect opinions and sentiment on a certain topic within an in-depth group interview. Data analysis followed the general approach of focus group discussion put forth by Krueger.

Result: Three major themes characterized the accounts of these women post treatment: (1) Changed body, (2) Negatively altered sexuality and intimacy, (3) I am still sick (non-supportive intimate husband), and (4) Sorry but I love you. These three themes detail the various aspects of living with breast cancer as women and also underscore women experiences of changes in sexuality as a consequence of their treatment.

Conclusions: This study outlined that changed body and its perception among breast cancer patients after treatment is essential for marital relationship. The possible impact of the knowledge by this study for healthcare practices is that health care professionals should provide support including sexuality as an important aspect in the care for women with breast cancer.

PO172

FERTILITY PRESERVATION FOR BREAST CANCER PATIENTS AMONG REPRODUCTIVE AGE - A SINGLE INSTITUTE EXPERIENCE

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Background: The number of newly diagnosed Japanese breast cancer patients is still increasing. Among these breast cancer survivors, population under age 40 increased from 1610 in 2006 to 3,182 in 2011. Since 2010, we have been cooperating with gynecologists to provide fertility preservation program in our institute.

Methods: We accessed our team management, clinical impact and outcome of fertility preservation among young breast cancer patients in our institute. A patient, 1) without distant metastasis, 2) systemic chemotherapy and/or hormonal therapy planned, 3) within reproductive age and 4) willing to preserve fertility, will be referred to oncofertility clinic. Chart review was done retrospectively.

Result: Ninety-five patients had consultation to the oncofertility clinic between April 2010 and April 2015. The average age at consultation was 34.1(range 22-44). Almost all patient had invasive cancer; cStage 0: 4%, cStage I: 31%, cStage II: 53%, cStage III: 11%. Fifty-five percent had estrogen receptor (ER) positive/HER2 negative, 31% had ER positive/HER2 positive, 2% had ER negative/HER2 positive and 12% had ER negative/HER2 negative breast cancer. Forty-five had counseling without any procedure, 22 underwent ovarian tissue cryopreservation, 17 underwent embryo cryopreservation and 8 underwent oocyte cryopreservation. Because observation period is still short, we haven't had any case that got pregnant or delivered, yet.

Conclusions: The number of patient who choose to underwent fertility preservation is increasing. Among them, we need to think when we shall lay aside adjuvant hormonal therapy to permit pregnancy, and evaluate the safety and outcome of each procedure which undergone multidisciplinary deliberate decision-making process.

CHANGES OF PSYCHOLOGICAL DISTRESS IN KOREAN WOMEN WITH NEWLY DIAGNOSED BREAST CANCER

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Background: Breast cancer diagnosis and treatment is considered a stressful life events and lead to psychological distress. Distress levels remained elevated over the first year of the diagnosis with breast cancer. The purpose of this study was to identify changes of psychological distress in Korean women with newly diagnosed breast cancer.

Methods: A longitudinal prospective study design was adopted. A total of 117 patients with breast cancer were administered the Distress Thermometer (DT) scale and Problem List at diagnosis (T1), after completing adjuvant therapy (T2), and 6 months after the completion of adjuvant therapy (T3). Data were analyzed using SPSS/Win 21.0 program.

Result: The mean DT score were 3.71 ± 2.85, 2.82 ± 2.34, and 2.13 ± 2.35 and the 48.7%, 29.9% and 17.9% (respectively) of patients had DT scores above the cut-off for distress. Level in psychological distress was higher at T1 than T2, and T3. At the T2 and T3 ($F = 16.25$, $p < 0.001$). At the T1, problems most frequently encountered were worry (72.6%), bathing/dressing (65.0%), fatigue (62.4%), fear (57.3%) and housing (55.6%). At the T2 and T3, problems most had treatment-related symptoms like fatigue (72.6% and 68.4%), worry (63.2% and 29.1%), appearance (53.0% and 30.8%), memory/concentration (47.9% and 48.7%) and fear (40.2% and 30.8%).

Conclusions: Psychological distress was significantly decreased but remained after treatment. Therefore, oncology specialists should be aware of the potential distress and problem lists that breast cancer patients may experience after treatment.

MIR-4653-3P AND ITS TARGET GENE FRS2 PREDICT THE OUTCOME OF HORMONE RECEPTOR POSITIVE BREAST CANCER PATIENTS RECEIVING TAMOXIFEN AS ADJUVANT ENDOCRINE THERAPY

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Background: Tamoxifen resistance remains a big challenge for hormone receptor-positive (HR+) breast cancer (BC) patients. We aimed to identify prognostic biomarkers for tamoxifen treatment and explore their role in tamoxifen resistance.

Methods: From 2001. 3 to 2013. 9, 400 non-metastatic HR+ BC women were treated with adjuvant tamoxifen for 5 years or until relapse in West China Hospital. We included a discovery set of 6 patients who experienced failure with TAM treatment and a validation cohort of 88 patients including 35 cases with relapse. MicroRNA microarray/real-time RT-PCR and immunohistochemistry were performed to detect miR-4653-3p and FRS2 levels, respectively. The effects of miR-4653-3p on FRS2 regulation and TAM sensitivity were explored in two tamoxifen-resistant cell models.

Result: MicroRNA microarray showed downregulation of miR-4653-3p in relapse lesions compared to the matched primary lesions from the discovery set. In the validation cohort, high miR-4653-3p level in the primary tumors significantly decreased the risk of relapse following tamoxifen treatment (adjusted hazard ratio [HR] = 0.22, $p = 0.002$). Conversely, high expression of FRS2, the key adaptor protein required by FGFR signaling, independently predicted poor disease-free survival (adjusted HR = 2.61, $p = 0.02$). Interestingly, levels of miR-4653-3p and FRS2 were negatively correlated in tumor tissues. By using two tamoxifen-resistant breast cancer cell models, we demonstrated that miRNA-4653-3p downregulated FRS2 by binding to its 3-UTR, and either overexpressing miRNA-4653-3p or attenuating FRS2 expression could restore TAM sensitivity.

Conclusions: MiR-4653-3p and its target FRS2 were independent predictors of disease-free survival in non-metastatic HR+ BC patients receiving TAM adjuvant therapy. FGFR/FRS2 signaling might be a promising target for reversing tamoxifen resistance.

LOW EXPRESSION OF MICRORNA-221-3P IS ASSOCIATED WITH POOR OUTCOME OF TRIPLE NEGATIVE BREAST CANCER VIA PARP1 TARGETING

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Background: The purpose of this study was to identify microRNAs (miRNAs) closely associated with the prognosis of triple negative breast cancer (TNBC) and their possible targets.

Methods: This study recruited 125 early TNBC patients, including 40 cases in the experimental group (20 cases with poor prognoses vs. 20 cases with good prognoses) and 85 cases in the validation group (27 cases with poor prognoses vs. 58 cases with good prognoses). The miRNA profiles were analyzed by miRNA microarray. Differentially expressed miRNAs were validated using real-time PCR. The potential targets of differentially expressed miRNAs were screened and validated.

Result: A total of 266 differentially expressed miRNAs were detected in patients with different prognoses in the experimental group. We selected 20 miRNAs for real-time PCR validation. Differential expression of miR-221-3p was further verified in the experimental and validation groups. A survival analysis of all125 patients showed that patients with high levels of miR-221-3p expression exhibited markedly longer disease-free survival (DFS) than those with low miR-221-3p expression levels (73% vs. 51.6%, $p = 0.015$). miR-221-3p was an independent prognostic factor in TNBC patients. Functional analysis demonstrated that miR-221-3p regulated Poly (ADP-Ribose) Polymerase 1 (PARP1) expression by targeting its 3-untranslated region (UTR).

Conclusions: Our study demonstrated that expression profile of miRNAs varied in cancer tissues of TNBC patients with different prognoses. Low expression of miR-221-3p may contribute to the poor outcome of TNBC patients. miR-221-3p likely plays a role as a PARP1 inhibitor by directly regulating PARP1 expression and thus affects the prognosis of TNBC patients.

DEPRESSIVE DISORDERS ARE ASSOCIATED WITH INCREASED RISK OF BREAST CANCER RECURRENCE FOLLOWING CURATIVE SURGERY

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Background: The relationship between newly onset of depression following curative surgery and subsequent recurrence of breast cancer remain unclear. This population-based study is aimed to assess the incidence and risk of recurrence after curative surgery among breast cancer patients with newly diagnosis of depressive disorders.

Methods: Using a nationwide database, the Taiwan National Health Insurance Research Database, newly diagnosed breast cancer patients with depressive disorders and age-, sex-, index-year, chemotherapy-, and radiotherapy-matched control patients who did not have depressive disorders were enrolled between 2003 and 2007. Patients who did not receive curative surgery were excluded. The 2 cohorts were observed until December 31, 2007. The primary endpoint was recurrence of breast cancer.

Result: A total of 1,147 breast cancer patients who developed depressive disorders following curative surgery, and 2,294 breast cancer patients who did not were enrolled. Of the 3,441 patients, 332 (9.65%) suffered from recurrence during a mean follow-up period of 4.547 years, including 139 (12.12%) from the depressive disorders cohort and 193 (8.41%) from the control group. In breast cancer patients, the Cox multivariate proportional hazards analysis showed that the risk increased with depressive disorders 1.373 (95% confidence interval (CI), 1.098-1.716; $p = 0.005$). Moreover, among depressive disorder cohort, younger (20 to 39 years) breast cancer patients had the higher risk of recurrence (HR = 1.7478, 95% CI = 1.0407 to 2.9355, $p = 0.0093$) compared with other patients (> = 40 years).

Conclusions: Depressive disorders were associated with a higher risk of breast cancer recurrence among younger patients after curative breast surgery.

THE REAL LIFE TREATING PATTERNS OF ADJUVANT THERAPY AND PROGNOSTIC ANALYSIS IN HR-POSITIVE BREAST CANCER PATIENTS IN SOUTHWEST CHINA

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Background: Hormone receptor-positive (HR+) is defined as estrogen and/or progesterone receptor-positive. It is the most common subtype of breast cancer. We aimed to explore the adjuvant treatment patterns and prognostic factors for HR+ breast cancer in Southwest China.

Methods: 5,256 women diagnosed with HR+ non-metastatic breast cancer at West China Hospital, Sichuan University, between 1989 and 2014 were enrolled. The patterns of adjuvant therapy and prognostic factors were analyzed retrospectively.

Result: The whole cohort had a 5-year overall survival (OS) rate of 94.0% and a 10 year OS rate of 88.0%. Luminal B was the most common subtype (58.1%). Luminal A tended to be diagnosed at an older age. Compared with Luminal A subtype, Luminal B patients had a poorer iDFS but a similar OS. Simutaneous ER and PR-positive was associated with improved prognosis compared with single receptor-positive. Endocrine therapy (ET) following chemotherapy was the predominant adjuvant treatment pattern and the percentage of this pattern displayed a fluctuant increase. Unfortunately, as ET duration increased, treatment adherence was on the decline. The whole cohort significantly benefited from ET. There was no statistical difference in prognosis between postmenopausal patients receiving different aromatase inhibitors. Receiving either chemotherapy or radiotherapy resulted in a better OS. However, radiotherapy did not improve the loco-regional relapse-free survival in patients with lymph node metastasis.

Conclusions: ET following chemotherapy was the predominant adjuvant treatment pattern in HR+ breast cancer. The impact of breast cancer subtype, hormone receptor status and treatment patterns on the prognosis is complex.

ASSOCIATION BETWEEN HEPATITIS B VIRUS AND RISK OF BREAST CANCER RECURRENCE FOLLOWING CURATIVE SURGERY

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Background: Tumor recurrence is a major issue for patients with breast cancer following curative breast surgery. This study is aimed to investigate the association between hepatitis B virus (HBV) and risk of tumor recurrence in patients with HBV after curative surgery.

Methods: Using a nationwide database, the Taiwan National Health Insurance Research Database, newly diagnosed breast cancer patients with hepatitis B virus and age-, sex-, index-year, chemotherapy-, and radiotherapy-matched control patients who did not have hepatitis B virus were enrolled between 2001 and 2007. Patients who did not receive curative surgery were excluded. The 2 cohorts were observed until December 31, 2007. The primary endpoint was recurrence of breast cancer.

Result: A total of 1,168 breast cancer patients with hepatitis B virus, and 4,672 breast cancer patients without hepatitis B virus were enrolled. Of the 5,840 patients, 426 (7.29%) suffered from recurrence during a mean follow-up period of 5.576 years, including 124 (10.62%) from the hepatitis B virus cohort and 302 (6.48%) from the control group. In hepatitis B virus patients, the Cox multivariate proportional hazards analysis showed that the risk increased with hepatitis B virus (adjusted hazard ration (aHR) 1.9513, 95% CI 1.3780 to 2.7631, $p < 0.001$), and younger age (20-39y/o) (aHR 2.1850, 95% CI 1.5762 to 3.0291, $p < 0.001$).

Conclusions: Hepatitis B virus was associated with a higher risk of breast cancer recurrence among young patients after curative breast surgery.

THE RELATIONSHIP BETWEEN NUCLEAR FACTOR (NF)-κB FAMILY GENE EXPRESSION REGULATED BY SP1 AND PROGNOSIS IN TRIPLE-NEGATIVE BREAST CANCER (TNBC) PATIENTS RECEIVING DOXORUBICIN CONTAINING ADJUVANT CHEMOTHERAPY

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Background: We investigated gene expression profiles of the nuclear factor (NF)-κB pathway in patients with triple-negative breast cancer (TNBC) receiving adjuvant chemotherapy to determine the prognostic value of NF-κB pathway genes according to chemotherapeutic regimen.

Methods: We performed the nCounter expression assay (NanoString) to measure expression of eleven genes (NFKB1, NFKB2, RELA, RELB, REL, TP53, FOXC1, TBP, SP1, STAT3, and IRF1 genes) belonging to the NF-κB pathway using mRNA extracted from paraffin-embedded tumor tissues from 203 patients diagnosed with TNBC.

Result: Two hundred and three patients were diagnosed with TNBC from 2000 to 2004 and received adjuvant chemotherapy after curative surgery. Of the 203 patients, 116 patients were treated with a chemotherapeutic regimen containing doxorubicin. As revealed by the expression profiles of the 11 genes in TNBC tissue specimens, increased expression of SP1 was associated with poor prognosis in TNBC patients treated with adjuvant doxorubicin chemotherapy in the survival analysis (5-year distant recurrence-free survival (5Y DRFS), low vs. high expression [cut-off: median]: 92.3% vs. 71.6%, $p = 0.001$). In a multivariate Cox regression model, SP1 expression was identified as a useful marker for predicting long-term prognosis in TNBC patients with doxorubicin treatment.

Conclusions: The level of SP1 expression could serve as a prognostic marker in TNBC patients receiving adjuvant doxorubicin chemotherapy.

THE DIFFERENT PROGNOSTIC ROLE OF BCL2 IN MOLECULAR SUBTYPES OF BREAST CANCER

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

Methods: We retrieved data from 1,356 patients in the breast cancer center of Seoul St. Marys Hospital between 2006 and 2011. We classified breast cancer into five molecular subtypes depending on 13th St. Gallen immunohistochemical classification, including Luminal A, Luminal B (HER2 negative), Luminal B (HER2 positive), HER2 overexpression, Basal-like. We analyzed the clinicopathologic features and assessed the correlation between BCL2 expression and clinical outcomes relapse free survival (RFS) and disease specific survival (DSS) according to the five molecular subtypes.

Result: A total of 605 (53.7%) breast cancer showed BCL2 expression. BCL2 positive expression was associated with young (< 50 years old) ($p = 0.036$), well histologic grade ($p = < 0.001$), low level of Ki-67 (< 14%) ($p < 0.001$), hormone receptor positive ($p < 0.001$), HER2 negative ($p < 0.001$), luminal type of breast cancer ($p < 0.001$), and low rate of recurrence ($p = 0.016$; BCL2 negative vs. positive; 5-year RFS; 86.3% vs. 91.4%). Although there was no significant difference, BCL2 positive expression was also associated with favorable 5-year DSS ($p = 0.074$). In Luminal A and HER2 overexpression group, patients with BCL2 positive showed a significantly favorable 5-year RFS and 5-year DSS (Luminal A group; $p = 0.023$; $p = 0.041$, HER2 overexpression group; $p = 0.019$; $p = 0.049$). In contrast, patients with BCL2 negative showed a favorable 5-year RFS and 5-year DSS though there was no significantly difference in Basal-like group ($p = 0.735$; $p = 0.181$).

Conclusions: The prognostic role of BCL2 in molecular subtypes of breast cancer is different. BCL2 positive expression is a favorable prognostic marker in Luminal A and HER2 overexpression breast cancer. In contrast, BCL2 negative expression is a prognostic marker in Basal-like breast cancer.

CLINICAL SIGNIFICANCE OF KI-67 EXPRESSION IN BREAST CANCER PATIENT

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Background: Numerous studies have shown a positive correlation between Ki-67 expression and the proliferative cell fraction in tumors. The objectives of this study were to assess the potential value of Ki-67 in predicting prognosis of breast cancer and to suggest a reasonable cut-off value for classifying Ki-67 expression.

Methods: This study included 824 breast cancer patients who underwent surgery between 2006 and 2010. We analyzed the correlation between the expression of Ki-67 and clinical outcome in breast cancer patients. To determine a optimal Ki-67 expression cut-off value, we compared disease free survival (DFS) according to each Ki-67 expression cut-off points.

Result: Ki-67 over expression was significantly correlated with large tumor size ($p = 0.027$), Lymph node metastasis ($p = 0.015$), hign histologic grade ($p = 0.009$), estrogen receptor (ER) negativity ($p = 0.019$), progesterone receptor (PR) negativity ($p = 0.034$). In terms of prognosis, Ki-67 over expression was associated with decreased DFS, especially there was the biggest DFS gap in 25% of Ki-67 cut-off point ($p = 0.011$).

Conclusions: Ki-67 expression in breast cancer tissue was effective factor for predicting prognosis of breast cancer patients. In addition, we suggest that a 25% level of Ki-67 expression is a reasonable cut-off value for predicting DFS in breast cancer patients.

ATTITUDES OF PATIENTS WITH CANCER TOWARDS RESEARCH BIOPSIES

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Background: Research biopsies from cancer patients assist the understanding of the molecular biology of cancer tissue. They can be a stand-alone procedure (research purposes only biopsy, RPOB) or performed during a clinically indicated biopsy (additional pass biopsy, AB). This study evaluates the attitudes of patients with different cancers towards research biopsies, and the attitudes of patients with early breast cancer compared with patients with metastatic breast cancer.

Methods: Patients completed a paper questionnaire that assessed patients' willingness to consider research biopsies. Outcomes were dichotomized into "yes" or "no", and inputs included biopsy history, sociodemographic information and information about prior trial and biopsy participation. Univariate and multivariable analyses were conducted using random-effects logistic regression.

Result: 165 patients with metastatic cancer (40 melanoma, 37 colorectal, 32 breast, 30 lung, 25 prostate), and 39 patients with early breast cancer completed the questionnaire. Patients with melanoma demonstrated the greatest willingness to consider a research biopsy compared to other cancer types (all $p < 0.05$), followed by patients with colorectal, breast, lung and prostate cancer. For patients with early breast cancer, 21/39 (54%) patients would consider an AB compared with 15/39 (38%) patients who would consider an RPOB. Similarly in patients with metastatic breast cancer, 19/32 (59%) patients would consider an AB compared with 11/32 (34%) patients who would consider an RPOB.

Conclusions: Patients with different cancers and different stages of cancers have different attitudes towards research biopsies. By performing a research biopsy in addition to a diagnostic biopsy, there would be an approximately doubling of the proportion of patients who would be willing to have a research biopsy. As research biopsies are critical building blocks for translational cancer research, further research into patient's attitudes towards this is important in improving their participation rates.

PATIENTS AND NURSES SATISFACTION WITH THE ROLE OF NURSE SPECIALISTS WORKING IN A DEPARTMENT OF BREAST SURGERY

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Background: In the present study, we conducted an education program targeting patients scheduled for breast cancer surgery and surveyed Patient's and clinical nurse's satisfaction and patients length of hospital stay.

Methods: A standardized education program was developed through a literature review on education for patients with breast cancer and a survey of educational needs. To test the effects of the program, we recruited 27 participants of the program who had undergone breast cancer surgery and had been discharged within September 2015 and administered them a questionnaire assessing their satisfaction. The length of hospital stay for these patients was obtained from their medical records. An additional survey was conducted to investigate clinical nurse's satisfaction.

Result: The survey results indicated that, after the patients with breast cancer had completed the standardized education program, 64% were very satisfied and 25.4% were mostly satisfied. The mean length of hospital stay also showed a statistically significant decrease from 4.30 days before the program to 4.06 days after the program ($p = 0.043$). Moreover, the survey results on clinical nurses satisfaction revealed that 38% of the nurses were very satisfied and 56% were mostly satisfied.

Conclusions: In conclusion, the standardized education program for patients with breast cancer was found to improve patient satisfaction and shorten their length of hospital stay, while also increasing the satisfaction of clinical nurses. It is believed that such a standardized education program will contribute to increased profitability for the hospitals by improving satisfaction and shortening the length of hospital stay among patients with breast cancer.

PO184

EFFECTS OF QIGONG TRAINING ON QUALITY OF LIFE (QOL) AND PSYCHOLOGICAL HEALTH IN BREAST CANCER SURVIVORS: A REVIEW

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Background: Breast cancer is a common cancer across the world. With the advancement in treatment, the survival rate has greatly improved. Unfortunately, most survivors reported to live with complications from the disease and treatments. In this review, the effects of Qigong training on quality of life (QOL) and psychological health of breast cancer survivors will be summarized.

Methods: Electronic databases were searched with different terms including qigong, breast cancer patients, breast cancer survivors, and breast cancer complications. Clinical controlled trials (CCTs) and randomized controlled trials (RCTs) studies, in English or were translated in English, were included. Original sources were reviewed and analyzed. The quality and validity of the included studies were evaluated by Jadad Scale and strength of the included studies by the Oxford Centre for Evidence-based Medicine Levels of Evidence respectively.

Result: Six studies published between 2006 and 2014, included four RCTs and two CCTs, were examined. There were 223 patients in the experimental groups, 236 patients in the control groups and 16 healthy adults in total. Jadad scores ranged from 2 to 3. Three studies were ranked as A in the level of evidence and others were ranked as B. All RCTs and one CCT showed favorable effects of Qigong training on QOL in the experimental group compared to the control group while one CCT showed that Qigong was not effective. These studies showed significant effects of qigong on improving mood and depression in the experimental groups.

Conclusions: Since the number of studies was limited, the effectiveness of Qigong exercise on QOL and psychological health of breast cancer survivors is still questionable. Further studies should be carried out to confirm the effects.

PO185

PRESCRIPTION DATA ANALYSIS OF HORMONAL TREATMENT IN BREAST CANCER PATIENTS

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Background: The adherence to oral hormonal treatment in breast cancer has association with breast cancer prognosis. However, there is no index for predict or monitor the adherence of oral medication in breast cancer patients. Therefore, we analyzed the prescription data and patients characteristics to predict the prognosis of breast cancer.

Methods: From January 1st 1997 to December 31st 2009, patients with stage 0-3 breast cancer, who underwent operation at Asan Medical Center were enrolled retrospectively. We excluded the patients with early recurrence, within five years. The prescription data of 6.628 patients with hormonal treatment were analyzed. The prescription ratio (PR) was calculated by the ratio of prescription date and the gap of the date of prescribed, during five years.

Result: The mean age at diagnosis was 48.2 years and the age at diagnosis was significantly lower ($p < 0.001$) in lower PR group (PR lower than 20%). The patients with high level of education and married status were tend to had high PR ($p = 0.001$, $p = 0.008$). The prognosis of the group with PR in lower 20% was significantly poor compared with the other patients, in all events of breast cancer recurrence, distant metastasis and breast cancer specific death ($p = 0.009$, $p < 0.001$, $p = 0.018$).

Conclusions: We analyzed prescription data and found out the correlations with breast cancer survival. The index of adherence calculated from prescription data could provide more immediate feedback to patients, than the public data or data from survey. Further study would be proceeded to give more prompt feedback to patients.

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