GBCC2019
Global Breast Cancer Conference 2019
April 25 (Thu) - 27 (Sat), 2019
Songdo ConvensiA, Incheon, Korea

eISSN 2508-1624
GBCC Abstract Book
www.gbcc.kr

Abstract Book

한국유방암학회
Korean Breast Cancer Society

Table of Contents

Program at a Glance

*(Invited Priority): The session is not for invitees only, but they will be given priority.

Program Details

Day 1 April 25 (Thu)

09:45-10:00 **Opening Ceremony** 2F, PBR AB

10:00-11:15 **Symposium 1** 2F, PBR AB

Tailoring Adjuvant Systemic Therapy

Moderator Masakazu Toi
Graduate School of Medicine, Kyoto Univ., Japan

Moderator Woochul Noh
Department of Surgery, Korea Cancer Center Hospital, Korea

Speaker Yoon-Sim Yap *11*
WHO NEEDS SYSTEMIC CHEMOTHERAPY?
Department of Medical Oncology, National Cancer Centre Singapore, Singapore

Speaker Masakazu Toi *12*
WHO ARE CANDIDATE FOR OVARIAN SUPPRESSION & EXTENDED ENDOCRINE THERAPY
Graduate School of Medicine, Kyoto Univ., Japan

Speaker Jee Hyun Kim *13*
WHAT'S NEW FOR HER2 POSITIVE EARLY BREAST CANCER?
Department of Internal Medicine, Seoul National Univ. Bundang Hospital, Korea

10:00-11:15 **Panel Discussion 1** 2F, PBR C

What Can We Do for the Excellent Responders of Neoadjuvant Chemotherapy?

Moderator Byung Ho Son
ASAN Medical Center, Korea

Moderator In Ah Kim
Department of Radiation Oncology, Seoul National Univ., Korea

Speaker Yong Wha Moon *39*
GOOD RESPONDERS: WHO ARE THEY?
Department of Medical Oncology, CHA Bundang Medical Center, CHA Univ., Korea

Speaker Mark Basik *40*
CAN WE ELIMINATE SURGERY IN EXCEPTIONALLY EXCELLENT RESPONDERS?
Segal Cancer Center, Canada

Speaker Mi Young Kim *41*
RADIATION ONCOLOGIST'S VIEW FOR ESCALATION OR DE-ESCALATION
Department of Radiation Oncology, Kyungpook National Univ. Hospital, Korea

10:00-11:15 **Education Session 1** 1F, 113-115

Recent Advance of Endocrine Treatment

Moderator Hiroji Iwata
Department of Breast Oncology, Aichi Cancer Center, Japan

Moderator Sung Hoo Jung
Department of Breast Thyroid Surgery, Chonbuk National Univ. Hospital, Korea

Speaker Sarat Chandarlapaty *70*
OPTIMAL SEQUENCE OF ENDOCRINE TREATMENT IN ADVANCED BREAST CANCER
Department of Medicine, Memorial Sloan Kettering Cancer Center, U.S.A.

Program Details

Day 1 April 25 (Thu)

Speaker Hiroji Iwata *71*
OVERCOME OF ENDOCRINE RESISTANCE
Department of Breast Oncology, Aichi Cancer Center, Japan

Speaker Ian Smith *72*
LATE RECURRENCE IN ER-POSITIVE BREAST CANCER: RISK PREDICTION & TREATMENT
The Royal Marsden NHS Foundation Trust, United Kingdom

10:00-11:15 Oral Presentation 1 1F, 107-109

Moderator Cheol Wan Lim
Department of Surgery, Soon Chun Hyang Univ. Hospital Bucheon, Korea

Moderator Kweon Cheon Kim
Department of Surgery, Chosun Univ. Hospital, Korea

Speaker Michael Co *142*
BREAST CANCER RATE AND MORTALITY IN FLIGHT ATTENDANTS
Department of Surgery, The Univ. of Hong Kong, Hong Kong

Speaker Tae-Kyung Yoo *143*
HORMONE REPLACEMENT THERAPY AND BREAST CANCER RISK IN A NATIONWIDE POPULATION-BASED COHORT
Department of Surgery, The Catholic Univ. of Korea, Seoul St. Mary's Hospital, Korea

Speaker Jeongshin An *144*
ASSOCIATION BETWEEN OBESITY AND FIRMICUTES/BACTEROIDETES RATIO IN BREAST CANCER PATIENTS
Department of Surgery, Ewha Womans Univ. Mokdong Hospital, Korea

Speaker Soojeong Choi *145*
NOVEL FUSION GENES IDENTIFIED FROM MATCHED PRIMARY AND RECURRED BREAST CANCERS BY RNA-SEQUENCING
Department of Surgery, ASAN Medical Center, Korea

Speaker Yisun Jeong *146*
BASAL AND IL-1β-INDUCED IL-8 IS SUPPRESSED BY CELASTROL IN TRIPLE NEGATIVE BREAST CANCER
Sungkyunkwan Univ. School of Medicine, Korea

Speaker Aisha Alzuhair *147*
APPLICATION OF 3D PRINTED BREAST SURGICAL GUIDE FOR BREAST CONSERVING SURGERY IN DCIS PATIENTS
Department of Surgery, ASAN Medical Center, Saudi Arabia

Speaker Hung-Wen Lai *148*
ROBOTIC VERSUS CONVENTIONAL NIPPLE SPARING MASTECTOMY AND IMMEDIATE PROSTHESIS BREAST RECONSTRUCTION IN THE MANAGEMENT OF BREAST CANCER- A CASE CONTROL COMPARISON STUDY
Department of Surgery, Changhua Christian Hospital, Taiwan

Speaker Jisun Kim *149*
PHASE II RANDOMIZED STUDY OF NEOADJUVANT METFORMIN PLUS LETROZOLE VERSUS PLACEBO PLUS LETROZOLE FOR ER-POSITIVE POSTMENOPAUSAL BREAST CANCER [METEOR STUDY]
Department of Surgery, ASAN Medical Center, Korea

Day 1 April 25 (Thu)

Speaker Alan Prem Kumar *151*
DEAD-BOX RNA HELICASE DP103 REGULATED SUMO/ACETYLATION SWITCH OF P53 DETERMINES RESPONSE TO DOCETAXEL IN ERα-POSITIVE BREAST CANCER
National Univ. of Singapore, Singapore

10:00-11:15 Oral Presentation 2 1F, 104-106

Moderator Heung Kyu Park
Department of Surgery, Gachon Univ. Gil Medical Center, Korea

Moderator Kyung-Hun Lee
Department of Hematology-Oncology, Seoul National Univ. Hospital, Korea

Speaker Seung Yeun Chung *152*
THE RISK OF CARDIAC DISEASE IN KOREAN BREAST CANCER PATIENTS: IMPACT OF PATIENT-SPECIFIC FACTORS AND HEART DOSE BASED ON INDIVIDUAL HEART DOSE CALCULATION FROM THREE-DIMENSIONAL RT PLANNING
Department of Radiation Oncology, Yonsei Univ. College of Medicine, Korea

Speaker Yujie Wang *153*
INTERNAL MAMMARY LYMPH NODES INVOLVEMENT IN PATIENTS WITH BREAST CANCER: ANATOMICAL CHARACTERISTICS AND IMPLICATION FOR TARGET DELINEATION
Department of Radiology, Shanghai Jiaotong Univ. Medical School Ruijin Hospital, China

Speaker Hwa Kyung Byun *154*
RISK OF LYMPHEDEMA FOLLOWING CONTEMPORARY TREATMENT FOR BREAST CANCER: AN ANALYSIS OF 7,426 CONSECUTIVE PATIENTS FROM A MULTIDISCIPLINARY PERSPECTIVE
Department of Radiation Oncology, Yonsei Univ. College of Medicine, Korea

Speaker Jee Suk Chang *155*
RADIATION PRACTICE PATTERNS AND IMPACT OF RADIOTHERAPY ON COMPLICATIONS AFTER BREAST RECONSTRUCTION: FINAL REPORT OF KROG 18-04
Yonsei Univ. College of Medicine, Korea

Speaker Hee Jun Choi *156*
EFFECT OF POLOXAMER-BASED THERMO-SENSITIVE SOL-GEL ON SHOULDER MOTION AFTER AXILLARY LYMPH NODE DISSECTION IN PATIENTS WITH BREAST CANCER: A MULTI-CENTER DOUBLE-BLIND, RANDOMIZED CONTROLLED TRIAL
Department of Surgery, Samsung Changwon Hospital, Korea

Speaker Jeea Lee *157*
GAS VERSUS GASLESS ROBOT-ASSISTED NIPPLE SPARING MASTECTOMY
Yonsei Univ. College of Medicine, Korea

Speaker Victor Chan *158*
PRE-OPERATIVE TOMOSYNTHESIS-GUIDED HOOKWIRE NEEDLE LOCALISATION OF IMPALPABLE, MAMMOGRAPHICALLY AND SONOGRAPHICALLY OCCULT BREAST LESIONS: A PRELIMINARY EXPERIENCE
Department of Radiology, Queen Mary Hospital, Hong Kong

Speaker Jung Hyun Yoon *159*
OUTCOMES OF DUCTAL CARCINOMA IN SITU ACCORDING TO DETECTION MODALITY: A MULTICENTER STUDY COMPARING RECURRENCE BETWEEN MAMMOGRAPHY AND BREAST US
Department of Radiology, Yonsei Univ. College of Medicine, Korea

Program Details

Day 1 — April 25 (Thu)

11:15-11:30 Break

11:30-12:15 Plenary Lecture 1 — 2F, PBR AB

Evolution of Therapeutic Strategies for Hormone Receptor-positive, HER2-negative Breast Cancer

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

Speaker Nadia Harbeck *2*
EVOLUTION OF THERAPEUTIC STRATEGIES FOR HORMONE RECEPTOR-POSITIVE, HER2-NEGATIVE BREAST CANCER
Univ. of Munich (LMU), Germany

12:15-12:30 Break

12:30-13:15 Satellite Symposium 1 — 2F, PBR AB

Leading the Way in the Treatment of HR+ HER2-mBC: Palbociclib & CDK4/6 Inhibitors in Clinical Practice

Moderator Joohyuk Sohn
Department of Internal Medicine, Yonsei Univ. College of Medicine, Korea

Speaker Hope S. Rugo *126*
LEADING THE WAY IN THE TREATMENT OF HR+ HER2-MBC: PALBOCICLIB & CDK4/6 INHIBITORS IN CLINICAL PRACTICE
Univ. of California San Francisco Medical Center, U.S.A.

13:15-13:45 Break

13:45-14:30 Plenary Lecture 2 — 2F, PBR AB

Current Trends and Future Directions in Bench to Bedside Translational Research in ER-positive Breast Cancer

Moderator Young-Hyuck Im
Department of Hematology-Oncology, Samsung Medical Center, Korea

Speaker Carlos Arteaga *4*
CURRENT TRENDS AND FUTURE DIRECTIONS IN BENCH TO BEDSIDE TRANSLATIONAL RESEARCH IN ER-POSITIVE BREAST CANCER
UT Southwestern Harold C. Simmons Cancer Center, U.S.A.

14:30-14:45 Break

14:45-16:00 Symposium 2 — 2F, PBR AB

TNBC: Where Are We and What's Next Destination?

Moderator Seock-Ah Im
Department of Internal Medicine, Seoul National Univ. Hospital, Korea

Program Details

Day 1 April 25 (Thu)

Moderator Shigeru Imoto
Kyorin Univ. School of Medicine, Japan

Speaker Sung-Bae Kim 14
POTENTIAL THERAPEUTIC TARGETS: ANDROGEN RECEPTOR, PI3KCA, MEK, ETC.
Department of Oncology, ASAN Medical Center, Korea

Speaker Seock-Ah Im 16
BRCA AND DNA REPAIR IMPAIRMENT
Department of Internal Medicine, Seoul National Univ. Hospital, Korea

Speaker Rebecca Alexandra Dent 17
OPTIMAL TREATMENT OF TNBC WITH CYTOTOXIC CHEMOTHERAPY
Department of Medical Oncology, National Cancer Centre Singapore, Canada

14:45-16:00 **Panel Discussion 2** 2F, PBR C

Up-to-date Management of Premalignant Lesion

Moderator Young-Jin Suh
Department of Surgery, The Catholic Univ. of Korea, St. Vincent's Hospital, Korea

Moderator Aeree Kim
Department of Pathology, Korea Univ. Guro Hospital, Korea

Speaker Aeree Kim 43
RISK STRATIFICATION OF PREMALIGNANT BREAST LESIONS
Department of Pathology, Korea Univ. Guro Hospital, Korea

Speaker Masahiro Takada 44
SURGERY FOR LOBULAR CARCINOMA IN SITU: TO DO OR NOT TO DO?
Kyoto Univ. Hospital, Japan

Speaker Jong Han Yu 45
HOW TO MANAGE SUSPICIOUS MICROCALCIFICATIONS?
Department of Surgery, Samsung Medical Center, Korea

14:45-16:00 **Education Session 2** 1F, 113-115

Prediction and Risk Assessment of Breast Imaging

Moderator Christiane Katharina Kuhl
RWTH Aachen, Germany

Moderator Woo Kyung Moon
Department of Radiology, Seoul National Univ. Hospital, Korea

Speaker Emily Conant 73
QUANTITATIVE IMAGING FOR BREAST CANCER RISK ASSESSMENT
Department of Radiology, Univ. of Pennsylvania, U.S.A.

Speaker Bong Joo Kang 74
EARLY PREDICTION OF RESPONSE FROM NEOADJUVANT THERAPY
Department of Radiology, The Catholic Univ. of Korea, Seoul St. Mary's Hospital, Korea

Speaker Eun-Kyung Kim 76
APPLICATION OF AI IN DIAGNOSIS OF BREAST CANCER WITH DIGITAL MAMMOGRAPHY
Department of Radiology, Yonsei Univ. Severance Hospital, Korea

Program Details

Day 1 April 25 (Thu)

14:45-16:00 **Survivorship Session 1** 1F, 107-109

Healthy Living after Breast Cancer Treatment from Psycho-oncologists' Perspectives

Moderator Richard Fielding
Univ. of Hong Kong, Hong Kong

Moderator Hyun Jo Youn
Department of Surgery, Chonbuk National Univ., Korea

Speaker Eun-Jung Shim *104*
COMPLEX RELATIONSHIP AMONG DEPRESSION, SELF-EFFICACY, ILLNESS PERCEPTION, AND FEAR OF PROGRESSION IN BREAST CANCER SURVIVORS
Department of Psychology, Pusan National Univ., Korea

Speaker Richard Fielding *105*
UNDERSTANDING THE CAUSES OF DISTRESS IN BREAST CANCER PATIENTS AND SURVIVORS
Univ. of Hong Kong, Hong Kong

Speaker Seockhoon Chung *106*
SLEEP & DEPRESSION: TWO IMPORTANT PSYCHIATRIC SYMPTOMS IN PSYCHO-ONCOLOGY
Department of Psychiatry, ASAN Medical Center, Korea

14:45-16:00 **Junior Doctors Forum 1 (Invited Priority)** 1F, 104-106

Moderator Woo-Chan Park
Department of Surgery, The Catholic Univ. of Korea, Seoul St. Mary's Hospital, Korea

Speaker Ian Smith *136*
MY JOURNEY WITH ENDOCRINE THERAPY AND FUTURE PERSPECTIVES ON YOUNG ASIAN DOCTORS
The Royal Marsden NHS Foundation Trust, United Kingdom

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

16:15-17:30 **Symposium 3** 2F, PBR AB

Immunity, Immunotherapy, and Breast Cancer

Moderator Prudence Francis
Department of Medical Oncology, Peter MacCallum Cancer Centre, Australia

Moderator Byung Joo Song
Department of Surgery, The Catholic Univ. of Korea, Bucheon St. Mary's Hospital, Korea

Speaker Eui-Cheol Shin *18*
CURRENT TRENDS IN IMMUNO-ONCOLOGY
Korea Advanced Institute of Science and Technology (KAIST), Korea

Speaker Prudence Francis *19*
IMMUNOTHERAPY IN BREAST CANCER: BIOMARKERS AND CORRELATIVE STUDIES
Department of Medical Oncology, Peter MacCallum Cancer Centre, Australia

Program Details

Day 1 April 25 (Thu)

Speaker Giuseppe Curigliano 20
BREAST CANCER SUBTYPES & IMMUNOTHERAPY
Istituto Europeo di Oncologia, Italy

16:15-17:30 **Panel Discussion 3** 2F, PBR C

Breast Cancer and Bone Metastasis: from Microenvironment to Macroenvironment

Moderator Jin Seok Ahn
Samsung Medical Center, Korea

Moderator Chang-Ok Suh
Department of Radiation Oncology, CHA Bundang Medical Center, CHA Univ., Korea

Speaker Sun Wook Cho 46
BONE PHYSIOLOGY AND PATHOGENESIS OF BONE METASTASIS
Department of Internal Medicine, Seoul National Univ. Hospital, Korea

Speaker Wanlim Kim 48
SURGICAL CONSIDERATION FOR BONE METASTASIS FROM BREAST CANCER
Department of Orthopedic Surgery, ASAN Medical Center, Korea

Speaker Haeyoung Kim 49
OPTIMIZATION OF RADIATION THERAPY FOR BONE METASTASIS
Department of Radiation Oncology, Samsung Medical Center, Korea

16:15-17:30 **Education Session 3** 1F, 113-115

Recent Advance of MRI and Its Application

Moderator Emily Conant
Department of Radiology, Univ. of Pennsylvania, U.S.A.

Moderator Boo-Kyung Han
Samsung Medical Center, Korea

Speaker Christiane Katharina Kuhl 77
ABBREVIATED BREAST MRI FOR HIGH RISK PATIENTS
RWTH Aachen, Germany

Speaker Hee Jung Shin 78
NON-CONTRAST MRI FOR SCREENING AND SURVEILLANCE OF BREAST CANCER
Department of Radiology, ASAN Medical Center, Korea

Speaker Nariya Cho 80
APPLICATION OF ULTRAFAST MRI TO REAL PRACTICE
Department of Radiology, Seoul National Univ. Hospital, Korea

16:15-17:30 **Survivorship Session 2** 1F, 107-109

Cancer Chronotherapy: A Right Time in the Day to Treat

Moderator Jong Won Lee
Department of Hematology-Oncology, Asan Medical Center, Univ. of Ulsan College of Medicine, Korea

Moderator Seockhoon Chung
Department of Psychiatry, ASAN Medical Center, Korea

Program Details

Day 1 April 25 (Thu)

	Speaker	Tae Kim ASSOCIATION BETWEEN CIRCADIAN DISRUPTION AND BREAST CANCER *Gwangju Institute of Science and Technology (GIST), Korea*	*107*
	Speaker	Carla Finkielstein MUTATIONS IN CIRCADIAN GENES AND THEIR MECHANISTIC CONNECTION TO CANCER DEVELOPMENT *Virginia Tech, U.S.A.*	*109*
	Speaker	Jae Kyoung Kim CIRCADIAN RHYTHM OF P53 TOWARD THE CHRONOTHERAPY OF CANCER *Department of Mathematical Sciences, Korea Advanced Institute of Science and Technology (KAIST), Korea*	*111*

16:15-17:30 **Junior Doctors Forum 2 (Invited Priority)** 1F, 104-106

Moderator	Jeong Eon Lee *Department of Surgery, Samsung Medical Center, Korea*	
Moderator	Byung Joo Chae *Department of Surgery, Samsung Medical Center, Korea*	
Speaker	Seigo Nakamura HOW TO GLOBALIZE THE SOCIETY YOU ARE INVOLVED IN *Department of Breast Surgery, Showa Univ. School of Medicine, Japan*	*137*
Speaker	Ho-Young Song HOW TO GLOBALIZE YOUR CAREER: 30 YEARS EXPERIENCE FROM THE MIND TO THE GLOBAL STENT MARKET *Department of Radiology, ASAN Medical Center, Korea*	*138*
Speaker	Yongsik Jung INTRODUCTION TO JOURNAL OF BREAST CANCER *Department of Surgery, Ajou Univ. Hospital, Korea*	*140*

17:30-18:00 **General Assembly (KBCS Only)** 2F, PBR C

18:30-20:00 **Welcome Dinner** 3F, Grand Ballroom, Sheraton Grand Incheon Hotel

Program Details

Day 2 — April 26 (Fri)

08:00-08:45 **Satellite Symposium 2** 3F, Grand Ballroom, Sheraton Grand Incheon Hotel

Understanding the Psychological Effects of Breast Cancer: Now and Future

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

Speaker Jong-Heun Kim 128
UNDERSTANDING THE PSYCHOLOGICAL EFFECTS OF BREAST CANCER: NOW AND FUTURE
Department of Psychiatry, National Cancer Center, Korea

08:45-09:00 Break

09:00-09:45 **Plenary Lecture 3** 2F, PBR AB

Past, Present, Future of Clinical Trials in Breast Cancer Surgery

Moderator Woo-Chan Park
Department of Surgery, The Catholic Univ. of Korea, Seoul St. Mary's Hospital, Korea

Speaker Terry Mamounas 5
PAST, PRESENT, FUTURE OF CLINICAL TRIALS IN BREAST CANCER SURGERY
Orlando Health, U.S.A.

09:45-10:00 Break

10:00-11:15 **Symposium 4** 2F, PBR AB

Nipple Sparing Mastectomy with Immediate Reconstruction

Moderator Hak Chang
Department of Plastic and Reconstruction Surgery, Seoul National Univ., Korea

Moderator Se Jeong Oh
Department of Surgery, The Catholic Univ. of Korea, Seoul St. Mary's Hospital, Korea

Speaker Hak Chang 21
RECONSTRUCTION AFTER NSM: AUTOLOGOUS TISSUE OR IMPLANT?
Department of Plastic and Reconstruction Surgery, Seoul National Univ., Korea

Speaker Teruhisa Sakurai 22
LONG-TERM FOLLOW-UP OF NIPPLE-SPARING MASTECTOMY
Department of Surgery, Wakayama Medical Univ. Kihoku Hospital, Japan

Speaker Jia-Yi Chen 24
RADIATION TREATMENTS AFTER NSM WITH RECONSTRUCTION
Department of Radiation Oncology, Ruijin Hospital, Shanghai Jiaotong Univ. School of Medicine, China

10:00-11:15 **Panel Discussion 4** 2F, PBR C

Overcoming Resistance to Neoadjuvant Chemotherapy

Moderator Yeon Hee Park
Department of Hematology-Oncology, Samsung Medical Center, Korea

Program Details

Day 2 April 26 (Fri)

Moderator Jin Zhang
Tianjin Medical Univ. Cancer Institute and Hospital, China

Speaker Yeon Hee Park 51
NEOADJUVANT CHEMOTHERAPY STRATEGIES BASED ON BREAST CANCER SUBTYPES
Department of Hematology-Oncology, Samsung Medical Center, Korea

Speaker Hee Jin Lee 52
PRIMARY TUMOR VS. RESIDUAL TUMOR: ANY DIFFERENCES?
Department of Pathology, ASAN Medical Center, Korea

Speaker Shaheenah Dawood 53
HOW TO TREAT PATIENTS WITH RESIDUAL DISEASE AT SURGERY?
Department of Medical Oncology, Mediclinic City Hospital, U.A.E.

10:00-11:15 **Education Session 4** 1F, 113-115

Updated Evidence between Breast Cancer and Environment, Hormones, Alcohol

Moderator Yongsik Jung
Department of Surgery, Ajou Univ. Hospital, Korea

Moderator Yoon-Sim Yap
Department of Medical Oncology, National Cancer Centre Singapore, Singapore

Speaker Sung Gwe Ahn 81
UPDATED EVIDENCE FOR ENVIRONMENT AND HORMONAL FACTORS AND BREAST CANCER
Department of Surgery, Gangnam Severance Hospital, Korea

Speaker Janice Tsang 82
UPDATED EVIDENCE FOR NUTRITION AND DIET AND BREAST CANCER
Hong Kong Breast Oncology Group, Hong Kong

Speaker Seung Pil Jung 83
UPDATED EVIDENCE FOR THE EFFECT OF ALCOHOL AND BREAST CANCER
Korea Univ. Anam Hospital, Korea

10:00-11:15 **Nursing Session 1 (Korean)** 1F, 107-109

Building a Better Cancer Care Delivery System

Moderator Eunkyung Hwang
Department of Nursing, Seoul National Univ. Hospital, Korea

Moderator Miok Kim
Department of Nursing, Dankook Univ., Korea

Speaker Dong-Young Noh 117
DISSEMINATION OF BREAST CANCER AWARENESS: PREVENTION AND EARLY DETECTION
Department of Surgery , Seoul National Univ. Hospital, Korea

Speaker Beomseok Ko 118
HEALTH INSURANCE SYSTEM FOR BREAST CANCER PATIENTS
Department of Surgery , ASAN Medical Center, Korea

Speaker Sorah Park 119
SOCIAL WORK SERVICES FOR LOW-INCOME PATIENTS WITH CANCER
Department of Social Work, Yonsei Univ. Medical Center, Severance Hospital, Korea

Program Details

Day 2 April 26 (Fri)

10:00-11:15 **ABRCA & HBOC** 1F, 104-106

Asia Breast Cancer Gene & Hereditary Breast Ovarian Cancer

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

Moderator Hyung Seok Park
Department of Surgery, Yonsei Univ. College of Medicine, Korea

Speaker Ava Kwong 113
GENETIC TESTING IN HEREDITARY BREAST CANCER IN ASIA
Department of Surgery, The Univ. of Hong Kong, Hong Kong

Speaker Hyung Seok Park 114
RISK REDUCTION STRATEGIES FOR WOMEN WITH PATHOGENIC VARIANTS IN MULTIGENE PANEL TESTS
Department of Surgery, Yonsei Univ. College of Medicine, Korea

Speaker Benjamin Sarfati 115
ROBOTIC NIPPLE SPARING MASTECTOMY WITH IMMEDIATE RECONSTRUCTION FOR WOMEN WITH BRCA1/2 MUTATION
Department of Plastic Surgery, Institut Gustave Roussy, France

11:15-11:30 **Break**

11:30-12:15 **Plenary Lecture 4** 2F, PBR AB

Ovarian Function Suppression for Premenopausal Women with Breast Cancer

Moderator Toshiaki Saeki
Saitama Medical Univ. International Medical Center, Japan

Speaker Woochul Noh 7
OVARIAN FUNCTION SUPPRESSION FOR PREMENOPAUSAL WOMEN WITH BREAST CANCER
Department of Surgery, Korea Cancer Center Hospital, Korea

12:15-12:30 **Break**

12:30-13:15 **Satellite Symposium 3** 2F, PBR AB

Recent Strategies to Reach the Best Clinical Outcomes in HER2-positive Early Breast Cancer Patients

Moderator Dae Sung Yoon
Department of Surgery, Konyang Univ. Hospital Cancer Center, Korea

Speaker In Hae Park 130
RECENT STRATEGIES TO REACH THE BEST CLINICAL OUTCOMES IN HER2-POSITIVE EARLY BREAST CANCER PATIENTS
National Cancer Center, Korea

13:15-13:45 **Break**

Program Details

Day 2 April 26 (Fri)

13:45-14:30 **Plenary Lecture 5** 2F, PBR AB

Innovative Approach for the Treatment of Refractory Breast Cancer

Moderator Sung-Bae Kim
Department of Oncology, ASAN Medical Center, Korea

Speaker Hope S. Rugo 9
INNOVATIVE APPROACH FOR THE TREATMENT OF REFRACTORY BREAST CANCER
Univ. of California San Francisco Medical Center, U.S.A.

14:30-16:00 **GBCC Sino-Korean Joint Meeting**

3F, Grand Ballroom, Sheraton Grand Incheon Hotel

Moderator Woochul Noh
Department of Surgery, Korea Cancer Center Hospital, Korea

Moderator Yongsheng Wang
Shandong Cancer Hospital, China

Speaker Sung Hwan Park
INTRODUCTION OF KBCS AND BBDS
Department of Surgery, Daegu Catholic Univ. Medical Center, Korea

Speaker Peng Yuan
INTRODUCTION OF KBCS AND BBDS
Cancer Hospital Chinese Academy of Medical Sciences, China

Speaker Sung Gwe Ahn
BIOLOGICAL CHARACTERISTICS OF YOUNGER BREAST CANCER IN ASIA (OR KOREA)
Department of Surgery, Gangnam Severance Hospital, Korea

Speaker Ling Xu
PROGRESS OF ENDOCRINE THERAPY FOR YOUNGER BREAST CANCER
Peking Univ. First Hospital, China

Speaker Woo Young Sun
CASE DISCUSSIONS
Department of Surgery, The Catholic Univ. of Korea, Daejeon St. Mary's Hospital, Korea

Speaker Huihui Li
CASE DISCUSSIONS
Shandong Tumor Hospital, China

14:45-16:00 **Symposium 5** 2F, PBR AB

Optimizing Anti-HER2 Therapies for HER2 Positive Breast Cancer

Moderator Hope S. Rugo
Univ. of California San Francisco Medical Center, U.S.A.

Moderator Keun Seok Lee
National Cancer Center, Korea

Speaker Hope S. Rugo 25
HER2 TARGETED THERAPY IN BREAST CANCER IN 2019
Univ. of California San Francisco Medical Center, U.S.A.

Speaker Toshimi Takano 26
OPTIMAL SEQUENCE OF ANTI-HER2 THERAPY IN THE METASTATIC SETTING
Department of Medical Oncology, Toranomon Hospital, Japan

Day 2 April 26 (Fri)

Speaker Kyung Hae Jung 27
OVERCOMING RESISTANCE TO ANTI-HER2 THERAPIES
Department of Oncology, ASAN Medical Center, Korea

14:45-16:00 **Panel Disscussion 5** 2F, PBR C

Oncoplastic Breast Surgery I

Moderator Jung Dug Yang
Department of Plastic and Reconstructive Surgery, Kyungpook National Univ. Hospital, Korea
Moderator Polly Suk Yee Cheung
Breast & Endocrine Surgery Centre, Hong Kong
Speaker Wonshik Han 54
EVIDENCE-BASED INDICATION OF ONCOPLASTIC BREAST SURGERY
Department of Surgery, Seoul National Univ. Hospital, Korea
Speaker Jeeyeon Lee 55
ONCOLOGICAL SAFETY OF ONCOPLASTIC BREAST SURGERY
Department of Surgery (Breast and Thyroid), Kyungpook National Univ. Hospital, Korea
Speaker Polly Suk Yee Cheung 57
HOW TO AVOID ONCOPLASTIC FAILURE IN SMALL-TO-MEDIUM SIZED BREASTS
Breast & Endocrine Surgery Centre, Hong Kong

14:45-16:00 **Education Session 5** 1F, 113-115

Partial Breast Irradiation

Moderator Su Ssan Kim
Department of Radiation Oncology, ASAN Medical Center, Korea
Moderator Frank Vicini
MHP Radiation Oncology Institute, U.S.A.
Speaker Ji Hyeon Joo 85
WHO CAN BE AN OPTIMAL CANDIDATES FOR PARTIAL BREAST IRRADIATION?
Department of Radiation Oncology, Pusan National Univ. Yangsan Hospital, Korea
Speaker Frank Vicini 87
TECHNICAL CONSIDERATIONS AND EMERGING MODALITIES FOR PARTIAL BREAST IRRADIATION
MHP Radiation Oncology Institute, U.S.A.
Speaker Yong Bae Kim 88
WHAT SHOULD BE CONSIDERED FOR PARTIAL BREAST IRRADIATION IN KOREA?
Department of Radiation Oncology, Yonsei Cancer Center, Korea

14:45-16:00 **Nursing Session 2 (Korean)** 1F, 107-109

New Approach for Developing Breast Cancer Nursing

Moderator Jinhee Park
Department of Nursing, Ajou Univ., Korea
Speaker Myungsun Yi 120
THE NEED FOR LEADERSHIP IN CANCER NURSING
Department of Nursing, Seoul National Univ., Korea

Day 2 April 26 (Fri)

Speaker Imryung Kim *122*
DEVELOPING AND IMPLEMENTING BREAST CANCER EDUCATION
Samsung Medical Center, Korea

Speaker Eunkyung Hwang *123*
A NEW APPROACH TO LYMPHEDEMA GUIDELINES: HOW TO OVERCOME DILEMMAS IN EDUCATING LYMPHEDEMA GUIDELINES
Department of Nursing, Seoul National Univ. Hospital, Korea

14:45-16:00 **Education Session 6** 1F, 104-106

How to Prevent and Screen the Breast Cancer?

Moderator Dong-Young Noh
Department of Surgery, Seoul National Univ. Hospital, Korea

Moderator Seigo Nakamura
Department of Breast Surgery, Showa Univ. School of Medicine, Japan

Speaker Byung Joo Chae *90*
GUIDELINES FOR PREVENTION OF BREAST CANCER
Department of Surgery, Samsung Medical Center, Korea

Speaker Emily Conant *92*
IMAGING SCREENING TOOL BEYOND MAMMOGRAPHY
Department of Radiology, Univ. of Pennsylvania, U.S.A.

Speaker Seigo Nakamura *93*
POPULATION BASED MUTATION SCREENING TO SELECT HIGH RISK PATIENTS: WHERE ARE WE NOW?
Department of Breast Surgery, Showa Univ. School of Medicine, Japan

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

16:15-17:30 **Symposium 6** 2F, PBR AB

Beyond Horizons: Current Landscape and Future Prospects of Breast Cancer Immunotherapy

Moderator Nadia Harbeck
Univ. of Munich (LMU), Germany

Moderator Jae Hong Seo
Department of Medical Oncology, Korea Univ. Guro Hospital, Korea

Speaker Nadia Harbeck *28*
CURRENT LANDSCAPE: REVIEW OF RECENT IMMUNOTHERAPY TRIALS
Univ. of Munich (LMU), Germany

Speaker Kyong Hwa Park *29*
EMERGING TARGETS BEYOND PD-1 AND PD-L1
Department of Internal Medicine, Korea Univ. Anam Hospital, Korea

Speaker Helena Chang *30*
IMMUNOTHERAPY BEYOND ANTIBODIES: THE ROLE OF CD 24 IN TNBC DRUG RESISTANCE AND TUMOR IMMUNITY
David Geffen School of Medicine at UCLA, U.S.A.

Day 2 April 26 (Fri)

16:15-17:30 **Panel Disscussion 6** 2F, PBR C

Oncoplastic Breast Surgery II

Moderator Ho Yong Park
Department of Surgery, Kyungpook National Univ. Chilgok Hospital, Korea

Moderator Hideko Yamauchi
Department of Breast Surgical Oncology, St. Luke's International Hospital, Japan

Speaker Yuko Kijima 58
ONCOPLASTIC SURGERY WITH THORACODORSAL ADIPOFASCIAL CUTANEOUS FLAP
Fujita Health Univ., Japan

Speaker Douglas Macmillan 59
ONCOPLASTIC SURGERY AFTER NEOADJUVANT THERAPY
Nottingham Breast Institute, United Kingdom

Speaker Eun-Kyu Kim 60
ONCOPLASTIC SURGERY WITH OMENTAL FLAP
Department of Surgery, Seoul National Univ. Bundang Hospital, Korea

16:15-17:30 **Education Session 7** 1F, 113-115

Fibroepithelial Tumors of the Breast

Moderator Byeong-Woo Park
Yonsei Univ. College of Medicine, Korea

Moderator Puay Hoon Tan
Singapore General Hospital, Singapore

Speaker Puay Hoon Tan 94
UPDATES ON MOLECULAR GENETICS AND CLASSIFICATION OF FIBROEPITHELIAL TUMORS OF THE BREAST
Singapore General Hospital, Singapore

Speaker Han Suk Ryu 95
DIFFERENTIAL DIAGNOSIS BETWEEN FIBROADENOMA AND PHYLLODES TUMOR ON CORE NEEDLE BIOPSY
Department of Pathology, Seoul National Univ. Hospital, Korea

Speaker Yoo Seok Kim 96
RISK FACTORS FOR RECURRENCE AND DISEASE MANAGEMENT OF PHYLLODES TUMORS
Department of Surgery, Chosun Univ. Hospital, Korea

16:15-17:30 **Oral Presentation 3** 1F, 107-109

Moderator Sung Yong Kim
Department of Surgery, Soon Chun Hyang Univ. Hospital Cheonan, Korea

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

Speaker Yolanda Ho Yan Chan 160
MAGNETIC TRACER: A NEW OPTION OF SENTINEL LYMPH NODE LOCALIZATION
Department of Surgery, Kwong Wah Hospital, Hong Kong

Day 2 April 26 (Fri)

	Speaker	Seo Hee Choi THE EFFECT OF REGIONAL NODE IRRADIATION ON THE THYROID GLAND IN THE BREAST CANCER PATIENTS: THE CLINICAL SIGNIFICANCE OF OPTIMIZATION OF RADIATION TARGET VOLUME *Department of Radiation Oncology, Yonsei Univ. College of Medicine, Korea*	*161*
	Speaker	Yurina Maeshima THE ACCURACY OF AXILLARY NODE ASSESSMENT BY ULTRASOUND AFTER NEOADJUVANT CHEMOTHERAPY IN CLINICALLY NODE POSITIVE PATIENTS *Department of Surgery, Cancer Institute Hospital, Japan*	*162*
	Speaker	Yumi Kim PLASMA PROTEIN BIOMARKER FOR EARLY DIAGNOSIS OF BREAST CANCER BY USING PROTEOMICS TECHNOLOGY *Department of General Surgery, Seoul National Univ. Hospital, Korea*	*163*
	Speaker	Holly Keane A SIMPLE INTERVENTION FOR LONG-TERM RELIEF OF CHRONIC POST MASTECTOMY PAIN *Department of Surgery, Peter MacCallum Cancer Institute, Australia*	*164*
	Speaker	Bong Kyun Kim COMPARATIVE STUDY BETWEEN SENTINEL LYMPH NODE BIOPSY AND AXILLARY DISSECTION IN PATIENTS WHO UNDERWENT TOTAL MASTECTOMY WITH 1 OR 2 METASTATIC LYMPH NODES *Department of Surgery, The Catholic Univ. of Korea, Daejeon St. Mary's Hospital, Korea*	*165*
	Speaker	Tiffany Sin Hui Bong FACTORS PREDICTIVE OF MALIGNANT UPSTAGING OF ATYPICAL DUCTAL HYPERPLASIA OF THE BREAST - CAN SURGICAL EXCISION BIOPSY BE AVOIDED? *Singapore General Hospital, Singapore*	*166*
	Speaker	Choong Man Lee OVEREXPRESSION OF ANDROGEN RECEPTOR (AR) INDICATE FAVORABLE PROGNOSIS IN PURE DUCTAL CARCINOMA IN SITU (DCIS) *Department of General Surgery, ASAN Medical Center, Korea*	*167*

16:15-17:30 **Asian Breast Cancer Networking Business Meeting (Invited Only)**

1F, 104-106

17:30-17:45 **Break**

17:45-18:30 **Satellite Symposium 4** 3F, Grand Ballroom, Sheraton Grand Incheon Hotel

Consensus in ER+ HER2- Asian Premenopausal Breast Cancer

	Moderator	Soo Jung Lee *Department of Surgery, Yeungnam Univ. College of Medicine, Korea*	
	Speaker	Hiroji Iwata CONSENSUS IN ER+ HER2- ASIAN PREMENOPAUSAL BREAST CANCER *Department of Breast Oncology, Aichi Cancer Center, Japan*	*132*

Program Details

Day 3 — April 27 (Sat)

08:00-08:45 **Satellite Symposium 5** 3F, Grand Ballroom, Sheraton Grand Incheon Hotel

Treatment of HR+ HER2- Advanced Breast Cancer: Practical Implication of Fulvestrant

Moderator Sung-Bae Kim
Department of Oncology, ASAN Medical Center, Korea

Speaker Kyong Hwa Park 134
TREATMENT OF HR+ HER2- ADVANCED BREAST CANCER: PRACTICAL IMPLICATION OF FULVESTRANT
Department of Internal Medicine, Korea Univ. Anam Hospital, Korea

08:45-09:00 Break

09:00-10:15 **Symposium 7** 2F, PBR AB

Controversies in Treatment for DCIS

Moderator Terry Mamounas
Orlando Health, U.S.A.

Moderator Eun Sook Lee
National Cancer Center, Korea

Speaker Bruce Mann 31
WHEN CAN WE OMIT RADIATION THERAPY AFTER BREAST CONSERVING SURGERY FOR DCIS?
The Royal Women's Hospital, Australia

Speaker Terry Mamounas 32
WHAT IS OPTIMAL MARGIN IN BREAST CONSERVING SURGERY FOR DCIS?
Orlando Health, U.S.A.

Speaker Kyubo Kim 34
CAN RADIATION THERAPY REPLACE RE-EXCISION OF POSITIVE MARGIN IN DCIS?
Department of Radiation Oncology, Ewha Womans Univ., Korea

09:00-10:15 **Panel Discussion 7** 2F, PBR C

Risk Reduction Strategies for High Risk Patients in Real Practice

Moderator Yongsheng Wang
Shandong Cancer Hospital, China

Moderator Ava Kwong
The Univ. of Hong Kong, Hong Kong

Speaker Hideko Yamauchi 61
IN WHOM, WHEN AND HOW DO WE PROVIDE RISK REDUCTION SURGERY?
Department of Breast Surgical Oncology, St. Luke's International Hospital, Japan

Speaker Hee Jeong Kim 63
IS RISK REDUCTION SURGERY MANDATORY FOR THE WOMEN WHO ALREADY TREATED FOR THE BREAST CANCER?
Department of Surgery, ASAN Medical Center, Korea

Day 3 April 27 (Sat)

Speaker Jihyoun Lee 65
ALTERNATIVE STRATEGIES OTHER THAN SURGERY TO REDUCE THE BREAST CANCER RISK
Department of Surgery, Soon Chun Hyang Univ. Hospital Seoul, Korea

09:00-10:15 **Education Session 8** 1F, 113-115

Challenge of Treatment for Brain Metastasis

Moderator Nancy Lin
Department of Breast Oncology, Dana-Farber Cancer Institute & Harvard Medical School, U.S.A.

Moderator Jin-Hee Ahn
Department of Medical Oncology, ASAN Medical Center, Korea

Speaker Joohyuk Sohn 97
FACT CHECK OF BRAIN METASTASIS IN BREAST CANCER
Department of Internal Medicine, Yonsei Univ. College of Medicine, Korea

Speaker Seok-Gu Kang 98
LOCAL TREATMENT OPTION OF BRAIN METASTASIS
Department of Neurosurgery, Yonsei Univ. Severance Hospital, Korea

Speaker Nancy Lin 99
BRAIN METASTASIS: NEW THERAPEUTIC APPROACH
Department of Breast Oncology, Dana-Farber Cancer Institute & Harvard Medical School, U.S.A.

09:00-10:15 **Oral Presentation 4** 1F, 107-109

Moderator Min Hee Hur
Department of Surgery, Inha Univ. Hospital, Korea

Moderator Je-Ryong Kim
Department of Surgery, Chungnam National Univ. Hospital, Korea

Speaker Daeun You 168
CCL2 DERIVED FROM EGFR AND HER2 (+) BREAST CANCER CELLS RECRUITS TUMOR ASSOCIATED MACROPHAGES
Samsung Medical Center, Korea

Speaker Han-Byoel Lee 169
ONCOGENIC CONTRIBUTION OF GERMLINE MUTATIONS IN LYSOSOMAL STORAGE DISEASE-RELATED GENES TO PATIENTS AT HIGH RISK FOR HEREDITARY BREAST CANCER
Department of Surgery, Seoul National Univ. Hospital, Korea

Speaker Hyeon Jeong Oh 170
PROTEOMIC LANDSCAPE OF FIBROEPITHELIAL TUMOR OF BREAST
Department of Pathology, Seoul National Univ. Hospital, Korea

Speaker Lu Wang 171
PRELIMINARY STUDY OF REAL-TIME THREE-DIMENSIONAL CONTRAST-ENHANCED ULTRASOUND OF SENTINEL LYMPH NODES IN BREAST CANCER
Sichuan Cancer Hospital and Institute, China

Day 3 April 27 (Sat)

Speaker Pengfei Qiu 172
THE EXPLORATORY STUDY ON INDICATIONS OF INTERNAL MAMMARY SENTINEL LYMPH NODE BIOPSY IN BREAST CANCER
Shandong Cancer Hospital & Institute, China

Speaker In Hee Lee 173
EVALUATION OF A DIRECT REVERSE TRANSCRIPTION LOOP-MEDIATED ISOTHERMAL AMPLIFICATION METHOD WITHOUT RNA EXTRACTION (DIRECT RT-LAMP) FOR THE DETECTION OF LYMPH NODE METASTASIS IN EARLY BREAST CANCER
Department of Medical Oncology, Kyungpook National Univ. Hospital, Korea

Speaker Hakyoung Kim 174
PROGNOSIS OF BREAST CANCER PATIENTS WHO HAD SENTINEL LYMPH NODE BIOPSY AFTER NEOADJUVANT THERAPY
ASAN Medical Center, Korea

Speaker Christina Dieli-Conwright 175
EFFECTS OF AEROBIC AND RESISTANCE EXERCISE ON ANDROID FAT IN BREAST CANCER SURVIVORS
Department of Biokinesiology and Physical Therapy, Univ. of Southern California, U.S.A.

09:00-10:15 **Practicing Breast Surgeons Session 1 (Korean)** 1F, 104-106

Integrative Medicine in Breast Disease

Moderator Se Min Oh
Dr. Oh's Breast Clinic, Korea

Speaker Eunseo Choi
EFFECTIVENESS OF VITAMIN THERAPY ON GRANULOMATOUS LOBULAR MASTITIS
Wellsu Breast Clinic, Korea

Speaker Eunchang Choi
PUNCTURE STIMULATION FOR LYMPHEDEMA
Department of Surgery, Nonsan Corea Hospital, Korea

Speaker Yang Soo Jung
NK CELLS AND BREAST CANCER
Department of Family Medicine, The NK Clinic, Korea

10:15-10:30 **Break**

10:30-11:45 **Symposium 8** 2F, PBR AB

Making the Most Out of Multigene Assays

Moderator Joon Jeong
Department of Breast Surgical Oncology, Gangnam Severance Hospital, Korea

Moderator Hong Liu
Tianjin Medical Univ. Cancer Institute and Hospital, China

Speaker Chiun-Sheng Huang 35
MULTIGENE ASSAYS DEVELOPED FROM WESTERN AND ASIAN COUNTRIES
Department of Surgery, National Taiwan Univ. Hospital, Taiwan

Day 3 April 27 (Sat)

Speaker Takayuki Ueno 36
ROLE OF MULTIGENE ASSAYS TO GUIDE DECISIONS FOR NEOADJUVANT THERAPY
Cancer Institute Hospital, Japan

Speaker Joon Jeong 37
CURRENT EVIDENCE FOR USE OF MULTIGENE ASSAYS IN NODE-POSITIVE DISEASE
Department of Breast Surgical Oncology, Gangnam Severance Hospital, Korea

10:30-11:45 **Panel Discussion 8** 2F, PBR C

Cutting Edge Trend of Breast Surgery

Moderator Eisuke Fukuma
Kameda Medical Center, Japan

Moderator Min-Hyuk Lee
Department of Surgery, Soon Chun Hyang Univ. Hospital Seoul, Korea

Speaker Antonio Toesca 66
RECENT PROGRESS IN ENDOSCOPIC BREAST SURGERY AND ROBOT-ASSISTED MASTECTOMY
European Institute of Oncology, Italy

Speaker Beomseok Ko 67
APPLICATION OF 3D PRINTING TECHNIQUE TO BREAST SURGERY
Department of Surgery, ASAN Medical Center, Korea

Speaker Eisuke Fukuma 68
UP-TO-DATE MINIMALLY INVASIVE PROCEDURES FOR BREAST CANCER TREATMENT
Kameda Medical Center, Japan

10:30-11:45 **Education Session 9** 1F, 113-115

Update of Treatment for Complications in Breast Cancer Patients

Moderator Jung Han Yoon
Department of Endocrine Surgery, Chonnam National Univ. Hwasun Hospital, Korea

Moderator Shinji Ohno
Cancer Institute Hospital, Japan

Speaker Jung Eun Choi 100
RISK FACTORS FOR LYMPHEDEMA AND PREVENTIVE INTERVENTIONS DURING SURGERY
Department of Surgery, Yeungnam Univ. College of Medicine, Korea

Speaker Eun Joo Yang 101
TREATMENT FOR BREAST CANCER PATIENTS WITH LYMPHEDEMA
Department of Rehabilitation Medicine, Seoul National Univ. Bundang Hospital, Korea

Speaker Seung Hyun Chung 102
MANAGEMENT OF BREAST SURGERY-RELATED MUSCULOSKELETAL COMPLICATIONS
Department of Rehabilitation, National Cancer Center, Korea

Program Details

Day 3 April 27 (Sat)

10:30-11:45 **Oral Presentation 5** 1F, 107-109

Moderator	Changwan Jeon *Department of Surgery, Kosin Univ. Gospel Hospital, Korea*	
Moderator	Sangdal Lee *Department of Surgery, MD Clinic, Korea*	
Speaker	Seungtaek Lim PROGNOSIS AND EFFECT OF ADJUVANT TREATMENT IN SMALL, NODE(-), HER2(+) BREAST CANCER *Yonsei Univ. Wonju College of Medicine, Korea*	*176*
Speaker	Akihiko Shimomura PREDICTION OF PATHOLOGICAL COMPLETE RESPONSE BY MICRORNA IN BREAST CANCER PATIENTS TREATED WITH NEOADJUVANT CHEMOTHERAPY *Department of Medical Oncology, National Cancer Center Hospital, Japan*	*177*
Speaker	Lu Wang HOW PREOPERATIVE SENTINEL LYMPH NODE CONTRAST-ENHANCED ULTRASOUND HELPS INTRAOPERATIVE SENTINEL LYMPH NODE BIOPSY IN BREAST CANCER: INITIAL EXPERIENCE *Sichuan Cancer Hospital and Institute, China*	*178*
Speaker	Jina Kim RADIOTHERAPY FOR INITIAL CLINICALLY POSITIVE INTERNAL MAMMARY NODES IN BREAST CANCER *Yonsei Univ. College of Medicine, Korea*	*179*
Speaker	Dong Hun Choi THE USEFULNESS OF ONCOPLASTIC BREAST SURGERY WITH ROTATION FLAP SUPERCHARGED WITH LATERAL THORACIC ARTERY PERFORATOR IN PARTIAL MASTECTOMY DEFECT *Department of Plastic and Reconstructive Surgery, Kyungpook National Univ. Hospital, Korea*	*180*
Speaker	Isaac Kim A PREDICTIVE MODEL FOR PATHOLOGIC COMPLETE RESPONSE IN BREAST CANCER PATIENTS TREATED WITH NEOADJUVANT CHEMOTHERAPY USING MACHINE LEARNING *CHA Bundang Medical Center, CHA Univ., Korea*	*181*
Speaker	Rahmawati Binti Pare CHARACTERISTIC AND PROGNOSTIC VALUE OF CELLULAR SENESCENCE-ASSOCIATED MARKERS IN BREAST CANCER DEVELOPMENT *Department of Medicine and Health Sciences, Universiti Malaysia Sabah, Malaysia*	*182*
Speaker	Tira Tan OPTIMIZING PD-L1 TESTING FOR THERAPEUTIC EFFICACY IN TRIPLE NEGATIVE BREAST CANCER (TNBC) *Division of Medical Oncology, National Cancer Centre Singapore, Singapore*	*183*

Day 3 April 27 (Sat)

10:30-11:45 **Practicing Breast Surgeons Session 2 (Korean)** 1F, 104-106

Breast Clinic Issue

Moderator Jin Woo Ryu
Angelot Woman Hospital, Korea

Speaker Sangwon Kim
IMMEDIATE IMPLANT BASED BREAST RECONSTRUCTION USING ALLODERM
Mother's Hospital, Korea

Speaker Bon Yong Koo
ANNUAL REPORT OF BREAST CLINICS IN KABTS (KOREAN ASSOCIATION OF BREAST AND THYROID SURGEONS)
Department of Surgery, U & U Surgery Clinic, Korea

Speaker Jae Yang Lim
WHAT'S HEALTHY FOOD?
Department of Surgery, Dr. Lim's Breast Clinic, Korea

11:45-12:00 **Break**

12:00-12:30 **Closing Ceremony** 2F, PBR AB

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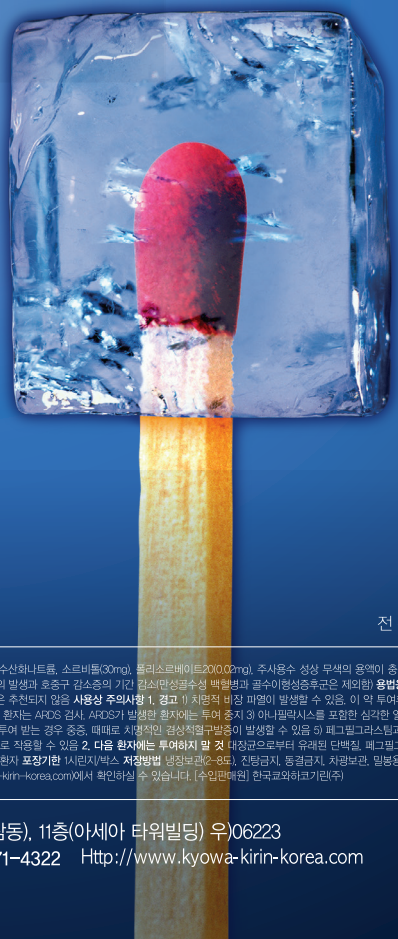

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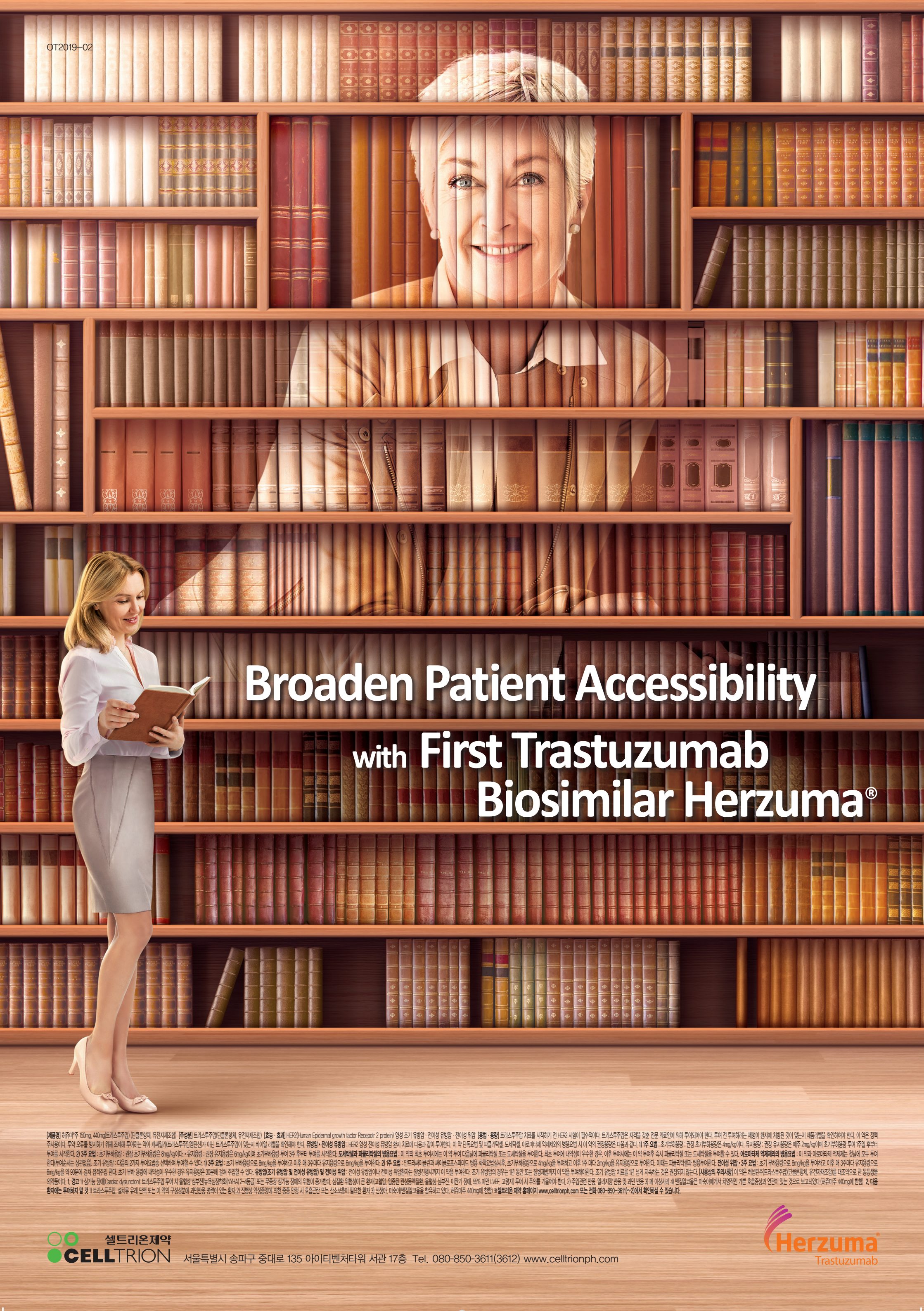
[원료약품 및 분량] 1바이알중 주성분 트라스투주맙 150mg **[성상]** 백색 내지 연한 황색의 동결건조분말이 든 무색 투명한 바이알. 재용해 후 탁도는 약한 탐탕 이하이여야 하고, 색상은 무색에서 밝은 노랑이어야 함 **[효능·효과]** 1.전이성 유방암 : HER2(Human Epidermal growth factor Receptor 2 protein) 양성 전이성 유방암환자 치료에 다음과 같이 투여한다. 1) 전이성 질환에 대해 1회 또는 그 이상의 화학요법 치료를 받은 적이 있는 환자에게는 단독투여 2) 전이성 질환에 대해 화학요법 치료를 받은 적이 없는 환자에게는 파클리탁셀 또는 도세탁셀과 병용투여 3) 이전에 트라스투주맙을 투여받은 적이 없는 호르몬 수용체 양성인 폐경기 이후 환자에게 아로마타제 억제제와 병용투여 2. 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) 2 ㎝인 종양에 대해 수술 전 보조요법(neoadjuvant)으로 이 약과 화학요법 병용투여 후 수술 후 보조요법(adjuvant)으로 이 약 단독 투여 3. 전이성 위암 : 전이성 질환으로 이전에 항암치료를 받은 적이 없는 HER2 양성 전이성 위 선암이나 위식도 접합부 선암환자에 백금계 약물과 카페시타빈 또는 5-FU와 병용투여 **[용법·용량]** 이 약의 치료를 시작하기 전 HER2 시험이 필수적이다. 이 약은 자격을 갖춘 전문 의료인에 의해 투여되어야 한다. 투여 전 투여하려는 제형이 환자에 처방된 것이 맞는지 제품라벨을 확인하여야 한다. 이 약은 정맥주사용이다. 투약 오류를 방지하기 위해 조제해 투여하는 약이 캐싸일라(트라스투주맙 엠탄신)가 아닌 이 약, 삼페넷주(트라스투주맙)가 맞는지 바이알 라벨을 확인해야 한다. 1. 전이성 유방암 HER2(Human Epidermal growth factor Receptor 2 Protein) 양성 전이성 유방암 환자 치료에 다음과 같이 투여한다. 이 약 단독요법 및 파클리탁셀, 도세탁셀, 아로마타제 억제제와의 병용요법 시 이 약의 권장용량은 다음과 같다. ▶1주 요법 : 초기부하용량 : 권장 초기부하용량은 4mg/kg이다. 유지용량 : 권장 유지용량은 매주 2mg/kg이며 초기부하용량 투여 1주일 후부터 투여를 시작한다. ▶3주 요법 : 초기부하용량 : 권장 초기부하용량은 8mg/kg이다. 유지용량 : 권장 유지용량은 6mg/kg이며 초기부하용량 투여 3주 후부터 투여를 시작한다. 도세탁셀과 파클리탁셀의 병용요법 : 이 약의 최초 투여시에는 이 약 투여 다음날에 파클리탁셀 또는 도세탁셀을 투여한다. 최초 투여에 내약성이 우수한 경우, 이후 투여시에는 이 약 투여후 즉시 파클리탁셀 또는 도세탁셀을 투여할 수 있다. 아로마타제 억제제와의 병용요법 : 이 약과 아로마타제 억제제는 찻날에 모두 투여한다(투여순서는 상관없음). 2. 조기 유방암 다음의 2가지 투여요법중 선택하여 투여할 수 있다. ▶3주 요법 : 초기 부하용량으로 8mg/kg을 투여하고 이후 매 3주마다 유지용량으로 6mg/kg을 투여한다. ▶1주 요법 : 안트라싸이클린과 싸이클로포스파미드 병용 화학요법 실시 후, 초기부하용량으로 4mg/kg을 투여하고 이후 1주마다 2mg/kg을 유지용량으로 투여한다. 이때는 파클리탁셀과 병용투여한다. 3. 전이성 위암 ▶3주 요법 : 초기 부하용량으로 8mg/kg을 투여하고 이후 매 3주마다 유지용량으로 6mg/kg을 약 90분에 걸쳐 점적주입한다. 초기 부하 용량에 내약성이 우수한 경우 유지용량은 30분에 걸쳐 주입할 수 있다. **[주입방법]** 이 약은 90분에 걸쳐 정맥주입한다. 이 약은 급속정맥주입(intravenous push or bolus)으로 투여해서는 안 된다. 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.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[제품명] 허쥬마®주 150mg, 440mg(트라스투주맙) (단클론항체, 유전자재조합) [주성분] 트라스투주맙(단클론항체, 유전자재조합) [효능 · 효과] HER2(Human Epidermal growth factor Recepotr 2 protein) 양성 조기 유방암 · 전이성 유방암 · 전이성 위암 [용법 · 용량] 트라스투주맙 치료를 시작하기 전 HER2 시험이 필수적이다. 트라스투주맙은 자격을 갖춘 전문 의료인에 의해 투여되어야 한다. 투여 전 투여하려는 제형이 환자에 처방된 것이 맞는지 제품라벨을 확인하여야 한다. 이 약은 정맥주사용이다. 투약 오류를 방지하기 위해 조제해 투여하는 약이 캐싸일라(트라스투주맙엠탄신)가 아닌 트라스투주맙이 맞는지 바이알 라벨을 확인해야 한다. 유방암 • 전이성 유방암 : HER2 양성 전이성 유방암 환자 치료에 다음과 같이 투여한다. 이 약 단독요법 및 파클리탁셀, 도세탁셀, 아로마타제 억제제와의 병용요법 시 이 약의 권장용량은 다음과 같다. 1) 1주 요법 : 초기부하용량 : 권장 초기부하용량은 4mg/kg이다. 유지용량 : 권장 유지용량은 매주 2mg/kg이며 초기부하용량 투여 1주일 후부터 투여를 시작한다. 2) 3주 요법 : 초기부하용량 : 권장 초기부하용량은 8mg/kg이다. • 유지용량 : 권장 유지용량은 6mg/kg이며 초기부하용량 투여 3주 후부터 투여를 시작한다. 도세탁셀과 파클리탁셀의 병용요법 : 이 약의 최초 투여시에는 이 약 투여 다음날에 파클리탁셀 또는 도세탁셀을 투여한다. 최초 투여에 내약성이 우수한 경우, 이후 투여시에는 이 약 투여후 즉시 파클리탁셀 또는 도세탁셀을 투여할 수 있다. 아로마타제 억제제와의 병용요법 : 이 약과 아로마타제 억제제는 첫날에 모두 투여한다(투여순서는 상관없음). 조기 유방암 : 다음의 2가지 투여요법중 선택하여 투여할 수 있다. 1) 3주 요법 : 초기 부하용량으로 8mg/kg을 투여하고 이후 매 3주마다 유지용량으로 6mg/kg을 투여한다. 2) 1주 요법 : 안트라싸이클린과 싸이클로포스파미드 병용 화학요법실시후, 초기부하용량으로 4mg/kg을 투여하고 이후 1주 마다 2mg/kg을 유지용량으로 투여한다. 이때는 파클리탁셀과 병용투여한다. 전이성 위암 • 3주 요법 : 초기 부하용량으로 8mg/kg을 투여하고 이후 매 3주마다 유지용량으로 6mg/kg을 약 90분에 걸쳐 점적주입 한다. 초기 부하 용량에 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. [사용상의 주의사항] 이 약은 허셉틴주(트라스투주맙)(단클론항체, 유전자재조합)를 대조약으로 한 동등생물의약품이다. 1. 경고 1) 심기능 장애(Cardiac dysfunction): 트라스투주맙 투여 시 울혈성 심부전[뉴욕심장학회(NYHA) 2~4등급] 또는 무증상 심기능 장애의 위험이 증가한다. 심질환 위험성이 큰 환자(고혈압, 입증된 관상동맥질환, 울혈성 심부전, 이완기 장애, 55% 미만 LVEF, 고령자) 투여 시 주의를 기울여야 한다. 2) 주입관련 반응, 알러지양 반응 및 과민 반응 3) 폐 이상사례 4) 벤질알코올은 미숙아에게서 치명적인 가쁜 호흡증상과 연관이 있는 것으로 보고되었다.(허쥬마주 440mg에 한함) 2. 다음 환자에는 투여하지 말 것 1) 트라스투주맙, 설치류 유래 단백 또는 이 약의 구성성분에 과민반응 병력이 있는 환자 2) 진행성 악성종양에 의한 중증 안정 시 호흡곤란 또는 산소보충이 필요한 환자 3) 신생아, 미숙아(벤질알코올을 함유하고 있다. 허쥬마주 440mg에 한함) ※셀트리온 제약 홈페이지 www.celltrionph.com 또는 전화 080-850-3611(~2)에서 확인하실 수 있습니다.
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- **GBCC PUBLICATION COMMITTEE**

- **EDITOR-IN-CHIEF**: SUNG-WON KIM
- **MEMBER**: DONGWON KIM
- **VOL. 04**
- **EDITORIAL OFFICE**
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  E-MAIL: GBCC@INTERCOM.CO.KR
- **eISSN:** 2508-1624

GBCC2019

Abstract Book

GLOBAL BREAST CANCER CONFERENCE SECRETARIAT

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Plenary Lecture

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Global Breast Cancer Conference 2019

EVOLUTION OF THERAPEUTIC STRATEGIES FOR HORMONE RECEPTOR-POSITIVE, HER2-NEGATIVE BREAST CANCER

Nadia Harbeck

Univ. of Munich (LMU), Germany

Therapeutic strategies in HR-positive HER2-negative breast cancer have substantially evolved over the last decade based on new drugs in metastatic and refined risk assessment algorithms in early disease.

In metastatic disease, availability of CDK 4/6 inhibitors has changed the treatment sequence and postponed chemotherapy for most patients. Except for life-threatening situations, patient should receive endocrine-based therapy. For all three available CDK 4/6 inhibitors (abemaciclib, palbociclib, ribociclib) plus endocrine therapy, phase III studies demonstrated substantial prolongation of PFS compared to endocrine therapy alone either in untreated patients or in those who progressed on prior endocrine therapy. The Paloma 3 study recently showed first phase III OS data with a non-significant prolongation of OS in the numerical range of the PFS advantage (~ 6 months) favoring fulvestrant plus palbociclib. In endocrine-sensitive patients, the OS advantage amounted to even 10 months. OS data from the other phase III trials and preferably even a metaanalysis need to be awaited before final conclusions can be drawn. After progression on CDK 4/6i, everolimus and exemestane or a monochemotherapy are effective therapy options. For PIK3CA mutated tumors, the SOLAR-1 trial presented an effective therapy option with alpelisib, an alpha-specific PI3K inhibitor, for which approval needs to be awaited.

In early disease, the key question is whether chemotherapy is needed in addition to endocrine therapy. For risk assessment. Here, prospectively evaluated multigene tests such as MammaPrint or Oncotype DX help with risk assessment in patients up to 3 involved axillary nodes based on the MINDACT, PlanB or TAILORx trials. In addition to the conventional static risk assessment, dynamic assessment of early endocrine response by Ki67 may add to individualize adjuvant therapy. The POETIC trial validated early Ki67 response as a prognostic factor for patient outcome: Patients with high initial Ki67 who respond well to a 2-week of endocrine therapy have a better outcome than those where Ki67 does not drop < 10%. The ongoing WSG ADAPT trial has used early Ki67 response (< 10%) to omit chemotherapy in intermediate-risk Oncotype DX patients. Using such static and dynamic markers together, more than half of HR+ HER2- EBC patients could be spared the burden of adjuvant chemotherapy. As patients with

poor endocrine response to short preoperative endocrine therapy do not respond well to chemotherapy, the upcoming WSG ADAPTcycle trial will evaluate the CDK 4/6i ribociclib together with an AI vs. conventional chemotherapy in these patients.

In conclusion, due to endocrine-based highly effective therapy sequences in metastatic as well as dynamic early response assessment in early breast cancer, chemotherapy will continue to play a less important role in HR+ HER2- breast cancer.

CURRENT TRENDS AND FUTURE DIRECTIONS IN BENCH TO BEDSIDE TRANSLATIONAL RESEARCH IN ER-POSITIVE BREAST CANCER

Carlos Arteaga

UT Southwestern Harold C. Simmons Cancer Center, U.S.A.

About 80% of breast cancers are estrogen receptor-positive (ER+) and estrogen dependent. Therapies for ER+ breast cancer inhibit ER signaling by directly antagonizing ER or by abolishing estrogen production. Adjuvant anti-ER therapies significantly reduce mortality in patients with ER+ breast cancer. However, ~20% of patients treated with adjuvant endocrine therapy eventually relapse with metastatic disease. To date, several mechanisms of de novo and acquired resistance to endocrine therapy have been reported. Large-scale tumor DNA sequencing has identified several actionable genetic alterations that promote endocrine resistance. Mutations in the ligand-binding domain of ESR1, the gene encoding ERα, confer resistance to estrogen suppression via ligand-independent ERα transcriptional activity. Amplification/mutation of growth factor receptors such as ERBB2 and FGFR1 has also been associated with endocrine therapy resistance. More recently, Razavi and colleagues reported that mutations in components of the MAPK pathway and the ER transcriptional program, found in approximately 20% of ER+ breast cancers, are associated with poor patient outcome after antiestrogen therapy. Finally, preclinical and clinical studies suggest a critical role of the activation in the phosphoinositide 3-kinase (PI3K)/AKT pathway in endocrine resistance. Bedside to bench approaches are increasingly used to identify these actionable mechanisms including short presurgical (aka, 'window') and neoadjuvant therapeutic trials, serial molecular profiling of ER+ tumors evolving and progressing through endocrine therapy, and the interrogation in patients' tumors of the molecular basis of exceptional clinical responses to targeted therapies. Several bedside to bench approaches and recent results with clinical trials of drugs targeting actionable mechanisms of endocrine resistance in hormone dependent breast cancer will be presented.

PAST, PRESENT, FUTURE OF CLINICAL TRIALS IN BREAST CANCER SURGERY

Terry Mamounas

Orlando Health, U.S.A.

The role of surgery in breast cancer has undergone significant evolution over the past 40 years, after the centuryold Halstedian paradigm of radical mastectomy as the primary treatment was challenged by the alternative hypothesis that breast cancer was a systemic disease from early on and its inception. Starting in the 1970s, a series of well-designed, randomized, phase 3 clinical trials demonstrated the equivalence between less radical breast surgical procedures and the Halstead radical mastectomy (Fisher B, et al: Cancer, 1977; Fisher B, et al: N Engl J Med, 1985; VeronesiU, et al: N Engl J Med, 1981). Based on these clinical trials, breast conserving therapy became the preferred surgical treatment approach for early stage breast cancer. (NIH Consensus Development Conference, JAMA, 1991).

In addition to breast conserving therapy, the approach to mastectomy has also evolved considerably over the past 25 years. Total mastectomy without reconstruction has now been replaced by skin sparing or nipple sparing mastectomy with immediate/delayed reconstruction with considerable improvement in cosmesis and patient satisfaction. This in turn, has led to a significant increase in the use of contralateral prophylactic mastectomy. The main reasons for this may partially relate to patient's overestimation of the risk of contralateral breast cancer, misperception that contralateral mastectomy may reduce the risk of distant recurrence, patient preference for better symmetry with bilateral reconstruction, increasing use of genetic testing and preoperative breast MRI as well as results of observational studies demonstrating an association between contralateral prophylactic mastectomy and lower breast cancer-specific and all-cause mortality, likely due to selection bias.

In the 1990s, the established reduction in the extent of breast surgery was also matched by a considerable reduction in the extent of axillary surgery with the development and validation of the sentinel lymph node biopsy (SLNB) concept. This has resulted in a substantial decrease in axillary morbidity, while preserving local control, prognostic information and information needed for appropriate adjuvant systemic therapy. Currently, SLNB has become the gold standard for staging the clinically negative axilla whether the SLNs are negative or whether 1 or 2 SLNs are involved.

The adoption of the alternative hypothesis also had a profound impact in identifying the need for adjuvant systemic therapy in order to reduce breast cancer recurrence (both loco-regional as well as distant). The efficacy of adjuvant systemic therapy was demonstrated through multiple randomized clinical trials in nodepositive and nodenegative breast cancer (EBCTCG Lancet 2012). The adoption of effective adjuvant systemic therapy has led to a dramatic reduction in the rates of local regional recurrence both after mastectomy and after breast conserving therapy. This demonstration also led to the hypothesis that if systemic therapy was effective when given after surgery, reversing the sequence and administering it before surgery could lead to primary breast tumor shrinkage that could, in turn, convert patients with inoperable breast cancer to operable candidates and convert mastectomy candidates to candidates for breast conserving therapy. In randomized clinical trials, equivalent outcomes were demonstrated between neoadjuvant and adjuvant chemotherapy. Achievement of pathologic complete response to neoadjuvant chemotherapy was identified as a significant predictor of good outcome. Following this demonstration and with increasing efficacy of neoadjuvant chemotherapy regimens, the next logical step was to attempt to also reduce axillary surgery, with the application of SLNB following neoadjuvant chemotherapy. Several single-institution, multicenter studies and overview analyses have demonstrated the safety and accuracy of SLNB following neoadjuvant chemotherapy in patients who presented with clinically negative axilla. In addition, prospective clinical trials have also demonstrated the safety and accuracy of SLNB in patients who present with biopsy-proven involvement of the axilla but become clinically node-negative after neoadjuvant chemotherapy.

Looking into the future, the next frontier is to challenge the role of breast surgery altogether for patients who are exceptional responders after neoadjuvant chemotherapy and can be identified with high accuracy as having a pathologic complete response based on preoperative imaging and minimally invasive core biopsy of the tumor bed. Also, elimination of SLNB as a staging procedure is being evaluated in prospective clinical trials for patients at low risk for nodal involvement. Results of clinical trials currently conducted on these approaches will shape the future of breast and axillary surgery in the years to come.

OVARIAN FUNCTION SUPPRESSION FOR PREMENOPAUSAL WOMEN WITH BREAST CANCER

Woochul Noh

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In Korea, approximately 50% of newly diagnosed breast cancer cases are premenopausal. Breast cancer in young women is more aggressive and has a worse prognosis compared with women with postmenopausal women. Special considerations should also be taken because of different tumor biology and quality of life issue including fertility preservation. One of the most effective strategies for premenopausal women with ER+ tumor is medical ovarian ablation using GnRT agonist.

Ovarian suppression for preservation of ovarian function and fertility

Young women facing chemotherapy have several options for their fertility preservation. Cryopreservation of embryo, ova, and ovarian tissue are the current standard. However, these strategies do not prevent the development of chemotherapy-induced premature ovarian failure. Currently, concurrent administration of GnRHa with cytotoxic chemotherapy was the only medical intervention to reduce the risk of premature ovarian failure. However, studies regarding this issue have been conflicting, and international guidelines still consider it controversial. Recently a patients level meta-analysis showed the evidence for its efficacy and safety of temporary use of GnRHa during the course of chemotherapy to reduce the POI and preserve fertility. The use of GnRHa was associated with reduced risk of POI and higher pregnancy rates with compatible disease-free survival of the patients. Now it should be considered a reliable strategy to preserve ovarian function and fertility.

Ovarian suppression for advanced/metastatic breast cancer

For the postmenopausal, HR+ advanced breast cancer, the treatment landscape has changed substantially in the recent years with introduction of target therapies in combination with endocrine therapy. However, premenopausal women with HR+ tumor are under-represented in clinical trials. There is a need for dedicated studies in premenopausal patients with advance cancer to derive an effective treatment for young women. MONALEESA-7 was the first trial fully dedicated to premenopausal women with HR+ advance breast cancer. The trial demonstrated that PFS was significantly prolonged with the addition of ribociclib to endocrine therapy with GnRHa.

Based on this study, treatment strategies for HR+ tumor in premenopausal women are usually extrapolated from data from postmenopausal patients with addition of ovarian suppression. This trial and recently on-going trials for premenopausal women provide evidence for new standard treatment for premenopausal women. The flexibility of endocrine therapy partner gives premenopausal women more treatment choice with application of GnRHa.

Ovarian suppression in adjuvant endocrine therapy

Recently, The SOFT and TEXT represents a landmark achievement, addressing a long standing question of optimal endocrine therapy for premenopausal women with HR+ breast cancer. In SOFT, with 8 year median follow-up, tamoxifen plus ovarian suppression significantly improved DFS and OS compared with tamoxifen alone. In contrast, exemastane plus ovarian suppression did not significantly improve OS compared with tamoxifen alone. Thus, many questions arise when translating results of SOFT and TEXT into clinical practice. Although it is generally accepted that adding OFS to tamoxifen provides benefits for premenopausal women with HR+ breast cancer, uncertainty exist about patients selection, the best timing, and optimal duration. Recently conducted Korean ASTRRA trial suggested that the use of OFS for 2 years from the point of the resumption of ovarian function after completion of chemotherapy could be an option. In this presentation, the results of ASTRRA trial will be reported in more detail with the suggestion of subsequent trials to address the unanswered questions.

INNOVATIVE APPROACH FOR THE TREATMENT OF REFRACTORY BREAST CANCER

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One of the biggest challenges in the treatment of advanced breast cancer is the development of resistance, which is cumulative over time and exposure to increasing lines of therapy. Resistance develops rapidly in triple negative disease, limiting treatment options, and more slowly in endocrine responsive disease. Several new approaches have significant promise, including novel chemotherapy agents, antibody drug conjugates, genomic profiling to identify targetable pathways with clinical utility, PARP inhibitors for germline BRCA mutated disease and immunotherapy.

Newer chemotherapy agents include the oral microtubule inhibitor tesetaxel, currently under evaluation in a randomized phase III trial in combination with capecitabine compared to capecitabine alone in hormone refractory hormone receptor positive metastatic breast cancer. Novel antibody drug conjugates appear to have activity across biologic subsets of disease, with modest and tolerable toxicity. Two agents with novel targets and toxins in late stage development include sacituzumab govitecan and trastuzumab deruxtecan (DS-8201). Genomic profiling is still exploratory in breast cancer, but one example is of particular interest. Somatic HER2 mutations are found more frequently in hormone receptor positive disease, and treatment of patients with these mutations with combined endocrine therapy and the HER2 targeted tyrosine kinase inhibitor neratinib has demonstrated clinical activity. Patients whose tumors harbor PI3KCA mutations are uniquely sensitive to inhibitors of this pathway, with recent positive results from the SOLAR-1 trial combining fulvestrant with the alpha specific inhibitor of PIK-3CA, alpelisib. Two PARP inhibitors were recently approved for the treatment of metastatic breast cancer associated with germline mutations in BRCA 1 or 2 due to marked increases in both response and progression free survival. Ongoing studies are evaluating the effectiveness of these agents in patients with other germline mutations affecting DNA repair, and with somatic mutations in BRCA.

Immunotherapy has met with great success in multiple malignancies, with variable data in triple negative and HER2+ breast cancer. Recent data from the IMPASSION130 trial demonstrating improvement in overall survival with the combination of atezolizumab and nab-paclitaxel compared to nab-paclitaxel alone led to regulatory approval of this combination for the treatment of PD-L1 immune cell positive triple negative breast cancer. Multiple studies are evaluating ways to increase PD-L1 expression and enhance the clinical impact of immunotherapy in all subsets of breast cancer, and in both early and late stage disease.

Symposium

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WHO NEEDS SYSTEMIC CHEMOTHERAPY?

Yoon-Sim Yap

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Adjuvant systemic chemotherapy has been a major advance in improving survival outcomes in non-metastatic breast cancer over the past few decades. This lecture will discuss the summary of the data demonstrating the benefits of adjuvant chemotherapy, as well as who needs systemic chemotherapy in the adjuvant setting. Key factors in the decision to use chemotherapy include the underlying tumor biology (grade, estrogen receptor, progesterone receptor and HER2 status) and disease burden (tumor size, nodal status), in addition to patient factors (age, comorbidities, personal preference). Benefit-risk calculators and genomic assays may help to refine the prediction of prognosis and potential benefit from chemotherapy further. Determination of the residual micrometastatic disease for accurate risk assessment in each patient is currently not feasible; neither can we predict sensitivity of individual tumors to the chemotherapy administered. While major progress has been made in tailoring adjuvant systemic therapy, we are still far from achieving the ideal goals in delivering personalised medicine to our patients.

WHO ARE CANDIDATE FOR OVARIAN SUPPRESSION & EXTENDED ENDOCRINE THERAPY

Masakazu Toi

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Breast cancer is a heterogenous disease. Annual risk of recurrence differs depending upon tumor stage at diagnosis and tumor properties.

In luminal diseases, recurrence risks tend to long over 15 years.

Therefore, precise evaluation of tumor stage and characteristics, and precise prediction of survival outcomes are crucial. In general, we consider adding ovarian suppression and extended endocrine therapy for patients having a certain level of recurrence risk. Obviously, clinicopathological staging, age, multigene signatures, tumor subtyping, and the composite model using these parameters help us to assess hormone sensitivity and predict survival in the presence or absence of treatments, which results in the treatment escalation or de-escalation for each patient. If neoadjuvant endocrine therapy is concerned, short-term responses may be important information as well.

Quality of life aspects are also extremely important for patients decision making. Recently, we have got multiple keynote publications and presentations so that it would be the time to discuss about the optimal indication for doing more and the value of the personalization of treatment.

WHAT'S NEW FOR HER2 POSITIVE EARLY BREAST CANCER?

Jee Hyun Kim

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There has been huge improvement in the systemic adjuvant treatment of HER2 positive early breast cancer, turning worst phenotype of breast cancer into highly treatable subtype. Efforts to achieve even better outcome with escalation strategy, as well as de-escalation strategies to achieve same good outcome yet with less treatment therefore less toxicity are ongoing.

In the year of 2018-2019, important results have been reported both in terms of escalation & de-escalation. In the APHINITY trial, addition of pertuzumab to standard adjuvant chemotherapy plus 1 year of trastuzumab resulted in modest, but significant increase in the disease free survival of HER2 positive early breast cancer (HR 0.81; 95% CI 0.66-1.00, $p = 0.0446$), albeit very little absolute gain of 0.9% in estimated 3-year invasive disease free survival rate. Lymph node positive patients seemed to receive most benefit, with 3-year rate of invasive disease free survival of 92.0% vs. 90.2%.

In KATHERINE trial, 1486 patients who had residual tumor after preoperative therapy with taxane +- anthracyclines plus HER2 targeted agents were randomized to T-DM1 vs. trastuzumab. The estimated percentage of patients who were free of invasive disease at 3 years was higher in T-DM1 arm (88.3% vs. 77.0%, HR 0,50, 95% CI 0.39-0.64, $p < 0.001$) than in the trastuzumab arm.

Attempts of de-escalation also continued with TRAIN-2 trial testing omitting anthracyclines, and PERSEPHONE and PHARE trial testing 6 months vs. 12 months of adjuvant trastuzumab. Other attempts of de-escalation included omitting chemotherapy and replacing it with hormone plus dual targeted therapy in triple positive patients in the neoadjuvant setting (PerElisa study), and comparing adjuvant trastuzumab with or without chemotherapy in the adjuvant setting in the elderly patients (RESPECT trial). The results of these trials, as well as studies on biomarkers to predict response and select optimal treatment strategy for HER2 positive early breast cancer will be shared in the meeting.

POTENTIAL THERAPEUTIC TARGETS: ANDROGEN RECEPTOR, PI3KCA, MEK, ETC.

Sung-Bae Kim

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Regardless of enriched chemosensitivity and immunogenicity, majority of Triple-negative breast cancer (TNBC) patients still suffer from dismal clinical outcomes including early relapse and metastatic spread.

There is an unmet need in TNBC patients to identify therapeutic targets and develop more effective stratified medicine for the treatment of TNBC. The potential therapeutic targets for TNBC based on its intrinsic subtype and. the aberrant activated signals found in different subgroups of TNBC, including androgen receptor (AR) and PI3K/AKT/mTOR, Notch, Wnt/β-catenin, Hedge-hog, and TGF-β signaling pathways, which play essential roles in multiple development stages of TNBC, will be covered. The careful analysis of these signaling pathways and therapeutic targets would have significant impact on the drug development and clinical trials, leading to effective therapies for this deadly disease.

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BRCA AND DNA REPAIR IMPAIRMENT

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Cancer has been defined as a genetic disorder caused by the accumulation of genetic alterations, which result from various internal and external DNA damages that are left unrepaired. One of main characteristics of cancer is partial loss of DNA damage repair (DDR) pathway resulting in increased DNA damage levels and replication stress. DDR inhibitors have been suggested as a new anticancer strategy, under the concept of synthetic lethality. The poly-(ADP-ribose) polymerase (PARP) inhibitor is the first DDR inhibitor to be used in clinical practice. PARP inhibitors have been tested in patients with BRCA1/2 germline mutations (gBRCA1/2mt) and shown robust clinical benefits in breast cancer with gBRCA1/2mt and serous ovarian cancer patients. The concept of synthetic lethality is not limited to gBRCAmt for PARP inhibitor, and discovering homologous recombination deficiency (HRD) markers beyond BRCA1/2 and identifying best candidates for DDR inhibitors are the active research areas. At the same time, various combinations of DDR inhibitors and other anti-cancer drugs are being tested both in preclinical and clinical studies. In addition, based on recent evidence of the immunemodulatory effect of PARP inhibitors, the combination of DDR inhibitors and immune checkpoint inhibitors is being actively investigated. Acquired resistance mechanism of DDR inhibitors, as well as defining best candidates and best combinations, would be future research topics for DDR inhibitors. Furthermore, it would be also crucial to establish a clinically relevant standardized method to detect HRD for future clinical use.

OPTIMAL TREATMENT OF TNBC WITH CYTOTOXIC CHEMOTHERAPY

Rebecca Alexandra Dent

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The molecular biology revolution in cancer began with the completion of the Human Genome Project in 2003. From there, large scale, international consortia such as the TCGA & ICGC, amongst others, have delivered a compendium of the complex make-up of the diseases we know as cancer.Triple negative breast cancer (TNBC), a diagnosis of exclusion, is being unravelled by this improved understanding into different subtypes. The issue is that we do not yet have a definitive breakdown of what constitutes separate types so that we can adopt pathway driven approaches to therapy. In the meantime, the management of TNBC relies on chemotherapy as its basis, albeit with a refined approach using platinum based chemotherapy for cancers with defects in HRD repair, anti-metabolites for HNEJ and eribulin for changes in EMT. Gene expression analyses are characterising general sensitivity algorithms to chemotherapy but in the main part are not used in day to day practice. This presentation will review current and possible future standards for chemotherapy treatment of TNBC.

CURRENT TRENDS IN IMMUNO-ONCOLOGY

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During immune responses, antigen-specific T cells are regulated by various mechanisms including inhibitory receptors and regulatory T cells to avoid excessive and persistent immune responses. These regulatory mechanisms, called 'immune checkpoint', suppress T cell responses particularly in chronic viral infection and cancer, in which viral antigens or tumor antigens persist for a longtime, and lead to T cell exhaustion in patients with chronic viral infection or cancer. Among them, cytotoxic T lymphocyte-associated protein 4 (CTLA-4) and programmed cell death 1 (PD-1) are the most well-known receptors and have been targeted for drug development. As a result, anti-CTLA-4 and anti-PD-1 (or anti-PD-L1) blocking antibodies were developed for cancer treatment and known as 'immune checkpoint inhibitors'. However, anti-CTLA-4 and anti-PD-1 (or anti-PD-L1) blocking antibodies fail to control tumors in a significant proportion of cancer patients. Therefore, it is an important question how the coverage of immune checkpoint inhibitors can be extended to the majority of cancer patients who do not have control or regression of their cancer. In this lecture, strategies to improve treatment responses of anti-PD-1 will be discussed, including novel immuno-modulators and biomarkers predicting treatment responses.

IMMUNOTHERAPY IN BREAST CANCER: BIOMARKERS AND CORRELATIVE STUDIES

Prudence Francis

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During the 21st century, immunotherapy has dramatically changed the treatment landscape for a variety of different types of cancer. Immunotherapy provides some patients with an improvement in progression-free and overall survival. However, not all types of cancer, or patients with a particular type of cancer, benefit from current immunotherapy treatments. In addition, given the cost of treatments, and the possibility of life-threatening or permanent toxicities, it is important to understand which patients are most likely and which patients have the capacity to derive benefit.

Historically in some types of solid tumor such as melanoma, the observation of occasional spontaneous regressions in the absence of therapy, suggested the immune system might play an important role in tumor control, while breast cancer was not traditionally considered a particularly immunogenic type of cancer. Results of more recent research indicates that the immune system is relevant in breast cancer, particularly in triple negative (TNBC) and HER2-positive cancers.

The recent results of the IMpassion 130 phase III trial reporting a significant improvement in progression-free survival in the first-line setting for incurable advanced or metastatic TNBC with the addition of atezolizumab to nab-paclitaxel, has clarified the importance of immunotherapy for at least some breast cancers. Apart from the use of ER, PR, and HER2 to identify breast cancer subtypes that may respond to immunotherapy, ongoing breast immuno-oncology research is important to identify and evaluate relevant biomarkers in tumors and patients.

BREAST CANCER SUBTYPES & IMMUNOTHERAPY

Giuseppe Curigliano

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Many new achievements have been reached in triple negative breast cancer research in the last year. The phase III IMpassion130 trial comparing chemotherapy plus atezolizumab versus chemotherapy plus placebo brought breast cancer into the immunotherapy era. Despite the encouraging results obtained in this trial, many open questions can be raised. The positive overall survival outcome provided only in the PD-L1-positive triple-negative breast cancers suggest that we need to enrich the patient population which more likely benefit from an immunotherapy approach. Moreover, we do not know whether single-agent immunotherapy might be a good option for some patients. In this context, the discovery and implementation of novel and proper biomarkers is an unmet need. Moving to the early setting of triple-negative breast cancer, neoadjuvant trials could represent excellent in-vivo platforms to test immunotherapy agents and the potential combinations allowing the opportunity to perform translational study for biomarkers implementations and a better patient selection. Limited data are available also in HER2 positive disease, where activity of pembrolizumab in combination with trastuzumab has been described in HER2 positive BC. In ER positive disease acritivity of immune-checkpoints is limited. The aim of my presentation is to present recent advances in triple negative, HER2 positive and ER positive breast cancer treatment and to discuss open issues in order to define potential future directions for immunotherapy in breast cancer.

RECONSTRUCTION AFTER NSM: AUTOLOGOUS TISSUE OR IMPLANT?

Hak Chang

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Recently, nipple-sparing mastectomy (NSM) has gained acceptance in the field of breast oncology, because the procedure appears to be oncologically safe with low risks of cancer recurrence. Thus, the number of patients undergoing NSM has increased due to its cosmetic merits of preserving the native skin and nipple of the breast, and its strength in immediate reconstruction, which can be performed following direct-to-implant breast reconstruction or buried free TRAM flap breast reconstruction and create a natural appearance of the breast in only a single surgery.

In NSM, final survival of mastectomy skin flap and NAC without any necrosis is a key factor for surgical success due to its relatively high complication rates (3%-37%, depending on studies) and may delay postoperative oncologic therapy with delayed wound healing, wound dehiscence, implant exposure, or wound infection, and deform the appearance of the breast resulting in emotional stress. Inadequate skin perfusion to the NAC is the Achilles heel of this operation, and perfusion deficits were greatest for incisions that combined circumareolar and radial approaches. In these recent circumstances, our institution aimed to analyze the intraoperative Indocyanine green (ICG) image of breast cancer patients who underwent NSM, and to evaluate the perfusion of NAC using intraoperative laser-assisted ICG dye angiography (SPY system, Novadaq Technologies, Canada) to predict NAC and skin flap necrosis.

For immediate reconstruction choice, using autologous tissue and implant-based reconstruction are the two basic categories. In case of using autologous tissue, free TRAM flap reconstruction is mostly considered, and in case of implant-base reconstruction, Direct-to-implant reconstruction is mostly considered. Both methods are very effective tools for most of the patients undergoing NSM, if they have no contraindication for each method. Because each treatment option has clear advantages and disadvantages, patients preference is firstly considered after consultation with the plastic surgeon. Then, each patients medical conditions such as age, obesity, peripheral vascular disease, history of radiation therapy, clinical cancer stage, and compliance are considered by the plastic surgeon for risk evaluation. For better surgical outcome with better patient satisfaction, treatment options should be applied adequately according to the patients.

LONG-TERM FOLLOW-UP OF NIPPLE-SPARING MASTECTOMY

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Background: Nipple-sparing mastectomy (NSM) is an increasingly popular surgical procedure for treatment of breast cancer. However, NSM is controversial because of its association with locoregional recurrence. We started performing NSM in 1978.

Methods: We investigated the surgical safety including nipple necrosis, and nipple-areola recurrence (NAR) and skin flap recurrence (SFR) after NSM for 1,071 patients with breast cancer, including 31 with stage 0, 414 with stage 1, 479 with stage 2,141 with stage 3 and 6 with stage 4, from 1985 to 2017. Our surgical notes for NSM included the following information: (1) Tissue thickness under the NAC was left at 5 mm, but the major ducts were removed from within its lumen. (2) A skin flap preparation was created based on a thick flap (> 1 cm-thick subcutaneous adipose tissue) created > 2 cm away from the tumor, but a thin flap was placed close to the tumor. No patients received radiotherapy. We herein provide a review of safety in NSM surgical technique involving the NAC and a discussion of nippleareola and skin flap recurrence, and prognosis of nipple-areola and skin flap cases. In 1,034 patients with stage 13 breast cancer treated with NSM who developed NAR or SFR, we evaluated cancer stage, nuclear grade, lymph node metastasis, tumor-nipple-areola distance, and histological classification as tubule forming, solid and schirrous type. In 748 patients with early stage 1 and 2A breast cancer treated with NSM, NAR, and SFR were evaluated for estrogen receptor and HER2 expression. We evaluated disease-free interval and frequency of late NAR and SFR.

Result: Median follow-up after NSM was 87 (33-97) months. There was only one case of total nipple necrosis among all 1,071 patients. There were 96 patients (9.0%) with local recurrence, including 44 (4.0%) with NAR and 52 (4.8%) with SFR. NAR was seen in 1 (3.1%), 14 (3.4%), 17 (5.1%), 5 (3.4%), 7 (5.0%), and 0 patients with stage 0, 1, 2A, 2B, 3, and 4 cancer, respectively. SFR was seen in 0, 15 (3.6%), 8 (2.7%), 7 (4.8%), 22 (15.6%), and 0 patients with stage 0, 1, 2A, 2B, 3, and 4 cancer, respectively. Median disease-free interval of NAR and SFR was 3.4 (0.96-22.3) and 2.5 (0.21-21.2) years, respectively. Twenty-three (53%), 12 (27.9%) and 6 (14%) patients had NAR at more than 3, 5, and 10 years after NSM, respectively. Twenty (38%), 13 (25%), and 6 (11.5%) patients had SFR at more than 3, 5, and 10 years after NSM, respectively. Therefore, late NAR and SFR were observed. Patients with stage 13 cancer treated with NSM who

had significantly more frequent NAR, were characterized by high nuclear grade and tubule-forming type cancer. Patients with significantly more frequent SFR were characterized by stage 3 cancer, positive lymph node metastasis and age ≤ 40 years. Patients with early stage breast cancer treated with NSM with significantly more frequent NAR had negative estrogen receptor expression, positive HER2 expression and shorter tumornipplеareola distance (≤ 2 cm). Overall survival was significantly better in patients with NAR (97% at 5 years and 80% at 10 years) than SFR (71% at 5 years and 50% at 10 years). Regarding SFR, overall survival was significantly worse for multiple (≥ 2) and diffuse (clinical inflammatory syndrome) recurrence than for single-nodule recurrence. There was no significant difference in prognosis between NAR and single-nodule SFR. The prognosis of nipple-areola recurrence was good with a 60-month overall survival of 93% and a 100-month survival of 84%. A total of 45% of nipple-areola recurrence cases were Pagets type recurrences. All cases of nipple-areola recurrence were able to undergo salvage surgery.

Conclusions: The nipple-areola recurrence rate after NSM was low, and its prognosis was good. Our data showed that clinicopathological features and prognosis differed between patients with NAR and SFR. There was no significant difference in prognosis between NAR and single-nodule SFR. Late NAR and SFR were seen, and careful long-term follow-up observation is necessary after NSM.

RADIATION TREATMENTS AFTER NSM WITH RECONSTRUCTION

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HER2 TARGETED THERAPY IN BREAST CANCER IN 2019

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Multiple advances in the treatment of HER2 positive breast cancer have markedly improved outcome for this subset. The combination of trastuzumab with pertuzumab and chemotherapy markedly improved survival in the first line metastatic setting and has become a standard of care. The addition of pertuzumab to neoadjuvant trastuzumab based chemotherapy improves pathologic complete response rate, but has a modest impact in high risk disease in the adjuvant setting. Trastuzumab emtansine improved survival compared to lapatinib and capecitabine following progression on trastuzumab, and with this data became the second line standard of care as treatment for metastatic HER2+ disease. A number of novel therapies have demonstrated some efficacy in the metastatic setting and have been or are being tested in phase III trials including the oral tyrosine kinase inhibitors neratinib and tucatinib, the novel HER2 antibody margetuximab, antibody drug conjugates including trastuzumab deruxtecan, and combinations with immunotherapy. Several agents may have specific activity in the CNS. In the early stage setting, results of the Katherine trial demonstrating improved disease free survival when trastuzumab emtansine was substituted for trastuzumab after surgery for patients with residual disease following trastuzumab based chemotherapy has significantly impacted the approach to HER2+ disease, with neoadjuvant therapy recommended for most early stage tumors. Although alternative therapy has proved very effective in patients with more resistant disease, overall response to taxane/trastuzumab and pertuzumab chemotherapy is very high. For this reason, response to neoadjuvant therapy is now being used as a way to de-escalate therapy in patient who will do well with less intensive therapy. Side effects from trastuzumab are minimal with reduction in cardiac muscle function remaining the primary toxicity. In patients receiving anthracyclines, this toxicity can be reduced by concomitant administration of cardiac medications. Lastly, access to trastuzumab is increasing with the increasingly widespread access to biosimilars with excellent clinical efficacy data.

OPTIMAL SEQUENCE OF ANTI-HER2 THERAPY IN THE METASTATIC SETTING

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Anti-HER2 agents such as trastuzumab, lapatinib, pertuzumab, and trastuzumab emtansine (T-DM1) have been widely used in HER2-positive metastatic breast cancer, and there remain many clinical questions on optimal sequence of these agents.

Trastuzumab+pertuzumab+taxane (HPT) for first-line treatment and T-DM1 for second-line treatment have been established as the standard of care by CLEOPATRA study and EMILIA study, respectively. Because T-DM1 was not superior to trastuzumab+taxane in MARIANNE study, HPT is considered to be superior to T-DM1 as first-line treatment; however, there may be some populations that benefit more from first-line T-DM1 therapy. A phase III trial (JCOG1607/HERB TEA) is ongoing to compare HPT and T-DM1 for first-line treatment in elderly patients. Another clinical question for first-line treatment is which cytotoxic agent is the best partner for trastuzumab and pertuzumab, and a phase III trial (JBCRG-M06/EMERALD) is ongoing to compare HPT and trastuzumab+pertuzumab+eribulin mesylate.

For third or more line treatment, we have several options including lapatinib+capecitabine (LX) and trastuzumab beyond progression+cytotoxic agents; however, there have been insufficient evidence to recommend one regimen over another. We conducted a randomized phase II trial (WJOG6110B / ELTOP) to compare LX and trastuzumab+capecitabine (HX) in patients previously treated with trastuzumab and taxanes and showed that LX yielded longer PFS and OS than HX, although this was not statistically significant. Another clinical question is the significance of pertuzumab beyond progression, and a phase III trial (JBCRG-M05/PRECIOUS) is ongoing to evaluate pertuzumab retreatment in patients previously treated with pertuzumab, trastuzumab, and chemotherapy.

Since recent studies have shown promising results of other anti-HER2 agents such as neratinib and trastuzumab deruxtecan (DS-8201a) and other molecular targeted agents such as CDK4/6 inhibitors and immune checkpoint inhibitors are also studied in patients with HER2-positive breast cancer, we will have more clinical questions in the near future.

OVERCOMING RESISTANCE TO ANTI-HER2 THERAPIES

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CURRENT LANDSCAPE: REVIEW OF RECENT IMMUNOTHERAPY TRIALS

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Immunetherapy has substantially changed the outlook of several solid tumors over the last decade. In breast cancer, studies so far have concentrated on triple negative disease. Early I-II studies for pembrolizumab and atezolizumab in the metastatic setting have demonstrated efficacy in only a small proportion of patients. Recently, the IMPassion 130 trial reached its primary endpoint and showed a significant improvement in PFS both in the overall cohort of triple negative metastatic breast cancer as well as in the PD-L1 (immune cells)-positive tumors favoring nab-paclitaxel plus atezolizumab vs. nab-paclitaxel alone in the first line setting. In the intention-to-treat analysis, the median OS was 21.3 vs. 17.6 months, again favoring the atezolizumab arm. In PD-L1+ tumors, median OS was 25.0 vs. 15.5 months, respectively (hazard ratio 0.62; 95% CI 0.45-0.86). Approval is still pending. Results of further trials in the metastatic setting, also with pembrolizumab are urgently awaited as there is still a number of open questions regarding immunotherapy in MBC. Optimal testing, sequence as well as combination partners are still unclear.

Also in early breast cancer, initial data from phase I-II neoadjuvant trials are quite promising in TNBC. High pCR rates up to 80% were demonstrated by standard chemotherapy plus pembrolizumab in the Keynote 173 trial. In i-SPY-2 trial, the probability that a pembrolizumab-containing regime is superior to standard chemotherapy was demonstrated for TNBC as well as HR+ HER2- disease. The GeparNuevo trial showed a numerical but not significant difference between standard chemotherapy +/- durvalumab. Interestingly, in patients who had received durvalumab before onset of chemotherapy in a window phase had a significantly better pCR compared to standard chemotherapy alone. More phase II III trials in the neoadjuvant setting for pembrolizumab but also atezolizumab or other immune therapies are still ongoing or already fully recruited.

In conclusion, initial phase III data with the anti PD-L1 inhibitor atezolizumab are very promising regarding this therapeutic approach in metastatic breast cancer. More data are awaited for PD-L1 as well as PD-1 inhibitors this year and will help to clarify the role of immunetherapy in metastatic and early breast cancer.

EMERGING TARGETS BEYOND PD-1 AND PD-L1

Kyong Hwa Park

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Introduction of immune checkpoint inhibitors to oncology has greatly changed clinical practice in cancer care. Recent researches achieved dissection of tumor immune environment according to cancer types and context of diseases. Moreover, extensive translational research enabled us to search new combinations for the better therapeutic strategies. Like other cancers, breast cancers have been investigated for efficacy starting from pretreated patients using single agent PD-1/PD-L1 antibodies. Early trials of single-agent checkpoint inhibitors in pretreated TNBCs showed very low response rates between 5-10%. The response rate was improved up to 20-25% when the patients were untreated first-line setting. Recently, a large phase III clinical trial comparing nab-paclitaxel/atezoliaumab with nab-paclitaxel/placebo showed a significant improvement in PFS in patients with untreated, metastatic TNBC. Additionally, investigators reported PD-L1 on immune cells was the most important single biomarker for response to ICI-combination. However, biomarkers to guide personalized approach according to subtypes and disease context are not clearly defined in breast cancer.

One of the most important indicator for response to ICI combination is the disease setting; earlier the better. Thus, in metastatic setting, there should be a biomarker to select patients for ICI single or combination therapy. In this context, MSI-high tumors might be an example and could be selected by NGS analysis. For the combination approach, optimization of standard of care chemotherapy or targeted agent might be an important determinant for the best efficacy. In case of IO combinations with other than PD-1/PD-L1 antibodies, exploration of immune microenvironment for resistant mechanisms (LAG-3, TIM-3, ICOS, TIGIT, IDO1, etc) should be conducted.

Environmental modifiers for anti-tumor immunity like gut microbiome, which was demonstrated in melanoma, is also deserve to be explored in clinical trials. Several ongoing trials are evaluating the potential associations in breast cancer.

IMMUNOTHERAPY BEYOND ANTIBODIES: THE ROLE OF CD 24 IN TNBC DRUG RESISTANCE AND TUMOR IMMUNITY

Helena Chang, Lihong Huo, Xinyu Deng, Xiang Huang, Xinfeng Zhang

Department of Surgery, David Geffen School of Medicine at UCLA, U.S.A.

Background: Increasing evidence indicates that the immune system plays a critical role in monitoring and regulating tumor growth and immune evasion is a hallmark mechanism of cancer progression. A recent success in adding immune checkpoint inhibitor to chemotherapy in treating triple negative breast cancer (TNBC) confirms that uplifting immunosuppression enhances tumor response to chemotherapy. We hypothesize that immunosuppression co-exists with chemotherapy resistance in TNBC.

Methods: 158 tumor specimens containing TNBC TMA were used to study the association among CD44, CD24, CD133, and ALDH with patients survival outcomes after adjuvant chemotherapy. The CD24- mediated chemotherapy resistance, autophagy, and immune-phenotyping in TNBC are being studied.

Result: We have demonstrated that CD44+CD 24+ high TNBC are resistant to Taxane-based chemotherapy not only in patients but also in vitro/in vivo studies. The CD24 expression in TNBC is regulated by TGF-β and Bcl2 through ATM-NDRG2-Stat 3 signaling. Downstream, CD24 regulates drug resistance through autophagy and is associated with immune suppressive signaling. Literature review of immunologic phenotyping in TNBC will be reported.

Conclusions: Understanding drug resistance mechanisms and its relationship with immunologic suppression present in tumor is essential in the success of TNBC treatment.

WHEN CAN WE OMIT RADIATION THERAPY AFTER BREAST CONSERVING SURGERY FOR DCIS?

Bruce Mann

The Royal Women's Hospital, Australia

Ductal carcinoma in situ is a highly controversial disease. It is viewed by some as part of the key to reducing breast cancer mortality a premalignant condition diagnosis of which can prevent breast cancer. It is viewed by others as a problem, with a large amount of over-diagnosis leading to unnecessary treatment, the side effects of which may balance or outweigh any benefits from breast cancers prevented.

In order to optimize the outcome of patients, the aims of diagnosis and treatment of DCIS must be identified, and both the risks and the benefits must be acknowledged.

Surgical excision alone is the minimal treatment recommended in the majority of cases. There is little evidence that adding further treatment reduces the risk of breast cancer specific or overall mortality, save in a small group with high risk disease. Most patients have a significant risk of local recurrence after wide excision alone, either as DCIS or invasive cancer, and for that reason, adjuvant radiation therapy is usually considered, and often recommended.

Limitations of current technology to determine the nature and extent of disease prior to surgery an important limitation, and the lack of effective biomarkers to identify those cases of DCIS at risk of invasive progression/recurrence has hindered the quest to appropriately tailor treatment.

The attitude of the individual patient is critical when answering the question: when can we omit radiation therapy after BCS for DCIS?. As there is generally no survival benefit, the treatment is given to improve the quality of life, and for many women, accepting a higher rate of local recurrence in order to avoid the costs, inconvenience and short- and long-term side effects of radiation treatment is their preferred choice.

This presentation will review the current status of DCIS diagnosis and management, and outline various initiatives and developments that may allow us to better avoid under- and over-treatment of the disease.

WHAT IS OPTIMAL MARGIN IN BREAST CONSERVING SURGERY FOR DCIS?

Terry Mamounas

Orlando Health, U.S.A.

The debate on the optimal margin width after breast conserving surgery for invasive breast cancer as well as for DCIS is as old as the procedure itself. From the time of inception of breast conserving surgery, two divergent approaches emerged, i.e. lumpectomy and quadrantectomy with diametrically opposed approaches to surgical margin width.

Lumpectomy was designed to remove the breast tumor with a limited normal rim of tissue around it. Pathologically negative margins were declared if on microscopic examination there was "no ink on tumor". On the other hand, quadrantectomy was designed to remove the quadrant where the tumor resided along with the overlying skin and underlying fascia "en block" resulting in wider margins.

Over the past three decades this debate continued unabated leading to great variability in perceptions and attitudes of what is an acceptable margin in breast conserving surgery. As a result, approximately 1 in 4 women treated with BCS undergo a re-excision in order to obtain more widely clear margins. Re-excisions result in additional discomfort, increase surgical complications, inferior cosmetic result, increase patient anxiety, increased health care costs and increased mastectomy rates.

In order to provide information on optimal resection margins following breast conserving surgery, the Society of Surgical Oncology (SSO), the American Society of Clinical Oncology (ASCO) and the American Society of Therapeutic Radiation Oncology (ASTRO) convened a multidisciplinary consensus panel that considered a meta-analysis of margin width and ipsilateral breast tumor recurrence (IBTR) for patients who underwent breast conserving surgery plus breast radiation for invasive breast cancer. The meta-analysis was a systematic review of 33 studies that included 28,162 patients. In addition, the panel considered the results of randomized trials, the reproducibility of margin assessment, and current patterns of multimodality care. Based on the above information, the multidisciplinary panel concluded that the use of no ink on tumor as the standard for an adequate margin in invasive cancer in the era of multidisciplinary therapy is associated with low rates of IBTR. These recommendations provided a much needed guidance regarding margin assessment but as with any new guideline there were

strengths and limitations of the recommendations: The guideline applies to patients with invasive breast cancer treated with whole breast radiation. The findings cannot be extrapolated to patients with pure DCIS, to those treated with neoadjuvant chemotherapy or accelerated partial breast irradiation or to those not receiving XRT. However, it was recognized that this approach has the potential to decrease re-excision rates, improve cosmetic outcomes, and decrease healthcare costs.

In order to address optimal margin for patients with DCIS, the Society of Surgical Oncology (SSO), the American Society of Clinical Oncology (ASCO) and the American Society of Therapeutic Radiation Oncology (ASTRO) convened another multidisciplinary consensus panel that considered a meta-analysis of margin width and ipsilateral breast tumor recurrence (IBTR) for patients who underwent breast conserving surgery plus breast radiation for DCIS. The meta-analysis of margin width and IBTR included 20 studies with a total of 7,883 patients and 865 IBTRs. Eligible studies required to have a minimum of 50 patients with DCIS who underwent local excision and reported IBTR in relation to microscopic margin width. The minimum median follow up was 4 years and the median proportion of patients receiving WBRT was 100% (range 53.3%-100.0%). The median proportion of patients receiving endocrine therapy was 20.8% and the median follow up was 78.3 months. The median incidence of IBTR was 8.3%. The results of the meta-analysis showed that negative margins halve the risk of IBTR compared with positive margins defined as ink on DCIS. In addition, 2-mm margin minimized the risk of IBTR compared with smaller negative margins but more widely clear margins did not significantly decrease IBTR compared with 2-mm margins. Based on the information from the meta-analysis and other published literature, the multidisciplinary panel concluded that use of a 2-mm margin as the standard for an adequate margin in DCIS treated with whole-breast irradiation is associated with lower rates of IBTR and has the potential to decrease re-excision rates, improve cosmetic outcomes, and decrease health care costs. They further stated that clinical judgment should be used in determining the need for further surgery in patients with negative margins narrower than 2-mm. This new guideline has the potential to decrease re-excision rates for patients with DCIS undergoing breast conserving surgery pus breast radiation.

CAN RADIATION THERAPY REPLACE RE-EXCISION OF POSITIVE MARGIN IN DCIS?

Kyubo Kim

Department of Radiation Oncology, Ewha Womans Univ., Korea

Breast conserving surgery followed by whole breast radiotherapy (RT) is the standard treatment for ductal carcinoma in situ (DCIS) of the breast. Recently, the omission of adjuvant RT is being actively investigated for selected low-risk DCIS patients, and conversely, the role of tumor bed boost after whole breast RT is another topic to be resolved in the treatment of high-risk DCIS.

High-grade tumor, larger tumor size, close resection margin (RM), younger age, and/or absence of hormonal receptor expression are considered as high risk factors of local recurrence after breast conserving surgery for DCIS. Among these, clear RM is the most important goal to be achieved for adequate local control, and a cut off of 2 mm is the adequate margin width in patients receiving whole breast RT, which is the consensus guideline by SSO, ASCO, and ASTRO. In those patients undergoing excision alone, the adequate margin width is not yet determined, but a wider RM would be required.

Involved RM itself is the high risk factor for local recurrence, and therefore, re-excision should be considered. However, adjuvant RT may be a treatment option if further excision is not eligible and adequate local control could be achieved with RT. In invasive carcinomas of the breast, RT dose escalation for involved RM had been tested through a randomized trial by EORTC. Tumor bed boost was given up to either 26 Gy or 10 Gy after 50 Gy of whole breast RT. There was no significant difference in local control, rather increased incidence of fibrosis was observed in the high dose group.

Regarding the role of tumor bed boost in DCIS, there is no consensus yet. Several retrospective studies were reported, but the results are conflicting. This issue is under investigation via two randomized trials, that is, BONBIS and TROG trials. Although both trials excluded those patients with involved RM from trial participation, their results would be helpful to understand the association between RT dose and local control in DCIS according to the margin width.

MULTIGENE ASSAYS DEVELOPED FROM WESTERN AND ASIAN COUNTRIES

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Breast cancer is the most common cancer in women. About 80% of node-negative and hormonal receptor-positive (HR+) patients remain disease-free at 12-year follow-up after primary treatment with surgery plus tamoxifen. To overcome the imprecise prediction of prognosis based on clinicopathologic factors, multigene tests for breast cancer prognosis are frequently used, especially in Western countries. The recent TAILORx trial demonstrated that about 70% of node-negative, HR+, and human epidermal growth factor receptor 2-negative (HER2-) patients can forgo adjuvant chemotherapy. These types of multigene assays are not commonly used in Asian countries. One reason could be due to that the majority of tests were developed from Caucasian populations. In fact, evidence has shown that Oncotype DX may overestimate the risk of recurrence among Japanese populations. Therefore, an 18-gene classifier (18-GC) based on the gene-expression profiling of Chinese breast cancer patients was developed. Genetic information and clinical variables, including age at diagnosis, tumor size, lymph node status, estrogen receptor status, lymphovascular invasion, and tumor grading, were combined to generate a clinical-genomic model: RI-DR, to predict the risk of distant recurrence. We evaluated the performance of the RI-DR model with that of the Oncotype DX assay in terms of prognosis assessment in a cohort of 138 Taiwanese patients. There was high concordance between the RI-DR and RS. This predictive model may fill the gap between the current and best practice in Chinese patients with hormone receptor positive and HER2 negative early breast cancer.

ROLE OF MULTIGENE ASSAYS TO GUIDE DECISIONS FOR NEOADJUVANT THERAPY

Takayuki Ueno

Cancer Institute Hospital, Japan

In the era of precision medicine, neoadjuvant therapy has huge potential to personalize perioperative systemic therapy. Neoadjuvant chemotherapy and neoadjuvant endocrine therapy are two major neoadjuvant therapies, which provide information not only on tumor sensitivity to chemo- and endocrine therapy but also on profound characteristics of tumor. The adjuvant strategy based on the pathological result of neoadjuvant therapy has been proven to be clinically useful in both HER2-negative and -positive breast cancers. However, it is not clear how to differentially apply chemotherapy and endocrine therapy to a certain patient in the neoadjuvant settings to optimize perioperative systemic treatment. Multigene assays give useful information on patient prognosis and chemo-sensitivity. We have shown that the multigene assay also provides information on sensitivity to endocrine therapy. Thus, multigene assays are promising tools to determine what kind of therapy will be likely to be most beneficial to the patient in the neoadjuvant settings. In addition, neoadjuvant endocrine therapy is useful to examine the biological responses to molecular targeted therapies such as CDK4/6 inhibitor and mTOR inhibitor. In this symposium, I would like to discuss how to optimize perioperative systemic therapy using multigene assays.

CURRENT EVIDENCE FOR USE OF MULTIGENE ASSAYS IN NODE-POSITIVE DISEASE

Joon Jeong

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Multigene assays generate crucial prognostic information particularly useful for cancer patients where clinical parameters and traditional immunohistochemical markers alone lead to equivocal prognosis. Clinicians are now provided with molecular tools that assist in the outline of adjuvant therapies, namely helping decide on the extension of adjuvant endocrine therapy or on suppressing adjuvant chemotherapy in patients were toxic effects are particularly deleterious or when this treatment is fundamentally not needed. The importance of cancer multigene prognostic assays is well elucidated in the guidelines for adjuvant systemic therapy in early-stage breast cancer and the guidelines on disease staging that are progressively integrating gene expression assays as classification biomarkers.

The role of multigene assay in identifying patients who need not chemotherapy remains controversial in node-positive breast cancer. Most studies evaluated the predictive ability of those gene signatures in node-positive patients with the retrospective analyses. However, in 2016, results of the MINDACT were announced, and MammaPrint became the first trial to support the predictive ability of multigene assay in node-positive luminal breast cancer through a prospective trial. Recent updated guidelines recommend MammaPrint in order to avoid chemotherapy in breast cancer patients with estrogen receptor (ER)-positive, lymph-node positive (LN+ 1-3). In addition, the role of Oncotype Dx for breast cancer with in ER-positive and N1 has been evaluated in the prospective study (RxPonder).

Herein, we compare the evidence of other molecular tests such as OncotypeDX, Prosigna, EndoPredict, and Breast Cancer Index, as well as MammaPrint in ER-positive, node-positive disease.

Panel Discussion

GBCC2019
Global Breast Cancer Conference 2019

GOOD RESPONDERS: WHO ARE THEY?

Yong Wha Moon

Department of Medical Oncology, CHA Bundang Medical Center, CHA Univ., Korea

Neoadjuvant systemic therapy is the standard treatment in locally advanced breast cancer. It is also being used increasingly in the treatment of early-stage breast cancer to control micrometastasis earlier and to improve the rate of breast conservation. In addition, neoadjuvant trials allow rapid assessment of drug efficacy and could expedite development and approval of treatments for early breast cancer. Pathologic complete response (pCR) is accepted as a validated and evaluable surrogate endpoint of long-term clinical benefit after neoadjuvant therapy, even though there have been some controversial results; pCR in the NeoALTTO trial could not predict DFS in the ALTTO trial. This failure to reach statistical significance may be explained by the small number of events in the NeoALTTO trial because the trial was not designed with sufficient sample size to reliably assess survival. Furthermore, in 2012 the US FDA distributed the draft guidance for industry. pCR in the neoadjuvant treatment of high risk early stage breast cancer: use as an endpoint to support accelerated approval; the guidance was finalized in 2014.

Thus, pCR has become a primary endpoint for clinical trials. To date, however, there has not been uniform definition of pCR. For example, some investigators have defined pCR as the absence of both in situ and invasive cancer, whereas others have considered only the invasive cancer following neoadjuvant chemotherapy. Some investigators have defined pCR as absence of residual cancer in the breast and regional lymph nodes at the time of definitive surgery, whereas others have defined pCR as a complete response in the breast, irrespective of axillary nodal involvement. Recently as reported in the CTNeoBC pooled analysis, pCR definition of ypT0N0 or ypT0/isN0, which predicted EFS and OS better, is more widely used.

Although patients who achieve a clinical complete response with neoadjuvant chemotherapy must still undergo surgical treatment in current clinical practice, more recently the concept of omitting breast surgery in excellent responders to neoadjuvant chemotherapy, is emerging. One of current limitations is that routine radiologic modalities cannot confirm pCR potentially to omit breast surgery. To predict pCR before surgery, many studies are underway using new imaging modalities and molecular techniques.

In the presentation, I will discuss controversial definitions of pCR. I will also introduce several studies regarding predictive factors of pCR in the pre-neoadjuvant and post-neoadjuvant periods.

CAN WE ELIMINATE SURGERY IN EXCEPTIONALLY EXCELLENT RESPONDERS?

Mark Basik

Segal Cancer Center, Canada

Neoadjuvant chemotherapy has resulted in very high rates of pathological complete response (pCR) in the breast, especially in HER2+ and triple negative breast cancers. Patients are not infrequently having surgery with no residual cancer in the breast. The question arises: is it possible not to operate these women? This question presupposes another question: is it possible to identify women with pCR prior to surgery? Previous attempts to avoid surgery that did not benefit from modern imaging have resulted in high local recurrence rate. More recently, trimodality imaging (mammography, ultrasound and MRI) has been found to provide higher negative predictive value for pCR, but still not enough to avoid surgery. The addition of image-guided biopsy to trimodality imaging holds the promise to reach a high degree of accuracy. Several clinical trials are ongoing to evaluate the value of imaging combined with tumor bed biopsies pre-operatively to predict pCR and/or detect residual tumor in the tumor bed. These have the potential to lay the groundwork for a clinical trial in which the omission of surgery will be formally evaluated.

RADIATION ONCOLOGIST'S VIEW FOR ESCALATION OR DE-ESCALATION

Mi Young Kim

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Neoadjuvant chemotherapy (NAC) is increasingly used for operable locally advanced breast cancer, inoperable locally advanced or inflammatory breast cancer. The NAC can permit inoperable disease to become operable, eradicate micrometastasis, and allow breast conserving surgery for patients who would have required a mastectomy. And NAC allows the assessment of tumor response to chemotherapy.

The current NCCN guidelines recommend that postmastectomy radiotherapy (PMRT) indication and RT field should be based on maximal disease stage from prechemotherapy tumor characteristics at diagnosis and post-chemotherapy pathology results. However, no randomized trials have been established to define which patient benefit from PMRT after NAC. Additionally, there is no evidence of PMRT benefit in patients who had excellent response to NAC. In a retrospective study of University of Texas MD Anderson Cancer Center (MDACC), clinical stage IIIB, four or more lymph node, or failure to use tamoxifen independently worsen the locoregional recurrence (LRR). The 5-year LRR rate for patients with a pCR was 19%. The updated analysis showed that patients with clinical stage III breast cancer who experience a pCR maintain a clinically relevant risk of LRR (10-year LRR rate 33% without PMRT) and the PMRT provides a significant clinical benefit(10-year LRR 7%). In contrast, results from studies performed in France have shown that no increase in the risk of distant metastasis, locoregional recurrence, or death when PMRT was omitted in breast cancer patients with pN0 status after NAC and mastectomy. In a multicenter retrospective study from Korea (KROG 1205), PMRT was no correlated with a significant difference in treatment results in patients with pN0 after NAC, regardless of clinical stage. They concluded that PMRT might not be necessary for pN0 patients after NAC and mastectomy. Recently, the study from China and France showed that PMRT could significantly improve locoregional recurrence free survival, and be therapeutic in the subgroup of patients with good response after NAC. Because of these conflicting results, it is hard to conclude whether PMRT is effective or not to patients with excellent response after NAC and mastectomy.

NAC can allow breast conserving surgery (BCS) for patients with locally advanced disease. Adjuvant RT has a significant role in breast conserving treatment in terms of LRR and overall sur-

vival. Although lymph node irradiation (LNI) reduces the risk of LRR in patients with lymph node involvement, the benefit of LNI for clinical stage II, III breast cancer with pN0 after NAC is unclear. Daveau et al. assessed the utility of LNI in breast cancer with pN0 after NAC and BCS. The results showed that breast irradiation does not appear to be associated with a higher risk of LRR or death in patients with pN0 status after NAC, compared with breast and regional lymph node irradiation. In multicenter retrospective study of Korea (KROG 1205), the study analyzed the effect of elective nodal irradiation (ENI) in clinical stage II, III breast cancer with pN0 after NAC. The results showed that whole breast irradiation without ENI may be a sufficient and feasible local treatment in patients with ypN0 after NAC. However, there are retrospective studies, so there is limitation to conclude. NSABP B18, B27 studies showed the 10-year cumulative incidence of regional recurrence of 0- 2.4% for patients with ypN0. In both NASBP B18 and B27 studies, patients undergoing lumpectomy received breast irradiation without lymph node irradiation. They developed nomogram to predict LRR after NAC. In nomogram, the 10 year LRR rate is approximately 5-10% in patients with clinically N0, pathologically N0, and breast pCR after NAC. But, for patients with clinically node positive, or pathologically node positive, or no breast pCR, the 10-year LRR rate is increasing, especially younger age.

To know the effect of radiotherapy after NAC, prospective randomized trial is needed. The NSABP B51/ RTOG1304 is a phase III randomized trial. This trial evaluates if PMRT or whole breast RT with regional nodal RT after BCS reduces invasive breast cancer recurrence free interval in patients with clinically positive node and pathologically negative node after NAC. The patients in that study are randomly assigned to regional nodal RT or no regional nodal RT. All the patients with BCS receive whole breast irradiation.

To date, we cannot safely omit the PMRT or regional nodal RT to patients with excellent responder after NAC without prospective studies. And also, we should consider the age, clinical T, N stage, hormonal receptor status, and Her2/neu receptor status to decide whether to treat or not.

RISK STRATIFICATION OF PREMALIGNANT BREAST LESIONS

Aeree Kim

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Since the follow-up study concerning breast cancer risk development from atypical ductal hyperplasia by Dr. Page in 1985, many studies to understand these lesions and to establish the appropriate management have been performed. The intraductal proliferative lesions are associated with different levels of risk for subsequent development of invasive breast carcinoma, which range from approximately 1.5- to 13- times that of the reference population.

The main contents of my presentation are (1) spectrum of proliferative breast disease of ductal or lobular, with or without atypia, (2) an overview of the risk of invasive breast carcinoma associated with these various proliferative lesions, (3) other proliferative lesions, such as flat epithelial atypia and papillomatosis, (4) differential points between atypical ductal hyperplasia and low grade DCIS, (5) recent changes of risk stratification in classic lobular carcinoma in situ [C-LCIS] in comparison with pleomorphic LCIS.

SURGERY FOR LOBULAR CARCINOMA IN SITU: TO DO OR NOT TO DO?

Masahiro Takada

Kyoto Univ. Hospital, Japan

Currently, there is a general agreement that lobular carcinoma in situ (LCIS) represents both a risk factor and a non-obligate precursor of breast cancer. Annual incidence of breast cancer after diagnosis of LCIS is 1-2% per year, and a relative risk is approximately 8 to 10 times that of the general population. Although several genetic analyses suggested that at least some of LCIS may be precursor of the breast cancer, they are generally managed as risk indicators rather than precursor lesions, as the cancers that subsequently develop may occur in either breast and not necessarily at the site of the LCIS. Optimal management of LCIS diagnosed on core needle biopsy is still debated. Surgical excision can be safely spared in classic LCIS cases with imaging-pathological concordance. Counseling for chemoprevention is also recommended by the guidelines. In cases with variant or pleomorphic LCIS, surgical excision is recommended, as the upgrade rates and natural history of the variant or pleomorphic LCIS have not been systematically evaluated. Clinical significance of attempts to clear margin, or that of post-operative radiation therapy is not clear. Surgical management of LCIS will be discussed in this session.

HOW TO MANAGE SUSPICIOUS MICROCALCIFICATIONS?

Jong Han Yu

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Microcalcification is a common finding in the breast. As mammography was established as a screening tool for breast cancer detection and developed into digital mammography, more frequent microcalcifications have been found. Various imaging techniques and biopsy techniques have been used for accurate diagnosis of suspicious microcalcifications. By using those techniques, diagnosis should be made appropriately. And appropriate surgical operation should be performed according to the pathologic diagnosis.

This presentation is organized in the following order.

Microcalcification

1. Background of microcalcification: Microcalcification result from the deposition of Calcium oxalate Calcium phosphate within the breast tissue (Louise Wilkinson et al., BJR 2016)

2. Diagnosis of microcalcification

   1) Mammography (analogue, digital), magnification, tomosynthesis

   2) Biopsy

      - Localization technique

      - Biopsy device

      - Surgical excision

      - Marker clip

   3) Post biopsy check of microcalcification

3. Surgery for Pre-malignant and malignant lesion with microcalcification

4. Another views

BONE PHYSIOLOGY AND PATHOGENESIS OF BONE METASTASIS

Sun Wook Cho

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The tumor microenvironment is composed of various stromal cells in addition to tumor cells. Increasing evidence now clearly supports the role of microenvironmental stromal cells in tumor progression and metastasis, yet the regulatory mechanisms and interactions among tumor and stromal cells remain to be elucidated.

The tumor microenvironment is composed of various stromal cells in addition to tumor cells. Increasing evidence now clearly supports the role of microenvironmental stromal cells in tumor progression and metastasis, yet the regulatory mechanisms and interactions among tumor and stromal cells remain to be elucidated.

Bone metastasis is the major problem in many types of human malignancies including prostate, breast and lung cancers, and the biological basis of bone metastasis let alone curative approaches are largely undetermined. Bone provides a unique microenvironment for the migrated tumor cells to survive and grow. The normal physiology of the skeletal system requires a tightly-regulated balance between osteoblasts and osteoclasts. The homeostasis of the human skeletal system is maintained by the coupling of bone resorption (by osteoclasts) and new bone formation (mainly by osteoblasts). However, this balance is frequently tipped during the process of bone metastases. The best-characterized example is the vicious cycle hypothesis of bone metastasis. Briefly, the migrated breast cancer cells express bone-modulatory factors such as a parathyroid hormone-related peptide (PTHrP), leading to up-regulation of receptor activator of nuclear factor κB (RANKL) and monocyte-colony stimulating factor (M-CSF) in adjacent osteoblasts. Subsequently, osteoclastogenesis occurs, followed by osteolysis and the release of bone matrix-embedded growth factors (e.g., transforming growth factor β [TGF-β]). These processes ultimately result in severely increased bone resorption and metastatic tumor growth.

In addition to the vicious cycle hypothesis described above, increasing lines of evidence now clearly support that alterations in the bone homeostasis contribute to the progression of bone metastases. Among the many cell types in the metastatic bone microenvironment, including osteocytes, osteoblasts, osteoclasts, mesenchymal stem cells, and hematopoietic bone marrow cells in diverse stages of differentiation, the majority of research data concentrate on osteoclasts,

and thus the current therapeutic approaches targeting the metastatic bone microenvironment are mostly osteoclast inhibitors (e.g., bisphosphonates, denosumab, and cathepsin K inhibitors). On the other hand, numerous research groups have demonstrated that other types of cells, particularly osteoblasts, are also important in the metastatic bone microenvironment, and also that osteoblasts play distinct and essential roles in metastatic progression. This lecture will summarize and highlight the recent updates of the environmental pathophysiology of bone as a metastatic niche.

SURGICAL CONSIDERATION FOR BONE METASTASIS FROM BREAST CANCER

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Bone is the 4th most common site of cancer metastasis. As survival of breast cancer patients increases, the number of patients with bone metastases is increasing; approximately 70% of patients with advanced breast cancer have bone metastases. However, clinicians who primarily treat breast cancer may have difficulty determining the proper treatment of bone metastasis. For example, in patients with multiple bony lesions, it can be difficult to determine which lesion should be treated surgically. Furthermore, because surgical treatment is usually performed late in the disease course, there are many complicating factors, such as concurrent chemotherapy or radiation, nutritional status, and cancer fatigue. It is therefore desirable to use a multidisciplinary approach with such cases. A thorough understanding of the benefits and risks of surgical treatment of bone metastases is needed to properly select patients who would most benefit. In addition, increased knowledge is helpful in organizing further treatment plans without unnecessarily immobilizing or interrupting treatment.

Indications for surgical treatment include pathological fractures, impending fractures, and painful bone metastases. Estimating life expectancy is not easy, but an accurate estimate should be provided to the treating orthopedic surgeon. This estimate will not only assist in deciding whether to perform treatment, but also allow the surgeon to tailor the process. In addition, anatomical location is important when deciding on surgical treatment. Weigh bearing bones, such as the femur and the weight-bearing portion of the pelvis, are the most common sites of surgical interest, as lesions in these areas cause significant loss of muscle tone and mobility. In contrast, conservative treatment of lesions in the upper extremities and non-weight bearing pelvic bones is relatively well-tolerated by patients. Pain is also an important factor, especially if pain is aggravated during weight-bearing activity or is not relieved by radiation therapy.

Practical goals of surgical treatment of bone metastases include alleviation of pain, restoration of skeletal stability, and functional independence. We prefer the fixation method, since, considering the factors discussed above, fixation often lasts longer than the remaining life expectancy of a patient. Fixation modalities include intramedullary nails, prosthetic reconstruction for articular involvement, plates, screws, and bone cement. After surgery, immediate weight bearing is allowed, and adjuvant radiation therapy is usually recommended if not given preoperatively.

This presentation will cover more detailed general surgical considerations of bone metastases, as well as recent breast cancer-specific issues.

OPTIMIZATION OF RADIATION THERAPY FOR BONE METASTASIS

Haeyoung Kim

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Bone is the most common site of metastasis, affecting over half of the patients with metastatic breast cancers [1]. Radiotherapy plays an important role in reducing pain from bone metastasis. Pain improvement is seen in 60-80% of patients and complete pain relief is seen in 15-40% of patients after palliative radiotherapy [2]. Besides these pain reducing effects, radiotherapy is performed to prevent pathologic fracture or to avoid of other treatments in patients with bone metastasis.

There have been several randomized prospective trials comparing shorter-course treatment to longer-course radiotherapy [3]. In these trials, single dose of 8 Gy provides similar pain relief to longer regimens (30 Gy in 10 fractions or 20-24 Gy in five to eight fractions). However, retreatment rates are significantly more frequent in the single fraction treatment, with 20% receiving additional treatment to the same site versus 8% in the multiple fractions treatment. Pathologic fracture risk and spinal cord compression rates are similar between the single fraction and multiple fractions treatments. For patients with a poor performance status, extensive visceral organ metastases, and/or a short life expectancy, appropriate treatment is a single fraction of 8 Gy. For patients with a longer life expectancy, bone-only metastases, and good performance status, a longer course of treatment may be more appropriate to minimize the risk of retreatment. Besides, for selected patients with a solitary bone metastasis, an even higher dose of treatment may be indicated.

Stereotactic radiosurgery has been evaluated for the treatment of bone metastasis. Single doses of 15-24 Gy to fractionated schedules delivering 15-35 Gy in three to five fractions used in radiosurgery. Over 80% of patients achieved pain relief, with similar rates of objective local control [4]. Toxicity is infrequently occurred after radiosurgery. Even in cases that have delivered re-irradiation the incidence of myelopathy was less than $< 1\%$ after radiosurgery for bone metastasis [4].

Radiotherapy is an effective treatment for patients with bone metastasis. Dose and fractions of

radiotherapy should be modified according to patients life expectancy and performance status.

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NEOADJUVANT CHEMOTHERAPY STRATEGIES BASED ON BREAST CANCER SUBTYPES

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Preoperative systemic neoadjuvant chemotherapy can offer a rapid assessment of efficacy of a given therapeutic approach using pathologic complete response (pCR) as a surrogate endpoint for long-term clinical outcomes, which therapeutic strategies mainly used for patients with triple-negative (TNBC) and HER2-positive breast cancers. Recently, this approach resulted in accelerated new drug approval of pertuzumab for HER2-positive cancers with pCR, and subsequently reached a final approval using adjuvant long-term favorable outcomes (disease free survival; DFS). This is the case that neoadjuvant chemotherapy provided us remarkable quicker timeline than would have been possible with its assessment in the adjuvant setting. However, there is still unmet medical need for TNBC subtype, in which pCR to conventional doxorubicin based neoadjuvant chemotherapy would show us good correlation with long-term prognosis. TNBC subtype.

Furthermore, the use of preoperative neoadjuvant chemotherapy remains controversial, as the higher response rates noted with newer approaches have not routinely translated into improved longer-term outcomes, nor have they been confirmed in larger adjuvant trials (Neo-ALTTO & ALTTO). Most of the neoadjuvant clinical trials have demonstrated that pCR is a robust prognostic marker in patients with TNBC and HER2-positive cancers, thus the insignificant correlation between pCR and event-free survival (EFS) or DFS may be caused by inadequate power in the trials with heterogeneity of breast cancer biology.

It has been very well known that pCR following preoperative chemotherapy is not prognostic in many hormone receptor (HR)-positive breast cancers, especially those with a luminal A phenotype, which typically has minimal response to chemotherapy.

Taken together, neoadjuvant systemic strategies could be also used for in vivo vehicle delivering and monitoring several new drugs using umbrella clinical trials to test innovative biomarkers irrespective of breast cancer subtypes. Overall, the use of neoadjuvant approaches offers a rapid assessment of efficacy of novel therapies and remains a useful research tool for drug evaluation.

In this lecture, clinical developments of neoadjuvant chemotherapy regimens mainly TNBC and HER2-BC subtypes and rational approaches for unmet medical need.

PRIMARY TUMOR VS. RESIDUAL TUMOR: ANY DIFFERENCES?

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Neoadjuvant chemotherapy (NAC) is the recent trend in therapy of breast cancer to shrink the locally advanced tumors. Pathologic complete response is achieved in 4-45% of tumors, but majority of locally advanced tumors show residual tumors after NAC. Studies comparing primary tumors with residual tumors in several aspects including mutation, gene and protein expression, and immune microenvironment will be discussed.

HOW TO TREAT PATIENTS WITH RESIDUAL DISEASE AT SURGERY?

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EVIDENCE-BASED INDICATION OF ONCOPLASTIC BREAST SURGERY

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To maximize the cosmetic result after breast cancer surgery, the advantage of oncoplastic surgery (OPS) has been acknowledged and become incorporated in routine practice. One of the most important benefit of OPS is to extend the indication of breast conserving surgery towards larger or multifocal tumors as alternative to mastectomy. Also, OPS can decrease the contour deformity of breast due to lumpectomy in 5-40% of women. At the same time OPS can make getting wider resection margin possible, which can reduce re-excision due to positive resection margins and furthermore reduce local recurrence event in the long term. In women with large breast, OPS usually reduces breast volume and corrects ptosis, and even reduce the incidence of new breast cancer.

There are many kind of OPS techniques are available now and they should be standardized. In 2010, Clough et al. classified the OPS techniques into level I and level II, and suggested optimal techniques according to the location of tumor. It is useful as a standard in clinical practice for indicating, planning, and performing the procedure. For the assessment of outcome after OPS procedure, patient-reported outcome measurement is mandatory. Breast-Q^{TM} Breast Conserving Therapy Module is a strong tool for patient satisfaction and quality of life measure.

Although there are growing bodies of publication that OPS is safe and effective procedure for many breast cancer patients, still there is a need for prospective multicenter studies to optimize patient selection and for standardized criteria to qualify and accredit OPS training centers.

ONCOLOGICAL SAFETY OF ONCOPLASTIC BREAST SURGERY

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Oncoplastic breast surgery (OPS) has been a standard surgical technique for breast cancer since 1993 [1]. Numerous surgeons have reported the oncological safety of OPS not only for early-stage breast cancer but also for advanced breast cancer. However, the success of OPS cannot be achieved without a systematic multidisciplinary team approach [2,3].

The oncological safety of OPS has been proven by many surgeons, including partial mastectomy with volume replacement or displacement technique, nipple, or skin-sparing mastectomy with immediate or delayed reconstruction [4-7]. The commonality of these studies was that the oncological safety of breast cancer has been obtained in the surgical field as a first priority. It means that obtaining negative surgical margins for breast cancer is nonnegotiable.

To improve the oncological outcome of OPS, a multidisciplinary team approach is necessary. In OPS, it is important to achieve not only a successful oncological outcome but also a cosmetic outcome. In this aspect, for the plastic surgeon, having options is more important than anything else. As the range of breast surgeries can be different in the surgical field, many surgical options in plastic surgery for breast reconstruction would be necessary.

In addition, the radiation oncologist should understand these various oncoplastic techniques. In particular, when the volume replacement or displacement technique is performed for breast reconstruction, the radiation oncologist should know the characteristics of the donor organ and operative process to prevent post-radiotherapeutic complications and conduct radiotherapy at accurate locations of breast cancer [8,9]. Of course, the breast surgeon should label the sites with surgical clips in the tumor bed so that they can be recognized by the radiation oncologist.

The oncologist is also a key member in the multidisciplinary team approach to improve the oncological outcome of OPS. The oncologist should be aware of the overall process of OPS and should consider oncological factors, including margin positivity, multifocality, existence of lymphovascular invasion, and the subtype of breast cancer, when determining the adjuvant treatment of breast cancer.

For physicians, it would be annoying and troublesome to organize a multidisciplinary team for determining the treatment of breast cancer. Physicians may experience several conflicts of interest during the discussion and must take their own time to decide. However, OPS based on a multidisciplinary team discussion would be the best approach to maximizing the oncological safety of OPS for breast cancer.

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HOW TO AVOID ONCOPLASTIC FAILURE IN SMALL-TO-MEDIUM SIZED BREASTS

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Oncoplastic Surgery in breast cancer combines the principles of oncology and plastic surgery, aiming at oncologic safety, at the same time creating a cosmetically acceptable breast after removal of tumour.

In small and medium sized breast, removing large tumours with contralateral breast reduction is not an option. Careful case selection based on tumour location, tumour-to-breast volume ratio, incision planning, techniques in parenchymal shifting, are all important factors in avoiding failures in oncoplastic breast surgery.

ONCOPLASTIC SURGERY WITH THORACODORSAL ADIPOFASCIAL CUTANEOUS FLAP

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When a breast conserving surgery, we pay an attention to not only tumors factor but also host factors such as breast size, shape, and degree of ptosis. We select volume displacement using breast reduction technique for patients with large or ptotic breasts, and volume replacement for patients with small or non-ptotic breasts as oncoplastic breast surgery (OBS). In volume replacement of the breast outside area, we reported that using thoracodorsal adipofascial flap provided good results. We add some modifications to an original method during those fourteen years, so we would like to show the results of them retrospectively.

Patients: From May 2004 to July 2018, we experienced 83 cases having with early breast cancer on the outer area of non-ptotic breasts in Kagoshima University. O: Original method, A: Crescent-shaped dermis on the distal edge of the flap, B: Crescent-shaped dermis on the proximal edge of the flap, C: B plus making of new inframammary line, D: C plus Benz-shaped dermis on the proximal edge of the flap. Patients number were 26, 9, 15, 22, 11 cases, respectively.

Results: 1) Postoperative complication (wound-healing delay) was seen in 5 (19%), 0, 2 (13%), 1 (5%), 0 cases, respectively. 2) Median of postoperative observation period was 115, 92, 67, 51, 32 months, respectively. By cosmetic assessment, 73, 63, 79, 83, 100% patients were evaluated as good-excellent, respectively. 3) Insufficient volume (9 cases) and deviation of nipple (3 cases) were seen in 4, 3, 3, 2, 0 cases, evaluated as poor-fair, respectively.

Conclusion: Modification and experience of immediate volume replacement using thoracodorsal adipofascial flap decrease postoperative complications and improve cosmetic results.

ONCOPLASTIC SURGERY AFTER NEOADJUVANT THERAPY

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There are now other reasons to consider the use of neo-adjuvant therapy, but its main indication remains its ability to facilitate or enable the option of breast conserving surgery. As the indications for breast-conserving surgery are also extended by the use of oncoplastic techniques, the combination can be employed to afford the surgeon the ability to tailor extent of surgery to treatment response.

For larger breast cancers, local recurrence risk correlates with response to systemic therapy; pCR is associated with a significantly reduced risk. Standardising the degrees of response to neoadjuvant therapy short of pCR remains problematic but studies with various criteria show that this also correlates with recurrence and non-responders have the highest risk.

Other surgical issues with breast conserving surgery after NACT are the lack of definition of an acceptable excision margin, lack of consensus on volume of target tissue or footprint to be removed and lack of definition as to overall criteria for safe conservation. In addition, associated calcifications and the need to remove them accounts for half of the reported reasons why mastectomy was recommended after neoadjuvant therapy. Oncoplastic surgery helps to resolve all of these issues by its ability to remove a proportionately large part of a breast, whilst still achieving the cosmetic aims of breast conserving surgery.

Any breast conserving surgery is an attempt at preserving the breast, ultimately depending upon the excision margins achieved and a judgment on recurrence risk for breast conservation versus mastectomy based on the pathological features of the cancer removed. However, success of this attempt can be weighted in favour of conservation by oncoplastic surgery and for large cancers, this is achieved in combination with neoadjuvant therapy. The art in breast conserving surgery is the ability to correctly select for breast conservation (and the surgical technique used for it), achieve success at one operation and obtain a cosmetic and functional result that easily outweighs any that can be achieved with mastectomy and reconstruction.

In summary, oncoplastic techniques can allow breast conserving surgery for large cancers and do so with good cosmesis. However, their role can be refined and enhanced in combination with neoadjuvant therapy and allow tailoring of local treatment to response, removal of associated calcifications, and reduction in the risk of completion mastectomy. Neoadjuvant therapy also allows time for genetic testing and for those who will always require a mastectomy, time for planning reconstruction.

ONCOPLASTIC SURGERY WITH OMENTAL FLAP

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For breast cancer patients in whom breast-conserving surgery (BCS) is impossible, a conservative mastectomy such as skin-sparing mastectomy (SSM) or nipple-sparing mastectomy (NSM) accompanied by an immediate reconstruction using an autologous tissue flap is one of the best surgical options. For these cases, a transverse rectus abdominis myocutaneous (TRAM) flap or latissimus dorsi (LD) flap has been used commonly. LD flap also can be used after BCS to fill the defect in case the remained breast tissues are insufficient for a tissue displacement flap. Breast reconstruction using TRAM or LD flaps, however, has a disadvantage of flap-associated complications as well as donor site morbidities. Moreover, these surgeries inevitably leave a large and noticeable scar on the donor site.

The use of the omentum for breast reconstruction was first described in 1963. Omentum is an ideal autologous tissue as a substrate for breast reconstruction because it is rich in blood supply, resistant to infection, insusceptible to radiation, and easily shaped for various breast defects. Nevertheless, the omental flap has not obtained wide-spread popularity because it requires a laparotomy at that time. However, recent advances in laparoscopic surgery have allowed the retrieval of omentum for the reconstruction after breast cancer surgery with less donor-site deformity and morbidity, which has made use of this flap more attractive. Recently, investigators have been reporting their successful experiences on immediate reconstruction with laparoscopically harvested omental flap after various breast cancer surgeries and demonstrated its safety and feasibility. In selected patients, this technique produces good results, creating a reconstructed breast with a natural, soft consistency, and with minimal donor site morbidity.

The omental flap reconstruction for breast cancer will be reviewed in this session, and I would like to share our experience of single-port laparoscopically harvested omental flap (SLHOF) for immediate breast reconstruction.

IN WHOM, WHEN AND HOW DO WE PROVIDE RISK REDUCTION SURGERY?

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Medical management has been shifted from curative medicine to preemptive medicine since Precision Medicine has been applied rapidly in this era. We can estimate ones cancer risk, plan precision screening to ones risk and consider preventive measures including pre-emptive surgery. While pre-emptive surgery is one of the established options for high-risk women in western country, it is not accepted well in Asian community, including Japan.

Hereditary Breast and Ovarian Cancer Syndrome (HBOC) is know as a syndrome that causes breast and ovarian cancer at exceptionally high rate in patients who have genetic mutations in BRCA 1 and 2. Penetration rate of BRCA 1 and 2 in Japanese population with strong family history showed 20% as high as the Western population. To protect the population from developing the disease, risk reducing mastectomy (RRM) or bilateral salphingo oophrectomy (RRSO) are strong strategies for women with mutated BRCA. Distribution of age at onset of breast cancer with/without BRCA1/2 mutations shows that BRCA1/2MUT+ breast cancer occurred at a younger mean age (41.7 years) than did BRCA1/2MUT breast cancer (45.8 years). In comparison to the 2013 National Registration for Breast Cancer Incidence in Japan, breast cancer with BRCA mutations occurred at a younger age. Even though the fee for the process are not covered by Japanese insurance since they are considered as preventive medicine. We performed cost-effective analysis by using the model whether BRCA1/2 (+) women receive risk reduction strategies or not and showed cost-effectiveness for the RRM and/or RRSO.Furteremore the occult cancer rate were 11% in the specimens of 51 RRM by using the registration data for Japanese HBOC consortium1.

It is urgently required to establish consensus and support system for pre-emptive surgery in Asian community. We should discuss how we can work together to develop precision medicine for BRCA1/2 (+) women.

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IS RISK REDUCTION SURGERY MANDATORY FOR THE WOMEN WHO ALREADY TREATED FOR THE BREAST CANCER?

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Over the past years, there has been an increasing rate of bilateral prophylactic mastectomy and contralateral prophylactic mastectomy surgeries. In this abstract, possible treatment options for patients already suffer from breast cancer are discussed. Topics covered include risk of ipsilateral recurrence, contralateral recurrence; overall survival; and issues related to quality of life and patient satisfaction. Predicting future breast cancer risk requires consideration of both genetic factors and primary disease situation, including types of existing mutation, age, prognosis of primary disease. A meta-analysis study showed that no signification increase of ipsilateral tumor recurrence after breast conserving surgery and radiation (17% vs. 11%, RR 1.45 95% CI 0.98-2.24, $p = 0.07$). But after classifying the studies according to the duration of treatment, a significant higher rate of Ipsilateral tumor recurrence after 7 years of surgery was shown for breast conserving surgery compared to mastectomy because of de novo carcinoma in patients with mutation(15.9% vs. 7% RR 1.51, 95% CI 1.150-1.98, $p < 0.003$) . The breast cancer patients with BRCA mutation (BRCA1 > BRCA2) with early onset of the disease and good prognosis of primary disease will benefit from a bilateral risk reducing mastectomy. Previous studies of women with breast cancer have found no clinically meaningful differences in quality of life (QOL) based on surgical procedure although body image has been lower in some settings in women who undergo mastectomy. However, recent QOL study for young women with breast cancer showed that both mastectomy and bilateral mastectomy is associated with significantly decreased satisfaction, psychosocial, and sexual well-being compared with BCS, but recent studies reported higher satisfaction with CPM than in the past due to improved methods of reconstruction.

Breast cancer risk reduction is important for known BRCA1/2 carriers. The younger patients and the better the prognosis of the primary disease, the higher is the benefit of risk reduction surgery. Future research should focus efforts to optimize surgical decision making in high risk patients with breast cancer

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ALTERNATIVE STRATEGIES OTHER THAN SURGERY TO REDUCE THE BREAST CANCER RISK

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The lifetime cumulative risk of breast cancer is elevated in *BRCA* mutation carriers up to 70% at age 80, and the risk of contralateral breast cancer (CBC) is also increased in affected carriers compared to non-carriers. Risk reducing mastectomy (RRM) is recommended to unaffected carriers for preventing breast cancer development. The morbidity of RRM has known up to 20%, including pain, loss of sensory in nipple, and change of body image. In *BRCA*-related breast cancer patients, the cumulative risk of CBC is reported more than 20% in *BRCA1* mutation carriers after 10 years from initial diagnosis. *BRCA2* carriers and noncarriers have less than 10% risk, lower than *BRCA1* carrriers. Contalateral risk reducing mastectomy (CRRM) showed significantly decreased the incidence of CBC, however, patient uptake of CRRM or dose not simply related to individual risk.

The annual breast surveillance is recommended for *BRCA1/2* unaffected carriers using MRI at age 25, or mammography at age 30. Other than surveillance, chemoprevention should be also discussed. Chemoprevention, also known as medical prevention is recommended by tamoxifene or aromatase inhibitors in some countries. From the result of NSABP P-1 study, tamoxifen was associated decreased risk of breast cancer in *BRCA2* mutation carriers. Tamoxifen also known protective effect of CBC in the *BRCA1* and *BRCA2* mutation. Use of aromatase inhibitors, a retrospective study was reported for CBC in *BRCA* related breast cancer. However, the uptake of chemoprevetion is less than one fourth. Older women showed more frequent use than young age group. The fear of adverse effect might related to the reluctance. The benefit of tamoxifen chemoprevention under age 35 is still unknown. Results of ongoing trails are expected about the chemoprevention for unaffected carriers by rovastatin, metformin, and aromatase inhibitor.

RECENT PROGRESS IN ENDOSCOPIC BREAST SURGERY AND ROBOT-ASSISTED MASTECTOMY

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The protocol design of pilot Robotic Mastectomy Trial, recruitment of patients and assessment of procedural technique of first 3 cases started at European institute of Oncology in Milan in late 2013.

After the first 3 Robotic Mastectomy and Immediate Robotic Reconstruction with Implant (R-NSM) in 2014, the first phase of the feasibility and safety trial ended in 2016 with the 2 publications on scientific journals Annals of Surgery and The Breast.

The results were so encouraging that a randomized controlled trial comparing R-NSM and classical open technique was designed. The aim was to conceive a new technique that could be taken into consideration by the scientific community as an alternative to the more classic open procedure, in selected and highly motivated patients, with the aim to perform a more conservative mastectomy and natural one step reconstruction.

Furthermore, during the past 4 years, a lot of efforts were spent through simulations, through experimental laboratory workshops and with the help of many grants, to develop a new technique that could be fast in terms of operative time, without post operative pain, with few complications, that allows a direct to implant reconstruction and that would be attractive for patients, with the aim to increase the request from the patients who need mastectomy themselves.

The accrual of randomized trial was reached in December 2018 and the first robust results concerning the safety and post-operative outcome of the randomized patients became impactful in few months. These preliminary data could help to conclude the authorization process and community consensus.

With this premises, the preliminary results of the randomized controlled trial are now available.

APPLICATION OF 3D PRINTING TECHNIQUE TO BREAST SURGERY

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There is no difference in prognosis according to the breast surgery method. Therefore, the surgeon tries Breast-conserving surgery (BCS) as much as possible for the quality of life and good cosmetic results of women. For good cosmetic results at BCS, it is important to preserve normal breast tissue as much as possible while ensuring adequate margin and completely removing the tumor, and an accurate method of predicting the extent of the tumor for precise surgery is needed. MRI is known to be more accurate than conventional mammography and ultrasonography, but it is difficult to use it directly by marking the lesion area on the breast. There have been many attempts to solve these problems, but due to technical difficulties, there is no universally practiced method. In this study, To solve these problems, we developed a customized 3D printing breast surgical guide (3DP-BSG) and applied it to patients.

If the tumor is not palpable, appropriate localization techniques are used for precisional BCS and wire localization is the most used method. The use of mammography or ultrasound-guided H-wire insertion is relatively straightforward, but it can lead to pneumothorax or hematoma during the procedure and can lead to complications such as migration, loss, and cutting during surgery. Above all, it can not provide information on the quantitative extent of the tumor, and there is a limitation that MRI data cannot be used. Radioactive occult lesion localization (ROLL) and radioactive seed localization (RSL) have been tried to overcome the limitations of WL. However, these new techniques also have a disadvantage in that it is difficult to mark the area of the tumor on MRI directly on the breast, and there is a limitation in providing information on the original tumor area before the treatment in patients receiving neoadjuvant systemic therapy. 3DP-BSG has many advantages such as not causing pain to the patient, no exposure to radiation, providing information on the quantitative extent of the tumor, and making available MRI data. Above all, it has the advantage of providing information on past original tumor areas that are not currently observed. 3DP-BSG is expected to be useful for breast cancer patients who will receive BCS.

UP-TO-DATE MINIMALLY INVASIVE PROCEDURES FOR BREAST CANCER TREATMENT

Eisuke Fukuma

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Education Session

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OPTIMAL SEQUENCE OF ENDOCRINE TREATMENT IN ADVANCED BREAST CANCER

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Estrogen receptor positive (ER+) metastatic breast cancer (MBC) remains an incurable but highly prevalent entity despite major advances in the management of early stage disease. Unlike the case for many metastatic solid tumors, a number of different forms of systemic therapy can exert temporizing disease control in ER+ MBC. Approved forms of therapy for ER+ MBC include hormonal treatments (aromatase inhibitors, ER antagonists, progestins), cell cycle inhibitors (CDK4/6i), signal transduction inhibitors (everolimus), and various chemotherapies (5-fluorouracil based drugs, taxanes, platinum salts, etc.). While these agents are all effective in aggregate, there is enormous diversity in the degree and duration of benefit. For instance, with single agent endocrine therapy, some tumors will immediately progress after 2-3 months of therapy, others will progress after 6-12 months, and others after 4-5 years. Moreover, some tumors appear to respond better to hormone therapy than chemotherapy and visa versa. And finally, it is also clear that the tumors themselves can undergo evolution that is dictated by the specific therapy exposure. For instance, exposure to aromatase inhibitor therapy leads to selection for constitutively active mutations in the estrogen receptor gene (ESR1) that may have additional phenotypes and implications. All of these lines of evidence suggest that the current clinical paradigm of uniform administration of the same sequence of agents based largely on toxicity profiles may be suboptimal. In this talk, we will assess how molecular and clinical profiling efforts may provide a deeper understanding of discrete subsets of ER+ MBC and enable more precise assignment of therapy that maximizes patient benefit.

OVERCOME OF ENDOCRINE RESISTANCE

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Endocrine therapy is the mainstay of treatment for patients with estrogen receptor-positive (ER+)/HER2-negative (HER2-) early (EBC) and metastatic breast cancer (MBC). Among EBC patients, primary endocrine resistant case is about 5% and presented the poor outcome regardless of adjuvant chemotherapy in all cases based on NEOS trial in Japan. Some new strategies such as CDK4/6 inhibitor or new targeting agents are required due to improve the long-term outcome in EBC patients with ER positive and high risk. Already enrollment of global trials (Penelope and PALLAs) which compare between endocrine therapy alone and combination with CDK4/6 inhibitor are completed in the world.

In advanced (Stage IV) or metastatic setting, there are some primary resistance cases and almost cases developed acquired resistance during long endocrine treatment. Due to overcome resistance, combination therapies with targeting agents as mTOR inhibitor and CDK inhibitors have been confirmed. The combination therapy with endocrine therapy and CDK inhibitor is recommended as standard treatment at 1st line and 2nd line setting for MBC based on several guidelines. Moreover the combination therapies endocrine therapy with new agents such as PI3CA inhibitor, IGF antibody and HDAC inhibitor have been developed in the world. The development of biomarker is also required due to determine the best combination regimen among many targeting agents at any points during long journey for MBC.

LATE RECURRENCE IN ER-POSITIVE BREAT CANCER: RISK PREDICTION & TREATMENT

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Late recurrence, up to 20 years or more after the initial diagnosis, has been recognized for many years in patients with ER positive breast cancer. A recent large meta analysis involving over 60,000 patients in 88 trials showed a continuing late risk in women given 5 years of adjuvant endocrine therapy (usually tamoxifen). Standard risk factors for late relapse included size, nodal status and grade. For women with 4 or more nodes the risk of late recurrence was around 35-40% depending on tumour size. For women with node negative cancers the risk was less, but still around 13-20%. Even in women with very good prognosis (T1 low grade cancers), the risk was around 10%.

Extended adjuvant endocrine therapy beyond 5 years has been used in several major trials to try to prevent late recurrence. The MA17 trial randomized 5,000 patients treated with 5 years of tamoxifen to have a further 5 years of letrozole or placebo and showed a very significant further reduction in the risk of 4 year disease free survival with a HR of 0.58. Similar results have been shown after 5 years of tamoxifen for exemestane (NSABP-B33 trial) and with anastrozole (ABCSG-6A trial).

For extended adjuvant endocrine therapy using tamoxifen, the large ATLAS trial involving 6846 patients has shown that 10 years of tamoxifen compared with 5 further reduces the risk of recurrence with an RR of 0.90 at 5-9 years and 0.75 at greater than 10 years. A similar slightly smaller reduction in breast cancer mortality has also been reported in this trial. In contrast, extended adjuvant AI after an initial 5 years of an AI have shown only very modest improvement if any in 3 trials.

Finally, the MA17R trial looked at continuing letrozole in patients who had already had up to 10 years of tamoxifen (5 years) followed by an AI (5 years). This trial showed a very modest improvement in disease free survival with up to 15 years treatment (95% 5 year disease free survival on letrozole versus 91% on placebo, HR 0.66). But much of this was made up by a reduction in contralateral breast cancers and there was only a 1% difference in distant recurrence.

Genomic platforms are increasingly being investigated to predict which patients are at greatest risk of late relapse beyond 5 years, to try to select who might benefit from long-term treatment. Current data show differences between different platforms with Nanostring PAM50 performing better than Oncotype DX in the period 5-10 years after diagnosis. Further work here is very important in selecting which patients are most likely to benefit from extended adjuvant endocrine therapy.

QUANTITATIVE IMAGING FOR BREAST CANCER RISK ASSESSMENT

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The assessment of an individual woman's risk for developing breast cancer has become increasingly important to guide precision screening as well as any necessary prevention strategies. Since mammography is the staple of breast cancer screening, methods to harness the rich image data to augment breast cancer risk prediction are an active research area. It is well known that increased mammographic breast density is associated not only with decreased screening accuracy but also with an increased risk of women with dense breast to develop breast cancer. Therefore, robust and reproducible methods to measure risk-associated characteristics of an individual woman's breast parenchyma are needed.

Clinical measures of breast density such as BI-RADS breast density categories have been shown to be associated with increased cancer risk in case-controlled studies however, such subjective measures of density are plagued with subjectivity and therefore, significant variability. Semi-automated methods of segmenting dense tissue areas have also been shown to be subject to be subject to reader variability. To provide more reproducible measures, entirely automated methods to quantitate percent area, percent volume and absolute volume of breast density have been developed. Recent studies suggest that even more refined measures of breast parenchymal texture play a complementary role in breast cancer risk assessment not reflected entirely by dichotomous measures (dense or not dense) breast tissue.

Breast MR, which leverages vascular physiology, has also been shown to be highly predictive of breast cancer risk in a few early studies. In addition, background parenchymal enhancement (BPE) of the fibroglandular tissue as seen on post-contrast MR imaging, can be followed as a surrogate for risk-reduction interventions such as prophylactic oophorectomy or tamoxifen therapy. In this presentation, examples of methods to quantitate breast parenchymal characteristics will be reviewed towards the goal of improving the accuracy of breast cancer risk assessment and precision screening at the individual level.

EARLY PREDICTION OF RESPONSE FROM NEOADJUVANT THERAPY

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Summary:
DCE MRI is accurately monitors response to neoadjuvant chemotherapy
- Functional tumor volume with an 80% enhancement threshold can predict response after one cycle of chemotherapy
ADC on DWI can predict response to chemotherapy at baseline, after one course and at mid treatment
PET MR offers opportunities for analysis of simultaneous physiological interactions

Content
1. Aim:
There are a lot of researches about the role of image in predicting pathologic complete remission in breast cancer patient treated with neoadjuvant chemotherapy and also about image performance in guiding response to neoadjuvant chemotherapy according to breast cancer subtypes.
Although MRI is widely recognized to be superior to mammography and ultrasound and is used in the assessment of response to neoadjuvant chemotherapy, there is not universal agreement as to which protocol or which time points are recommended.
The aim of this talk is about imaging (mainly MRI) performance for early prediction of response in breast cancer patients treated with neoadjuvant chemotherapy.

2. Neoadjuvant Chemotherapy:
Primary neoadjuvant chemotherapy is used to reduce tumor size and allow more conservative surgery.
Survival is the same regardless of whether the treatment is given before or after surgery. However it is potentially advantageous to be able to accurately monitor response to allow a change in the treatment regimen if a treatment is shown to be ineffective and also to allow testing of novel therapies.

3. Current and research breast MRI techniques in Neoadjuvant Chemotherapy:

1) DCE MRI
DCE MRI is accepted as the most accurate method of assessing response compared to mammography and ultrasound.

- The large multicenter American I-SPY trial measured tumor volume and signal enhancement rate (SER) and studied the rate of change during chemotherapy using receiver operating characteristic curve (AUC) measures for predicting response.
- The I-SPY II trial demonstrated that an 80% enhancement threshold of functional tumor volume predicted response to chemotherapy. Similarly the Signal Enhancement Ratio (SER) was equally predictive of response.
- A number of studies have demonstrated that quantifiable parameters derived from pharmacokinetic modeling can accurately determine response due to reduced tumor blood flow as a result of effective chemotherapy.

2) DWI
Breast malignancies demonstrate restricted diffusion, with high signal intensity on diffusion-weighted imaging (DWI) and low apparent diffusion coefficient (ADC) values, attributed to increased cellularity and decreased extracellular space.
Simple ADC is used in assessing response with those tumors with very low ADC values showing the greatest change following chemotherapy. Early changes in ADC can be seen after one or two courses of chemotherapy as a result of cell death.
- Results of ACRIN 6,698 support ADC as a predictive marker of response. In 242 subjects undergoing neoadjuvant chemotherapy for breast cancer at 10 participating institutions, mid-treatment (after 12 weeks of taxane-based therapy) change in tumor ADC was predictive of pathologic complete response, with predictive value varying across biologic subtypes (area under the receiver operating characteristic curves, AUCs, ranged 0.56 0.76). On the other hand, neither pre-treatment nor early-treatment (after the first 3 weeks of therapy) ADC measures were found to be predictive of pathologic outcome.

3) PET MR
PET MR is able to simultaneously measure metabolic activity using a radiotracer while dynamic contrast can assess delivery of the tracer and the influence of perfusion. Using multiparametric approach it is possible to better understand the tumor microenvironment in real time.

APPLICATION OF AI IN DIAGNOSIS OF BREAST CANCER WITH DIGITAL MAMMOGRAPHY

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Mammography is the only recommended examination for breast cancer screening, although the starting age and screening interval has been debated. Performance of screening mammogram is recommended as sensitivity over 85% and specificity over 90%, however it has been reported to be variable according to the radiologists experience or working area (academic vs. nonacademic, general vs. specific). Computer-aided detection (CAD) acts as an automated second reader by marking potentially suspicious spots for radiologists to review and several early reports emphasized that it can improve mammographic sensitivity, but several recent studies reported CAD does not improve diagnostic accuracy of mammography. New AI based algorithm derived from large scale medical image data by using deep learning technology can provide more accurate guidance for mammographic interpretation. Here, we will disscuss application of AI in diagnosis of breast cancer in digital mammorgraphy.

ABBREVIATED BREAST MRI FOR HIGH RISK PATIENTS

Christiane Katharina Kuhl

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NON-CONTRAST MRI FOR SCREENING AND SURVEILLANCE OF BREAST CANCER

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Diffusion-weighted imaging is a noncontrast MR imaging technique that provides information on tissue cellularity and microstructure and has the potential to aid in the detection, diagnosis, and evaluation of treatment response for breast cancer. With a short scan time, DWI may be performed as an adjunct to DCE-MRI to improve diagnostic accuracy or as an alternative to gadolinium-enhanced MR evaluation in patients at risk for nephrogenic systemic fibrosis. Moreover, there is also promise in using DWI as a noncontrast alternative screening modality in women at intermediate or high risk of breast cancer. On DWI, malignant tumors are more cellular than normal breast tissue, they often appear hyperintense to surrounding tissues on DWI. In a study of 118 mammographically and clinically occult breast lesions, Partridge et al. found that 89% of malignancies were hyperintense on DWI, with lower ADC values for malignant compared with benign lesions. Balzer et al. also reported comparable sensitivity and specificity between DCE-MRI and unenhanced sequence (T2WI and DWI) for breast cancer detection. McDonald et al. reported that DWI can identify mammographically occult cancers in elevated-risk women with dense breasts, with a sensitivity of 45%, specificity of 91%, PPV of 62%, and NPV of 83%. In the reader study by Yabuuchi et al., DWI was more accurate than mammography, with an AUC of 0.73 compared with 0.64 for mammography. Such data show potential for using DWI as an adjunct to mammography without the costs and toxicity associated with DCE-MRI. However, DWI cannot detect all lesions identified by DCE-MRI. In a blinded reader study of 42 lesions, 42% of malignant breast lesions were not visible on DWI. Tozaki and Fukuma also reported that 32% of nonmass DCIS could not be detected on DWI.

Considering the limitations of DCE-MRI in length, cost, and contrast related safety, DW-MRI could be a useful stand-alone screening tool if proven to supplement mammography and outperform other supplemental screening modalities for cancer detection. Another benefit of DW-MRI is that lesion detection remains independent of background parenchymal enhancement, breast density, menopausal status, or timing during menstrual cycle, all factors which influence mammographic and/or DCE-MRI lesion detection. It is important to note that readers were not blinded to DCE-MR images when identifying mammographically occult cancers with DW-MRI and US in these preliminary studies. Furthermore, recent technical advances in DWI have resulted in improved image quality. High-resolution DW-MRI could improve sensi-

tivity and allow more accurate characterization of breast lesions by better visualizing lesion margins and internal features. To improve resolution and overcome poor imaging quality, several recent studies employed acquisition techniques such as DW readout-segmented EPI. Another advanced technique that aims to reduce the required matrix size is reduced field-of-view DW-MRI (rFOV). The smaller field-of-view in rFOV allows for higher spatial resolution and/or shorter readout duration and enables exclusion of air-tissue interfaces, therefore reducing distortion from susceptibility artifact and heterogeneous fat suppression. rFOV may be superior to readout-segmented EPI in lesion conspicuity and image quality. However, a limitation of rFOV is the restriction to unilateral imaging and need for multiple acquisitions for full bilateral coverage, lengthening scan times. Furthermore, absolute ADC values in rFOV DW-MRI were lower than when using readout-segmented and standard single-shot EPI techniques, which may render prior published ADC cutoffs less useful for interpretation of rFOV DW-MRI. Other advanced techniques improve cancer conspicuity on DW-MRI through enhancing image display. Several studies used maximum intensity projections (MIPs), which can conveniently display DW-MRI in a 3-dimensional representation as opposed to standard slice-by-slice evaluation.

In summary, DWI is a fast, non-contrast modality that shows promise in identifying mammographically-occult malignancy and warrants further investigation as an alternative supplemental breast cancer screening tool. Multiple previous studies suggest that DWI may have sensitivity lower than DCE-MRI, but superior to that of mammography and US. The ability of DW-MRI to detect cancer may further be enhanced by emerging advanced acquisition and post processing techniques, protocol optimization, and more experienced readers. Additional DW-MRI investigations that use standard imaging and interpretation protocols on larger patient cohorts are essential prior to widespread implementation.

APPLICATION OF ULTRAFAST MRI TO REAL PRACTICE

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Ultrafast breast MRI is a dynamic contrast-enhanced MRI obtaining 17 to 20 post-contrast series of images with a 4 to 7-second temporal resolution during the first minute before standard image acquisition. The early kinetic information has shown similar accuracy in differentiation of benign and malignant lesions compared to conventional MRI. The better lesion to background conspicuity at ultrafast breast MRI can be useful in women with moderate to marked parenchymal enhancement for evaluation of tumor extent. In addition, combined approach using abbreviated MRI and ultrafast MRI to improve feasibility of screening MRI by reducing study time, while maintaining diagnostic performance will be presented.

UPDATED EVIDENCE FOR ENVIRONMENT AND HORMONAL FACTORS AND BREAST CANCER

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For millions of women with breast cancer, environmental factors including chemical and hormonal exposure affect development and progression of breast cancer disease in various ways, although etiologies of disease are multi-factorial. With respect to environmental factors, several studies are conducted using prospective cohort and revealed the role of environmental agents in the initiation and progression of cancer, as well as research on chemical risk factors and genetic susceptibility in human populations. In addition, it is well-known that estrogen promotes and largely involves carcinogenesis of breast cancer. Thus, the effects of hormonal agents including hormonal replacement therapy and oral contraceptives on breast cancer are intensively investigated in large-scaled epidemiologic studies as well as several cohort studies. More research is needed to pinpoint the environmental and hormonal factors that determine breast cancer susceptibility. Once researchers can identify the elements that are associated with cancer risk, appropriate interventions and precautions can be designed for those who are most likely to develop the disease. Herein, we will review updated evidence for the influence of environmental and hormonal factors on breast cancer.

UPDATED EVIDENCE FOR NUTRITION AND DIET AND BREAST CANCER

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"We are what we eat." While breast cancer is the most common female cancer in the world as well as in the Asia-Pacific region, little information is available with regard to specific dietary guidelines in accordance of better breast health, be it preventive for breast cancer or enhancement of nutritional status of breast cancer patients during their treatment process.

There has been evidence of taste and smell changes among cancer patients, and the nutritional status of breast cancer patients weakens as the treatment sessions take place. This change is multifactorial including biology of the tumour with its size, tumour load, as well as the general physical status of the patients such as negative digestive symptoms with negative emotions, and increased nutritional requirement. There has been increasing data showing correlation with different dietary requirement and unmet needs among breast cancer subtypes. Nutrition and diet do play a vital role in the nutritional health status of all breast cancer patients, and personalized diet advice should be based on one's nutritional status, dietary habits, eating schedule, daily activities and cultural preferences. Formal assessment of nutritional status followed by dietary advice to all breast cancer patients are of paramount importance.

In parallel, there has been various reviews on healthy diet reducing the risk of breast cancer. This lecture will give an overview of the current most up-to-date evidence for nutrition and diet for breast cancer with particular reference of unmet needs of breast cancer patients and survivors, as well as the added value for better breast health.

UPDATED EVIDENCE FOR THE EFFECT OF ALCOHOL AND BREAST CANCER

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Alcohol consumption is a major risk factor for the global burden of disease and injuries. Alcohol was established as carcinogenic by the International Agency for Research on Cancer (IARC) in 1987, and a causal relationship between alcohol and breast cancer was accepted in 2007. The mechanisms underlying alcohol-induced cancer are still not well defined, although plausible events include: genotoxic effect of acetaldehyde, increased estrogen concentration, cellular stress, altered folate metabolism and inflammation. Amongst all, ethanol metabolism plays an important role in carcinogenesis.

More than 100 empirical studies have established a positive correlation between moderate or chronic ethanol consumption and the incidence of breast cancer in pre- and post-menopausal women. Several recent articles found associations between modest or high alcohol consumption and a correspondingly moderate or higher increased risk of breast cancer and concluded that there is a positive dose-response relationship between alcohol drinking and breast cancer. In addition, several articles reported an association between alcohol consumption and specific subtypes of breast cancer. However, alcohol was not associated with all breast cancer subtypes.

Several meta-analyses have examined the association between alcohol consumption and breast cancer risk. While some studies reported a weak, non-linear, positive association between alcohol consumption and breast cancer, others observed a linear increase of breast cancer risk with an increasing level of alcohol consumption. A meta-analysis based on 20 prospective studies reported a highly suggestive association between heavy alcohol intake and ER+ breast cancer. The association between alcohol and ER-breast cancers was classified as weak, based on 17 meta-analyses.

Further research is needed on how drinking patterns, alcohol consumption during specific periods of life, and genetic differences may modify the risk relationship between alcohol consumption and the risk of breast cancer

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WHO CAN BE AN OPTIMAL CANDIDATES FOR PARTIAL BREAST IRRADIATION?

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Accelerated partial breast irradiation (APBI) describes radiotherapy techniques in which radiation dose is restricted to the tumor bed and limited breast tissue as opposed to whole breast irradiation (WBI). The rationale for APBI is that the majority of local recurrences occur in the region of the initial lumpectomy site, whilst recurrences in elsewhere in the breast is less than 20%. Potential advantages of APBI over whole breast irradiation include shorter treatment time, improved cosmesis, and cost reduction. The first randomised trials comparing APBI with WBI began in the 1980s. Unfortunately, these early pioneering trials showed an unacceptable increase in local recurrence, although APBI proved its effectiveness in treatment related toxicities.

Based on the rapid improvements in systemic therapies, pathological diagnosis (enabling more proper patient selection), and radiotherapy techniques, the APBI regained interest in the 2000s. The radiation techniques were heterogeneous, including some that placed radioactive sources into the tumor bed and others that used external radiation delivered via a linear accelerator.

In 2009, in the light of burgeoning off-trial use of APBI, the ASTRO developed consensus guidelines on selection of patients for APBI outside a clinical trial. The recommendations were predominantly based on data from four prospective randomized clinical trials (RCTs), together with 10 prospective single-arm studies. Based on the clinicopathological inclusion criteria of patients reporting ipsilateral breast tumor recurrence (IBTR) rates of $< 10\%$, a group suitable for off-trial APBI was defined. This included females ≥ 60 years with unifocal T1N0 ER-positive ductal carcinomas, excision margins of ≥ 2 mm and absence of lymphovascular invasion or extensive intraductal component.

After modern RCTs were released, the ASTRO updated guidelines on the eligibility criteria for off-trial use of APBI as well as considering the role of intraoperative radiotherapy (IORT) in 2017. The age criterion was reconsidered based on three RCTs of WBI versus APBI. The GEC-ESTRO trial, randomized females of 40 years or above to WBI versus APBI delivered using multicatheter brachytherapy. The 5 year risk of IBTR was $< 2\%$ in both arms of the study but only 14% of patients were under 50 years. Hungarian and Italian RCTs also recruited females > 40 years and reported similarly low recurrence rates, again with females < 50 years less well-

represented. The ASTRO recommended that females of ≥ 50 years may now be included in the group considered suitable for APBI outside a clinical trial. Females aged 40 to 49 are now included in the cautionary group and females of < 40 years in the unsuitable group. The updated guidelines also review suitability of patients with ductal carcinoma in-situ (DCIS). They refer to data from RCTs of radiotherapy vs. observation after breast conservation surgery for low-risk DCIS and highlight 7-year IBTR rates of 6-7% in patients with surgery alone. A pooled analysis of females treated with APBI reported a 2.6% risk of IBTR at 5 years. Females with low-risk DCIS are therefore defined as being suitable for APBI in current guideline. With regard to excision margins, the updated ASTRO APBI guidelines adhere to the original recommendation for margins of ≥ 2 mm. Following publication of results from the Intraoperative Radiotherapy with Electrons (ELIOT) and risk-adapted radiotherapy using single-dose targeted intraoperative radiotherapy (TARGIT), the updated guidelines newly considered IORT. The main recommendations therefore that, whilst data mature, patients interested in cancer control equivalent to that achieved with WBI post-lumpectomy for breast conservation should be counseled that in 2 clinical trials the risk of IBTR was higher with IORT (than with WBI).

Outside US, the GEC-ESTRO Breast Cancer Working Group defined groups of females considered to be at low risk of IBTR (and therefore suitable for APBI); patients ageing at least 50 years with unicentric, unifocal, pT12 (30 mm) pN0, non-lobular invasive breast cancer without the presence of an extensive intraductal component (EIC) and lympho-vascular invasion (LVI) and with negative surgical margins of at least 2 mm.

APBI has been tested in many trials with more than 1,000 patients over the past 10 years. These trials show that, in properly selected breast cancer patients, APBI has provided outcomes similar to WBI. Until the maturity of the ongoing prospective randomized phase III trials (NSABP B39/RTOG 0413, RAPID, IRMA, SHARE), conservative criteria such as the ones published by ASTRO/GECESTRO should be considered for choosing patients for APBI.

TECHNICAL CONSIDERATIONS AND EMERGING MODALITIES FOR PARTIAL BREAST IRRADIATION

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Purpose: Partial breast irradiation (PBI) represents an alternative to whole breast irradiation (WBI); this approach treats the lumpectomy cavity and a margin of adjacent breast tissue allowing for a reduction in treatment volume as well as the opportunity to reduce treatment duration and toxicity.

Methods: Multiple PBI techniques are available; interstitial brachytherapy (IB) represents the oldest PBI technique. Mature data from randomized trials are available with 5-10 year follow-up and demonstrate comparable local control and toxicity profiles. Applicator based brachytherapy has evolved from single-lumen applicators to multi-lumen and strut devices increasing the degrees of freedom for treatment planning and improving target coverage and reducing toxicities. Prospective, non-randomized 5-10 year data are available with applicator based brachytherapy demonstrating low rates of recurrence, comparable rates of toxicity, and high rates of excellent/good cosmetic outcomes. External beam radiation therapy includes 3D-CRT, IMRT and proton based techniques. Data from 3D-CRT PBI studies have suggested potentially higher toxicities and inferior cosmetic outcomes as compared to WBI. However, randomized studies evaluating IMRT PBI have not, demonstrating comparable or improved toxicity and cosmetic outcomes and may represent the superior external beam PBI strategy.

Result: Multiple retrospective studies and data from 7 prospective randomized trials in over 10,000 cases with follow-up > 10 years will be presented and continue to confirm, the efficacy of this treatment approach.

Conclusions: Partial breast irradiation represents a standard of care strategy for appropriately selected patients following breast conserving surgery; multiple techniques exist to deliver PBI with different technical considerations and data available.

WHAT SHOULD BE CONSIDERED FOR PARTIAL BREAST IRRADIATION IN KOREA?

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Recent clinical trials have demonstrated that accelerated partial breast irradiation (A-PBI) has shown non-inferior local control compared with whole breast irradiation, but late toxicity and cosmesis has varied according to applied techniques. The latest developments of high precision intensity modulated radiotherapy techniques with image based localization have made it more feasible in clinical practice. However, A-PBI is still far from widespread in Korea. In a pattern-of-care study, clinical application rate of A-PBI in practice stayed only at 4.7% (1). This situation might result from patient selection, relatively small breast volume, inexperience of technology and hypofractionation, and reimbursement in Korean national health insurance system.

Because A-PBI can be selectively applied to low risk breast cancer patients, the selection criteria has been the most important issues. In Korea, the peak incidence is around 45 year, ten to fifteen years earlier compared with Western countries. However, treatment outcomes of Korea are similar to those of Western countries. Current guidelines has the recommendation to exclude the younger patients less than 45 or 50 year, but no data exists whether different cutoff is available or not. At any rate, the population is much smaller based on the guidelines in Korea.

A-PBI in Korean women has been considered impracticable due to relatively small breast volumes, underlining the need for technological breakthrough. A phase I/II trial by Korean Radiation Oncology Group (KROG) has been conducted to evaluate technical feasibility of A-PBI with 3 dimensional conformal radiotherapy (3DCRT) (2). The study showed that A-PBI with 3DCRT cannot be reproduced in Korean breast cancer patients, especially in breasts with small volume, mainly due to major dosimetrical violation in surrounding ipsilateral normal breast. This volume issue should be considered in terms of definition and technical viewpoint.

A-PBI has the radiobiological background based on α/β ratio from the previous clinical trials. In Korea, this accelerated hypofractionation has not been familiar for PBI as well as whole breast irradiation yet. In clinical practice, many technologies can be considered for A-PBI, such as intensity modulated radiotherapy, interstitial brachytherapy, intraoperative radiotherapy, etc. However, most radiation oncologist are still conservative to adopt these newer technologies for breast cancer in Korea. Therefore, it may take time for A-PBI to incorporate into the practice in

Korea.

Reimbursement is one of the most important issues to perform PBI. In Korea, radiotherapy fee almost depends on the decision by Korean National Health Insurance Corporation that entirely controls the reimbursement system without private insurances. Because hospital is more paid if patients receive more fraction numbers of radiotherapy, radiation oncologists have cautious attitudes to decide to reduce fraction numbers. Especially, breast cancer is No. 1 cancer that patients receive radiotherapy, regardless of treatment aim, in Korea. Therefore, application of PBI may cause to reduce the income of radiation oncology department and have the impact to maintain the facility.

In summary, currently, many things should be considered for A-PBI in Korea as mentioned above. However, the application of A-PBI will be gradually more expanded for early breast cancer in Korea.

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GUIDELINES FOR PREVENTION OF BREAST CANCER

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Breast cancer is the most commonly diagnosed cancer in American women, with an estimated 268,670 cases of invasive breast cancer and an estimated death toll of 41,400 women in 2018 and affects approximately 1.67 million women annually worldwide. Early detection by screening, with or without the use of preventive medications, can reduce the burden of disease but has drawbacks, including overdiagnosis, anxiety related to additional testing, and costs associated with screening.

Cancer can take years, or even decades to develop, yet many people believe that getting cancer is due to genes, fate or bad luck. But scientific research shows that our cancer risk depends on a combination of our genes, our lifestyle and our environment – things we can and cannot control. So, when we talk about cancer prevention, we focus on the areas we can control and how we can lower our risk. This is important: there are things you can do today that can help to prevent, delay, or even stop the cancer process at all stages of life.

When we talk about risk factors we can control we often use the word "lifestyle." AICR's research shows that the choices you make about maintaining a healthy body weight, eating a healthy, balanced diet, and staying active can reduce your chances of developing cancer.

All of us are at some risk for developing cancer at some point in our lives. It's difficult to know how much risk, exactly. Some smokers never get lung cancer whereas some healthy, non-smoking individuals do develop lung cancer. Similarly, there are people with obesity who never develop any of the 12 cancer linked to this condition while some lean individuals do.

But for the vast majority of us, our cancer risk is something we can increase or decrease. And that's what we mean, when we talk to individuals about cancer prevention. You can help protect yourself against cancer. And given that the science says, strongly and consistently, that healthy everyday choices can and do decrease cancer risk, it makes sense to make those choices.

There are no guarantees when it comes to cancer. But every time you decide to go for a run or choose a fresh salad over a fast-food burger, you're playing the odds. And those odds are very good.

Decades of research into the science of cancer prevention show that a healthy overall lifestyle is

the smartest, safest bet you can make.

We have to review the risk factors for breast cancer so that discuss about preventing about breast cancer. Also, control of specific modifiable breast cancer risk factors as well as effective integrated prevention of non-communicable diseases which promotes healthy diet, physical activity and control of alcohol intake, overweight and obesity, could eventually have an impact in reducing the incidence of breast cancer in the long term.

IMAGING SCREENING TOOL BEYOND MAMMOGRAPHY

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Two-dimensional (2-D) mammography is the only screening modality that has been shown to decrease breast cancer mortality. However, it is well known that 2-D mammography has both limited specificity and sensitivity due to the confounding effect of superimposed breast tissue causing both false positive as well as false negative studies. While the quasi 3-D format of digital breast tomosynthesis (DBT) improves both specificity and specificity by presenting the reader with reconstructed slices of the breast, the modality is still primarily, an anatomic imaging technique. Screening ultrasound, has been shown to be complimentary to mammography by increasing cancer detection especially in denser breasts. However, ultrasound is very operator dependent and should be performed in combination with mammography to optimize cancer detection. Ultrasound is also, primarily an anatomic imaging technique.

Imaging modalities such as contrast enhanced mammography (CESM) or contrast enhanced DBT, contrast enhanced breast MRI (CE-MRI), and molecular breast imaging (MBBI) which leverage degrees of vascular and cell physiology have the potential to detect not only additional cancers, but also cancers that are more biologically aggressive. The detection of these poor prognosis cancers (and possibly, the lack of detection of indolent or, over-diagnosed cancers) has the potential to significantly improve long term outcomes of breast cancer screening beyond that achieved with 2-D mammographic screening. This lecture will review some of these additional breast imaging methods and outcomes in breast cancer screening.

POPULATION BASED MUTATION SCREENING TO SELECT HIGH RISK PATIENT:WHERE ARE WE NOW?

Seigo Nakamura

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Recently, the incidence of breast cancer in Japan has rapidly increased up to 90,000 cases per year. It is nearly 4times higher compared to 30 years ago and come closer to the western countries. This tendency is due to the changes of environmental factors including high calorie diet, early menarche, delayed menopause, elderly birth and decrease in the number of children. This trend is almost the same in some of Asian countries. Therefore, early detection with mammography screening for general population over 40 has become standard in each country.

However, dense breast issue has become a big problem especially under 50. Several western countries have changed the beginning age of mammography screening from nearly 50.

Women in Asian countries have more dense breast and ultrasonography could detect more breast cancers by the large scaled RCT called J-START conducted in Japan. How to utilize mammography and ultrasonography for breast cancer screening is urgent issue especially in Asian countries.

About 5-10% of primary breast cancers are thought to be hereditary. *BRCA* related breast cancer sometimes occurs in 20's or early 30's. For those women, breast MRI is much better to detect tiny cancers shaded behind dense breast. Breast MRI showed survival benefit compared to conventional MRI through several studies. However, this method costs extremely high and takes time consuming, therefore, another convenient methods will be warranted. One of the promising methods is liquid biopsy including miRNA or cfDNA. This method is still investigational, however, evolution of sequencing will make it possible in the clinical setting in the near future.

In Netherland or U.S., there are ongoing trials related to personalized screening depending on breast density and germline mutation. Those are promising to improve weak points of the mamography screening at present.

UPDATES ON MOLECULAR GENETICS AND CLASSIFICATION OF FIBROEPITHELIAL TUMORS OF THE BREAST

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Breast fibroepithelial tumours are a heterogeneous group of neoplasms comprising the common fibroadenoma and the less frequently occurring phyllodes tumour. While fibroadenomas are benign and affect approximately 10% of the female population, phyllodes tumours may be classified into benign, borderline and malignant grades, with borderline and malignant phyllodes tumours behaving more aggressively, potentially metastasizing and causing death.

Both fibroadenomas and phyllodes tumours are diagnosed histologically based on well recognized microscopic parameters. There are however, challenges in histological classification between cellular fibroadenoma and benign phyllodes tumour, as well as among malignant phyllodes tumour, spindle cell metaplastic carcinoma and sarcoma. Accurate categorization is important due to differences in clinical management.

In recent years, molecular characterization found frequent MED12 mutations in both fibroadenomas and phyllodes tumours, with additional mutations discovered in phyllodes tumours of increasing grades. Apart from providing further insights into the pathogenesis of fibroepithelial tumours, these molecular changes can be utilized to improve diagnostic accuracy. For instance, presence of TERT mutations in a cellular fibroepithelial lesion favours the diagnosis of phyllodes tumour. In a malignant spindle cell tumour for which differential considerations are metaplastic spindle cell carcinoma and malignant phyllodes tumour, the discovery of MED12 mutations would support the latter. Derangements in cancer driver genes in malignant phyllodes tumours may also offer targets for therapy.

Diagnosis of fibroepithelial neoplasms remains premised on microscopic morphology, with molecular discoveries in recent years being possibly harnessed for refining diagnostic categorization.

DIFFERENTIAL DIAGNOSIS BETWEEN FIBROADENOMA AND PHYLLODES TUMOR ON CORE NEEDLE BIOPSY

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Fibroepithelial neoplasms are biphasic tumors consisting of epithelial and stromal components, and include broad heterogeneous disease spectrum, from fibroadenoma to malignant phyllodes tumor. Fibroadenoma has benign appearance whereas, phyllodes tumor shows wide spectrum of behavior, from benign to malignant. Discrimination of phyllodes tumor from fibroadenoma in biopsy specimen is quite difficult, but there is no known diagnostic molecular marker for it. Predictive molecular markers for aggressive features of phyllodes tumor are also poorly studied.

RISK FACTORS FOR RECURRENCE AND DISEASE MANAGEMENT OF PHYLLODES TUMORS

Yoo Seok Kim

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Phyllodes tumors are uncommon breast diseases, accounting for 0.3 to 1% of breast tumors in females.

The basic principle of local treatment for all kinds of phyllodes tumors is local excision to negative margins. Most studies recommend at least 1 cm margin. The desired 1 cm margin width is based on retrospective analysis because these diseases are rare. A normal tissue containing microscopic projections of the lesion microscopic projections of the lesion commonly surrounds phyllodes tumors. So more tissue typically needs to be removed to achieve the desired histologic margin than might be predicted on the basis of preoperative physical examination or imaging findings.

When phyllodes tumors are excised with positive or closed margins, reexcision should be performed. The role of adjuvant radiation is controversial, with some studies indicating improved local control but no increased survival when used in patients with borderline or malignant tumors. Locally recurrent tumors may warrant adjuvant chest wall radiation following reexcision.

Routine adjuvant systemic treatment following initial excision is not recommended. When used for treatment of metastatic disease, guidelines for treating sarcoma should be followed.

Recurrence of phyllodes tumors is possible for all lesions with recurrence rates as high as 46%. Best predictor of local recurrence is surgical resection margins. Additionally, stromal atypia, necrosis and fibroproliferation are associated with local recurrence according to previous studies. On the other hand, the factors associated with risk of metastatic recurrence are mitotis index, stromal overgrowth and tumor size.

FACT CHECK OF BRAIN METASTASIS IN BREAST CANCER

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Development of brain metastasis in breast cancer patient is sometimes a life-threatening crisis during the lifetime course of metastatic breast cancer (MBC). Brain metastasis can affect the quality of life to the great extent so that the patients are not able to undertake any more systemic treatment because of reduced performance status and also it sometimes leads to death. Therefore, brain metastasis is one of the most troublesome events during the treatment course of MBC.

In terms of epidemiology, 15% to 35% of patients with breast cancer are found to have brain metastasis in autopsy studies. Lifetime cumulative incidence of brain metastasis in MBC patients reaches around 40% in HER2 positive and triple negative breast cancer but about 20% in hormone receptor positive breast cancer (unpublished data). In a population based large scaled study, 0.41% of the entire cohort of breast cancer and 7.56% of the subset with metastasis disease to any site were found have brain metastasis. The median survival of among the entire cohort with brain metastases was 10.0 months and 6.0 months in triple negative breast cancer, which is even dismal prognosis considering the survival of breast cancer patients without brain metastasis.

If we could identify brain metastasis earlier than the patients feel symptomatic deterioration, we might have better survival and quality of life in these affected patients facilitating earlier intervention with better clinical outcome, as we do in lung cancer patients. A prospective cohort study to detect brain metastasis earlier in MBC will be introduced in this talk.

LOCAL TREATMENT OPTION OF BRAIN METASTASIS

Seok-Gu Kang

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Even if there is a brain metastasis, the survival of the whole patient is mostly determined by the treatment of primary cancer. However, Increased intracranial pressure (IICP) causes life threatening at the moment of brain metastasis, and neurologic deficit has an absolute impact on quality of life. Thus, local control of brain metastasis improves the quality of life of breast cancer and also excludes life threatening cases caused by IICP. In this presentation, we will present an indication of local control options for brain metastasis to breast cancer. We will also introduce local control options, such as surgery, radiosurgery, and whole brain radiation therapy, to properly combine these four methods to treat patients. In addition, we present local control principals and new attempts at brain metastasis in Severacne Hosptial with cases.

BRAIN METASTASIS: NEW THERAPEUTIC APPROACH

Nancy Lin

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Brain metastases affect up to half of patients with advanced, HER2-positive breast cancer, 25-46% of patients with advanced triple-negative breast cancer, and 10-15% of patients with estrogen receptor (ER) positive/HER2-negative breast cancer. Local therapies such as surgical resection (for patients presenting with single or highly symptomatic metastases), stereotactic radiosurgery (SRS), and whole brain radiotherapy (WBRT) have long been considered standard-of-care. However, over the past decade, several systemic approaches have emerged as promising alternatives to localized approaches. For patients with HER2-positive breast cancer, clinically relevant central nervous system (CNS) activity has been reported with lapatinib-capecitabine, trastuzumab-emtansine, and neratinib-capecitabine. The combination of trastuzumab-capecitabine-tucatinib is currently under evaluation in a randomized phase 3 study which includes (but is not restricted to) patients with active brain metastases. For ER-positive breast cancer, preliminary evidence of CNS activity has been reported with the CDK4/6 inhibitor abemaciclib, and older case reports have indicated activity of standard hormonal therapies such as tamoxifen and aromatase inhibitors. Several commercially available chemotherapy agents also have reported activity, either in small, single-arm prospective studies, or case series, and these include capecitabine, platinum salts, and anthracyclines. Several novel approaches are now under investigation in clinical trials. In patients with HER2-positive breast cancer, new combinations of HER2-directed therapies with other targeted agents (for example, targeting the PI3K pathway) are being tested in clinical trials. Across tumor subtypes, there is great interest in testing cytotoxic chemotherapy agents with an improved profile either with respect to penetration across an intact blood brain barrier, and/or other characteristics that lead to longer residence time in brain metastases. Examples of novel chemotherapeutic agents under investigation are ANG1005, tesetaxel, and NKTR-102, among others. Finally, there are early efforts to determine whether the potential benefits of immune checkpoint inhibitors can be extended to breast cancer patients with brain metastases.

RISK FACTORS FOR LYMPHEDEMA AND PREVENTIVE INTERVENTIONS DURING SURGERY

Jung Eun Choi

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Lymphedema is a result of the functional overload of the lymphatic system and breast cancer related lymphedema is a negative sequela of breast cancer treatment. About 21.4% (14.9-29.8) patients experience lymphedema and report long-term decrease in their quality of life as well as chronic pain and depression.

The risk factor of lymphedema is related with treatment modality and patient's factor. Patients who receive ALND (axillary lymph node dissection) have a lymphedema incidence four times higher than those who receive SLNB (sentinel lymph node biopsy) [19.9% (95% CI: 13.5–28.2) and 5.6% respectively]. The number of removed LNs, mastectomy, radiotherapy to the regional LNs and chemotherapy including taxane are also the risk factors of lymphedema related with treatment.

Preventive intervention during surgery is including SLNB, Axillary reverse mapping (ARM) and LYMPHA (LYmphedema Microsurgical Preventive Healing Approach) technique. ALND is now performed more selectively on the basis of such studies as ACOSOG Z0011 and ACOSOG Z1071. For the patients who still requires axillary dissection, ARM and LYMPHA are possible. The ARM (axillary reverse mapping) procedure is based on the hypothesis that breasts and arms have different lymphatic pathways in the axillary area. The purpose of ARM is to preserve the arm lymph nodes and the lymphatic pathways and to prevent the ipsilateral arm. During LYMPHA technique, Arm lymphatics are identified and preserved at the time of axillary dissection, and microsurgical anastomosis to an axillary vein branch is performed. Here, the effect and safety will be reviewed.

TREATMENT FOR BREAST CANCER PATIENTS WITH LYMPHEDEMA

Eun Joo Yang

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Breast cancer survivors suffer from fear of lymphedema which is a chronic, debilitating, and disfiguring condition because lymphedema can be developed or progressed by vigorous activities and require lifelong management. Therefore, breast cancer patients should be monitored during exercise due to the secondary risk of breast cancer-related lymphedema. Early assessment of lymphedema may be important to correct subtle subclinical lymphedema because, if left untreated, it may progress to chronic and severe lymphedema.

Patients who already had symptoms of lymphedema such as heaviness or tightness after some exercise or activities showed satisfaction about monitoring their symptom and modification the exercise protocol according to their symptoms and counseling form their clinicians. Breast cancer survivors need personalized and exact information about their symptoms and experiences on their daily life. Communication with their clinicians with objective and subjective data can facilitate the motivation and health life style. Personal health record -based care program for breast cancer survivors could be helpful for those with fear of lymphedema when integrating with clinicians for decision making for safe and effective exercise program.

MANAGEMENT OF BREAST SURGERY-RELATED MUSCULOSKELETAL COMPLICATIONS

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After breast surgery, breast cancer patients have many problems on their shoulder and arm. Several studies have shown the prevalence of symptoms and upper limb dysfunction and effect of some rehabilitation programs, however, previous treatment still need more logical knowledge about pathophysiology, natural course and treatment of upper limb dysfunction and symptoms.

First, we should focus on the physical impairment by treatment such as surgery or radiation therapy. Breast conserving surgery could not prevent the upper limb dysfunction totally. Even after surgery without injury on the fascia, muscle and joint of shoulder, many patients complain their symptoms. This discrepancy should be explained to find the effective rehabilitation programs. For example, the breast surgery did not injure the rotator cuff tendon directly. What mechanism develop the rotator cuff disease? We can explain this phenomenon by the imbalance of shoulder motion. Dynamic stenosis on the rotator cuff pathway could damage the tendon. The causes of dynamic stenosis are 1. pectoralis minor shortening, 2. weakness of shoulder stabilizer muscles. 3. Postural change, named round shoulder. In this condition, uncontrolled shorts activities or activity of daily living could exaggerate the damage. In this case, we can plan the rehabilitation in four steps: 1. elongate shortened pectoralis minor muscles and frontal fascia of upper extremity 2. strengthen the shoulder stabilizing muscles, 3. modify the posture. 4. achieve full ROM of shoulder.

In this lecture, I will introduce the principle of comprehensive rehabilitation strategy. The goal of rehabilitation is not to come back to the previous status before surgery, but to go forward better life.

Survivorship Session

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COMPLEX RELATIONSHIP AMONG DEPRESSION, SELF-EFFICACY, ILLNESS PERCEPTION, AND FEAR OF PROGRESSION IN BREAST CANCER SURVIVORS

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The fear that breast cancer may progress or recur (hereafter, the FOP) is a prevalent concern that lingers even years after diagnosis and treatment. Moving forward despite this uncertainty and anxiety can be challenging to patients with breast cancer. To some extent, the fear that the illness may progress can motivate patients to engage in healthy behavior and promote adherence. However, excessive fear may be debilitating. In this presentation, we will review the factors associated with the FOP, as well as its relationship with patient reported outcomes. Moreover, the results from a longitudinal observational study with breast cancer patients will be presented. The study sample consisted of 204 patients with breast cancer on adjuvant endocrine therapy at a university hospital in Seoul, South Korea. The patients completed a self-report survey, including the Fear of Disease Progression Short Form, the Center for Epidemiologic Studies Depression Scale (CES-D), Brief Illness Perception Questionnaire (BIPQ), Beliefs About Medicines Questionnaire (BMQ)-Specific, and Menopause Rating Scale (MRS). The surveys were administered four times: at baseline and at 3, 6, and 12 months. The results of latent class growth analysis identified three classes based on the patterns of the FOP over time. These classes reflect the overall severity of the FOP: Class 1 (moderate and increasing FOP); Class 2 (low FOP); and Class 3 (high and persistent FOP). The patients with a higher level of baseline MRS scores were more likely to be in Class3 than in Classes 1 and 2. Moreover, the patients with higher emotional representation scores were more likely to be in Classes 1 and/or 3 than in Class 2. The patients with higher baseline CES-D scores were more likely to be in Class 1 than in Class 2. Furthermore, subscales scores of the BMQ (i.e. necessity and concern) showed significant differences across these classes. Perceived necessity of taking medication was higher in Class 3 (high FOP) as compared to Classes 1-2. The concern about potential negative consequences of taking medication was the highest in Class 3, followed by Classes 1 and 2. While no statistically significant differences were observed in the rates of adherence across these classes, the rates appeared to be lower in Class 3 as compared to Class 1. Taken together, these results indicate that a high FOP can potentially have adverse effects on medication adherence. Moreover, the FOP tends to increase over time in a proportion of patients with breast cancer. In conclusion, in order to improve medication adherence in breast cancer patients, the FOP should be monitored and managed.

UNDERSTANDING THE CAUSES OF DISTRESS IN BREAST CANCER PATIENTS AND SURVIVORS

Richard Fielding

Univ. of Hong Kong, Hong Kong

Breast cancer (BC) can have profound detrimental effects on the psychosocial functioning of women, leaving longstanding deficits in mental wellbeing and social function. Between 15-40% of women having experienced breast cancer report persisting psychological difficulties one or more years after primary breast surgery, depending on the study in question and the population. However, most women with breast cancer make good adjustment and return to normal life quite swiftly once treatment ends. What differentiates women who adjust well from those experiencing difficulties for often many years after treatment ends? While traditional studies of psychosocial distress indicate a long-term decline in psychological distress over the 12 months following BC diagnosis, more recent studies of sub-group trajectories indicate that the presence of unresolved physical symptoms is a major predictor of poor psychosocial adjustment, and a prior history of psychological difficulties may compound this problem. This talk will review the research on psychosocial distress after BC and draw inferences for intervention strategies based on preventive rather than curative strategies.

SLEEP & DEPRESSION: TWO IMPORTANT PSYCHIATRIC SYMPTOMS IN PSYCHO-ONCOLOGY

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Sleep disturbances and depression are common among cancer patients throughout the entire course of the illness, from diagnosis, through treatment, possible recurrence, and well into survivorship. Although many cancer patients experience insomnia and depression, only small number of these patients will seek evidence-based treatment. Both patients and their healthcare providers often consider sleep problems or depression as a normal reaction to cancer diagnosis and treatment, and become accustomed to those patients. This is unfortunate because of the significant physical and psychological health ramifications of untreated, chronic sleep disturbances or depressive symptoms within a patient population already at high risk for the development of medical co-morbidities. Most of cancer patients can suffer cancer-related fatigue symptom, and fatigue is associated with depression or sleep disturbance. Patients spend a lot of time lying in bed during daytime, and it may impair the sleep-wake cycle and decrease sleep quality at night. Time in bed during 24 hours (TIB/d), rather than time in bed (TIB), can be a useful sleep index for cancer patients who spend their time sleeping during the day. Cancer patients who suffer depression and insomnia also tend to be overconcerned about the negative consequences of poor sleep on their health. For example, sleep during a specific time period (e.g., 10 pm to 2 am) is critical for immune functioning or poor sleep affects cancer progression, are common cancer-related dysfunctional beliefs about sleep observed among patients with cancer experiencing insomnia. Such catastrophic thinking and pressure to sleep may lead them to go to bed earlier than their habitual sleep time before the diagnosis of cancer and try to fall asleep even though they are not sleepy. In this talk, the prevalence, etiology, and management of depression and sleep disturbance among cancer patients will be discussed. Especially, the Sleep Clinic for cancer patients, run in Asan Medical Center, will be presented.

ASSOCIATION BETWEEN CIRCADIAN DISRUPTION AND BREAST CANCER

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Circadian rhythms are biological cycles that govern many physiological processes such as body temperature, hormone secretion and sleep-wake control based on a 24-hour period. Epidemiological studies showed that the circadian disruption is associated with increased likelihood of various cancers, including breast cancer. Shift-working has been suggested to increase the cancer risk in human by the International Agency for Research on Cancer. Crosstalk between 17beta-estradiol (E2)-estrogen receptor (ER) signaling pathways and circadian clock-related molecules play a role in tumorigenesis of the breast cancer cells. In physiological condition, the dimerized E2-ER complex is translocated to the nucleus and bound to the estrogen response element. Afterward, transcription of the target gene is initiated by the co-activators such as the circadian locomotor output cycles kaput (CLOCK) and brain and muscle Arnt-like protein 1 (BMAL1) proteins which are essential components of the molecular circadian clock. Overexpressed CLOCK gene may be related to tumor cell proliferation. On the other hand, a decreased level of period 2 (PER2) causes an increased amount of E2-ER complex that leads to the activation of Akt and Ras/MAPK pathway followed by tumor proliferation, survival, and invasion. Decreased BMAL1 that inhibits the Akt/MMP2 pathway can also result in tumor proliferation.

Recently many reports showed an inverse association between serum vitamin D concentration and incidence of cancers in breast, colon, kidney, lung, and pancreas. Given that the incidence of breast cancer rises recently, and vitamin D deficiency becomes highly prevalent, there might be an association between vitamin D and breast cancer. Indeed, many studies have shown the inverse association between vitamin D level and incidence of breast cancer and the link between genetic polymorphisms of vitamin D receptor and breast cancer. The meta-analysis of the relationship between vitamin D and breast cancer showed that women in the highest quantile of vitamin D have a 45% lower risk than those in the lowest quantile. Genomic effects of vitamin D are exerted by binding to the vitamin D receptor, by which the transcription of more than 60 genes that are responsible for antiproliferative, pro-differentiating, antimetastatic, and proapoptotic effects on cells are regulated. Thus, decreased serum vitamin D levels result in enriched cellular growth, neoangiogenesis, and cancer development. In addition to the direct ef-

fect of vitamin D deficiency, there might be an indirect effect via circadian disruption. We found that an animal model of vitamin D deficiency showed the disrupted circadian rhythm and altered sleep-wake behavior. Further investigation into the biological mechanism of the causal relationship between vitamin D deficiency and breast cancer is warranted.

MUTATIONS IN CIRCADIAN GENES AND THEIR MECHANISTIC CONNECTION TO CANCER DEVELOPMENT

Carla Finkielstein

Virginia Tech, U.S.A.

A key aspect of breast cancer research is identifying new regulatory pathways involved in proliferation and differentiation of cells. Disruption of circadian rhythm, the mechanism that keeps our physiology and behavior running in a 24 hours cycle, has recently emerged as a new potential risk factor in the development of cancer, pointing to the human core transcription factor gene period 2 (PER2) as tumor suppressor. More recently, increasing evidence has established functional links between circadian clock components and the cell division processes. Remarkably, about 10% of all known circadian-controlled genes, including those encoding tumor-suppressors, caspases, cyclins, transcription factors, and ubiquitin-associated factors, regulate either cell-cycle progression or cell death mechanisms.

Our current findings show that PER2 directly interacts with the tumor suppressor p53 and its negative regulator, the proto-oncogene mouse double minute 2 homolog (MDM2). In unstressed conditions, binding of PER2 to p53 controls p53's stability, transcriptional activity, and time-of-day-dependent nuclear-cytoplasmic p53's shuttling, thus, generating an asymmetric distribution of each protein in different cellular compartments. Binding of PER2 to the E3-ligase MDM2 also occurs in the absence of p53, leading to PER2 ubiquitination and degradation in a process that directly influences the circadian period length of the cell. Interestingly, TP53, PER2, and MDM2 missense mutation data, obtained from human tumor samples show a great number of mutations map within the interface of binding of PER2 to p53 and MDM2. Known mutations in the TP53 gene have been deposited in the TP53 database and in the International Agency for Research in Cancer database (http://p53.free.fr/index.html and http://www-p53.iarc.fr/, respectively). At present, 23,544 somatic mutations and 376 germline alterations, including missense, nonsense, and frame-shift insertions and deletions in p53, have been reported in all human cancers in 2248 references (http://www-p53.iarc.fr/). The majority of mutations lie in the hydrophobic mid-region of the protein and are predicted to cause conformational changes that will prevent binding of p53 to its specific response element (RE) in the DNA. Importantly, 40 missense and nonsense mutations in breast cancer patients have been identified in the C-terminus domain where PER2 binds to p53 (http://www-p53.iarc.fr/). It in-

cludes mutations found in normal, pre-neoplastic and neoplastic tissues, including metastases as well as mutations found in individuals carrying a TP53 germline mutation. At present, we pinpoint hot spot mutations within the C-terminus of p53, and identified in sporadic and familial breast cancer patients, that modulate PER2 recognition, stability, and expression of downstream target genes. Furthermore, we found the effect of therapeutic drugs aimed at reversing the p53 mutant (p53mut) phenotype in cancer cells to be compromised when PER2 is co-expressed and thus, chronomodulation of drug administration, based on specific PER2 and p53 tumor genotypes, would need to be considered when designing clinical trials.

CIRCADIAN RHYTHM OF P53 TOWARD THE CHRONOTHERAPY OF CANCER

Jae Kyoung Kim[1], Tetsuya Gotoh[2], John Tyson[2], Carla Finkielstein[2]

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The circadian (~24 hours) core clock mechanism exerts a multilevel regulation of the cell division process. This is particularly relevant when it comes to the mechanism by which the core circadian clock components such as PER2 modulates the cellular response to genotoxic stress that leads to cell cycle arrest. In this talk, I will describe how PER2 generates circadian rhythms of a tumor suppressor, p53. In particular, I will illustrate how the combination of mathematical modeling and experimental works is used to reveal complex interactions between the clock regulator and the tumor suppressor. Finally, I will describe the potential role of p53 rhythms for the cancer chronotherapy, which treats cancer at the right time.

ABRCA & HBOC

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GENETIC TESTING IN HEREDITARY BREAST CANCER IN ASIA

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Background: Data from whole exome sequencing and whole genome sequencing presented other predisposition genes, besides *BRCA* genes, increased the risk of breast cancer. Generation of overwhelming amount of genetic data are imposed challenges in the interpretation of test results and identification of molecular-driven pathways for personalized medicine, especially when gene mutations (e.g. *MUYTH* mutation) are found with low penetrance and unknown pathogenicity. Currently, there is no standard guidelines for clinical management and genetic counseling of some of the variants and variant of uncertain significance (VUS). The prevalence of germline mutation in Asian is similar to the West, yet there are disparities in HBOC-related mutation spectrum across different ethnicity. For instance, *PALB2* and *RAD51D* mutations are commonly seen in Asian, *CHEK2* and *PMS2* mutations are more frequently seen in Americans. Understanding the mutation spectrum improves early diagnosis and clinical management in the region, however, lack of access to genetic testing and counseling are the common barriers for implementing genetic screening in Asia. It is important to implement genetic testing as part of the health care services, this need to be done together with the government and healthcare providers by increasing the public awareness and counseling resources, so that more of the high-risk patients can be benefited and moving towards personalized medicine.

Improvements in variant interpretation and bioinformatics pipelines.

RISK REDUCTION STRATEGIES FOR WOMEN WITH PATHOGENIC VARIANTS IN MULTIGENE PANEL TESTS

Hyung Seok Park

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Identification of various germline variants in cancer-susceptibility genes such as TP53, BRCA1, BRCA2, and PTEN improved the diagnosis and management of hereditary cancer syndrome. Recent advances in next-generation sequencing for cancer susceptibility genes relating to hereditary breast cancer provide more detailed and comprehensive information about those genes. Particularly, women with high risk factors without *BRCA* mutations can receive the multigene panel tests that include various cancer-susceptibility genes to identify their hereditary cancer risk. However, there are several issues that arise about management for women with pathogenic variants in multigene panel tests: validation of this novel techniques, selection of candidate susceptibility genes, difference in ethnicities, and lack of robust evidence for risk reduction strategies for various variants with moderate to high risks. In this lecture, I will discuss those issues relating to potential risk and benefit and several examples of real clinical practice for risk reduction strategies for women with pathogenic variants in multigene panel tests.

ROBOTIC NIPPLE SPARING MASTECTOMY WITH IMMEDIATE RECONSTRUCTION FOR WOMEN WITH BRCA1/2 MUTATION

Benjamin Sarfati

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Robotic nipple sparing mastectomy and immediate breast reconstruction with implant could be a significant advancement in the treatment of breast cancers and prophylaxis because the mastectomy is performed without any scar on the breast. Since December 2015 we built a prospective study to collect the data of our procedure to prove the advantages of this technique. The primary endpoint was the rate of skin or Nipple areola complex necrosis. The rate of conversion to open technique, the duration of the procedure, the postoperative complications were also analyzed.

Preliminary data attest to the feasibility, the reproducibility and the safety of this approach. However, long-term data are needed to confirm the oncological safety and the aesthetic stability of the result.

Nursing Session

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DISSEMINATION OF BREAST CANCER AWARENESS: PREVENTION AND EARLY DETECTION

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Physicians are supposed to treat patients disease, however they need to think about their life after disease as well. In this aspect, I have wondered what could I play a role in the relationship of physicians and patients, and what contribution I could make to the dissemination of breast cancer awareness.

In the year 2000, I established a patient survivor's group, Koreavenus Association. The purpose of the group was to understand breast cancer, to help each other, and to perform social activities as volunteers for specific activities such as awareness campaigns and fund raising for the poor. In addition, Q&A Corner was opened daily to relieve patients' questions, resulting in more than 45,000 valuable questions and answers.

Officially my big contribution to the patients and society is establishment of Korea Breast Cancer Foundation (KBCF) in 2000. More than 2 years of business and official arrangement from government was required and finally driving support from Kyung-Bae Suh, CEO of Amore-Pacific Co. KBCF was born with a mission to improve womens health from breast cancer. Moreover, Pink ribbon campaign, breast cancer awareness campaign to arouse public attention to breast cancer and importance of early detection was also started by myself at the same period in Seoul Korea.

I hope all these models will be propagated further to all over the nation and also give good influence to the society to the early detection and survival of the breast cancer and to improve their human right as well.

HEALTH INSURANCE SYSTEM FOR BREAST CANCER PATIENTS

Beomseok Ko

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Strengthening the protection of health insurance is a major issue and a task for the Korean health care policy. Strengthening the protection that citizens can experience should not only reduce cost barriers but also ensure adequate quality medical services. To do this, it is necessary to build a medical system that produces high-quality services at low cost. However, there are various problems such as poor insurance finances, unrealistic medical costs, unreasonable health insurance law provisions, insufficient protection, unreasonable insurance management system, and difficulties in running health insurance policy. In the case of vacuum-assisted resection, which is currently a problem, it is a matter of long-term problem-free behavior.

Vacuum-assisted resection is a technique in which vacuum is applied to pull tissue into a probe and then cut into a rotating blade. It is designed to cut the skin and cut it with a knife. It was introduced in 1995 and has been actively used in Korea since the early 2000s. This technique is replacing the practices performed in the past by surgical resection because of the advantage of minimizing the incision of the breast and resecting the breast lesion. Recently, it has been widely used as a non-surgical alternative for patients requiring surgical resection of benign lesions. In some reports, it is known that there is a considerable residual disease rate in long-term follow-up, but there are few reports of residual disease in more reports. Therefore, patients who fully understand the advantages and disadvantages of surgical resection and vacuum assisted resection I think there is a possibility of using. This is the reason why the foreign guidelines and the textbooks of domestic and foreign countries have expressed the opinion that they can be used as abstinence for benign tumors as an expert opinion even though some of the residual disease rates are reported.

It is clear that the abnormal profit structure of the medical system is one of the causes of distrust of the overall medical care. A reasonable number of adjustments should be made considering the difficulty, the frequency, and the medical resources to be used for medical treatment.

SOCIAL WORK SERVICES FOR LOW-INCOME PATIENTS WITH CANCER

Sorah Park

Department of Social Work, Yonsei Univ. Medical Center, Severance Hospital, Korea

Patients with breast cancer experience various problems in the psychological, social and functional aspects as well as physical difficulties while receiving short-term or long-term cancer treatment. And the quality of life is decreased. Families who need to take care of patients can also feel psychological and physical burdens such as imbalance in the family systems, management of patient's medical and emotional status changes, and changes in the role of the family caused by patients' diseases. Especially, if patients and their families have financial problems, they feel burdened not only with treating diseases itself, but also with financial problems from treating diseases.

Therefore, social welfare services and psychological and social resources are needed for low-income patients and families when they are diagnosed with cancer and receive treatment. The socioeconomic support systems for cancer patients can be largely divided into public and private resources. Public resources are government-centered support services and include disaster medical expenses support project, emergency medical expenses support project, and cancer patients medical expenses support project by community health center. Among private resources, there are sponsorship projects from the hospitals by means of suggesting proper support proposals for each corporate's social contribution business. Psychological support services for cancer patients include managing and supporting self-help groups and supporting mentoring programs for cancer patients.

THE NEED FOR LEADERSHIP IN CANCER NURSING

Myungsun Yi

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Cancer, which is the second leading cause of death globally and the primary cause of death in Korea, is still remained as a disease to be feared and is associated with inevitable death. Indeed, living with cancer is regarded as a continuous battle for their own survival with social stigma as well as inappropriate information and support and insensitive communication. Cancer nurses are positioned to play a pivotal role in improvement of health status and quality of life of people with cancer by demonstrating their leadership with an expert power base and a good insight into health care problems.

This presentation focuses on leadership in cancer nursing. Nursing leadership exemplars were demonstrated to show how successful nursing leaders set goals and challenged to meet these goals. And three essential elements that cancer nurses should consider in leadership were suggested: Awareness; Challenge; and Transformation. Awareness was stressed as the first step to becoming a leader. Clear awareness about social and nursing situation and problems would help nurse leaders establish their own goals and eliminate barriers that can undermine nurses achievements and limit their advancement. As nursing still remains a women-dominant discipline, feminist perspectives were introduced to help raise self-awareness on life conditions and situations that could be gender-biased. This awareness and the sense of empowerment will nourish nurse leaders in their effort to claim, fight for, and defend their own rights in hierarchical and male-oriented culture in health care settings.

Second, challenge was emphasized as leaders must face and confront situations and problems with courage. The differences that exist between men and women were identified. Relationship- and harmony- oriented characteristics of women and high capabilities to nurture were described as strength of women. Diverse views and insights of women were also highlighted to utilized them as good resources in challenging. At the same time, the weaknesses of women, such as lack of self-directedness and lower level of identity, which can be defined as value and concern for self, were emphasized in order to strengthen them to overcome the barriers that arise during challenge.

Lastly, transformation was highlighted as the ultimate goal of leadership. To help guide cancer nurses' leadership journey in improvement and expansion of cancer nursing, four leadership frames; structural frame, human resource frame, political frame, and symbolic frame were in-

troduced.

All cancer nurses need to be empowered to realize their potentials and make the care of people with cancer better no matter what positions they are in. Future cancer nursing leaders must demonstrate their impact by significantly enhancing health status and quality of life of people with cancer. This presentation would help empower cancer nurses in establishing and accomplishing their goals to improve quality of life of people with cancer in nursing policies as well as practice, research, and education.

DEVELOPING AND IMPLEMENTING BREAST CANCER EDUCATION

Imryung Kim

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Breast cancer patients and their families have diverse informational and educational needs throughout their cancer journey: from diagnosis to survivorship. Cancer education not only helps patients to make treatment decisions but also manage side effects and psychological distress encouraging them to adherence to their treatments.

Breast cancer patients can learn to cope with these conditions by effective education including counseling and support. So, health provider should be educated in a way that patients understand using plain language easy-to-understand written materials and teach-back, and also designed plain language written materials including visuals to provide more culturally and linguistically appropriate health education and enhance web-based information.

In particular, 'Appearance management' was the most difficult issue for patients to deal with. Patients wanted to obtain information to cope with hair loss, but it was difficult to provide information and education during the clinical care. So, education should be provided that reflects these unmet needs.

The topic on sexuality was very private and because it was difficult to open up to other people. It was necessary, but it was unmet need. Because the education gave detailed information to patients who wanted it, it was very essential to cancer patients.

In summary, there are three considerations for the education of breast cancer patients. First, durability: Continued education is needed according to the cancer treatment journey. Second, health provider should provide an easy-to-understand education considering health literacy. Third, Education appropriate to the patient's unmet needs should be provided.

In additional, breast cancer treatment advances are enhanced by expansion of health information technology platforms, new approaches to cancer prevention and screening and a greater emphasis on health provider and patient relationships. Advances in cancer care for breast cancer and treatment over the past 40 years have led to stunning gains. Therefore, medical staff should provide the correct information to help them receive the appropriate treatment.

A NEW APPROACH TO LYMPHEDEMA GUIDELINES : HOW TO OVERCOME DILEMMAS IN EDUCATING LYMPHEDEMA GUIDELINES

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Lymphedema is the accumulation of protein-rich fluid in tissues with inadequate lymphatic drainage.

People at risk of lymphedema are those who have impaired lymphatic system but dont undergo the signs and symptoms of lymphedema yet.

In an attempt to reduce its incidence and severity, patients are instructed to avoid skin and venous puncture and blood pressure measurements on the treated arm. However, these precautions are not possible to take in some cases and, moreover, efforts to keep taking those precautions can cause anxiety and destress for both patients and their health-care providers.

But even National Lymphedema Network comments that they lack scientific evidence regarding risk reduction practices for how to reduce the risk of developing lymphedema, or how to minimize lymphedema.

Recently, there are updated studies which suggest that blood draws, injections, blood pressure readings and air travel may not be associated with increasing arm volume.

And it must be also taken into account that generally not only lymphedema dissection and radiation but also old ages, obesity and neoadjuvant chemotherapy can increase incidence of lymphedema.

So its time to try a new approach to lymphedema guidelines. And oncology nurses should provide well balanced education considering both quality of life and lymphedema prevention to breast cancer patients.

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IBRANCE + AI and IBRANCE + fulvestrant[1]

JOINING FORCES, CHANGING THE OUTLOOK

As a **1st line therapy** for mBC, IBRANCE® + letrozole has demonstrated **>2 years mPFS**.*[2] And, when combined with fulvestrant, it offers **enhanced efficacy** to a **wide patient population**.*[3]

IBRANCE is indicated for the treatment of HR+/HER2- locally advanced or mBC:[1]
- in combination with an **AI**
- in combination with **fulvestrant in patients who have received prior ET**

In **pre- or peri-menopausal women**, the ET should be combined with an LHRH agonist

*Based on results from a Phase III RCT.

AI = aromatase inhibitor; ET = endocrine therapy; HR+/HER2– = hormone receptor positive, human epidermal growth factor receptor 2 negative; LHRH = luteinising hormone-releasing hormone; mBC = metastatic breast cancer; mPFS = median progression-free survival; RCT = randomised controlled trial.

1. IBRANCE® Product Information. **2.** Finn RS, et al. N Engl J Med. 2016;375(20):1925-1936.
3. Cristofanilli M, et al. Lancet Oncol. 2016;17(4):425-439.

[Product information] IBRANCE Capsules 75 mg, 100 mg, 125 mg [Active ingredient] Palbociclib [Indications] IBRANCE is indicated for the treatment of hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer in combination with: • an aromatase inhibitor as initial endocrine based therapy in post-menopausal women, or • fulvestrant in women with disease progression following endocrine therapy. [Dosage and administration] The recommended dose of IBRANCE is a 125 mg capsule taken orally once daily for 21 consecutive days followed by 7 days off treatment to comprise a complete cycle of 28 days. IBRANCE should be taken with food. Administer the recommended dose of an aromatase inhibitor when given with IBRANCE. (Please refer to the registered information of the aromatase inhibitor being used). When given with IBRANCE, the recommended dose of fulvestrant is 500 mg administered on Days 1, 15, 29, and once monthly thereafter. (Please refer to the registered information of fulvestrant). Patients should be encouraged to take their dose of IBRANCE at approximately the same time each day. If the patient vomits or misses a dose, an additional dose should not be taken. The next prescribed dose should be taken at the usual time. IBRANCE capsules should be swallowed whole (do not chew, crush or open them prior to swallowing). Capsules should not be ingested if they are broken, cracked, or otherwise not intact. Pre/perimenopausal women treated with the combination IBRANCE plus endocrine therapy should be treated with luteinizing hormone-releasing hormone (LHRH) agonists according to local clinical practice standards. [Precautions for use] 1. Warnings 1) Neutropenia: Decreased neutrophil counts have been observed in clinical studies with IBRANCE. Monitor complete blood counts prior to the start of IBRANCE therapy and at the beginning of each cycle, as well as on Day 15 of the first 2 cycles, and as clinically indicated. Dosing interruption, dose reduction or delay in starting treatment cycles is recommended for patients who develop Grade 3 or 4 neutropenia. Physicians should inform patients to promptly report any episodes of fever. 2) Embryo-fetal Toxicity: Based on findings from animal studies and its mechanism of action, IBRANCE can cause fetal harm when administered to a pregnant woman. In animal reproduction studies, administration of palbociclib to pregnant rats and rabbits during organogenesis resulted in embryo-fetal toxicity at maternal exposures that were ≥ 4 times the human clinical exposure based on area under the curve (AUC). Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with IBRANCE and for at least 3 weeks after the last dose. 2. Contraindications 1) This medicinal product contains lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp-lactase deficiency or glucose-galactose malabsorption should not take this medicine. [Latest HA approved date] 07 Nov 2018 ※ Please refer to latest product information for detailed information and you can find latest product information on Pfizer website(www.pfizer.co.kr).

Pfizer Oncology

IBRANCE® palbociclib

PP-IBR-KOR-0433-15Mar2021

LEADING THE WAY IN THE TREATMENT OF HR+ HER2- MBC: PALBOCICLIB & CDK4/6 INHIBITORS IN CLINICAL PRACTICE

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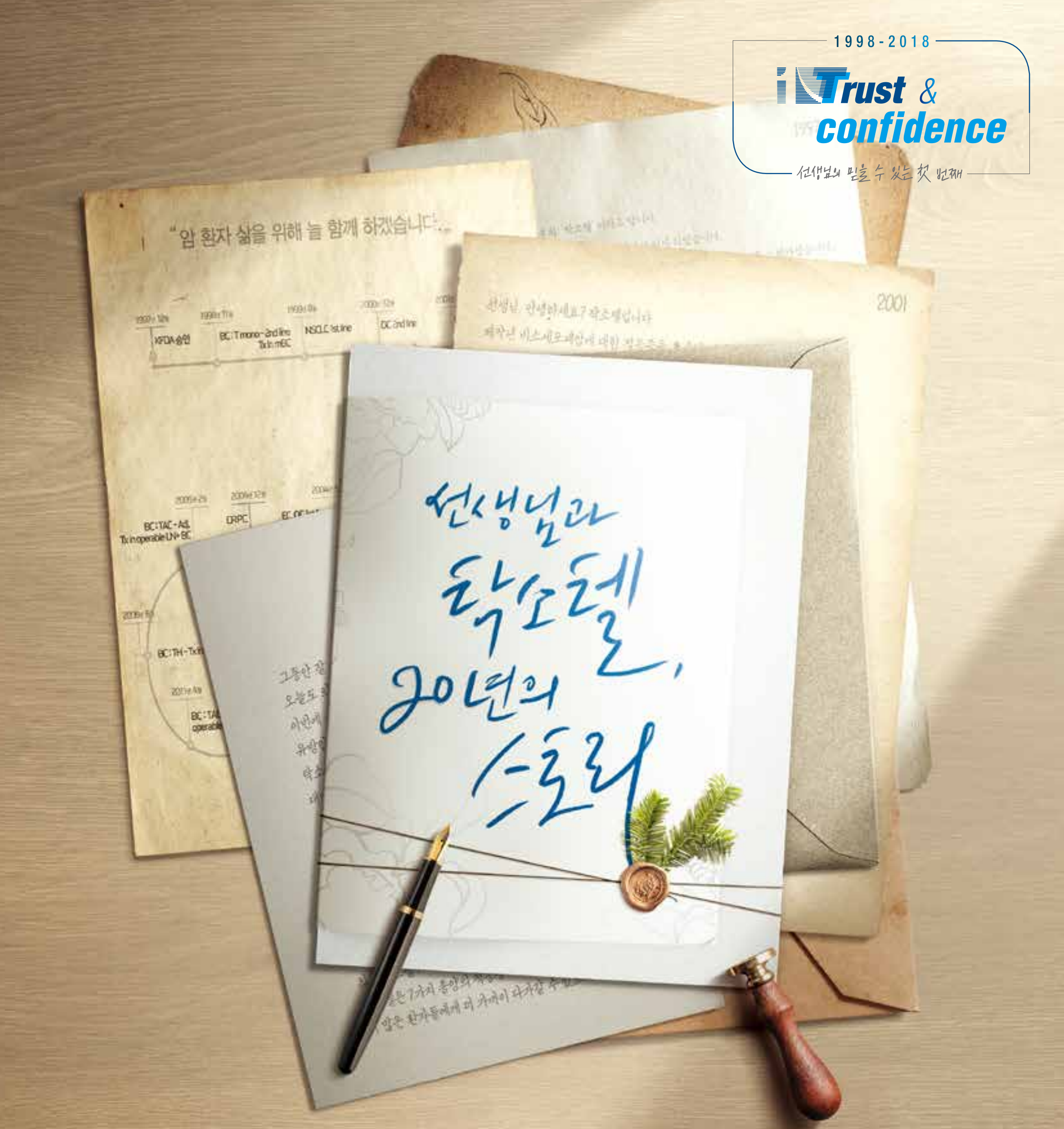
Hormone receptor positive (HR+) breast cancer represents the most common subtype of breast cancer. The goal of treatment for metastatic disease is to help patients live for as long as possible with the best quality of life. Although sequential hormone therapy can provide disease control for metastatic disease, resistance to hormone therapy develops over time, resulting in the need for treatment with chemotherapy. Considerable research has identified pathways of endocrine resistance, including dysregulation of the cell cycle, activating mutations of PIK3CA and alternations in the PIK3CA pathways, loss of estrogen receptor expression or mutations in the estrogen receptor itself, and upregulation of alternate growth factor receptor signaling pathways, as well as others. There is considerable interest in improving response and delaying resistance to endocrine therapy by targeting these pathways in combination with standard endocrine therapy.

Everolimus was the first targeted therapy to be approved as treatment for progressive hormone receptor positive disease in combination with exemestane. Although therapy was initially complicated by significant stomatitis, this was eventually controlled by use of a prophylactic steroid mouthwash. Nonetheless, treatment was still complicated by fatigue, hyperglycemia, and rare cases of pneumonitis and is used to treat disease already progressing on first- or second-line hormone therapy.

Subsequently, preclinical studies identified potent and selective inhibition of the cyclin dependent kinases 4 and 6 with palbociclib as an effective mechanism of suppression growth of endocrine responsive cell lines; this and subsequent extensive clinical data has revolutionalized the treatment of hormone receptor metastatic breast cancer. CDK4/6 inhibitors block the kinase mediated phosphorylation and therefore inactivation of the tumor suppression gene Rb, preventing dysregulated proliferation mediated by upregulated cyclin D which in turn activates CDK4/6 enzymatic activity. Based on encouraging data from both phase I and II studies in combination with endocrine therapy, several phase III trials were launched. Two additional potent CDK4/6 inhibitors also demonstrated significant activity and have also undergone testing in definitive phase III trials. Palbociclib and ribociclib are dosed daily for 3 weeks, followed by one week off to allow bone marrow recovery before restarting the 28-day cycle. Abemaciclib is dosed daily. Phase III trials in the first-line metastatic setting in combination with nonsteroidal aromatase inhibitors or fulvestrant, as well as in the second or greater line setting in combination with fulvestrant have demonstrated almost doubling of progression free survival, even in patients with visceral disease and with short disease-free intervals. Activity has been shown regardless of menopausal status, and abemaciclib has been demonstrated to cross the blood brain barrier with some degree of activity in CNS disease.

Aside from marked clinical activity, and delayed deterioration or improvement in quality of life, in general these agents are well-tolerated, with little in the way of serious toxicity. The most common toxicity from palbociclib and ribociclib is neutropenia without an increase in febrile neutropenia, and with abemaciclib the most common toxicity is diarrhea. Fagigue is also a common side effect. Ribociclib has been associated with rare prolongation of the QT interval and occasional elevation in liver enzymes; both must be monitored early in treatment.

With the marked clinical efficacy and tolerability of CDK4/6 inhibitors, there has been tremendous interest in moving treatment into the early stage setting to prevent recurrence, and in sequential or additional combinatons to improve efficacy. Over 15,000 women will be randomized in early stage clinical trials, and 3 of 4 trials have already completed accrual. Ongoing studies in the metastatic setting include novel combinations with immunotherapy or PIK3CA inhibitors, continuing CDK 4/6 inhibition through progression, and combinations in HER2 positive disease based on preclinical efficacy.



탁소텔® 1-바이알주 (도세탁셀수화물)

[원료약품 및 그 분량] 이 약 본액1mL중 주성분 도세탁셀수화물(별규) 21.34mg (도세탁셀무수물로서 20.0mg), 첨가제 폴리소르베이트80(별규), 무수에탄올(EP) [효능효과] 1. 유방암 • 국소적으로 진행된 또는 전이성 유방암 1) 독소루비신과 병용하여 국소적으로 진행된 또는 전이된 유방암의 1차 치료 2) HER2(Human Epidermal growth factor Receptor 2 protein)가 과발현(IHC 3+ 또는 FISH 양성)되고 화학요법 치료를 받은 경험이 없는 전이성 유방암에 트라스투주맙과 병용요법3) 이전의 화학요법에 실패한 국소적으로 진행된 유방암 또는 전이성 유방암 4) 카페시타빈과 병용하여 Anthracycline계 약물을 포함한 화학요법에 실패한 국소적으로 진행된 유방암 또는 전이성 유방암 • 수술 후 보조요법 – 독소루비신과 시클로포스파미드와 병용하여 다음 환자의 수술 후 보조요법 (TAC regimen) 〈림프절 양성의 수술 가능한 유방암환자, 림프절 음성의 수술 가능한 유방암환자 (고위험인자가 하나 이상 있는 환자(종양크기〉2cm, 연령〈35세, 호르몬수용체음성, 종양분화도2~3))〉 – 독소루비신과 시클로포스파미드 사용 후, 트라스투주맙과 병용하여, HER2가 과발현된 수술 가능한 유방암 환자의 수술 후 보조요법 (AC-TH regimen) – 카보플라틴과 트라스투주맙과 병용하여, HER2가 과발현된 수술 가능한 유방암 환자의 수술 후 보조요법 (TCH regimen) – 시클로포스파미드와 병용하여 수술가능한 유방암 환자의 수술 후 보조요법 (1cm≤원발종양크기〈7cm) (TC regimen) 2. 비소세포폐암 : 백금화학요법제로 치료효과를 얻지 못한 환자들을 포함한 국소적으로 진행된 비소세포폐암 또는 전이성 비소세포폐암 3. 전립샘암 : 프레드니솔론과 병용하여 안드로겐 비의존성(호르몬불응성) 전이성 전립샘암 4. 난소암 : 카보플라틴과 병용하는 1차요법제로서 진행된 또는 전이된 상피성 난소암 5. 두경부암 : 시스플라틴 및 플루오로우라실과 병용하여 국소 진행성 두경부 편평세포암의 유도화학요법 6. 위암 1) 진행성 및 전이성 또는 국소재발성 위암의 단독용법 2) 시스플라틴 및 플루오로우라실과 병용하여 전이성 또는 국소재발성 위암의 1차 치료 7. 식도암 : 진행성 또는 재발성 식도 편평세포암 [용법용량] 1. 유방암 • 국소적으로 진행된 또는 전이성 유방암 1) 유방암에 대한 일차적 요법에서 독소루비신(50 mg/m²)과 병용시 도세탁셀 75 mg/m²을 투여. 2) 화학요법 치료를 받은 적이 없는 HER2 과발현 전이성 유방암에 트라스투주맙과 병용요법제로 사용하는 경우, 도세탁셀 100 mg/m²를 매 3주마다 60분에 걸쳐 점적정주. 트라스투주맙 첫 투여 다음날 도세탁셀 투여를 시작할 수 있고, 이전 투여한 트라스투주맙의 내약성이 좋았다면 트라스투주맙 투여 직후 도세탁셀 투여를 시작할 수도 있다. * 트라스투주맙은 초기용량으로 체중 kg 당 4mg을 90분에 걸쳐 점적 정주한 후 다음 주부터는 매주 체중 kg 당 2mg을 투여(트라스투주맙 제품의 용법,용량 참조) 3) 이전 화학요법에 실패한 유방암에서는 도세탁셀 75~100mg/m²을 매 3주마다 1시간 동안 정맥 투여. 4) 카페시타빈과 병용하여 Anthracycline계 약물을 포함한 화학요법에 실패한 국소적으로 진행된 유방암 또는 전이성 유방암에서는 3주마다 도세탁셀을 75 mg/m² 투여하면서 카페시타빈을 2주간 1일 2회, 1회 1,250 mg/m² 투여하고(식후 30분 이내) 1주간 휴약하는 것(3주를 주기로 함)이 권장된다. 카페시타빈 용량은 카페시타빈의 제품설명서를 참조하여 체표면적에 따라 결정. • 수술 후 보조요법 1) TAC regimen: 매 3주마다 독소루비신 50 mg/m² 과 시클로포스파미드 500 mg/m² 투여 1시간 후 도세탁셀 75 mg/m²를 6주기 투여. 혈액학적 독성 위험을 줄이기 위해서는 예방적 G-CSF 투여가능 (용량조절항 참조). 2) AC-TH regimen : • AC: 1~4 주기(3주/1주기)동안 매 3주마다, 독소루비신 (A) 60 mg/m² 투여하고, 시클로포스파미드 (C) 600 mg/m² 투여. • TH : 5~8 주기(3주/1주기)동안 매 3주마다 도세탁셀 (T) 100mg/m²를 1시간 동안 투여하고, 트라스투주맙 (H)은 매주 아래와 같은 일정으로 투여한다. • 트라스투주맙 : 5주기의 1일차에 초기부하용량으로 트라스투주맙 4 mg/kg을 90분간 투여. 이후 1주마다 유지용량으로 2mg/kg를 30분간 투여.(5주기의 8일차부터, 8주기까지) • 도세탁셀: 5주기의 2일차에 투여. 6~8주기에는 1일차에 투여. 보조화학요법이 완료된 후에 트라스투주맙 6mg/kg를 단독요법으로 3주마다 30분간 투여. 트라스투주맙은 총 1년간 투여. 3) TCH regimen(1~6주기) • 도세탁셀 및 카보플라틴: 3주마다 도세탁셀 (T) 75 mg/m²를 1시간 동안 투여 및 카보플라틴 (C) AUC 6m g/mL/min를 30~60분간 투여하며, 1주기에는 2일차에 투여, 2~6주기에는 1일차에 투여. • 트라스투주맙: 1일차에 초기부하용량으로 트라스투주맙 4 mg/kg을 90분간 투여. 이후 1주마다 유지용량으로 2 mg/kg를 30분간 투여. • 보조화학요법이 완료된 후에 트라스투주맙 6mg/kg를 3주마다 30분간 투여. 트라스투주맙은 총 1년간 투여. 4) TC regimen: 3주를 1주기로 하여 4주기 동안, 매 주기의 1일차에 도세탁셀 75mg/m²을 1시간 이상 주입하고, 시클로포스파미드 600mg/m²을 30~60분간 정맥 주입. 도세탁셀 투여 1일 전, 전처치로 경구용 덱사메타손 8mg, 1일 2회 투여를 시작하며, 총 5회 동안 계속 복용. 2. 비소세포 폐암 : 도세탁셀 75 mg/m²을 매 3주마다 1시간동안 정맥 주사한다. 백금 유도체와 복합화학요법으로 치료시 최대 75 mg/m²으로 정맥 투여한다. 3. 전립샘암 : 프레드니솔론과 병용시 도세탁셀 75 mg/m²을 매 3주마다 1시간동안 정맥주사한다. 프레드니솔론은 1일 2회, 1회 5mg을 지속적으로 경구투여한다. 4. 난소암 : 진행된 또는 전이된 상피성 난소암에 대한 일차적 요법으로는 카보플라틴과 병용하여 3주마다 도세탁셀 75 mg/m² 1시간동안 정맥 주사 후 즉시 카보플라틴 AUC 6.0 mg/ml.min 을 30~60분간 정맥주사한다. 5. 두 • 경부암 1) 방사선요법 전의 유도화학요법: 75mg/m²을 1시간동안 정맥주사한 후, 시스플라틴 75mg/m²을 1시간 이상 정맥주사한다 (제 1일). 그 후 플루오로우라실을 750mg/m²/day로 5일동안 연속 정맥주사한다. 3주를 1주기로 하여 4주기 동안 투여한다. 화학요법을 받은 후 방사선 요법을 받도록 한다. 2)화학방사선요법 전의 유도화학요법: 75mg/m²을 1시간동안 정맥주사한 후, 시스플라틴 100mg/m²을 30분~3시간 동안 정맥주사한다 (제 1일). 그 후 플루오로우라실을 1,000mg/m²/day로 연속 정맥주사한다 (제1~4일). 3주를 1주기로 하여 3주기 동안 투여한다. 화학요법을 받은 후 방사선 요법을 받도록 한다. 6. 위암 1) 단독요법: 75 mg/m² 매 3주마다 1시간동안 정맥 주사한다. 2) 시스플라틴 및 플루오로우라실과 병용투여 : 75 mg/m²을 1시간 동안 정맥주사 후, 시스플라틴 75mg/m²을 1~3시간 동안 정맥주사한다. 시스플라틴 정맥주사가 끝난 후부터 플루오로우라실을 750 mg/m²/day 용량으로 5일동안 연속주입한다 (1주기). 3주마다 같은 방법으로 투여한다. 7. 식도암 : 상용량은 성인에게 1일 1회 도세탁셀 70 mg/m²을 1시간 이상 3~4주 간격으로 정맥 주사하며, 환자의 상태에 따라 적절히 감량한다. 〈전치료 〉 이 약 투약 시 발현될 수 있는 중증의 과민반응 및 체액저류를 최소화 하기위해 전치료를 해야 하며 전치료로는 금기사항이 아닌 한, 이 약 투약 하루 전부터 3일 동안 경구용 코르티코스테로이드(덱사메타손의 경우 매일 16mg (예:8mg씩 2회)을 투여)를 투여한다. 혈액학적 독성의 위험을 완화하기 위하여 예방적으로 G-CSF를 투여할 수 있다. 〈용량조절〉 이 약 투여시 다른 화학요법제와 마찬가지로 호중구수를 면밀히 측정해야 하며, 필요시 용량조절을 하여야 한다. [사용상의 주의사항] 경고 1) 간기능의 이상이 있고, 고용량을 받는 경우, 이전 백금을 기본으로 한 치료경험이 있는 비소세포폐암 환자 중 단독으로 100mg/m²을 투여 받는 경우 이 약과 관련된 사망 건수가 증가하였다. 2) 간장애 환자 : 이 약 100mg/m²을 단독으로 투여받은 환자 중에서 혈청 아미노전달효소가 ULN보다 1.5배 이상 높고, 혈청 ALP가 ULN보다 2.5배 이상 높은 경우에는 중증의 이상반응이 나타날 위험이 높다. 3) 호중구수가 1,500/mm³ 미만인 경우 이 약을 투여해서는 안 된다. 4) 이 약 투여시 환자가 과민반응을 나타내는지, 특히 첫번째 또는 두번째 투여시, 주의깊게 관찰해야 한다. 5) 3일 동안 덱사메타손 전치료를 받았음에도 불구하고 중증의 체액저류가 6.5% 발생하였다. 견디기 힘든 말초부종, 전신부종, 긴급한 배출이 필요한 흉막삼출, 심낭삼출, 호흡곤란, 복부팽창(복수에 의한)과 같은 이상반응이 발생하였다. 금기 1) 이 약 및 이 약의 구성성분, 폴리소르베이트 80에 대해 과민반응의 병력이 있는 환자 2) 호중구수가 1,500 /mm³ 미만인 환자 3) 임부, 가임부 및 수유부 4) 중증 간기능장애 환자 5) 병용투여시, 병용약물에 금기인 환자(중증 신기능장애 환자, 파라플라틴, 백금화합물, 만니톨에 과민한 환자 등) 6) 감염증의 합병증이 있는 환자 7) 감염성 발열이 의심되는 환자 8) 중증의 골수 억제가 있는 환자 신중투여 1) 골수억제가 있는 환자 2) 간기능장애 환자 3) 신기능장애 환자 4) 간질성 폐렴 또는 폐섬유증이 있는 환자 5) 부종이 있는 환자 6) 임신할 가능성이 있는 환자(남성 및 여성) ※기타 자세한 내용은 제품설명서 또는 홈페이지를 참조하십시오. (최종문안개정년월일 : 2016.06.23)

SAKR.DOC.18.02.0235(02.21)

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TAXOTERE® (docetaxel)

UNDERSTANDING THE PSYCHOLOGICAL EFFECTS OF BREAST CANCER: NOW AND FUTURE

Jong-Heun Kim

Department of Psychiatry, National Cancer Center, Korea

Many women with breast cancer suffer psychologically during their course from the diagnosis through treatments and to survivorship or the end-of-life. Psychological effects of cancer have been most extensively studied among breast cancer patients at each stage of disease and during survivorship.

Their psychological distress may extend to become severe enough to interfere with the ability to cope with cancer. Anxiety, depression, and insomnia often occur among cancer patients. Although distress is prevalent in cancer patients, it is often under-recognized and under-treated in oncology setting. Psychological distress may have a negative effect on patients quality of life. The prevention, early detection, and proper management of distress are important for improving the quality of life during and after cancer treatment. Therefore it is necessary to develop a system for assessing and managing distress. The US National Comprehensive Cancer Network developed guidelines for distress management in 1999. Korean recommendation of distress management was published in 2009. The Korean government recently designated 8 integrated supportive care centers for survivors (ISCC-sv) in the National Cancer Center and 7 regional cancer centers. The service is provided for cancer survivors who finished the first-line anti-cancer treatment. The psychosocial care is one of the most important components in the services.

There are many benefits from distress management for cancer patients. But the reality is that less than 10% of significantly distressed patients are properly referred for psychosocial care. The goal is that all distressed patients should be properly referred for psychosocial care. The psychosocial care of breast cancer patients should be a routine part of cancer care practice. We still have a long way to go before we reach the goal.

PERJETA®
pertuzumab

Roche

Risk of recurrence,

It's more than just numbers.

The Perjeta-Herceptin combination therapy demonstrated **23% of relapse risk reduction** in LN+, HER2+ eBC patients.[1]

LN, lymph node. eBC, early breast cancer

Study design. APHINITY was conducted as a prospective, two-group, randomized, multicentec multinational, double-blind, placebo-controlled trial. A total of 4805 patients with node-positive or high-risk node-negative HER2-positive, operable breast cancer were randomly assigned to receive chemotherapy and trastuzumab plus either pertuzumab (2400 patients) or placebo (2405 patients). The primary end point, invasive-disease-free survival, was defined as the time from randomization until the date of the first occurrence of one of the following events (hereafter referred to as invasive-disease events): recurrence of ipsilateral invasive breast tumor, recurrence of ipsilateral locoregional invasive disease, a distant disease recurrence, contralateral invasive breast cancer, or death from any cause.

Reference. 1. von Minckwitz G, Procter M, de Azambuja E, et al., for the APHINITY Steering Committee and Investigators. Adjuvant pertuzumab and trastuzumab in early HER2-positive breast cancer. N Engl J Med. 2017;377:122-131.

PERJETA inj. (Pertuzumab) prescription medicine **[INDICATIONS]** • Metastatic breast cancer: Perjeta is indicated for use in combination with trastuzumab and docetaxel in adult patients with HER2-positive metastatic or locally recurrent unresectable breast cancer, who have not received previous anti-HER2 therapy or chemotherapy for their metastatic disease. • Early breast cancer: Perjeta is indicated for use in combination with trastuzumab and chemotherapy in: • the neoadjuvant treatment of adult patients with HER2-positive, locally advanced, inflammatory, or early stage breast cancer (greater than 2cm)• the adjuvant treatment of adult patients with HER2-positive early breast cancer at high risk of recurrence. **[DOSAGE AND ADMINISTRATION]** Perjeta is subject to restricted medical prescription and therapy should only be initiated under the supervision of a physician experienced in the administration of anti-cancer agents. Perjeta should be administered by a healthcare professional prepared to manage anaphylaxis and in an environment where full resuscitation facilities are immediately available. Patients treated with Perjeta must have HER2-positive tumour status, defined as a score of 3+ by immunohistochemistry (IHC) and/or a ratio of ≥ 2.0 by in situ hybridisation (ISH) assessed by a validated test. • Metastatic and early breast cancer: The recommended initial loading dose of pertuzumab is 840 mg administered as a 60 minute intravenous infusion, followed every 3 weeks thereafter by a maintenance dose of 420 mg administered over a period of 30 to 60 minutes. When administered with Perjeta the recommendation is to follow a 3-weekly schedule for trastuzumab administered as either • an IV infusion with an initial loading dose of trastuzumab 8 mg/kg body weight followed every 3 weeks thereafter by a maintenance dose of 6 mg/kg body weight or • a fixed subcutaneous dose of trastuzumab by injection (600 mg) every 3 weeks irrespective of the patient's body weight. In patients receiving a taxane, Perjeta and trastuzumab should be administered prior to the taxane. When administered with pertuzumab the recommended initial dose of docetaxel is 75 mg/m², administered thereafter on a 3 weekly schedule. In patients receiving an anthracycline-based regimen, Perjeta and trastuzumab should be administered following completion of the entire anthracycline regimen. • Metastatic breast cancer: Perjeta should be administered in combination with trastuzumab and docetaxel. Treatment with Perjeta and trastuzumab may continue until disease progression or unmanageable toxicity even if treatment with docetaxel is discontinued. • Early breast cancer: In the neoadjuvant setting, Perjeta should be administered for 3 to 6 cycles in combination with trastuzumab and chemotherapy, as part of a complete treatment regimen for early breast cancer Four preoperative cycles of Perjeta in combination with trastuzumab and docetaxel followed by 3 postoperative cycles of fluorouracil, epirubicin, and cyclophosphamide (FEC). Three or four preoperative cycles of FEC alone followed by 3 or 4 preoperative cycles of Perjeta in combination with docetaxel and trastuzumab . Six preoperative cycles of Perjeta in combination with docetaxel, carboplatin, and trastuzumab (TCH) (docetaxel at docetaxel above 75 mg/m² is not recommended). Four preoperative cycles of ddAC/dose dense doxorubicin and cyclophosphamide followed by 4 preoperative cycles of Perjeta in combination with docetaxel and trastuzumab. Following surgery patients should continue to receive trastuzumab to complete 1 year of treatment (max 18cycle). In the adjuvant setting, Perjeta should be administered in combination with trastuzumab for a total of one year (up to 18 cycles or until disease recurrence, or unmanageable toxicity, whichever occurs first) as part of a complete regimen for early breast cancer and regardless of the timing of surgery. Treatment should include standard anthracycline- and/or taxane-based chemotherapy. Perjeta and trastuzumab should start on Day 1 of the first taxane-containing cycle and should continue even if chemotherapy is discontinued. • For delayed or missed doses, if the time between two sequential infusions is less than 6 weeks, the 420 mg dose of PERJETA should be administered. Do not wait until the next planned dose. 6mg/kg of trastuzumab intravenous infusion should be administered as soon as possible without regard to the next planned dose. Trastuzumab 600mg SC should be administered as soon as possible without regard to the next planned dose. If the time between two sequential infusions is equal or more than 6 weeks, the loading dose of 840 mg Perjeta IV should be re-administered as a 60 minute infusion, followed by a maintenance dose of 420 mg IV administered over a period of 30 to 60 minutes every 3 weeks thereafter. The loading dose of 8 mg/kg of Herceptin IV should be re-administered over approximately 90 minutes, followed by a maintenance dose of 6 mg/kg IV administered over a period of 30 or 90 minutes every 3 weeks thereafter • Dose modification: If trastuzumab treatment is discontinued, treatment with Perjeta should be discontinued. Dose reductions are not recommended for Perjeta or trastuzumab. For details regarding trastuzumab, please refer to the product information. Patients may continue therapy during periods of reversible chemotherapy-induced myelosuppression but they should be monitored carefully for complications of neutropenia during this time. For docetaxel and other chemotherapy dose modifications, see relevant product information. • Hypersensitivity reactions/anaphylaxis: Perjeta must be permanently discontinued in case of severe hypersensitivity. • Left Ventricular dysfunction: The recommendations on dose modifications in the event of LVEF dysfunction refer to 1. Warnings. • Infusion-Related Reactions: The infusion rate of PERJETA may be slowed or interrupted if the patient develops an infusion-related reaction. The infusion may be resumed when symptoms abate. Treatment including oxygen, beta agonists, antihistamines, rapid iv fluids and antipyretics may also help alleviate symptoms. Perjeta must be permanently discontinued in case of NCI-CTCAE Grade 4 hypersensitivity reactionsdyspnea), bronchospasm or acute respiratory distress syndrome. • Method of administration: It should not be administered as an intravenous push or bolus. For the initial dose, the recommended infusion period is 60 minutes. If the first infusion is well tolerated, subsequent infusions may be administered over a period of 30 minutes to 60 minutes. **[SPECIAL WARNINGS AND PRECAUTIONS FOR USE]** *Warnings 1) Left ventricular dysfunction • Decreases in LVEF have been reported with medicinal products that block HER2 activity, including Perjeta. Patients who have received prior anthracyclines or prior radiotherapy to the chest area may be at higher risk of LVEF declines. The majority of cases of symptomatic heart failure reported in the adjuvant setting were in patients who received anthracycline based chemotherapy. • Perjeta has not been studied in patients with a pre-treatment LVEF value of < 50%, a prior history of congestive heart failure (CHF), LVEF declines to < 50% during prior trastuzumab adjuvant therapy, or conditions that could impair left ventricular function such as uncontrolled hypertension, recent myocardial infarction, serious cardiac arrhythmia requiring treatment or a cumulative prior anthracycline exposure to > 360 mg/m² of doxorubicin or its equivalent. • Assess LVEF prior to initiation of Perjeta and at regular intervals during treatment with Perjeta (e.g. once during neoadjuvant treatment and every 12 weeks in the adjuvant or metastatic setting) to ensure that LVEF is within normal limits. Patients with metastatic breast cancer should have a pre-treatment left ventricular ejection fraction (LVEF) of ≥ 50%. Perjeta and trastuzumab should be withheld for at least 3 weeks for: • a drop in LVEF to less than 40% • a LVEF of 40%-45% associated with a fall of ≥ 10% points below pre-treatment values. Perjeta and trastuzumab may be resumed if the LVEF has recovered to > 45%, or to 40-45% associated with a difference of < 10% points below pre-treatment values. Patients with early breast cancer should have a pre-treatment LVEF of ≥ 55% (≥ 50% after completion of the anthracycline component of chemotherapy, if given). Perjeta and trastuzumab should be withheld for at least 3 weeks for: • a drop in LVEF to less than 50% associated with a fall of ≥ 10% points below pre-treatment values. Perjeta and trastuzumab may be resumed if the LVEF has recovered to ≥50% or to a difference of < 10% points below pre-treatment values. If the LVEF has declined as indicated above and has not improved, or has declined further at the subsequent assessment, discontinuation of Perjeta and trastuzumab should be strongly considered, unless the benefits for the individual patient are deemed to outweigh the risks. 2) Infusion reactions • Perjeta has been associated with infusion reactions including fatal outcomes. Close observation of the patient during and for 60 minutes after the first infusion and during and for 30 minutes after subsequent infusions of Perjeta is recommended. If a significant infusion reaction occurs, the infusion should be slowed down or interrupted and appropriate medical therapies should be administered. Patients should be evaluated and carefully monitored until complete resolution of signs and symptoms. Permanent discontinuation should be considered in patients with severe infusion reactions. This clinical assessment should be based on the severity of the preceding reaction and response to administered treatment for the adverse reaction. 3) Febrile neutropenia • In the CLEOPATRA trial in metastatic breast cancer, Patients treated with Perjeta, trastuzumab and docetaxel are at increased risk of febrile neutropenia compared with patients treated with placebo, trastuzumab and docetaxel, especially during the first 3 cycles of treatment. nadir neutrophil counts were similar in Perjeta-treated and placebo-treated patients. The higher incidence of febrile neutropenia in Perjeta-treated patients was associated with the higher incidence of mucositis and diarrhoea in these patients. Symptomatic treatment for mucositis and diarrhoea should be considered. No events of febrile neutropenia were reported after cessation of docetaxel. 4) Hypersensitivity reactions/anaphylaxis. • Patients should be observed closely for hypersensitivity reactions. Severe hypersensitivity, including anaphylaxis and fatal outcomes, has been observed in clinical trials with Perjeta. Medicinal products to treat such reactions, as well as emergency equipment, should be available for immediate use. Perjeta is contraindicated in patients with known hypersensitivity to pertuzumab or to any of its excipients. *** Precautions for use** 1. Fertility, pregnancy and lactation 1) Women of childbearing potential and her partner should use effective contraception while receiving Perjeta and for 7 months following the last dose of pertuzumab. 2) There is limited amount of data from the use of pertuzumab in pregnant women. Studies in animals have shown reproductive toxicity. Administration of pertuzumab to pregnant cynomolgus monkeys during the period of organogenesis resulted in oligohydramnios, delayed fetal kidney development, and embryo-fetal death. 3) Perjeta is not recommended during pregnancy and in women of childbearing potential not using contraception. Considering these animal studies and the mechanism of action of Perjeta, it is believed that this drug may cause harm to the fetus when administered to pregnant women. The safe use of Perjeta during labor and delivery has not been established. 4) Because human IgG is secreted in human milk and the potential for absorption and harm to the infant is unknown, a decision should be made to discontinue breast-feeding or to discontinue treatment, taking into account the benefit of breast-feeding for the child and the benefit of Perjeta therapy for the woman. 5) No specific fertility studies in animals have been performed to evaluate the effect of pertuzumab. Only very limited data are available from repeat-dose toxicity studies with respect to the risk for adverse reactions on the male reproductive system. No adverse reactions were observed in sexually mature female cynomolgus monkeys exposed to pertuzumab. Perjeta® 2018-11-22-1.0

- Please report to Roche Korea (02-3451-3600) straight away, if you get pregnant during treatment with Perjeta or during the 7 months after stopping treatment.
- Additional information may be requested from pregnancy to fyr after birth for your infant. This information will help Roche to better understand the safety of Perjeta and to provide appropriate information to health authorities, health care professionals and patients.
- If you want to get detailed product information and report adverse events, please contact Roche Korea (02-3451-3600).
- You can find latest product information on the Roche Korea website (www.roche.co.kr).

Roche Korea, 17F, 411, Seocho-daero, Seocho-gu, Seoul, Republic of Korea
TEL: 02-3451-3600 FAX: 02-561-7200

MC20190314-002

RECENT STRATEGIES TO REACH THE BEST CLINICAL OUTCOMES IN HER2-POSITIVE EARLY BREAST CANCER PATIENTS

In Hae Park

National Cancer Center, Korea

Human epidermal growth factor receptor 2 (HER2) is overexpressed in 20-25% of breast cancer and shows an aggressive clinical course and a poor patient outcome. Although the introduction of anti-HER2 therapies, trastuzumab to the treatment of patients with HER2 positive breast cancer has led to significant improvement of the survival outcomes, long term follow-up data indicated that 15-24% of patients still experience disease recurrence during their life time. Therefore, most research has been focusing on the enhancing clinical outcomes by adding new novel drugs on the standard therapy. Currently, many novel anti-HER2 drugs with standard treatment are achieving statistically significant improvement of clinical outcomes. Based on the pCR results from the NeoSphere and TRYPAENA trials, neoadjuvant pertuzumab in combination with trastuzumab got FAD approval for operable HER2 positive breast cancer. In addition, through phase III APHINITY trial, pertuzumab also gained the approval for adjuvant treatment as the combination with trastuzumab. Ado-trastuzumab emtansine (T-DM1), antibody drug conjugate also showed its impressive role at adjuvant setting for patients who have residual disease after neoadjuvant therapy though the KATHERINE trial. A potent irreversible pan-HER2 tyrosine kinase inhibitor, Neratinib demonstrated the clinical benefit in disease free survival rate at 5 years compared to placebo when administered one more year after the completion of one-year adjuvant treatment of trastuzumab, especially for hormone receptor positive and HER2 amplified breast cancer. As noted, continuous improvements of clinical outcomes have been achieved through intense therapeutic escalating strategies. However, biologic heterogeneity within HER2 positive tumors can cause different treatment sensitivities and survival outcomes to those novel treatment. Therefore, the optimization of current available drugs should be done in parallel by identifying adequate biomarkers of response and resistance. It would be also helpful in avoiding unnecessary treatments and their related toxicities in select patients.

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타이커브(Lapatinib)

Tykerb® (lapatinib)

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EGF100151 Study:
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Study 010:
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페마라(Letrozole)

Femara® (letrozole)

2001년 12월 승인[7]

BIG-1-98:
폐경 후, Early breast cancer 환자에게 효능과 안전성 입증[8]

HR= Hormone Receptor, **HER2-**= Human Epidermal growth factor Receptor 2 negative, **HER2+**= Human Epidermal growth factor Receptor 2 positive, **ABC**= Advanced Breast Cancer, **MBC**= Metastatic Breast Cancer

References 1. 아피니토 허가정보, 식품의약품 안전처 의약도서관 http://drug.mfds.go.kr/html/index.jsp#n 2. José Baselga et al. N Engl J Med 2011;1-10 3. 타이커브 허가정보, 식품의약품 안전처 의약도서관 http://drug.mfds.go.kr/html/index.jsp#n 4. Charles E. Geyer et al. N Engl J Med 2006;355:2733-43 5. 조메타허가정보, 식품의약품 안전처 의약도서관 http://drug.mfds.go.kr/html/index.jsp#n 6. Lee S, Rosen, et al. The Cancer Journal 2001;7(5):377-87 7. 페마라 허가정보, 식품의약품 안전처 의약도서관 http://drug.mfds.go.kr/html/index.jsp#n 8. Meredith M Regan et al. Lancet Oncol 2011;12:1101-08

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CONSENSUS IN ER+ HER2- ASIAN PREMENOPAUSAL BREAST CANCER

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The ratio of premenopausal breast cancer is higher in Asian than non-Asian population among all breast cancer. But the ratio of premenopausal breast cancer has been decreased in Asian population because of increasing the incidence of postmenopausal breast cancer based on life style changing. The distribution of subtype (luminal, HER2, TN subtypes) may be similar between pre and postmenopausal population. We should not consider the change about chemotherapy and targeting therapy for early breast cancer (EBC) and metastatic breast cancer (MBC) according to menopausal status. The regimen of chemotherapy and targeting therapy would be determined based on pathological and clinical factors excluding menopausal status. However endocrine therapy is different according to menopausal status for EBC and MBC with ER+ HER2-.

In Japan, Tamoxifen (TAM) alone or combined therapy with TAM and LH-RH analogue (LH-RHa) as adjuvant endocrine therapy are usually used for premenopausal EBC with ER+ HER2-. The frequency of TAM alone and TAM plus LH-RHa has moved by era according to new evidence. Currently we recommend the TAM and LH-RHa for premenopausal EBC with high risk, ER+ HER2- as adjuvant endocrine therapy after chemotherapy based on SOFT and TEXT data. Contrary we recommend TAM alone for EBC with low risk population. Unfortunately aromatase inhibitor (AI) plus LH-RHa is not usually used in Japan because of heterogynous situation about covered by insurance among Japan.

For MBC, TAM+LH-RHa and AI+LH-RHa are standard treatment as 1st line and 2nd line endocrine therapy, respectively during long time. Currently Paloma-2,3 and Monarch 2 and 3 using CDK4/6 inhibitors were published and Fulvestrant+LH-RHa+CDK4/6 inhibitor may be one of option as 2nd line after for MBC with ER+ HER2-. In Japan, this triplet regimen has been approved and frequency of this regimen has been increased.

I consider the system of reimbursement is different among Asian countries. The building of standard treatment based on consensus for EBC and MBC with ER+ HER2- among Asian countries is very tough. However the consensus guideline of treatment strategy should be made among Asian countries based on hard discussion among expert panels.

FASLODEX™
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Faslodex,
with extended therapeutic indications.

Monotherapy

This medicine is indicated for the treatment of hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer in postmenopausal women.

Combination therapy

This medicine is indicated in combination with palbociclib for the treatment of hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer in women who have received prior endocrine therapy.

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PRODUCT INFORMATION

FASLODEX (fulvestrant)

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

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

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

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

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KR-1533 I Exp 20191201

TREATMENT OF HR+ HER2- ADVANCED BREAST CANCER: PRACTICAL IMPLICATION OF FULVESTRANT

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Fulvestrant is a selective oestrogen receptor downregulator (SERD) which was introduced to clinical practice in 2002, initially for the treatment of postmenopausal women with hormone-receptor-positive advanced breast cancer as second-line therapy after progression from aromatase inhibitors or tamoxifen. Later, fulvestrant has also been shown to be effective in patients previously untreated in the neoadjuvant and metastatic setting, alone or combination with other targeted agents. COFIRM study investigated optimal dose of fulvestrant and conformed 500 mg as standard dose with loading dose.

With the understanding of biological pathways contributing to endocrine resistance, targeted agents, such as mTORi or CDK4/6 inhibitors, were approved in combination with endocrine therapies. However, optimal sequence or choice of endocrine therapies has not been clearly defined.

Fulvestrant is a favorite combination partner with new targeted agents in HR(+), HER-2(-) breast cancer due to its unique mode of action. After the initial approval in combination with palbociclib in 2016 by US FDA, more extended applications are expected from the recent extensive studies.

Recent data from FALCON phase III study also demonstrated its efficacy and tolerability in comparison with anastrozole single therapy in the first-line setting. Although combination therapy with CDK 4/6 inhibitors are the current standard of care for this clinical setting, fulvestrant single therapy might play a role in patients with non-visceral metastasis.

In summary, fulvestrant has a unique mode of action and is active for the patients with metastatic HR(+)/HER-2(-) breast cancer, alone or in combination with targeted agents. More research is needed to identify biomarkers for accurate selection of patients likely to benefit from monotherapy or combinations.

Junior Doctors Forum

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MY JOURNEY WITH ENDOCRINE THERAPY AND FUTURE PERSPECTIVES ON YOUNG ASIAN DOCTORS

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Endocrine therapy is the oldest form of targeted therapy in cancer medicine. Oopherectomy as a treatment for metastatic breast cancer in young women was described at the end of the 19th century.

The anti-oestrogen, tamoxifen was developed in the early 1970s and revolutionised the treatment of patients with ER positive breast cancer. In metastatic disease this achieves a response rate of about 30% with a further 20% of patients having stable disease. The key question is of course why the others do not benefit and why resistance develops while ER positivity persists

Adjuvant tamoxifen for 5 years in early breast cancer has been shown to reduce the risk of recurrence by around 13% over a 15 year period and the risk of death by almost 10%.

The next major development in endocrine therapy for breast cancer were aromatase inhibitors which inhibit the synthesis of oestrogen. 3 of these, letrozole, anastrozole and exemestane, have been shown to give a small but significant improvement over tamoxifen in both advanced and early (adjuvant) breast cancer.

In recent years it has become apparent that adjuvant chemotherapy is frequently of no clinically meaningful benefit in many patients with early ER positive breast cancer, including in patients with up to 3 involved nodes, and genomic platforms including Oncotype DX and PAM50 are increasingly used to give a more accurate prognosis in the individual patient and to determine which patients do not need chemotherapy in addition to adjuvant endocrine therapy.

The latest development in endocrine therapy has been the use of CDK46 inhibitors and it has been shown that palbocicilb, ribociclib and abemaciclib all help overcome resistance to endocrine therapy and improve progression-free survival compared with endocrine therapy alone. The addition of these drugs to an AI as neoadjuvant therapy in early breast cancer supresses proliferation as measured by Ki67 more than the AI alone, and the results of adjuvant trials are awaited.

A recent discovery is that genomic mutations can contribute to resistance to endocrine therapy and may direct treatment selection. The best example is ESR1, which is very rarely mutated in early breast cancer but frequently so in metastatic disease and this is a associated with a significantly worse prognosis. To some extent the resistance to an AI conferred by this mutation can be overcome with fulvestrant or with the addition of a CDK4/6 inhibitor palbociclib.

It is likely that in the near future further mutations will lead to the development of newer and more effective targetted therapies that will further help to overcome endocrine resistance.

HOW TO GLOBALIZE THE SOCIETY YOU ARE INVOLVED IN

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The incidence of breast cancer has rapidly been increased in Asian countries including South Korea and Japan. And the strategies to conquer breast cancer are common aim in both countries at present.

Previously, breast cancer has been treated by surgery such as mastectomy with axillary dissection in the era of Halsted at the beginning of 1900. However, the importance of systemic therapy has been clarified by large-scaled randomized clinical trials in the era of Fishers between 1980 and 2000.

Nowadays, neoadjuvant chemotherapy with new agents has brought high rate of pCR (pathological Complete Remission) which shows good prognosis later on and also the potential of non-surgical approach in the future.

The new agents such as CDK4/6 inhibitors, mTOR inhibitors and immune-check point inhibitors are promising drugs for breast cancer. But the clarification of efficacy for each drugs should be efficiently confirmed by international collaborative work. Therefore, mutual understanding in English are essential. The presentation skill and discussions either just after speech or on the floor should be brushed up in the international conference such as GBCC.

To study abroad for 1 or 2 years either for research or clinical training is also useful to deepen communication skill in English.

To master EBM process in the early phase of doctoral training is another key factor for young doctors.

In daily practice, to pick up clinical questions properly during each patient is the first step for EBM. Then how to search PubMed or the other database to solve the clinical question is the second step.

Lastly, the critical appraisal is the most important skill to read the article. To modify the solution in the article is another crucial point according to each patients life style or view of values.

Don't be afraid of making mistakes. Innovation & Challenge is privilege of youth.

HOW TO GLOBALIZE YOUR CAREER: 30 YEARS EXPERIENCE FROM THE MIND TO THE GLOBAL STENT MARKET

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When I was an assistant professor at Chonbuk National University in 1987, I used esophageal tubes such as the Celestin tube and the Wilson Cook tube for palliative treatment of patients with inoperable esophageal cancer. It was very difficult to place these into a narrowed esophagus, particularly in patients who had radiation therapy, because the outer diameter of the delivery systems was 25 mm. So, the esophageal rupture rate was as high as 11%. I still, vividly, remember how difficult this was. I would toss and turn the night before the procedure, worried about rupture and failure. Helping these patients was very stressful because of the limitations of these devices.

Later that year, I read an article on endovascular self-expandable Z-stents. I was so excited, that I visited the authors at the MD Anderson Cancer Center in Houston for one month after the 1988 RSNA conference. Dr. Wright was kind enough to show me how to fashion Z-stents.

First generation of esophageal stent

In 1991, we described the first covered metallic stent placement in the human esophagus. We placed the Z-stent with two barbs in 8 patients with an unresectable malignant esophageal stricture. Although the Z-stent with two barbs had larger internal diameter than the conventional tubes, it needed a much lower profile delivery system because of the advantage of compression.

Second generation of esophageal stent

Instead of the two barbs, we made the proximal and distal part of the stent 8 mm wider than the middle part to prevent stent migration. We placed the stent in 119 patients with a malignant or a benign stricture with use of a 13 mm polyethylene tube. The esophageal perforation rate was 0%. Although it had advantages over the conventional tubes, however, the migration rate was up to 10% and needed a 13 mm stent delivery system.

Third generation of esophageal stent

We designed a polyurethane covered retrievable expandable Z-stent. To make the stents re-

movable, we attached two drawstrings to the upper inner margin of the stents. To remove the stent, we used a 13-F dilator and sheath.

Fourth, fifth, and sixth generations of esophageal stent

To improve the flexibility of the stent and to decrease the size of stent delivery system, we decided to construct a stent using a nitinol wire. After trial and error, we designed three more generations of retrievable expandable nitinol stents which needed a 6 mm delivery system. The forth generation was somewhat rigid and needed ice water to place the stent because temperature-dependent shape memory was used for fabrication of the stent. The fifth and sixth generations were flexible and did not need ice water because non-temperature-dependent superelasticity was used for fabrication of the stent.

Seventh generation of esophageal stent

We found that 3% of removed polyurethane covered stents showed partial disruption of covering membrane. To solve the problem, we designed 7th generation stent. We covered the stent with PTFE membrane sutured to both ends of the stent. We reported our experience with the 7th generation stent in 270 patients with a malignant esophageal stricture in 2008. However, separation of the PTFE membrane from the nitinol wire occurred in 0.7 % of the patients causing stent lumen obstruction.

Eighth generation of esophageal stent

To overcome the problem with separation of the PTFE membrane from the nitinol wire as well as to make a stent with less migration and with better conformability, we designed an eighth-generation line of esophageal stents. To prevent stent migration, both ends of the stent have two shoulders. To improve the conformability of the stent, only the outside of the middle segment of the stent is covered with nylon mesh.

Other non-vascular stents

We have devised 5 generations of gastroduodenal stents as well as 7 generations of colorectal stents. We have also devised other non-vascular stents, such as tracheobronchial stents, biliary stents, lacrimal stents, urethral stents, and prostatic stents.

Five tips on doing research from my personal experience

1. Building close relationships with patients is the name of the game in clinical research.
2. It is important to collaborate with physicians and scientists in other disciplines because invaluable ideas emerge from the interaction of different disciplines.
3. It is crucial to find mentors to help you and keep in touch with them.
4. Another important strategy is to train new scholars and cooperate with them.
5. Always thank your spouse and family.

INTRODUCTION TO JOURNAL OF BREAST CANCER

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The official journal of the Korean Breast Cancer Society was launched in June 1998 under the title 'Journal of Korean Breast Cancer Society'. The journal, which was published twice a year since its launch, has been converted to a quarterly magazine since 2002 and was listed on KoreaMed in 2003. From March 2005, we changed the title of 'Journal of Breast Cancer (JBC)' from 'Journal of Korean Breast Cancer Society' and prepared the leap to international journals by renewing the design. JBC was indexed in SCIE, SCOPUS, Embase in 2008 and became a full-scale international academic journal. Since March 2011, the journal has been fully published as English, and it has been indexed in PubMed central. The proportion of overseas contributions has also started to increase since this time and has grown rapidly in quantitative terms. As of last year, the number of annual submission has exceeded 500, and the number of overseas contributors is about 80%, rejection rate is over 80%, and JCR impact factor is 2.456.

However, as the number of submissions increases, issues such as delays in evaluation and delay in issuance also arise, and it is time to prepare new solutions such as expanding the number of judges and shortening the publication period.

Since last year, we have been replacing our submission system with an Editorial Manager, the most widely used platform in the world and implemented the epub ahead system for rapid release and access. In March of this year, we stopped off-line printing and switched to online journals. Also, we plan to change the publication interval from quartery to bimonthly starting next year.

JBC editorial committee hopes that more researchers from all over the world will be able to access JBC, and this journal to contribute to researches in breast cancer.

Oral Presentation

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BREAST CANCER RATE AND MORTALITY IN FLIGHT ATTENDANTS

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Background: Previous reports have suggested that breast cancer is more common among flight attendants than that in the general population. Constant exposure to cosmic radiation and circadian disruption are postulated to be the culprits to the problem.

Methods: A comprehensive review was performed on Medline, EMBASE, CINAHL, and Cochrane databases using predefined strategy. Retrieved studies were independently screened and rated for relevance. Data were extracted and analyzed by two researchers according to PRISMA protocol for systematic review and meta-analysis.

Result: Forty three studies were identified using the preset keywords defined in the study protocol. After excluding irrelevant papers, 12 studies were included for pooled analysis. Ten studies (4 American, 6 European) evaluated the breast cancer prevalence in flight attendants, Pooled analysis found that, 1,061 (2.35%) out of the 45,111 flight attendants censored had breast cancer. The standardized prevalence ratio (SPR) was 1.08 (90% CI, 0.30-2.58), when compared to the Surveillance, Epidemiology, and End Results (SEER) data in 2015. Two European studies evaluated breast cancer mortality among flight attendants, pooled analysis found that, out of the 34,898 flight attendants censored, 61 (0.17%) had breast-cancer related mortality. None of the 12 studies were able to demonstrate an association between cosmic irradiation, circadian disruption and breast cancer in flight attendants.

Conclusions: Overall breast cancer prevalence was 235/100,000 female flight attendants, with SPR of 1.08. The current evidence is insufficient to associate breast cancer with workplace risks like cosmic radiation and circadian disruption.

HORMONE REPLACEMENT THERAPY AND BREAST CANCER RISK IN A NATIONWIDE POPULATION-BASED COHORT

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Background: Hormone replacement therapy (HRT) increased breast cancer risk, but this association may vary by patient factors. We investigated the association between HRT and breast cancer in a nationwide Korean cohort with risk stratification according to breast cancer risk factors.

Methods: Using the Korean National Health Insurance Service database, 4,558,376 postmenopausal women who underwent breast cancer screening and regular health checkup between 2009-2014 were included. Subjects were classified into four groups according to self-reported drug history of HRT; none, < 2 years, 2 to < 5 years, 5 ≤ years. Follow-up for breast cancer diagnosis was performed up to 2016. Cox proportional hazard regression analysis was used to evaluate the association between HRT and breast cancer risk.

Result: A total of 696,084 (15.3%) women reported to have had current or previous HRT medication. The hazard ratio (HR) of breast cancer risk in HRT users was 1.253 (95% CI 1.216-1.292) compared to women with HRT non-users. Breast cancer risk increased according to HRT duration; adjusted HR (95% CI) were 1.079 (1.037-1.123) for < 2 years, 1.325 (1.254-1.401) for 2 to < 5 years and 1.722 (1.630-1.819) for > 5 years. The risk of breast cancer related to HRT was higher when women were leaner, had dense breasts or had no breast cancer family history.

Conclusions: HRT use increases breast cancer risk proportionally to HRT duration. This risk differs according to breast density, obesity and breast cancer family history. Risk stratification could help when advising HRT use for relief of menopausal symptoms.

ASSOCIATION BETWEEN OBESITY AND FIRMICUTES/ BACTEROIDETES RATIO IN BREAST CANCER PATIENTS

Jeongshin An[1], Jinho Yang[2], Won-Hee Lee[2], Jong Bin Kim[3], Eun Yeol Yang[1], Hyungoo Kim[1], Sehyun Paek[1], Jun Woo Lee[1], Joohyun Woo[1], Hyungju Kwon[1], Woosung Lim[1], Nam Sun Paik[1], Yoon-Keun Kim[2], Byung-In Moon[1]

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Background: Obesity is associated with breast cancer; particularly postmenopausal obesity is considered as a risk factor for breast cancer. Obesity is known to correlate with the microbiome. This study investigated the relationship among breast cancer, body mass index (BMI), and dietary habits by comparing the microbiome of breast cancer patients and normal healthy controls.

Methods: The symbiotic bacteria secrete extracellular vesicles into the blood and lymphatic fluid. And these vesicles contain bacterial nucleic acids and metabolites. We analyzed the blood microbiome of 95 female breast cancer patients and 192 healthy controls by NGS using a universal bacterial primer of 16S rDNA.

Result: We examined the Firmicutes/Bacteroidetes (F/B) ratio in normal controls and breast cancer patients and observed that the F/B ratio in the control group was 2.6-fold higher than in breast cancer group. In the control group, Firmicutes were 5-fold higher than Bacteroidetes. Among Firmicutes, Staphylococcus and Bacillus were especially higher. Bacteroidetes levels in the breast cancer patients were elevated, particularly Bacteroides and Parabacteroides levels were increased. In breast cancer patients, the F/B ratio was 1.3-fold higher in patients with high BMI (BMI > 30) compared to patients with normal BMI (BMI 20-24). The F/B ratio was the highest in breast cancer patients of meat-eater (F/B ratio: 2.3), followed by vegetarian patients (F/B ratio: 2.0), and omnivorous patients (F/B ratio: 1.8). Menopause had no considerable impact on the F/B ratio.

Conclusions: Changes in F/B ratio of microbiome that are affected by BMI and dietary status may be related to the breast cancer.

NOVEL FUSION GENES IDENTIFIED FROM MATCHED PRIMARY AND RECURRED BREAST CANCERS BY RNA-SEQUENCING

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Background: Breast cancers display substantial inter/intra-tumor heterogeneity. While numerous fusion genes have been identified, most are found to be subclonal, passenger alterations. To discover fusion genes which drive tumor progression and metastasis, we performed RNA-sequencing of matched primary and metastatic breast cancer samples.

Methods: RNA-sequencing was performed from sixteen patients matched primary-recurred tumor tissue and RNA-sequencing data was successfully achieved from sixteen primary tumors and eight recurred tumors. DeFuse program was used to identify fusion transcripts (FT).

Result: Among the sixteen patients, six were hormone receptor positive, three were HER2 positive and seven were triple negative tumors. Three cases displayed loco-regional recurrence only and other patients had distant metastases. Overall, 516 numbers of fusion transcripts were identified. Mean numbers of fusions in primary and recurred tumors were 28 and 14.6 FTs per sample. Numbers of fusions were greater in two cases with BRCA1 pathogenic germline mutations while no significant difference were observed across subtypes. Novel inter-chromosomal fusion transcript, BCL2-ESR1, CSMD1-ESR1 and HPGDS-ESR1 were found in one hormone receptor positive patients metastasis and/or primary tumor. All fusions resulted in preservation of DNA binding domain and ligand binding domain (exon4-10) of the ESR1 gene, with high ESR1 FPKM expression value. Fusions of ERBB2-, MALAT1- and CDK6- genes were found. Among the identified FTs, three cases harbored a previously reported recurrent fusion transcript EEF1DP3-FRY.

Conclusions: RNA-sequencing revealed numerous fusion transcripts. Among them we found novel fusions including ESR1 fusions which need further validation and functional annotation to confirm their role in tumor progression and metastasis.

BASAL AND IL-1β-INDUCED IL-8 IS SUPPRESSED BY CELASTROL IN TRIPLE NEGATIVE BREAST CANCER

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Background: Aberrant IL-8 expression is associated with poor prognosis in various cancers such as breast and colorectal cancer. Previously, we also reported that IL-8 induction in response to IL-1β treatment triggers cell motility in TNBC cells. In this study, we investigated the effect of celastrol on IL-1β-induced IL-8 expression.

Methods: Levels of various genes mRNA and protein expression were analyzed by real-time PCR and western blotting, respectively. Secreted IL-8 protein levels were measured by ELISA. Cell motility were analyzed by wound healing assay and invasion assay.

Result: Both IL-1β and IL-8 mRNA expression significantly increased in TNBC cells compared with non-TNBC cells. We also observed that IL-8 expression is increased by IL-1β treatment. While IL-1β expression did not changed by IL-8 treatment. We found for the first time that basal and IL-1β-induced IL-8 expression was decreased by celastrol in TNBC cells. In addition, IL-1β-induced cell invasion was significantly suppressed by celastrol. Interestingly, we found that the phosphorylation of ERK by IL-1β was decreased by celastrol but not STAT3, p38 and JNK. Finally, we observed that IL-1β-induced IL-8 expression is suppressed by a specific MEK inhibitor, UO126.

Conclusions: Celastrol suppresses basal as well as IL-1β-induced IL-8 expression through the inhibition of MEK/ERK pathway in TNBC cells. In addition, cell motility of TNBC is prevented by celastrol. Therefore, we suggest that celastrol may be a promising therapeutic drug for treatment of TNBC.

APPLICATION OF 3D PRINTED BREAST SURGICAL GUIDE FOR BREAST CONSERVING SURGERY IN DCIS PATIENTS

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Background: Breast conserving surgery (BCS) is being attempted in small size DCIS. For precise partial resection, it is important to know precisely the extent of the tumor before surgery. When removing tumors that are not well palpable, wire guide localization is usually performed, but WGL has a disadvantage that it is hard to know the boundary of tumor and it is difficult to use MRI. To solve these problems, 3D printed breast surgical guide (BSG) was developed using supine MRI information and 3D printing technology and applied to breast cancer patients. We report our experience with the application of BSG in DCIS patients.

Methods: BSG was modeled according to the surface of the breast. BSG was designed as a hybrid type with a column to inject blue dye directly into the boundary of the tumor inside the breast and a groove to mark the skin.

Result: A total of 50 BCS using BSG were implemented from July, 2017 to January, 2018, and 6 cases were DCIS cases. The median age of the patient was 48 years (range, 39 to 68). The median operation time was 53 minutes (range, 40 to 88). In both frozen biopsy and permanent pathology results, all patients had tumor free resection margins. The median distance from the tumor to the margin was 10 mm (range, 1 to 20).

Conclusions: The use of BSG in DCIS patients has the advantage of marking the tumor extent directly to the breast and not causing the patient to suffer pain.

ROBOTIC VERSUS CONVENTIONAL NIPPLE SPARING MASTECTOMY AND IMMEDIATE PROSTHESIS BREAST RECONSTRUCTION IN THE MANAGEMENT OF BREAST CANCER- A CASE CONTROL COMPARISON STUDY

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Background: Few evidence was available comparing the effectiveness and safety of robotic nipple sparing mastectomy (R-NSM) with conventional nipple sparing mastectomy (C-NSM) in the management of breast cancer.

Methods: A case control comparison study was conducted for patients received C-NSM versus R-NSM at single institute to compare the clinical outcome, medical cost, and patient-reported cosmetic results.

Result: Thirty-six patients received R-NSM with immediate prosthesis breast reconstruction (IPBR) and 62 patients received C-NSM with IPBR were enrolled. The mean operation time for C-NSM and R-NSM groups were 197.1 ± 79.9 mins, and 246.6 ± 60.6 mins, separately ($p = 0.002$). The mean blood loss was 34.6 ± 31.8 mL in R-NSM group, and 104.3 ± 71.0 mL for C-NSM group ($p < 0.001$). There was no statistically significant difference in the NAC ischemia/necrosis ratio between R-NSM and C-NSM (8.3% versus 14.5%, $p = 0.53$). The overall complication rate was 27.8% in R-NSM group compared with 46.8% in C-NSM group ($p = 0.09$). The positive surgical margin involved rate was 0% and 2.6% in C-NSM and R-NSM group, separately ($p = 0.187$). The overall mean cost for patients received C-NSM and R-NSM with IPBR was 5,702.3 ± 660.8, and 10,876.6 ± 796.2 United State Dollars, separately ($p < 0.01$). The overall satisfaction rate was higher in R-NSM group (96.4% excellent, and 3.6% good) than C-NSM group (75.6% excellent and 24.4% good, $p = 0.019$).

Conclusions: R-NSM compared with C-NSM had comparable clinical outcome, a decrease of blood loss and higher patients' satisfaction in the cost of longer operation time, and higher medical expanse.

PHASE II RANDOMIZED STUDY OF NEOADJUVANT METFORMIN PLUS LETROZOLE VERSUS PLACEBO PLUS LETROZOLE FOR ER-POSITIVE POSTMENOPAUSAL BREAST CANCER [METEOR STUDY]

Jisun Kim[1], Wonshik Han[2], Eun-Kyu Kim[3], Yongsik Jung[4], Hyun-Ah Kim[5], Soo Min Chae[3], Eun Sook Lee[6], Sei Hyun Ahn[1], Tae Hyun Kim[7], Joon Jeong[8], Su Yun Choi[9], Seok Jin Nam[10], Nam Sun Paik[11], Lee Su Kim[12], Gyungyub Gong[1], Jong Han Yu[10], So-Youn Jung[6], Hee Jeong Kim[1], Sung Gwe Ahn[8], Min Kyoon Kim[13]

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Background: Neoadjuvant endocrine therapy has shown comparable efficacy to chemotherapy in postmenopausal breast cancer (BC) and metformin have shown anti-tumor activity. We report the result of prospective, multicenter, phase II randomized, placebo controlled trial aiming to evaluate direct anti-tumor effect of metformin in postmenopausal women with hormone-receptor (HR) positive BC.

Methods: Two hundred three postmenopausal women diagnosed with HR positive, T1-3/N0-2 invasive BC were randomized to 24 weeks of neoadjuvant letrozole (2.5 mg/day) and either metformin (2,000 mg/day) or placebo. Primary endpoint was clinical response rate (complete, partial response by caliper). Breast conservation rate, Ki67 level, PEPI score and toxicity profile were analyzed.

Result: A total of 153 intention-to treat population were analyzed (72 metformin, 75 placebo group). Overall clinical response rate was 61.4% (94/153) and didn't reach statistical significance between two groups (66.7% versus 56.4%). Overall, breast conservation rate was 68.0% (100/147), 87.3% (103/118) displayed Ki67 < 10% at surgery and 16.7% (21/126) had zero PEPI score with no difference between two groups. However, Ki67 at 4-weeks biopsy was lower in metformin group (patient with Ki67 < 10%, 87.5% versus 33.3%, $p = 0.017$). Patients with 4week Ki67 < 10% had higher clinical response rate (100% versus 57.1%, $p = 0.038$). Grade 3 side effects were reported in three patients and no hypoglycemia event was observed.

Conclusions: 61.7% overall clinical response was achieved after 24-weeks of neoadjuvant le-

Oral Presentation

trozole, with numerically > 10% higher response rate with metformin. 4-weeks Ki67 < 10% level was predictive of clinical response. With minor side effects, preoperative letrozole (+/- metformin) followed by 4-week Ki67 evaluation may indeed serve as primary choice for HR positive postmenopausal BCs.

DEAD-BOX RNA HELICASE DP103 REGULATED SUMO/ ACETYLATION SWITCH OF P53 DETERMINES RESPONSE TO DOCETAXEL IN ERA-POSITIVE BREAST CANCER

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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: Gene expression analysis and immuno-histochemistry profiling of patient samples, variety of in vitro assays, in vivo mouse model.

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 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. ChIP-Seq analysis and estradiol-stimulation studies validated DP103 to be an estrogen-inducible gene. Interestingly, DP103 was also indentified as a potential modulator of ERα transcriptional activity. Silencing DP103 inhibited estradiol-induced ERα DNA-binding activity, expression of ERα target genes, cell growth and colony forming ability.

Conclusions: These findings summarise a novel role of DP103 in acquired drug resistance; presenting a potential surrogate biomarker for predicting drug response in breast cancer. 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.

THE RISK OF CARDIAC DISEASE IN KOREAN BREAST CANCER PATIENTS: IMPACT OF PATIENT-SPECIFIC FACTORS AND HEART DOSE BASED ON INDIVIDUAL HEART DOSE CALCULATION FROM THREE-DIMENSIONAL RT PLANNING

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Background: The impact of incidental exposure of radiation on cardiac disease in Korean breast cancer patients has not been studied well. Here we studied the risk of radiation-related cardiac toxicity in these patients, focusing on patient-specific factors.

Methods: A total of 1294 women who received primary breast surgery for breast cancer from 01/2005 to 05/2013 were analyzed. As for mean heart dose (MHD), all patients' dose distributions were retrospectively evaluated for the mean value of radiation dose the heart received. Major coronary event (MCE) was defined as a diagnosis of myocardial infarction, coronary revascularization, or death resulting from ischemic heart disease.

Result: Median follow-up period was 78.6 months (range, 60.0-153.7). The 10-year MCE rate was 3.9%. As MHD increased per 1 Gy, the risk of cardiac disease significantly increased with an adjusted hazard ratio (HR) of 1.21. Additionally, history of hypertension (HR 2.07) and diabetes (HR 3.43) were found to be adverse risk factors, whereas regular physical exercise (HR 0.20) was a protective factor. In a subgroup analysis, the impact size of increasing MHD (per Gy) was similar in women without or minimal risk factor (HR 1.17), as compared to women with multiple risk factors (HR 1.18).

Conclusions: This is the first study to report a radiation dose-effect relationship for cardiac disease in Korean breast cancer population. This result could increase physicians' awareness to adopt technical approaches to minimize heart dose in breast cancer patients undergoing adjuvant RT, even in those without any risk factor for heart disease.

INTERNAL MAMMARY LYMPH NODES INVOLVEMENT IN PATIENTS WITH BREAST CANCER: ANATOMICAL CHARACTERISTICS AND IMPLICATION FOR TARGET DELINEATION

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Background: The current study aims to collect and analyze the imaging information of IMN involvement so as to provide information for optimize IMN delineation.

Methods: Patients with IMN involvement were retrospectively identified from single-center database. The image information included thoracic CT, breast MRI, ultrasound and PET/CT. Anatomical characteristics from axial imaging including distribution of involved ribs, distance from the internal mammary vessels (IMV) were collected for each metastatic node. Natural extension orientation of IMNs from IMV was also calculated in this study.

Result: In total, 83 metastatic IMNs in 70 breast cancer patients were located from axial CT image. The percentage of metastatic nodes in the 1st, 2nd, 3rd, and 4th intercostal space were 36.1%, 77.1%, 26.5% and 4.8% respectively. The percentage of including IMN with a 4 mm, 5 mm, 6 mm and 7 mm medial/lateral distance to the IMV were 54.2%, 75.9%, 89.2.6%, and 92.3% respectively. Over 98% of the nodes were encompassed into 7 mm depth to the dorsal/ventral direction. In patients with visible metastatic IMNs, 65.3% of them were found to tend to grow closer to the sternum. Analysis of diagnostic reports demonstrated that MRI had an impressive diagnostic rates of 90.3%, while CT had a high misdiagnosis rate of 65.1% (41/63).

Conclusions: Clinical target volume of IMN can be delineated with a 7 mm medial/dorsal distance to the IMV on the same axial CT image. In patients with visible metastatic IMNs, deliberate delineation towards sternum might be reasonable in terms with our study. Multimodal image information may help to improve the sensitivity of diagnosis in IMN metastasis.

RISK OF LYMPHEDEMA FOLLOWING CONTEMPORARY TREATMENT FOR BREAST CANCER: AN ANALYSIS OF 7,426 CONSECUTIVE PATIENTS FROM A MULTIDISCIPLINARY PERSPECTIVE

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Background: To find and assess the comprehensive risk factors of lymphedema to help clinical decision making in the multidisciplinary discussion.

Methods: We identified 5,549 patients who underwent breast surgery between 2007 and 2015. Lymphedema was defined based on objective (difference in arm circumference ≥ 2 cm) and subjective methods assessed by rehabilitation physicians. Patients were categorized according to RT field and dose/fraction. First, we identified risk factors for lymphedema, and then developed a nomogram, and validated the model both internally (1,000 bootstrapping) and externally (external dataset; n = 1,877).

Result: With a median follow-up of 60 months, the 5-year lymphedema rate was 11.9%. As expected, greater number of lymph nodes removed (HR, 1.04) and greater BMI (HR, 1.05) were independently associated with the increased lymphedema. Significant additional findings were those that the greater irradiated volumes (no regional RT < regional RT without AXL 1-2, HR 1.36 < regional RT with AXL 1-2, HR 1.73), greater radiation dose (hypo < conventional, HR 1.36), more tissue removed (PM < MRM, HR 1.65), and more potent chemotherapy used (non-taxane < taxane-containing, HR 2.16) increased lymphedema (all $p < 0.001$). Using all identified variables, a nomogram was built to predict the lymphedema risk of an individual patient, which showed excellent discrepancy internally (c-index: 0.77) and externally (c-index 0.83).

Conclusions: Efforts to decrease lymphedema risk by focusing either on modifying regional RT field or selecting hypofractionated regimen are likely to have a major effect. Our findings suggest that de-escalation strategy to minimize lymphedema risk should be discussed in a multidisciplinary team.

RADIATION PRACTICE PATTERNS AND IMPACT OF RADIOTHERAPY ON COMPLICATIONS AFTER BREAST RECONSTRUCTION: FINAL REPORT OF KROG 18-04

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Background: Much heterogeneity exists with respect to reconstruction and radiation therapy (RT) following mastectomy.

Methods: We conducted a multicenter cohort study of women who underwent adjuvant RT after mastectomy and breast reconstruction for breast cancer from 01/2016 to 12/2017 from 15 hospitals (304 patients account for 28.4% of entire post-mastectomy RT patients [n = 1,072]).

Result: Prosthetic techniques (59.2%) were more often used than autologous techniques (40.1%), and delayed reconstruction was rare (0.7%). Time to adjuvant RT from mastectomy was median 3.9 months. A total of 14.1% of patients received a boost with a median of 10 Gy. 199 (65.5%) patients received conventional fractionation and 105 (34.5%) hypofractionation. Overall reconstruction-related complication rates before and after RT were 13.5%, and 24%, respectively. The major complication rates (requiring re-operation for implant explantation, flap failure or bleeding) were 2.3% and 6.3%, respectively. In multivariate analysis, current smoking history had adverse effect and autologous reconstruction protective effect on development of post-RT major complication. Interestingly, biological equivalent dose in 2 Gy-fractions (hazard ratio, 1.44 per EQD2-Gy$\alpha/\beta = 3.5$) and time interval from surgery to RT (hazard ratio, 0.77 per month) were significantly associated with major complication risk. Hypofractionated regimen of 40 Gy in 15 fractions has the lowest biological equivalent dose in 2 Gy-fractions (44.7 EQD2-Gy$\alpha/\beta = 3.5$).

Conclusions: Our analysis documents practice pattern variation for the use of breast reconstruction and RT in patients undergoing mastectomy seen today in Korea. The ongoing Korean prospective study (NCT03523078) could help guide clinicians to optimize the outcomes in this clinical setting.

EFFECT OF POLOXAMER-BASED THERMO-SENSITIVE SOL-GEL ON SHOULDER MOTION AFTER AXILLARY LYMPH NODE DISSECTION IN PATIENTS WITH BREAST CANCER: A MULTI-CENTER DOUBLE-BLIND, RANDOMIZED CONTROLLED TRIAL

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Background: Restricted shoulder motion is a major morbidity related to lower quality of life and disability after axillary lymph node dissection (ALND) in patients with breast cancer.

Methods: We designed a double-blind, multi-center randomized controlled study to evaluate the anti-adhesive effect and safety of poloxamer based thermo-sensitive sol-gel type to reduce of upper limb dysfunction after ALND. The primary outcome was ROM of the shoulder (sum of forward flexion and horizontal abduction) before surgery and at 1 month after ALND. Secondary outcomes included ROM of the shoulder at 6 month, axillary web syndrome and lymphedema.

Result: A total of 170 patients with planned ALND were randomly assigned to one of two groups and 18 patients were dropped. In the poloxamer group (n = 74), a poloxamer was applied to the surface of operation field after ALND. In the control group (n = 78), ALND was performed without the use of poloxamer. Compared with the control group, the poloxamer group showed greater reductions in postoperative restriction of total shoulder ROM at 1 month (-30.58 ± 27.8 vs. -43.14 ± 36.71; change from baseline, $p = 0.0476$). Especially poloxamer group showed bettter result in horizontal abduction at 1 month ($p = 0.0026$). Any adverse effect was not found in both groups. ROM at 6 months ($p = 0.5692$), axillary web syndrome ($p = 0.3025$) and lymphedema ($p = 0.6809$) were not significant difference between both groups.

Conclusions: These results provide evidence that poloxamer improve ROM of the shoulder without causing adverse effect after ALND.

GAS VERSUS GASLESS ROBOT-ASSISTED NIPPLE SPARING MASTECTOMY

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Background: There are various methods for nipple-sparing mastectomy (NSM) including conventional or endoscopic mastectomy. Robot-assisted nipple-sparing mastectomy (RANSM) is one of the recently introduced techniques for NSM. Since the introduction of RANSM, two different techniques have been attempted: gasless and gas techniques. The aim of this study is to compare different methods of carbon dioxide (CO_2) gas-inflated and gasless RANSM in terms of clinicopathologic characteristics and post-operative outcomes.

Methods: We conducted the retrospective study of the gas and gasless RANSM with immediate breast reconstruction for women with early breast cancer, bilateral interstitial mastopathy, and BRCA1/2 mutations from November 2016 to December 2018. Lapsingle (Sejong Medical Inc., Korea) or Octo-port (DalimSurgNet., Korea) was utilized for gas RANSM. A Chungs or modified Chungs retractor was utilized for gasless RANSM. The general characteristics of the study population, post-operative complication, and operation time were analyzed.

Result: The gas and gasless RANSM were performed in 18 and 14 cases, respectively. The median age of all patients was 44 years old. There was no significant difference between the gas and the gasless group in terms of the general characteristics of the study population, total operation time ($p = 0.675$), and post-operative complication ($p = 0.456$).

Conclusions: Both gas and gasless techniques can be used for RANSM with immediate reconstruction.

PRE-OPERATIVE TOMOSYNTHESIS-GUIDED HOOKWIRE NEEDLE LOCALISATION OF IMPALPABLE, MAMMOGRAPHICALLY AND SONOGRAPHICALLY OCCULT BREAST LESIONS: A PRELIMINARY EXPERIENCE

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Background: Breast cancer is one of the leading causes of death in women. In recent times, rapid advances in diagnostic imaging modalities have resulted in early detection of breast cancer. Impalpable breast lesions now constitute a larger proportion of breast lesions which subsequently require pre-operative image-guided hookwire localization (HWL) to facilitate surgical excision. As the use of digital breast tomosynthesis (DBT) increases, mamographically and sonographically occult lesions have also been increasingly detected, leading to an inherent drive towards DBT-guided HWL as the next step in clinical management of these once difficult-to-detect breast lesions. The authors sought to evaluate the feasibility, accuracy and safety of this relatively new technique in a single tertiary referral centre.

Methods: A retrospective review was made for all DBT-guided HWL performed over a 6-month period from April to October 2018. A query of the electronic patient database identified 10 consecutive women (average age = 51 years, age range = 41-64 years) with a total of 10 targeted lesions for DBT-guided HWL with the use of commercially available equipment.

Result: The presence of a microcalcification cluster was the imaging finding identified in 100% of patients. Histological findings were malignant in 1 of the 10 lesions (10%). Technical success of DBT-guided HWL was achieved in all patients (100%). No peri-procedural complications were noted (0%).

Conclusions: DBT-guided HWL is a feasible and safe image-guided technique which can be applied in the impalpable, mammographically and sonographically occult breast lesion.

OUTCOMES OF DUCTAL CARCINOMA IN SITU ACCORDING TO DETECTION MODALITY: A MULTICENTER STUDY COMPARING RECURRENCE BETWEEN MAMMOGRAPHY AND BREAST US

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Background: To determine whether disease recurrence and intrinsic characteristics of ductal carcinoma in situ (DCIS) are associated with the imaging method of detection in asymptomatic women diagnosed with DCIS.

Methods: This multicenter, retrospective, observational study was conducted from February 2003 to February 2011, at 8 institutions. Eight hundred forty-four women treated for asymptomatic, primary pure DCIS who had preoperative mammography and breast ultrasonography (US) studies available for review were included. Mean follow-up interval after treatment was 91.2 months (standard deviation: 53.3, range: 6.4-180.9 months). Medical records and breast images were reviewed by 8 breast-imaging dedicated radiologists for clinicopathologic information and image analysis. The Kaplan-Meier analysis and univariable/multivariable Cox proportion hazard model were used to analyze recurrence-free survival rates and factors associated with recurrence after DCIS treatment.

Result: Of the 844 women, 25 (3.0%) developed recurrences. Patients with US-detected DCIS had significantly lower 5- and 10-year recurrence-free survival rates compared to patients with mammography-detected DCIS ($p = 0.011$). US-detected DCIS showed significantly lower 5- and 10-year recurrence-free survival rates compared to mammography-detected DCIS in patients < 50 years or with mammographically-dense breasts ($p = 0.002$, and 0.002, respectively). Multivariable analysis showed that US as the detection modality (HR: 4.451, 95% CI: 1.530, 12.950, $p = 0.006$) and HER2 positivity (HR: 4.036, 95% CI: 1.438, 11.330, $p = 0.008$) were significantly associated with recurrence.

Conclusions: US as the detection modality and HER2 positivity were factors significantly associated with recurrence in patients treated for asymptomatic DCIS.

MAGNETIC TRACER: A NEW OPTION OF SENTINEL LYMPH NODE LOCALIZATION

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Background: The use of radioisotope has long become the gold standard for sentinel lymph node (SLN) localization in breast cancer. European trials have proven that a new tracer agent, Magtrace, is non-inferior to the standard method. It has yet been tried in most Asian countries.

Methods: This is a single-centre prospective trial comparing the new magnetic technique with the standard one. Breast cancer patients undergoing SNOLL (Sentinel node and occult lesion localization) were recruited and received subcutaneous injection of Magtrace in the morning of operation. On-table transcutaneous detection with the handheld magnetometer, as well as intraoperative and ex-vivo counts of excised nodes were measured. SLN identification rates by each method were compared. Duration of the procedure was recorded. Skin discoloration after Magtrace injection was also followed and documented.

Result: Forty-five patients were included and underwent SLN biopsy mapped by both radioisotope and Magtrace. The total number of SLN excised was 157. The SLN identification rates by Magtrace were higher than those by the standard technique per patient (97.1% vs. 53.3%) as well as per node (73.9% vs. 53.5%). The procedure took 25 minutes on average from skin incision on the axilla to the excision of the last SLN. Discoloration following Magtrace injection faded slowly and was still detectable in approximately 40% of patients after six months postoperatively.

Conclusions: Our findings echoed that Magtrace is a safe and effective option for SLN localization. Effort should be made on optimizing technical workflow and evaluating cost-effectiveness. Potential skin discoloration is a concern in breast conservation.

THE EFFECT OF REGIONAL NODE IRRADIATION ON THE THYROID GLAND IN THE BREAST CANCER PATIENTS: THE CLINICAL SIGNIFICANCE OF OPTIMIZATION OF RADIATION TARGET VOLUME

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Background: Radiation-induced-hypothyroidism (RIH) has largely been ignored in adjuvant radiotherapy (RT) for breast cancer. Here we studied the risk of RIH and whether optimizing RT target could minimize its risk.

Methods: We identified 4,073 patients who received adjuvant RT for breast cancer between 2007 and 2016 at a single institution. Patients were divided into three groups by the volume of regional RT field: no regional node irradiation (RNI) (n = 2,468), ESTRO-RNI (cranial border at the subclavian artery, n = 215), and RTOG-RNI (cranial border at the cricoid cartilage, n = 1,390). The incidences of RIH were retrospectively reviewed by medical chart reviews, and the dosimetric analysis was performed to estimate the Dmean to the thyroid in randomly-sampled matching patients (n = 200).

Result: At a median of 60 months, 89 patients developed RIH (1.5% subclinical, 0.7% biochemical) after 30 ± 24 months of RT (3- and 5-year rates: 1.3% and 2.2%, respectively). RNI significantly increased RIH (3.4% vs. 1.4%, $p < .001$). In subgroup analysis, ESTRO-RNI significantly decreased RIH risk compared to RTOG-RNI (0.5% vs. 3.8%, $p < .001$). After adjusting all confounders, RTOG-RNI was the only independent risk factor for the development of RIH (HR 1.46, 95% CI, 1.05-2.03). In the dosimetric analysis, mean radiation dose to the thyroid was significantly lowered in ESTRO-RNI group than RTOG-RNI group (2.9 ± 1.9 Gy vs. 9.3 ± 8.4 Gy $p < 0.001$).

Conclusions: RNI was associated with an increased risk of new incidence of RIH in breast cancer survivors. However, optimization of RT target volume could reduce the lifelong RIH risk, which further supports the adoption of ESTRO-guideline in early-stage breast cancer.

THE ACCURACY OF AXILLARY NODE ASSESSMENT BY ULTRASOUND AFTER NEOADJUVANT CHEMOTHERAPY IN CLINICALLY NODE POSITIVE PATIENTS

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Background: The use of SLNB following NAC for patients with cN1 is controversial. We studied the accuracy of cN0 assessment by ultrasound after NAC in patients with originally cN1 disease.

Methods: Two hundreds and eighty primary breast cancer patients who had cytologically proven axillary metastasis before NAC, and underwent axillary dissection after NAC were enrolled. We assessed the accuracy of axillary US after NAC in association with the response of primary tumor.

Result: Of 280 patients, 124 patients (44%) showed normal US findings in the axilla after NAC (ycN0) and 101 patients (36%) showed pathologically node-negative at surgery (ypN0). The rate of ypN0 was 20.1% in the luminal, 76.8% in the HER2, and 52.5% in the TN disease. The accurate prediction rate of node-negative status after NAC by US was 51% in total, and 29.7% in the luminal, 88.2% in the HER2, and 68.8% in the TN disease. The accuracy was highest in the HER2, and lowest in the luminal, with statistically significant difference ($p < 0.001$). The accurate prediction rate was 100% in patients with HER2 or TN breast cancer that showed cCR in the breast after NAC by MRI.

Conclusions: The accuracy of axillary US after NAC depended on subtypes, which was highest in the HER2 disease. The accuracy increased by combing with the tumor response in the breast assessed by MRI. We suggest that it is of clinical importance to take account of tumor subtypes in combination with axillary US in selecting patients for SLNB after NAC.

PLASMA PROTEIN BIOMARKER FOR EARLY DIAGNOSIS OF BREAST CANCER BY USING PROTEOMICS TECHNOLOGY

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Background: Breast cancer is the most common diagnosed cancer type and the most leading cause of cancer-related deaths among women worldwide. Although image screening (mammography) is available, there is an ongoing interest in improved early detection and prognosis. Research investigating biomarkers for early detection, prognosis and the prediction of treatment responses in breast cancer is rapidly expanding. However, no validated biomarker currently exists for use in routine clinical practice, and breast cancer detection and management remains dependent on invasive procedures We aimed to develop biomarker for early diagnosis of breast cancer by using proteomics technology.

Methods: We created the performance algorithm of the 3-protein diagnostic model to predict of the breast cancer. We performed several experiments for establishment and validation of cut-off value. Furthermore we conducted test for acquisition of sample stability and more experiments to achieve the reproducibility and level of evidence, compared with other cancers.

Result: Total 1,226 samples was analyzed. The sensitivity, specificity and accuracy from confirmation experiment was 71.58%, 85.25% and AUC 0.8323, respectively. The result of comparison with other cancers, there are no statistical significant difference and no relevance with effects of anesthesia. With these results, we recently got permission it to use for in vitro diagnostic use from Korea Food and Drug Administration.

Conclusions: In this study, we developed a plasma protein biomarker that may use to diagnosis of breast cancer in the real clinical practice. By using MRM approach, the 3-protein biomarker was validated in an independent cohort with acceptable accuracy for early diagnosis of breast cancer.

A SIMPLE INTERVENTION FOR LONG-TERM RELIEF OF CHRONIC POST MASTECTOMY PAIN

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Background: Post-mastectomy pain syndrome (PMPS) is a common and often debilitating condition. One common cause likely results from injury to the T4 and T5 sensory nerves during breast surgery, with resulting neuroma formation. It manifests as a pain syndrome diagnosed by trigger points that reproduce exquisite pain upon palpation. A combination of corticosteroids and local anaesthetic given through perineural infiltration, at other sites, effective in alleviating these neuromas or trigger points. Utilizing this principle, we initiated a quality improvement project to treat PMPS. This perineural injection led to remarkable, long-lasting relief of the first few patients, we therefore continued treating patients with clinical symptoms suggestive of a neuroma. We report on long-term pain relief after trigger point injections (TPI) for women with PMPS.

Methods: An observational cohort study of women with PMPS and clinical evidence of neuroma was undertaken. We injected a 2mL mixture of equal parts 0.5% bupivacaine and 4 mg/mL dexamethasone into each trigger point. Descriptive statistics are reported, univariate and bivariate analyses were conducted using Stata 12 (College Station, TX).

Result: We identified 104 trigger points in 54 patients with PMPS. Long term relief was achieved in 88.5% of patients. Effectiveness of the TPI was assessed by physical examination immediately (1-3 minutes) after the injection, then with telephone interview (at >/=3 months post TPI).

Conclusions: Perineural infiltration with bupivacaine and dexamethasone is a safe, simple, and effective treatment option for PMPS with an associated trigger point. This technique should be added to the armamentarium of all surgeons who perform breast surgery.

COMPARATIVE STUDY BETWEEN SENTINEL LYMPH NODE BIOPSY AND AXILLARY DISSECTION IN PATIENTS WHO UNDERWENT TOTAL MASTECTOMY WITH 1 OR 2 METASTATIC LYMPH NODES

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Background: Sentinel lymph node biopsy (SLNB) is a standard axillary procedure in early breast cancer patients with clinically negative node. In a randomized trial, SLNB was performed in patients who underwent breast conserving surgery with 1 or 2 lymph node metastases, and the survival rates were not different even if axillary lymph node dissection (ALND) was omitted. The goal of this study was to compare outcomes in patients who underwent total mastectomy (TM) with 1 or 2 positive nodes in the final pathology according to the types of axillary surgeries.

Methods: A total of 79,058 patients who underwent TM from the Korean Breast Cancer Society registration database were analyzed. Inclusion criteria were T stage 1 or 2, 1 or 2 positive axillary lymph nodes, and having TM, no radiation therapy, and no neoadjuvant therapy. We analyzed retrospectively the differences in overall survival (OS) among patients who received SLNB or SLNB + ALND.

Result: A total of 883 patients who were 1:4 matched for SLNB only group (n = 179) and SLNB +ALND group (n = 704) in the matched cohort from 1999 to 2014. There were no significant differences in OS between the two groups (HR = 0.728, $p = 0.413$). Subgroup analysis showed significant survival benefit in the SLNB+ALND group in T2 subgroup (HR = 0.353, $p = 0.012$).

Conclusions: There were no significant differences in OS between SLNB only and SLNB+ ALND in early breast cancer patients who underwent TM with 1 or 2 positive axillary lymph nodes.

FACTORS PREDICTIVE OF MALIGNANT UPSTAGING OF ATYPICAL DUCTAL HYPERPLASIA OF THE BREAST - CAN SURGICAL EXCISION BIOPSY BE AVOIDED?

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Background: Atypical ductal hyperplasia (ADH) of the breast is a high risk lesion associated with malignancy. Once diagnosed on core needle biopsy (CNB), excision biopsy is routinely performed to rule out malignancy. This study aims to identify factors predictive of malignant upgrade for ADH.

Methods: Retrospective analysis was performed on patients diagnosed with ADH on CNB conducted under the BreastScreen Singapore (a national breast screening programme) at the National Cancer Centre Singapore (NCCS) between 2010 and 2015.

Result: From 2010-2015, 47,934 patients underwent mammographic screening under BreastScreen Singapore, and 5,742 CNBs were performed. 2,686 of these women underwent CNBs at the NCCS and 89 patients (91 lesions) were diagnosed with ADH. 27 lesions (29.7%) were upstaged to DCIS (n = 25,27.5%) and invasive cancer (n = 2,2.2%) on excision biopsy. Univariate analysis identified the following factors associated with malignant upgrade: presence of a mass on either ultrasound ($p = 0.019$) or mammogram ($p = 0.001$), presence of microcalcification ($p = 0.047$), microcalcification distribution ($p = 0.019$), lower mammographic parenchymal density ($p = 0.008$), smaller needle gauges ($p = 0.019$) and use of Trucut biopsy method ($p = 0.031$). Mammographic parenchymal density ($p = 0.014$) and mass on ultrasound ($p = 0.009$) remained significant on multivariate analysis.

Conclusions: Incidence of malignant upgrade of CNB-diagnosed ADH at our institution is 29.7%, comparable with other regional studies. Decreased mammographic parenchymal density and presence of a mass on ultrasound were independently associated with malignant upgrade. Future work looks to develop a comprehensive predictive nomogram identifying lesions of low likelihood for malignant upgrade, reducing the necessity of excisional biopsy in these patients.

OVEREXPRESSION OF ANDROGEN RECEPTOR INDICATE FAVORABLE PROGNOSIS IN PURE DUCTAL CARCINOMA IN SITU

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Background: Ductal carcinoma in situ (DCIS) display favorable outcome while little is known about the factors associated with invasive recurrence. To identify better prognostic biomarkers we performed gene expression analysis followed by immunohistochemistry (IHC) staining validation.

Methods: Differential gene expression analysis of 29 pure DCIS patients was performed using nanostring platform. RNA was extracted from paraffin blocks from age/size matched 11 recurrence-free and 18 invasive-recurrence cases (disease free interval > 5 years). Gene annotation enrichment analysis was done for differentially expressed genes (DEG) using DAVID. Eighty-two pure DCIS cases were selected for external validation by IHC staining. Allred score cutoff 1 was used for survival analysis.

Result: Ninety-nine differentially expressed genes were found statistically significant (p-value < 0.05). Androgen receptor (AR) gene, which encodes a transcription factor AR, has recently been highlighted as a favorable prognostic marker and a therapeutic target in invasive tumor (fold change = -1.35, $p < 0.001$). AR protein expression was externally validated by IHC staining of 82 pure DCIS cases (24 invasive-recurrence versus 58 recurrence-free). Similar to gene expression analysis result, patients with invasive recurrence showed lower AR staining score than recurrence-free patients ($p = 0.007$). Cox regression analysis showed lower AR level as an independent risk factor of long-term invasive recurrence (HR 7.43, 95% CI 1.50 to 36.62). Gene enrichment analysis revealed enrichment of kinase pathway and cell cycle pathway in recurred cases (Enrichment Score = 2.43, 2.41 respectively).

Conclusions: DEG pattern was observed among pure DCIS cases. AR may serve as a prognostic biomarker and targeting kinase, cell proliferation may be effective for higher risk DCIS patients.

CCL2 DERIVED FROM EGFR AND HER2(+) BREAST CANCER CELLS RECRUITS TUMOR ASSOCIATED MACROPHAGES

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Background: Dimerization of EGFR and HER2 expression are associated with various tumor growth such as breast and lung adenocarcinoma. So far, the correlation between breast cancer and tumor microenvironment are not fully elucidated. Here, we focused on secreted cytokines between breast cancer cells and tumor associated macrophages (TAMs).

Methods: Disease free survival and overall survival were analyzed through the clinical database of the breast cancer center at Samsung Medical Center. Secreted proteins were analyzed by Proteome Profiler Human Cytokine Array. Levels of various genes mRNA and protein expression were analyzed real-time PCR and western blotting, respectively. Cell motility was analyzed by transwell chamber assay.

Result: Clinically, EGFR and HER2(+) breast cancer patients have poor prognosis comparing EGFR alone. We found that the levels of CCL2, CCL5, IL6, and IL8 are significantly increased in EGFR and HER2(+) breast cancer cells. Induction of CCL2 by HER2 overexpression was suppressed by src kinase inhibitors, saracatinib or PP2. Furthermore, recombinant human CCL2 and conditioned culture media of EGFR and HER2(+) breast cancer cells promoted cell motility of TAMs. Activated TAMs secreted tremendous IL-8 and elevated IL-8 triggered.

Conclusions: CCL2 derived from EGFR and HER2(+) breast cancer cells recruited TAMs. Activated TAMs secreted IL-8. Elevated IL-8 expression augmented cells growth and invasiveness of breast cancer cells. Therefore, we demonstrated that CCL2 derived from EGFR and HER2(+) breast cancer cells plays an important role on recruitment of TAMs. In addition, IL-8 by activated TAMs is involved with invasiveness of EGFR and HER2(+) breast cancer cells.

ONCOGENIC CONTRIBUTION OF GERMLINE MUTATIONS IN LYSOSOMAL STORAGE DISEASE-RELATED GENES TO PATIENTS AT HIGH RISK FOR HEREDITARY BREAST CANCER

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Background: Lysosomal storage diseases (LSD) are caused by inborn errors of metabolism. It has been suggested that lysosomal dysfunction contributes to carcinogenesis and carriers of potentially pathogenic variants (PPVs) of LSD-related genes are at increased risk of cancer. We aimed to elucidate the oncogenic contribution of germline mutations in LSD genes to patients at high risk for hereditary breast cancer (BC).

Methods: A total of 153 patients with high risk of hereditary BC (multiple primary cancer, age < 40, family history of BC ≥ 3, bilateral BC) who showed no pathogenic germline mutation on 64-gene hereditary cancer panel were analyzed. DNA extracted from blood samples of these patients underwent targeted sequencing for 42 LSD-related genes. Germline variants classified as PPVs were analyzed according to risk category.

Result: PPVs were detected in 18.9% (29/153) of samples sequenced. Compared to the PPV rate of 13.5% in the normal population from the 1,000 Genome Project, it showed an odds ratio (OR) of 3.24 (p-value = 0.072). Samples from patients with multiple primary tumors showed a PPV rate of 20.1% and an OR of 4.46 (p-value = 0.035). Samples from patients with age < 40, ≤ 35, and ≤ 25 showed PPV rates of 15.6%, 17.7%, and 22.2%, respectively.

Conclusions: High risk patients who do not possess germline mutations in commonly known hereditary cancer-related genes have a tendency to carry higher rate of PPVs in LSD-related genes compared to the normal population, especially in patients with multiple primary cancer which shows statistical significance. It may also contribute to developing cancer at a younger age.

PROTEOMIC LANDSCAPE OF FIBROEPITHELIAL TUMOR OF BREAST

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Background: Fibroepithelial neoplasms are biphasic tumors consisting of epithelial and stromal components, and include broad heterogeneous disease spectrum, from fibroadenoma to malignant phyllodes tumor. Discrimination of phyllodes tumor from fibroadenoma in biopsy specimen is quite difficult, but there is no known diagnostic molecular marker for it. Predictive molecular markers for aggressive features of phyllodes tumor are also poorly studied.

Methods: We selected total 64 patients who were underwent surgery for fibroepithelial lesion of breast. Fresh frozen paraffin embedded (FFPE) tissue of 17 fibroadenomas, 15 benign phyllodes tumors, 15 borderline phyllodes tumors, 17 malignant phyllodes tumors were used for proteomic analysis. After tumor dissection from FFPE samples, well defined proteomic strategies for protein identification including protein extraction, sample preparation, high-pH peptide fractionation based on stage-tip, and high-resolution quadruple Orbitrap LC-MS/MS were performed. Data analysis were performed using MaxQuant and Perseus program.

Result: Totally about 4,500 proteins were identified, of which 240 functional components were found in gene ontology analysis. Of them, some proteins were confirmed to be significantly altered related to disease aggressiveness. From the patient group with borderline to malignant phyllodes tumor, we featured several significantly upregulated proteins based on domain knowledge for text-mining and public network databases for network analysis. In addition to that, pathway network analysis using cytoscape and String DB for the proteins are on processing.

Conclusions: In this study, proteomic profiles of fibroepithelial tumors of breast were illucidated. Several differentially expressed proteins in each disease entity of fibroepithelial tumor can be used as predictive marker for appropriate therapeutic plan.

PRELIMINARY STUDY OF REAL-TIME THREE-DIMENSIONAL CONTRAST- ENHANCED ULTRASOUND OF SENTINEL LYMPH NODES IN BREAST CANCER

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Background: Sentinel lymph nodes (SLNs) are defined as the initial lymph nodes which receive lymphatic drainage from the primary tumor. The main methods for detection of SLNs include dye-guided method, radioisotope method and indocyanine green fluorescence (ICG) imaging. This is the first study to investigate the value of 3D-CEUS in the preoperative assessment of SLNs and LCs in patients with early breast cancer.

Methods: The study was performed in 187 women with pathology confirmed early breast cancer between June 2016 and December 2017. 146 in 187 patients were randomly divided into two groups: 73 patients received two-dimensional ultrasound (2D-US), and two-dimensional contrast-enhanced ultrasound (2D-CEUS, 2D-CEUS group), the other 73 patients immediately received 3D-CEUS after 2D-US (3D-CEUS group). The number, size, location, enhancement pattern of SLNs and the lymphatic drainage patterns were reviewed, the routes, location of SLNs and lymph channels (LCs) on the surface were marked. All patients underwent blue dye-guided sentinel lymph node biopsy finally.

Result: According to the postoperative pathology findings and the blue stained of the lymphatic drainage routes, the coincidence rate of the 2D-CEUS group and the 3D-CEUS group were 93.2% and 94.5%, respectively ($p > 0.05$); the LN detection rate were 90.4% and 95.6% ($p > 0.05$); the correct diagnosis rate were 91.8 and 93.2% ($p > 0.05$); the time of operative was 15.42 ± 1.10 and 13.49 ± 0.94 min ($p < 0.05$).

Conclusions: Compare to the 2D-CEUS, the 3D-CEUS can clearly display SLNs and lymph drainage routes, and help the clinicians recognize the spatial location and depth of SLNs, and reduce the time of finding the SLNs during operation.

THE EXPLORATORY STUDY ON INDICATIONS OF INTERNAL MAMMARY SENTINEL LYMPH NODE BIOPSY IN BREAST CANCER

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Background: The internal mammary sentinel lymph node biopsy (IM-SLNB) is a minimally invasive method to assess internal mammary lymph node (IMLN) metastatic status for breast cancer. However, IM-SLNB is performed only in clinically axilla lymph node (ALN) negative (cN0) patients in clinical practice, which result in low clinical benefit and limit application. In this study, the impact of IM-SLNB on the diagnostic and prognostic value were analyzed both in cN0 and clinically ALN positive (cN+) patients.

Methods: A total of 725 patients with biopsy-proven invasive breast cancer (cN0 554 and cN+ 171) were enrolled in this prospective study. The radiotracer was injected with our modified technique. IM-SLNB was performed for IMLN visualized patients and clinical benefits were accessed according to current guidelines.

Result: CN0: IM-SLNB was performed in 284 patients with IMLN visualized (visualization rate 70.0%). The IMLN metastases rate was 8.8%, systemic and radiotherapy treatment were changed only in 1.3% and 8.8%. However, for the patients with positive ALN and medial tumor, staging and radiotherapy treatment were changed both in 31.3%. cN+: IM-SLNB was performed in all patients with IMLN visualized (visualization rate 71.9%), and the IMLN metastasis rate was 39.8%. 123 patients who underwent IM-SLNB received more accurate staging, among which 49 IMLN positive patients received internal mammary radiotherapy (IMRT), the other 74 IMLN negative patients avoided IMRT.

Conclusions: As a minimally invasive technique, IM-SLNB should be routinely performed, especially in the cN+ patient. Based on this IM-SLNB indication above, more accurate IMRT indication and individualized radiotherapy strategies could be put forward.

EVALUATION OF A DIRECT REVERSE TRANSCRIPTION LOOP-MEDIATED ISOTHERMAL AMPLIFICATION METHOD WITHOUT RNA EXTRACTION (DIRECT RT-LAMP) FOR THE DETECTION OF LYMPH NODE METASTASIS IN EARLY BREAST CANCER

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Background: Determining lymph node metastasis, tumor-derived DNA or RNA has been widely studied in place of immunohistochemical assay. As a direct reverse transcription loop-mediated isothermal amplification method (direct RT-LAMP) was developed to rapidly identify virus without RNA extraction, we hypothesized that a direct RT-LAMP assay can be a substitute to detect tumor involvement of lymph node in breast cancer patients.

Methods: A total of 92 lymph nodes dissected from 40 patients with breast cancer were collected at Kyungpook National University Chilgok Hospital between November 2015 and February 2016. All of the samples were evaluated and compared by both a direct RT-LAMP assay and routine histopathologic examination. At first, cutoff values of CK19, CK20, and CEA for direct RT-LAMP was determined using different mRNA levels.

Result: We set the cutoff value of direct RT-LAMP assay for CK 19 mRNA at 1ng to distinguish status of LN metastasis. The sensitivity and specificity of the RT-LAMP assay were 85.7% and 100%, respectively. The positive predictive value and negative predictive value were 100% and 94.4%.

Conclusions: Direct RT-LAMP assay can allow detection of SLN metastasis in breast cancer patients intraoperatively with a good sensitivity through cost-effective and timesaving manner.

PROGNOSIS OF BREAST CANCER PATIENTS WHO HAD SENTINEL LYMPH NODE BIOPSY AFTER NEOADJUVANT THERAPY

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Background: The purpose of this study was to evaluate the prognosis of breast cancer patients who had neoadjuvant chemotherapy and had sentinel lymph node biopsy (SNB) only as axillary surgery regardless of clinical and pathological lymph node (LN) status.

Methods: We reviewed records of 1821 patients from Asan medical center who were diagnosed stage I-III breast cancer and had neoadjuvant chemotherapy between 2003-2014. Median follow up was 54 months (5-181). We selected patients who had SNB as axillary surgery (n = 816) and divided these patients into 4 groups via clinical (C) and pathological (P) LN status; C-P-(n = 382), C-P+(n = 40), C+P-(n = 254), C+P+(n = 140). In these groups, we compared axillary LN recurrence(including axillary recur only and axillary recur with others), locoregional recurrence, distant metastasis-free survival (DMFS), disease-free survival (DFS) and overall survival (OS) using Kaplan-Meier analysis.

Result: When we compared prognosis of C-P- group and C+P- group to find out whether SNB alone is enough treatment even in patients who were clinically LN positive before neoadjuvant therapy but negative SNB pathology, axillary recurrence rate and locoregional recurrence rate were not significantly different between two groups ($p = 0.09$, $p = 0.095$, $p = 0.081$). However, C+P- group had lower DMFS, DFS and OS than C-P- group ($p = 0.029$, $p = 0.047$, $p = 0.006$). When we compared 4 groups, axillary recurrence rate and locoregional recurrence rate were significantly different in four groups with pathologically LN negative groups (C-P-, C+P-) showing lower recurrence rates ($p = 0.036$, $p = 0.005$, $p = 0.002$). DMFS and OS were also significantly different in four groups with clinically LN negative groups (C-P-, C-P+) showing better survivals ($p = 0.019$, $p = 0.012$).

Conclusions: In conclusion, there are significant differences in recurrence rate and survival rates according to the clinical and pathological LN status.

EFFECTS OF AEROBIC AND RESISTANCE EXERCISE ON ANDROID FAT IN BREAST CANCER SURVIVORS

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Background: Android fat (AF) is associated with increased risk of cardiovascular disease and type 2 diabetes in breast cancer survivors (BCS). Exercise reduces fat mass in BCS; however, few studies have focused on AF. The study purpose was to examine the effects of a 16-week aerobic and resistance exercise intervention on AF among BCS. We assessed whether exercise-induced changes in AF were associated with improved insulin resistance.

Methods: BCS (Stage I-III) were randomized to exercise (n = 50) or usual care (n = 50). The thrice weekly 16-week intervention included supervised, progressive moderate-vigorous aerobic and resistance exercise. AF was obtained from a whole-body dual-energy x-ray absorptiometry. Insulin resistance was estimated using homeostatic model assessment of insulin resistance (HOMA-IR) calculated from fasting insulin and glucose levels. Within and between group differences were assessed by paired t-test and repeated measures ANOVA. Pearsons correlation was computed to assess the association between AF and HOMA-IR in the exercise group.

Result: Participants were 53 ± 10.4 years old, overweight (BMI > 25.0 kg/m^2; 54%), Hispanic (63.1%), and had undergone a mastectomy (90%) and chemotherapy+radiation therapy (76%). Adherence to the intervention was 95% and post-intervention assessments were available on 91% of participants. Post-intervention, AF significantly decreased in the exercise group from baseline and when compared to usual care ($p < 0.001$). Post-intervention, strong correlations were found between AF and HOMA-IR ($r = 0.91$; $p < 0.01$).

Conclusions: A progressive aerobic and resistance exercise intervention is an effective way to decrease AF in BCS. BCS who experience exercise-induced improvements in AF may also experience improved insulin resistance.

PROGNOSIS AND EFFECT OF ADJUVANT TREATMENT IN SMALL, NODE(-), HER2(+) BREAST CANCER

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Background: There remains uncertainty regarding prognosis and treatment effect in small, node negative breast cancer. We described overall prognosis of small (< 1 cm), node (-), HER2 (+) breast cancer after curative surgery, and effect of adjuvant treatment.

Methods: We identified patients who fulfilled inclusion criteria (curative surgery, < 1 cm, N0, and HER2(+) breast cancer) by medical chart review. We collected data of baseline characteristics, receptor status , surgical method, histologic type, histologic and nuclear grade, adjuvant treatment (chemotherapy, radiotherapy, endocrine therapy, and trastuzumab. We compared baseline characteristics between patients with or without adjuvant treatment (Chi-square), and the prognosis between them (Kaplan meier curve and log-rank test). SPSS version 18.0 was used for statistical analysis.

Result: A total of 427 patients (pT1a = 205, pT1b = 222) were identified. In patients with pT1a , with median follow up duration of , only 1 patient experienced systemic recurrence and death. No difference was observed in DFS and OS between patients with adjuvant chemotherapy and/or adjuvant trastuzumab. In pT1b, HR(-) patients (N = 52), longer DFS was observed in patients who received adjuvant chemotherapy ($p = 0.013$). There was no difference in DFS according to trastuzumab treatment ($p = 0.441$). Adjvuant chemotherapy remains statistically significant variable after adjustment of other variables (histologic grade, nuclear grade, and adjuvant trastuaumab). No difference was found according to adjuvant treatment in overall or HR(+) pT1b patients.

Conclusions: In conclusion, our result showed overall prognosis of small (< 1 cm), node (-), and HER2+ breast cancer and patients with pT1b and HR(-) patients can benefit from adjuvant chemotherapy. Subsequent study with large sample size is warranted.

PREDICTION OF PATHOLOGICAL COMPLETE RESPONSE BY MICRORNA IN BREAST CANCER PATIENTS TREATED WITH NEOADJUVANT CHEMOTHERAPY

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Background: We reported the combination of five serum microRNAs (miRNAs) can be used to detect breast cancer (BC). miRNAs are potentially useful in the evaluation of treatment of cancer.

Methods: Serum sample of patients who received neoadjuvant chemotherapy (NAC) before treatment between 2008 and 2014 were collected. A comprehensive quantitative expression analysis of miRNA was performed using the by DNA chip 3D-Gene (Toray Industries Inc.) Clinicopathological data was retrieved from medical records. Pathological complete response (pCR) was defined as the absence of residual invasive and in situ cancer of the resected breast specimen and all sampled regional lymph nodes.

Result: Ninety-one patients received NAC and surgery. Median age of patients was 49 years (range 28-77). Forty-two patients were hormone receptor-positive (HR+) and HER2-negative (HER2-), 24 were HR+ and HER2-positive (HER2+), 11 were hormone receptor-negative (HR-) and HER2+ and 14 were HR- and HER2-. pCR was observed in 19 (20.9%) of NAC patients. pCR in each subtypes were 3 (7.7%) in HR+ and HER2-, 6 (33.3%) in HR+ and HER2+, 4 (57.1%) in HR- and HER2+ and 3 (27.3%) in HR- and HER2-. Serum before NAC were obtained from 19 pCR patients and 71 non-pCR patients. miR-X (fold change >2, $p<0.01$) and miR-Y (fold change >2) were differentially expressed in the patients with pCR.

Conclusions: MiR-X and miR-Y are the potential predictive marker of pCR in patients with BC treated with NAC.

HOW PREOPERATIVE SENTINEL LYMPH NODE CONTRAST-ENHANCED ULTRASOUND HELPS INTRAOPERATIVE SENTINEL LYMPH NODE BIOPSY IN BREAST CANCER: INITIAL EXPERIENCE

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Background: We aimed to evaluate the value of sentinel lymph node contrast-enhanced ultrasound (SLN-CEUS) and surface tracing for the biopsy of intraoperative sentinel lymph nodes (SLN).

Methods: Between June 2015 and December 2017, a total of 473 patients with early invasive breast cancer were recruited. Patients received an intradermal injection of microbubble contrast agent around the areola on the day before surgery. The locations and sizes of lymphatic channels (LCs) and SLNs were marked on the body surface using gentian violet. Then, injection of double blue dye was performed half an hour before the surgery. We compared the pathway of LCs and the location of SLNs obtained from SLN-CEUS and blue dye during surgery.

Result: Among the 473 patients, the mean number of LCs and SLNs detected by SLN-CEUS was 1.42 and 1.72, respectively, and the coincidence rate was 98.1% compared with blue dye during surgery. The median distance of SLN to skin measured by preoperative CEUS and blue dye was 1.95 ± 0.69 cm and 2.03 ± 0.87 cm, $p = 0.35$. There were three enhancement patterns of SLN in our research, including homogeneous enhancement, inhomogeneous enhancement, and no enhancement, with the sensitivity, specificity, negative predictive value of SLN-CEUS for the diagnosis of SLN of 96.75%, 91.80%, 88.17%, respectively.

Conclusions: SLN-CEUS with skin marking can identify the pathway of LCs and the location of the SLN before surgery, measure the distance of the SLN to skin, and determine if the SLN is metastatic. SLN-CEUS can be used as an effective complement of the blue dye method.

RADIOTHERAPY FOR INITIAL CLINICALLY POSITIVE INTERNAL MAMMARY NODES IN BREAST CANCER

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Background: Internal mammary lymph node (IMN) involvement is associated with poor prognosis in breast cancer. This study investigated the treatment outcomes of initial clinically IMN-positive breast cancer patients who received adjuvant radiotherapy (RT) including IMN irradiation following primary breast surgery.

Methods: We identified 95 breast cancer patients with clinically detected IMNs at diagnosis treated with surgery and RT between June 2009 and December 2015. Patients received adjuvant RT to the whole breast/chest wall and regional lymph node areas. Twelve patients received an additional boost to the IMN area.

Result: The median follow-up was 43.2 months (range, 4.5-100.5 months). Among 77 patients who received neoadjuvant chemotherapy, 52 (67.5%) showed IMN normalization and 19 patients (24.6%) showed a partial response to IMN. There were three and 24 cases of IMN and any recurrences, respectively. The 5-year IMN failure-free survival, disease-free survival (DFS), and overall survival (OS) rates were 96%, 70%, and 84%, respectively. The IMN failure rate was significantly affected by resection margin status (97.5% vs. 75%, $p = 0.009$). All three patients with IMN failure had initial IMN size ≥ 1 cm, and did not receive IMN boost irradiation. The median age of the three patients was 31 years and all had hormone receptor-negative tumors. No adverse reaction following IMN boost irradiation was seen in the intensity-modulated radiotherapy (IMRT) group.

Conclusions: RT provides excellent IMN control without the support of IMN surgery. IMRT is a safe and effective technique of regional lymph node irradiation, including IMN boost for breast cancer patients.

THE USEFULNESS OF ONCOPLASTIC BREAST SURGERY WITH ROTATION FLAP SUPERCHARGED WITH LATERAL THORACIC ARTERY PERFORATOR IN PARTIAL MASTECTOMY DEFECT

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Background: With advancements in screening and radiotherapy, breast conserving surgery (BSC) is becoming a safe option in the treatment of early breast cancer patients. Rotation flap is a type of oncoplastic breast surgery that involves transposition of tissue from the lateral aspect of the partial mastectomy defect. The outcomes of the rotation flap in various locations over the past 13 years are reviewed.

Methods: We performed a retrospective study of 77 patients who underwent rotation flap between 2007 and 2018. We analyzed patient information using medical chart review, and classified patients into groups according to the location of the defect. The incidence of fat necrosis according to supercharging of lateral thoracic artery perforator was also analyzed.

Result: The mean tumor weight was 83.67 g and a defect was a moderate size as it was 25.02% of a total breast volume. In terms of defect locations, the most common was superomedial in 34 patients, followed by superocentral in 25 patients, superolateral in 12 patients, and 6 patients in inferior. Complications included fat necrosis and wound dehiscence. Fat necrosis was significantly less in the supercharged group.

Conclusions: The results shows that rotation flap can cover most moderate sized defects after BCS. Among these, for the superomedial aspect, volume displacement techniques are insufficient to cover moderate sized defects, while donor morbidity is an issue for volume replacement. Conversely, rotation flap could be a useful method for such cases, since it is a relatively simple procedure, shows fewer complications and lower donor morbidity, and shows excellent aesthetic outcomes.

A PREDICTIVE MODEL FOR PATHOLOGIC COMPLETE RESPONSE IN BREAST CANCER PATIENTS TREATED WITH NEOADJUVANT CHEMOTHERAPY USING MACHINE LEARNING

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Background: Neoadjuvant chemotherapy (NAC) has long been used for advanced breast cancer. In patients with NAC, pathological complete response (pCR) is known to be associated with long-term outcome. In previous reports, various ways have been used to predict pCR. However, no study has used machine learning to predict pCR.

Methods: We performed a retrospective chart review of 377 patients who underwent NAC followed by surgery and CancerSCANTM for gene data between August 2008 and June 2017 at Samsung Medical Center. After exclusion of 139 cases due to incomplete data, 238 cases were included for analysis. We built a supervised machine learning classification model using this Azure ML platform and Two-class Bayes point machine method was used to predict pCR.

Result: The no pCR group had 200 patients and the pCR group had 38 patients. In our predictive model with gene data, AUC of the ROC curve was 0.909 and the accuracy was 0.875. In another model without gene data, the AUC of the ROC curve was 0.743 and the accuracy was 0.800. We also conducted prospective internal validation with 72 patients. When we applied a threshold value of 0.4, the accuracy was 0.806 for the predictive model with gene profiles and 0.778 for the model without gene profiles.

Conclusions: Our predictive model presented a useful and easy-to-access tool for predicting pCR in breast cancer patients treated with NAC. After additional evaluation with a larger patient group and external validation, our model could be used more widely.

CHARACTERISTIC AND PROGNOSTIC VALUE OF CELLULAR SENESCENCE-ASSOCIATED MARKERS IN BREAST CANCER DEVELOPMENT

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Background: Breast cancer displaying distinct intertumour and intratumour heterogeneity. Cellular senescence-associated biomarkers exhibit distinguishing molecular changes at different stages of cancer development. Therefore, we aim to characterize expression pattern of senescence-associated markers within intratumour progression.

Methods: A retrospective study of 1,080 patients with invasive ductal carcinoma, of no special type, spanning over an 11-year period, was investigated. Immunohistochemical staining was performed on tissue microarrays that include normal, benign hyperplasia, ductal carcinoma in situ and invasive ductal carcinoma from each patient.

Result: There was a significant correlation between normal, benign, premalignant and malignant tissues with P14, P21, P16, P53, DCR2, and DEC1 expression. Univariate analysis showed strong P16 expression associated with poor survival and increased risk of relapse, whereas high P14 and high P53 expression correlated only with increased risk of relapse. Multivariate analysis of all tumour markers showed that P16 and P14 were important prognostic factors for disease-free survival. Moreover, patients displaying both strong P16 and P14 expressions had an adjusted 3-fold increased risk of disease recurrence and 2-fold increased risk of all-cause related death. Besides, patients whose breast cancer tissues exhibited both high P53 and P16 expression had an adjusted 4-fold increased risk of having disease recurrence and 3-fold increased risk of all-cause related death. High expression of P14 and P53 had an adjusted 3-fold increased risk of having recurrence.

Conclusions: In conclusion, these findings suggest P16, P14, and P53 expression may play a major role in the progression of proliferative breast tissue to invasive cancer and may be useful as prognostic factors.

OPTIMIZING PD-L1 TESTING FOR THERAPEUTIC EFFICACY IN TRIPLE NEGATIVE BREAST CANCER

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Background: There are several immunohistochemical (IHC) based assays approved as companion diagnostics to select for treatment with specific programmed death (PD)-1/PD-ligand-1 (L1) inhibitors. There is no uniformity in the assessment of PD-L1 positivity across trials. We evaluated and compared PD-L1 expression in triple negative breast cancer (TNBC) using different PD-L1 IHC assays.

Methods: A total of 269 TNBC tumors were stained with 3 PD-L1 clones of antibodies (22c3, SP142 and SP263). Quantitative multiplex Immunofluorescent (QmIF) staining method, cytokeratin and CD45 were used to detect tumor and immune cells. Expression of PD-L1 on tumor and immune cells were correlated with PD-L1 RNA expression, clinicopathological parameters as well as disease free survival (DFS) and overall survival (OS)

Result: We observed a weak correlation between SP142 and SP263 clones (R = 0.265) for PD-L1 staining SP142 and 22C3 demonstrated a weak inverse correlation (R = -0.256). There was no significant correlation to clinical outcomes using Combined Positive Score (CPS). Using Tumour Proportion Score (TPS), only high 22C3 TPS is significantly associated with better DFS but not OS. SP142 expression on immune cells is associated with both better DFS and OS. Correlations between protein and mRNA levels of PD-L1 are ongoing and will be reported.

Conclusions: We observed poor correlation of PD-L1 positivity across different assays. Further analysis and harmonization of assays is required to develop PD-L1 testing as a complementary diagnostic in TNBC. QmIF technique used to simultaneously detect and quantitate multiple PD-L1 clones in tumor and immune compartment is a promising tool in the era of cancer immunotherapy.

Poster Presentation

GBCC2019

Global Breast Cancer Conference 2019

UNDERSTANDING DELAYED PRESENTATION OF BREAST CANCER: A QUALITATIVE STUDY

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Background: Patients health seeking behavior is becoming increasingly relevant as a contributing factor of delayed presentation of breast cancer. Unlike other prognostic factors, reasons for this are poorly understood.

Methods: A purposive nested stratified sampling strategy was employed to recruit breast cancer patients within 6 months of diagnosis at the National University Hospital, Singapore. Based on patients narratives of their breast cancer journey, an analytical framework was developed to identify themes associated with delay in presentation to a healthcare professional. We inferred that a breast lump measuring more than 2 cm would be palpable by the patient. Late presenters were defined as patients with a mass of more than 2 cm while early presenters had breast masses 2 cm or less in diameter.

Result: Twenty seven of 36 patients analysed were late presenters. Thematic analysis revealed clear differences in interpretation and response to symptoms and diagnosis between the 2 groups. Lack of knowledge, financial and emotional restraints played a prominent role in delayed presentation. Fear of disease outcomes with the perception that cancer is uniformly fatal was prevalent in both groups. Interestingly, early presenters displayed rationality in actions and health seeking behavior despite these barriers. Healthcare resources and its availability were enabling factors.

Conclusions: Delayed presentation of breast cancer in Singapore is influenced by a combination of knowledge gaps, impact of social support mechanisms and fear. Our study provides valuable insight to formulate effective strategies to encourage earlier presentation of breast cancer which may translate into survival benefits.

HIGH INTENSITY INTERVAL TRAINING DID NOT IMPROVE LEFT VENTRICULAR EJECTION FRACTION IN BREAST CANCER PATIENTS UNDERGOING ANTHRACYCLINE CHEMOTHERAPY

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Background: Anthracycline-based chemotherapy is a cardio-toxic regimen which causes progressive cardiac damage in breast cancer patients, typically measured by left ventricular ejection fraction (LVEF) using echocardiography. High intensity interval training (HIIT) has been shown to increase LVEF compared to moderate intensity exercise in patients with heart failure. We sought to determine the effects of an 8-week HIIT intervention on LVEF in breast cancer patients undergoing anthracycline chemotherapy.

Methods: Thirty breast cancer patients were randomized to either HIIT or delayed (DEL) groups. The HIIT group participated in an 8-week aerobic HIIT intervention occurring 3 times per week on a cycle ergometer. The DEL group was offered the HIIT intervention after 8 weeks. At baseline (wk 0) and week 9, LVEF was assessed using standard M-mode assessment ultrasound. Paired t-test and repeated measures ANOVA was performed to assess changes in LVEF.

Result: At baseline, the HIIT group (n = 15) and DEL group (n = 15) groups did not differ by age (46.9 ± 9.8 years), BMI (31.0 ± 7.5 kg/m^2), systolic/diastolic blood pressure (116.1 ± 11.8/72.3.9 ± 5.6 mmHg) and ejection fraction (60.8 ± 3.3%). Post-intervention, LVEF did not significantly change from baseline in the HIIT group (wk 0: 60.2 ± 2.9%, wk 9: 60.3 ± 3.1%), as well as the DEL group (wk 0: 61.4 ± 4.6%, wk 9: 60.6 ± 5.6%) in the DEL group ($p > 0.05$).

Conclusions: An 8-week of HIIT intervention did not improve LVEF in breast cancer patients undergoing anthracycline chemotherapy, possibly due to shorter duration of intervention. Larger randomized trials are needed to establish the optimal exercise strategy to attenuate anthracycline-induced cardio-toxicities.

COMPARISON OF CLINICAL FEATURES AND ONCOLOGIC OUTCOMES BETWEEN FAMILIAL (NON-HEREDITARY) AND HEREDITARY BREAST CANCER

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Background: The authors compared the clinical features between familial (non-hereditary) and hereditary breast cancer. And we also analyzed their oncologic outcomes to establish appropriate surveillance protocol for familial (non-hereditary) and hereditary breast cancer.

Methods: Among 232 patients with breast cancer who were performed BRCA gene evaluation, twenty-eight patients were diagnosed as hereditary breast cancer with BRCA gene mutation and one-hundred and seventy-six patients were familial (non-hereditary) breast cancer. The clinical characteristics and oncologic outcomes were compared between two groups.

Result: While the incidence of multifocality was higher in familial (non-hereditary) breast cancer group ($p < 0.001$), the bilaterality was higher in hereditary breast cancer group ($p < 0.001$). And the rate of pathologic complete remission was also significantly higher in hereditary breast cancer group ($p = 0.030$). The characteristics of tumor were different between familial (non-hereditary) breast cancer and hereditary breast cancer. The oncologic outcome was better in familial (non-hereditary) breast cancer group than hereditary breast cancer group except death.

Conclusions: The clinical characteristics of familial (non-hereditary) breast cancer were different from those of hereditary breast cancer but similar to those of sporadic breast cancer. The prognosis of the familial (non-hereditary) breast cancer was significantly better than hereditary breast cancer.

MOUSE EMBRYONIC STEM CELL-BASED FUNCTIONAL ANALYSIS OF FIVE UNCLASSIFIED BRCA2 VARIANTS IDENTIFIES ONE DELETERIOUS AND FOUR NEUTRAL VARIANTS

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Background: Next-generation sequencing (NGS) has yielded a multitude of sequence variants in cancer predisposing genes that are of unknown clinical significance (VUS). Interpreting such variants pose significant challenges for both clinicians and patients. Mouse embryonic stem (ES) cell-based assays were conducted to determine the functional significance of five VUS in the BRCA2 gene identified through NGS testing of Sri Lankan families with hereditary breast cancer.

Methods: The following BRCA2 unclassified variants were tested: NM_000059.3:c.2353A > G|NP_000050.2:p.Ile785Val|rs747748537;NM_000059.3:c.9117G > T|NP_000050.2:p.Pro3039 = |rs28897756;NM_000059.3:c.2488A > G|NP_000050.2:p.Asn830Asp|rs574039421;NM_000059.3:c.784G > A|NP_000050.2:p.Ala262Thr|rs397507393;NM_000059.3:c.6231G > C|NP_000050.2:p.Lys2077Asn|rs541826447. The desired BRCA2 variants were generated in bacterial artificial chromosomes and electroporated into mouse ES cells. The assay is based on the observation that BRCA2 is essential for ES cell viability. The ability of human BRCA2 to rescue the lethality of mouse Brca2-deficient ES cells was used to evaluate the functional significance of the variants. Variants that failed to rescue Brca2-deficient ES cells were considered to be deleterious. Surviving ES cells were subsequently tested for sensitivity to several drugs (Cisplatin, Camptothecin, Mitomycin C, Methyl methanesulfonate, Poly ADP-ribose polymerase inhibitors) and irradiation.

Result: The p.Pro3039 = variant was clearly pathogenic. Though silent at the coding level, it resulted in skipping of exon 23 and production of an unstable and non-functional protein. p.Ile785Val, p.Ala262Thr, p.Asn830Asp and p.Lys2077Asn variants were neutral as they rescued ES cell lethality and were indistinguishable from wild-type BRCA2 in their sensitivity to DNA damaging agents.

Conclusions: These findings highlight the value of mouse ES-cell based assays for determining the functional significance of VUS and provide valuable information regarding risk estimation and genetic counseling of families carrying these BRCA2 variants.

Poster Presentation

FUNCTIONAL STUDIES IMPLICATE XRCC2:RS3218550C>T AS A PUTATIVE FUNCTIONAL GENETIC VARIANT FOR SUSCEPTIBILITY TO SPORADIC BREAST CANCER

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Background: A previous study undertaken by our team to identify common genetic variants associated with sporadic breast cancer in Sri Lankan women showed that the T allele of rs3218550, located in the 3'untranslated region of X-ray repair cross-complementing gene-2 (XRCC2), increased breast cancer risk by 1.5-fold. Dual luciferase reporter assays performed in MCF-7 breast cancer cells showed a putative transcriptional repressor effect exerted mainly by the T allele. Electrophoretic mobility shift assays were conducted to further investigate the interaction of this variant with DNA-binding protein, using nuclear protein extracts derived from MCF-7 cells.

Methods: Synthetic biotinylated and non-biotinylated probes containing the wild-type and variant allele sequences of rs3218550 were synthesized. The probes were incubated with nuclear protein extracts from MCF-7 cells, in the presence or absence of competitors, i.e. unlabeled probes. Protein-DNA complexes were resolved by polyacrylamide gel electrophoresis and detected using a Light-Shift Chemiluminescent EMSA kit (Profacgen, USA).

Result: An allele-specific differential binding was observed. The T allele resulted in differential DNA-protein complex binding as evidenced by the presence of multiple bands of increased intensity compared to the wild-type C allele. This implies possible alteration in binding of regulatory proteins by the variant allele.

Conclusions: These results implicate XRCC2:rs3218550C > T as a putative functional genetic variant for susceptibility to sporadic breast cancer. XRCC2 is known to play an essential role in homologous recombination repair of DNA double-strand breaks. It is plausible that this variant may be exerting regulatory effects on XRCC2 gene expression leading to altered DNA repair capacity.

CHARACTERISTICS OF SOMATIC MUTATIONS IN KOREAN YOUNG BREAST CANCER PATIENTS

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Background: Breast cancer in young patients may be biologically distinct from older patients; however, these characteristics have been less well investigated. The purpose of our study was to identify characteristics of somatic mutations in Korean young breast cancer patients.

Methods: Tumors from 273 breast cancer patients were prospectively collected from single institution between May, 2017 and October, 2018. Targeted next-generation sequencing including 143 gene panels was conducted.

Result: In our analysis, 41 (15.0%) and 232 (85.0%) patients were ≤ 40 and > 40 years of age. Totally 936 somatic mutations were identified in 259 of 273patients (94.9%), with the mutation frequency of PIK3CA as 37.7%, TP53 as 34.8%, TET2 as 17.6%, GATA3 as 13.6% and CDH1 as 10.6%. The prevalence of TP53 mutation was significantly higher in younger patients than older patients (51.2% vs. 31.9%, $p = 0.021$). Tumors from patients that carried the TP53 mutation were more likely to have higher expressions ($\geq 20\%$) of Ki-67 (83.7% vs. 30.5%, $p < 0.001$), higher grade (grade 3, 50.5% vs. 10.7%, $p < 0.001$) and estrogen receptor negative tumors (56.8% vs. 14.0%, $p < 0.001$). In the meanwhile, PIK3CA mutation was significantly lesser in young patients than older (22.0% vs. 40.5%, $p = 0.024$). PIK3CA mutations were associated with lower expressions of Ki-67 (69.6% vs. 40.1%, $p < 0.001$), ER positive (83.5% vs. 63.5%, $p = 0.001$) and low grade (85.4% vs. 69.4%, $p = 0.004$).

Conclusions: Aggressive phenotype of tumor in young breast cancer patient might be associated with high prevalence of TP53 mutation and less PIK3CA mutation.

PATTERN OF GERMLINE GENETIC VARIANTS IDENTIFIED USING NEXT-GENERATION SEQUENCING-BASED TESTING IN A SRI LANKAN COHORT WITH HEREDITARY BREAST CANCER

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Background: In 2015, using the Illumina MiSeq Next-generation sequencing (NGS) platform and an in-house developed validated bioinformatics pipeline, multi-gene cancer panel testing and clinical exome sequencing were successfully implemented at our centre for the genetic evaluation of patients with inherited cancers. Herein, the frequency and spectrum of germline genetic variants in cancer predisposing genes (CPGs) identified in a Sri Lankan cohort with hereditary breast cancer are described.

Methods: Clinical and genetic test data of consecutive patients from families with two or more patients with hereditary breast cancer who underwent NGS-based testing between January 2015 and December 2018 were maintained prospectively in a database and analysed retrospectively. Variants were classified after thorough assessment and review of available evidence which included population frequency databases, in-silico functional predictions, evolutionary conservation, clinical databases/published literature and co-segregation data.

Result: Thirty three (68.8%) were cancer affected. Fifteen (31.3%) were pre-symptomatic. Germline variants were identified in 28 (84.8%) cancer affected and 8 (53.3%) pre-symptomatic individuals. Variants were detected in the following CPGs: BRCA1-8 (22.2%); BRCA2-11 (30.6%); MSH2-1 (2.8%); PMS2-1 (2.8%); ATM-3 (8.3%); FANC1-1 (2.8%); CDKN2A-1 (2.8%); CHEK2-4 (11.1%); MLH3-1 (2.8%); PALB2-1 (2.8%); BARD1-1 (2.8%); BRIP1-1 (2.8%); STK11-2 (5.6%). They consisted of: non-synonymous variants-25 (69.4%); small deletions-10 (27.8%); and synonymous variants-1 (2.8%). They were clinically classified as: variants of unknown clinical significance (VUS)-11 (30.6%); pathogenic-14 (38.9%); and likely pathogenic-11 (30.6%). Six (16.7%) were novel variants.

Conclusions: Several VUS and novel variants were identified in this cohort. Further investigations are needed to validate the functional significance of these variants.

MAMMOGRAPHY DENSITY AND REPRODUCTIVE FACTORS BY NATIONAL CANCER SCREENING PROGRAMS FROM 2009 TO 2013: AN ANALYSIS OF THE NATIONAL HEALTH INSURANCE CLAIMS DATA

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Background: To overcome the limitation in women with high mammography density (MD) and to suggest the new guideline of Korean Breast Cancer Screening, we need to survey status of MD reporting and its interaction with screening results and detection of breast cancer.

Methods: Descriptive design with follow-up was used in the study, Data from breast cancer screening and health insurance claim data were used. The study population consisted of all participants in breast cancer screening of NCSP from 2009 to 2013. We used the logistic regression analysis for evaluating the relationship between MD and reproductive factors according to menopause status and analyzed an interaction between age and MD.

Result: MD was reported in 57.5% of participants. In both pre- and post-menopause women (3,417,319 participants), age, early menarche (≤ 15 years), lower live birth (≤ 1 birth) and previous breast benign disease correlated with increased MD. In postmenopausal women, early-onset menopause and longer hormone replacement therapy (≥ 2 years) also increased MD, independently. In interaction analysis, MD and age influenced on both screening results ($p < 0.001$) and a cancer detection ($p = 0.001$), respectively.

Conclusions: MD Reporting rate was relatively low. Reproductive factors correlated with MD in both pre-and post-menopausal Korean women. MD could be changed with age and concurrently influenced screening results and a cancer detection. MD could be not only a limitation of breast cancer screening but also meaningful information to postmenopausal women.

DOES PREOPERATIVE BREAST MRI HAVE BENEFIT FOR IPSILATERAL AND CONTRALATERAL BREAST TUMOR RECURRENCE OF BREAST CANCER PATIENTS?

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Background: This study aims to determine if magnetic resonance imaging (MRI) before breast conserving surgery (BCS) is associated with reduced ipsilateral and contralateral breast tumor recurrence.

Methods: Data from 542 consecutive patients with invasive breast cancer undergoing BCS between 2008 and 2015 at Dongsan Medical Center were reviewed. Ipsilateral breast tumor recurrence (IBTR) free survival and bilateral breast tumor recurrence (BBTR) free survival were compared between the patients with preoperative breast MRI (MRI group) and without preoperative breast MRI (non-MRI group).

Result: Preoperative breast MRI was not performed for 264 patients from 2008 to 2011. Routine preoperative breast MRI was performed for 278 patients from 2012 to 2015. Median follow-up period of the MRI group and the non-MRI group were 54.4 months and 86.5 months respectively. In the MRI group, IBTR was observed in 7 cases, and no contralateral breast tumor recurrence was observed. In the non-MRI group, IBTR was observed in 7 cases and contralateral breast recurrence was observed in 3 cases. Cumulative IBTR free survival and BBTR free survival were not different in the two groups (log rank $p = 0.111$ and 0.174 respectively). In multivariate analysis, among patient age, T stage, hormone receptor status, HER2 status, adjuvant chemotherapy, adjuvant radiotherapy and presence of preoperative MRI, no variable had significant relationship to IBTR and BBTR.

Conclusions: There was no significant difference in IBTR and BBTR, whether preoperative MRI is performed or not.

BREAST CANCER IN INDONESIA: WHERE DO WE STAND AND WHERE DO WE GO?

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Background: Breast cancer is the second most common cancer in Indonesia, a low income country in Southeast Asia. Perhimpunan Ahli Bedah Onkologi Indonesia (PERABOI) is association of oncologist surgeon in Indonesia provide hospital based registry breast cancer in tertiary referral hospital in Indonesia. The objective of this study is to characterize the presentation, evaluation diagnosis and management of breast cancer in Indonesia.

Methods: A total 9,770 women newly diagnosed with breast cancer from January 2012 until December 2017 were studied. Age at diagnosis, tumor size, histological type, tumor grade, ER, PR, lymph node involvement, treatment modalities were recorded.

Result: The median age was 49.55 years old. Initial diagnosis at 42.40 years old. 42.33% were diagnosed with stage 3 and 4 session and 75.1% underwent mastectomy, of which 47.3% the intent was palliative. Of those whose ER were known, only 26.9% positive and 36.5% of breast cancer weren't assessed immunohistochemistry evaluation.

Conclusions: Breast cancer presents at a late stage, because treatment is suboptimal, survival is poor in Indonesia. A more aggressive approach to early detection and treatment needs be developed in improve outcome from this potentially curable disease.

ARE THERE ANY DIFFERENCES BETWEEN THE VERY YOUNG AGE AND VERY OLD AGE WOMEN BREAST CANCER?

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Background: The incidence of breast cancer rate is highest among the age between 40-60. However, both very young (age ≤ 35) and very old age (age ≥ 75) breast cancer incidence are increasing. In this study, we investigated the clinicopathologic differences of women breast cancer between the age ≤ 35 and ≥ 75.

Methods: Among the 902 women patients underwent breast cancer surgery in our institution from March 2003 to December 2014, 81 patients were included in this study; group I, patients younger than age 35 (n = 36) and group II, patients older than age 75 (n = 46). Clinicopathologic characteristics were retrospectively reviewed from medical records.

Result: The mean age of patient was 31.8 in group I and 78.2 in group II, respectively. Elderly patients were tended to detect primary breast cancer incidentally via routine health screening, while young patients represented symptoms ($p = 0.037$). Very young age was significantly associated with higher rate of multifocal cancer, mastectomy, axillary dissection, breast reconstruction, either neo-adjuvant or adjuvant chemotherapy and adjuvant radiotherapy. ($p = 0.010$, 0.005, 0.005, < 0.001, < 0.001, and < 0.001, respectively). Either systemic or local recurrence rate were slightly higher in group I with no significance. Disease related death rate was not different between two groups.

Conclusions: Very young age breast cancer patients are tended to undergone more aggressive treatment. However, the disease related death rate in very young age breast cancer is not differ from that of very old age. Careful selection of treatment modality with balancing between the quality of life and the oncologic safety is needed in this group.

BONE METASTASIS IN PREMENOPAUSAL WOMEN WITH HORMONE RECEPTOR-POSITIVE BREAST CANCER TREATED WITH NEOADJUVANT CHEMOTHERAPY

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Background: Factor associated with bone metastasis is not well known. The purpose of this study was to find factors associated with bone metastasis in high risk estrogen receptor (ER)-positive breast cancer.

Methods: Two hundred ninety-seven premenopausal ER-positive/HER2-negative breast cancer patients who underwent breast surgery after neoadjuvant chemotherapy (NAC) from January 2004 to December 2009 were included. At least 5 years tamoxifen was routinely received. Patients with bone metastasis were compared to patients who developed distant metastasis without bone. Clinicopathological factors, including family history, parity, NG (1-2 vs. 3), ER (low: 1-4 vs. high: ≥ 5 by Allred score) and PR (low: 1-4 vs. high: ≥ 5) before and after NAC, cT and ypT (1-2 vs. 3-4), ypN (0 vs. ≥ 1), LVI, response to NAC (CR/PR vs. SD/PD), age (< 40 vs. ≥ 40) were assessed.

Result: At the median follow up period of 121 months (range: 9-174 months), 51 of the 297 patients (17%) developed distant metastases and 35 patients (12%) had bone metastases at the diagnosis of first metastasis. cT and age were independent factors of distant metastasis ($p = 0.012$, 0.054, respectively). With respect to bone metastasis, high ER was significantly associated with bone metastasis compared with low ER (OR: 3.667, 95% CI: 1.097-12.250, $p = 0.035$).

Conclusions: We showed that high ER expression level was the only clinical factor that was associated with bone as a first site of distant metastasis in premenopausal ER-positive/HER2-negative breast cancer patients who received NAC.

HETEROGENEITY OF ESTROGEN RECEPTOR AND PROGESTERONE RECEPTOR EXPRESSION IN LUMINAL B BREAST CANCER

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Background: Luminal subtype of breast cancer have very heterogeneous biologic characteristics according to estrogen receptor (ER) and progesterone receptor (PR) expression pattern. We planned to analyze the pattern of ER or PR expression and find out the clinically relevant prognostic factors of more aggressive luminal B breast cancer.

Methods: We collected the clinical and pathologic data of total 217 breast cancer patients who were classified as luminal B subtype defined as ER and/or PR positive and high Ki 67 proliferation index (> 14%) and/or HER2 positive. We classified them into four subgroup according to ER and PR expression pattern. We evaluated clinical factors such as age at diagnosis, recurrence pattern and pathologic factors such as bcl-2, Ki67.

Result: Among total 217 luminal B breast cancer patients, we had 106 intact ER and PR (group 0) (48.8%), 17 ER low or loss (group 1) (7.8%), 75 PR low or loss (group 2) (34.6%), 19 ER and PR low or loss (group 3) (8.8%). PR low or loss (group2) was related with age over 50 years old ($p = 0.0001$) and low bcl-2 ($p = 0.0009$) and non-skeletal metastasis ($p = 0.0019$). Disease free survival was statistically significantly worst in PR low or loss ($p = 0.0465$) and overall survival was best in group1 and worst in group 2 but statistically not significant ($p = 0.1485$).

Conclusions: This study supported that PR low or loss is important prognostic factor in luminal B breast cancer when we compared them to intact ER and PR, ER low or loss, ER and PR low or loss group.

A PI3KAΔ INHIBITOR COMBINED WITH IRRADIATION ENHANCE THE EFFECT OF ANTI-PD1 IN SYNGENIC TRIPLE NEGATIVE BREAST CANCER MODEL

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Background: We hypothesize that in situ tumor vaccination via radiation and suppression of immune tolerance via PI3Kδ inhibition could enhance the clinical efficacy of immune checkpoint blockade and evaluated whether RT combined with novel PI3Kαδ inhibitor could enhance the efficacy of PD-1 blockade in syngenic TNBC model.

Methods: 4T1 murine breast cancer cells were grown subcutaneously in the hind limb of BALB/c mice. Tumors were irradiated using 24 Gy/3 fractions. PD-1 blockade (10 mg/kg) and PI3Kαδ inhibitor (4 mg/kg) were administered every other day for two weeks, respectively.

Result: Triple combination of RT, PD-1 blockade, and PI3Kαδ inhibitor significantly delayed tumor regrowth whereas PD-1 inhibitor alone showed only modest effect in 4T1 syngenic TNBC model. FACS and IHC study for immune repertoire using tumor samples showed that RT and PD-1 blockade modestly increased the proportion of cytotoxic CD8+ T cells and PI3Kαδ inhibitor led to decrease the proportion of Treg. Triple combination showed remarkable increase of cytotoxic CD8+ T cells suggesting synergistic immune modulatory effect of RT, PD-1 blockade and PI3Kαδ inhibitor. Triple combination led to significant upregulation of c-GAS/STING pathway in the tumor and increased IFN-gamma level in blood as well compared to each modality alone.

Conclusions: Taken together, combination of RT and PI3Kαδ inhibitors maximized immune stimulatory effect in immune competent syngenic TNBC model and enhanced the response of PD-1 inhibitor via non-redundant synergistic immune modulatory effect. This study provides a preclinical rationale for the combination of PI3Kαδ inhibitor and RT with PD-1 blockade to overcome the immune tolerance of breast cancer.

MICRORNA-496 INHIBITS TRIPLE NEGATIVE BREAST CANCER CELL PROLIFERATION BY TARGETING DEL-1

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Background: Del-1 is linked to the pathogenesis of various cancers including breast cancer; however, the regulation of Del-1 expression remains unclear. The current study investigated how microRNA-496 (miR-496) regulates Del-1 expression in triple negative breast cancer (TNBC).

Methods: Del-1 mRNA and miR-496 were measured by quantitative PCR in breast cancer cells (MDA-MB-231, MCF7, SK-BR3, and T-47D) and tissues from 30 patients with TNBC. The effects of miR-496 on cell proliferation, migration, and invasion were determined in MTT, wound healing, and Matrigel Transwell assays, respectively.

Result: In MDA-MB-231, miR-496 levels were remarkably low and Del-1 mRNA was higher compared to other breast cancer cell lines. Luciferase reporter assays revealed that miR-496 binds the 3'-UTR of Del-1 and that Del-1 expression is downregulated by miR-496 mimics. Furthermore, miR-496 inhibited the proliferation, migration, and invasion of MDA-MB-231 cells. The effects of miR-496 on cell proliferation were additive with those of miR-137, another miRNA that regulates Del-1 expression. Moreover, in the 30 TNBC specimens, miR-496 was downregulated ($p < 0.005$) and the levels of Del-1 in the plasma was significantly elevated as compared to normal controls ($p = 0.0142$). TCGA data showed the correlation of miR-496 expression with better overall survival in patients with early TNBC.

Conclusions: In in silico and in vitro analyses, we showed that Del-1 is a target of miR-496 in TNBC and thereby affects cancer progression. Our findings suggest that miR-496 and Del-1 might act as modulating factors in TNBC and are new biomarkers for patients with TNBC.

A NOVEL APPROACH TO TRIPLE-NEGATIVE BREAST CANCER CELL TREATMENT TARGETED IN CALORIE RESTRICTION AND NHE-1 INHIBITION

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Background: Overexpression of P-glycoprotein (P-gp) plays a critical role in drug resistance in many cancer cells. Activation of Na^+/H^+ exchanger 1 (NHE-1) 1 leads to elevated intracellular pH (pHi), which reduces drug accumulation and promotes drug resistance. P-gp is an ATP-dependent transporter, and ATP is also required for NHE1 activity by regulation of the intracellular PIP2. In this study, we investigated whether calorie restriction and NHE-1 inhibition enhance therapeutic efficacy of anticancer drug on MDA-MB-231 cells.

Methods: RT-PCR, real time PCR and western blot were used to investigate the expression pattern of glucose metabolism-related, pHi-related and multidrug resistance signaling pathways. BCECF-AM was used to measure intracellular pH (pHi) by flow cytometry. The cell viability was evaluated by EZ-CYTOX cell viability assay kit.

Result: Multidrug resistance (MDR1) was upregulated at both the mRNA expression and protein expression levels after paclitaxel treatment in a time- and dose-dependent manner. Co-treatment with cariporide (a NHE-1 inhibitor) reversed the elevated expression of MDR1. A relative higher pHi was observed in low-glucose group than normal-glucose group, and the pHi was decreased by paclitaxel treatment in a time-dependent manner, and the pHi was rapidly decreased after 72 hours. Application of cariporide significantly reduced the pHi compared with control or paclitaxel treatment group. There was significantly reduced in cell viability by the combination of paclitaxel and cariporide in low-glucose group compare with high-glucose group.

Conclusions: Our results indicate that combination of calorie restriction and NHE-1 inhibition has a potential to become co-adjuvant target for triple-negative breast cancer.

IMPACT OF NEOADJUVANT DUAL HER2 BLOCKADE IN NON-METASTATIC HER2 POSITIVE BREAST CANCER FOR BREAST CONSERVATION SURGERY AND TUMOR SHRINKAGE

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Background: In current literature there is no data regarding how dual HER2 blockade affects surgical outcome in neoadjuvant setting, despite sufficient evidence showing its superiority, when compared to single blockade, in achieving pathological complete response. This study aims to compare the two in breast conservation therapy (BCT) rate and tumor response.

Methods: A retrospective study was performed on a prospectively-maintained database in an academic-based hospital, including patients with non-metastatic, HER2 positive breast cancer receiving neoadjuvant systemic therapy (NST) between January 2014 and December 2018.

Result: A total of 142 patients were analyzed: 75 received trastuzumab (Herceptin [H]) -based NST and 67 received H+pertuzumab (P) -based NST. Before NST, 65 patients (45.8%) were eligible for BCT; and this increased to 103 (72.5%) after NST. Thirty-seven out of 77 patients (48.1%), who were not suitable for BCT, converted to BCT-eligible after NST. Interestingly, 53.4% patients, who were BCT-eligible, opted for mastectomy. PH-based comparing to H-based NST did not differ significantly in BCT rate (35.5% vs. 32%, $p = 0.72$); but there was a trend of increase in conversion to BCT-eligible rate (43.9% to 52.8%) and reducing tumor volume (69.5% to 80.0% reduction).

Conclusions: This is the first study to compare H-based and PH-based NST on surgical outcome, and documented a trend of increasing tumor shrinkage and BCT eligibility with PH-based NST. However, actual BCT rate was not significantly increased, with more than half of BCT candidates choosing mastectomy. Further study on surgical choice would complement this finding and allow interventions to increase BCT rates.

CHANGES IN PATTERN OF MAMMOGRAPHIC MICROCALCIFICATIONS DO NOT CORRELATE WITH HISTOPATHOLOGIC RESULT AFTER NEOADJUVANT CHEMOTHERAPY FOR BREAST CANCER

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Background: Aim of this study is to assess mammographic microcalcification pattern of change before and after NAC, to correlate residual mammographic microcalcifications with histopathologic findings of the tumor.

Methods: From June 2011 to August 2018, breast cancer patients who underwent NAC and demonstrated suspicious microcalcifications within or near the tumor bed were included. To assess change in size of microcalcification, the greatest diameter was compared and categorized as follows; increase, decrease, no change and new microcalcifications.

Result: Of 150 patients who underwent NAC, 96 had visible microcalcifications on mammogram. The mean (±SD) age was 45.1±6.6 years (range, 3270 years). The most common histologic type at initial presentation was invasive ductal carcinoma (IDC), [n=141 (94.0%)]. The mean (±SD) size of microcalcifications on the pre and post-NAC mammograms was 4.02±2.7 cm (range, 0.413.0 cm) and 3.82±2.7 cm (range, 0.4 14.1 cm). After NAC, 72 (48.0%) showed no change, 12 (8.0%) decreased, 7 (4.7%) increased, and 5 (3.3%) showed new microcalcification. Of 23 patients who achieved pathologic complete response (pCR), microcalcifications were associated with benign pathology in 11 (47.8%), previous site of cancer in 8 (34.8%). Of the 127 (84.7%) patients who had non-pCR, microcalcifications were associated with invasive or in situ disease in 70 (55.1%), benign pathology in 36 (28.3%), previous site of cancer in 7 (5.5%).

Conclusions: The extent of calcifications on mammography after NAC does not correlate with the extent of residual disease in 82.6% of women who achieved pCR.

Poster Presentation

CONSECUTIVE 300 GYNECOMASTIA SURGERIES BY A SINGLE SURGEON

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Background: Gynecomastia is occurring in 5-10% men. When fibrotic tissue develops in gynecomastia, medical therapy is less helpful and surgical treatment may be the only way to overcome gynecomastia.

Methods: Three hundred patients who have been treated with gynecomastia from September 2017 to December 2018 at the Spring Day Clinic were analyzed for clinical factors retrospectively. Subcutaneous mastectomy and liposucion were performed on all cases by single surgeon (Dr. Hwang).

Result: The mean age was 25.3 years and the most frequent age group in gynecomastia patients was twenties (53.3%). According to type of gynecomastia, fibro glandular type was 107 patients (35.7%), mixed type was 126 patients (42.0%), pseudo type 67 patients (22.3%). Symmetric gynecomastia was found in 279 patients (93.0%) and asymmetric gynecomastia in 21 patients (7.0%). According to Simons classification, type I was 42 patients (14.0%), type IIA 216 patients (72.0%), type IIB 40 patients (13.3%), Type III two patients (0.7%). The mean amount of mammary tissue was 92.6 g and the mean amount of liposuction was 483 ml. Postoperative bleeding was seen in 5 patients (1.7%), remnant mammary tissue was seen in two patients (1.7%) and nipple retract was seen in one patient (0.3%). In our study, 96.3% of patients enjoyed cosmetically satisfying outcomes.

Conclusions: Patients with gynecomastia who are not responding to medical treatment and suffering psychosocially will have stable and reliable results with surgical treatment.

CLINICOPATHOLOGICAL CHARACTERISTICS OF BREAST CANCER CASES IN JAPANESE MEN

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Background: Male breast cancer is a rare disease that accounts for 0.5% of all breast cancer cases. While there have been sporadic case reports concerning this disease in Japan, there have been few case series reports.

Methods: Clinicopathological characteristics were extracted from the medical records of 44 male patients (including 1 bilateral case) diagnosed with breast cancer at the National Cancer Center Hospital from 1997 to 2017. Descriptive statistics were prepared with respect to patient age, cancer stage at time of diagnosis, hormone receptor status, HER2 status, and perioperative drug therapy. Overall survival time and disease-free survival time were analyzed using the Kaplan-Meyer method.

Result: The median patient age was 66.5 years (range: 31-88 years), and there were 38 cases (86.4%) of stage 0-II cancer, 4 cases (9.1%) of stage III cancer, and 1 case (2.3%) of stage IV cancer. 36 cases (81.8%) were hormone-positive, 3 cases (7.0%) were HER2-positive, perioperative chemotherapy was administered in 13 cases (30.2%), and anthracycline was administered in 12 cases (92.3%). Trastuzumab was administered to all HER2-positive patients. Postoperative hormone therapy was administered in 35 cases, and tamoxifen was administered in all cases. Distant metastasis recurred in 6 patients (14.0%). The median disease-free survival period was 2 years (95% CI: 1.5-N/A), and the median survival period was 6.3 years (95% CI: 5.1-7.8).

Conclusions: The age of onset in male breast cancer cases was higher than in cases involving female patients, hormone receptor positivity was high, and complicating cancers was found to appear more frequently.

DEMOGRAPHIC PROFILE AND OUTCOMES OF PREGNANCY ASSOCIATED BREAST CANCER PATIENTS IN A TERTIARY CARE CENTER IN INDIA

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Background: Pregnancy associated breast cancer (PABC) is defined as breast cancer diagnosed during pregnancy or one year post-partum, is a unique situation with issues regarding maternal ontological outcome and fetal safety together. There is sparse data, with unmet need especially in Lower and Middle income countries (LMICs) and merits exploration.

Methods: A prospective and retrospective registry study of PABC is carried out from 2013-2018 at Tata Memorial Center in India.

Result: There are 83 patients with a median age of 31(23-42) years; 37% diagnosed during pregnancy while 63% postpartum; 72% had delayed diagnosis. Twenty nine had family history however, 1 was positive for BRCA mutation (185 DelAG). Of these, 91% had IDC grade III tumours, 50% were triple-negative and 37% were Her2-positive. Majority 69 (71%) received anthracyclines & taxanes based therapies; grade III/IV complications occurred as: 10 febrile-neutropenias, 3 mucositis, 1 hypersensitivity. Of 49 non-metastatic patients, 43 received neoadjuvant-chemotherapy and 38 had partial response, 25 underwent breast-conservations and 2 achieved pathological complete remission. Of total, 31 patients diagnosed during pregnancy (19-first, 8-second, 4-third trimester).There were 11 medical terminations (6 metastatic) and 20 successful deliveries with average birth-weight of 3 (1.7-4) kgs. No congenital abnormality noted, however, two required ventilatory support due to prematurity. All 20 babies were alive with normal milestones. At median follow up of 23 (1-36) months, two years predicted overall survival is 87% & event free survival is 77%.

Conclusions: PABC is associated with delayed, advanced presentation and aggressive biology; a national registry, multidisciplinary care with avoidance of premature deliveries and optimizing oncologic outcome are highly needed in LMICs.

COMPLIANCE OF ENDOCRINE THERAPY IN YOUNG WOMEN WITH BREAST CANCER

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Background: Breast cancer is the most common cancer among Singaporean women. Incidence has increased threefold from 1980 to 2015, and young women make up 20% of those affected. Age-specific incidence rates for women below 30 remained similar (< 5 per 100,000 per year). For women aged 30-39, it increased from 25.8/100,000 per year in 1998-2007 to 35.6 in 2008-2017. The disease carries significant socioeconomic impact as these young women are a major contributor to the productive workforce and within their reproductive years, hence compliance to endocrine treatment (ET) is important.

Methods: A review of breast cancer patients aged 40 and below at diagnosis recruited prospectively in our Singhealth Joint Breast Cancer Registry was performed. Patient demographics, tumour characteristics, survival and duration of endocrine treatment were analyzed.

Result: Two thousands three hundreds fourteen patients were identified from 1998-2017. Cancer stage at diagnosis was similar to that of Singaporean woman of all ages in the national registry. 45.3% underwent breast conserving surgery and 94.5% of them received radiotherapy. 54.5% were hormone receptor positive cases, of which 84.7% were prescribed endocrine therapy. Overall survival rate at 5 years for those who received more than 3 years of ET was 98% compared to 76% for those who did not ($p < 0.001$).

Conclusions: Disease characteristics of breast cancer in young women in our healthcare cluster are similar to that of the general population. Despite the recommended duration of ET as 5 years, many studies have shown younger age is associated with lower compliance. The mean duration of ET in our study is 3 years.

ULTRASOUND-GUIDED VACUUM ASSISTED BREAST BIOPSY FOR DIAGNOSIS AND TREATMENT OF BREAST LESIONS

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Background: Vacuum assisted breast biopsy (VABB) is effective for complete removal of lesions of the breast. Ho Chi Minh City Oncology hospital is the first institution in Vietnam in which this procedure is performed.

Methods: Breast lesions which are completely removed by ultrasound guided VABB and local anesthesia at Ho Chi Minh City Oncology Hospital.

Result: One hundred nineteen patients with 229 lesions are removed with ultrasound guided VABB since 2/2017 to 10/2018. Mean age is 38.6 (11-63), mean size is 15.2 mm (4-50 mm). Most patients have 1-2 lesions, the highest number of lesion removed in one patient is 6. Most histology is benign with the majority is fibroadenoma. Eight cases (3.5%) are carcinoma. There is no severe complication, 46 (38.3%) cases with skin echymosis and 1 case with hematoma. Two cases have moderate bleeding in the procedure and need IV saline transfusion. There are 10 (8.3%) cases report of mild pain (mean score 3.5/10) in the first 3 days after the procedure. There is only one case (galactocele) has residue in ultrasound checking.

Conclusions: VABB is effective for breast lesions biopsy. This is also a diagnosis and treatment method for benign breast lesions. This gives Vietnamese patients another option besides open surgery.

NIPPLE-SPARING MASTECTOMY THROUGH ONLY PERIAREOLAR INCISION WITH IMMEDIATE RECONSTRUCTION

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Background: Nipple-sparing mastectomy (NSM) has become increasingly popular due to improved cosmesis without compromising oncologic safety. Radial and inframammary incisions are usually used to achieve NSM, with periareolar incisions usually being avoided because of the risk to nippleareola complex (NAC) viability. In an attempt to maximize esthetic effects, we performed NSM through only periareolar incision with immediate reconstruction. We report our initial experience.

Methods: This case series consisted of all consecutive patients (N = 23) who underwent NSM through a periareolar incision in our institution between August 2017 and November 2018. All patients underwent NSM through only periareolar incision followed by immediate reconstruction with an implant or deep inferior epigastric perforator (DIEP) flap. Patient demographics, tumor and treatment characteristics, and short-term postoperative outcomes were reviewed.

Result: The mean patient age was 47.76 ± 6.35 years (range, 38 to 62 years), and the mean operation time was 106.47 ± 26.07 minutes. Indications included in situ cancer in 8 cases and invasive cancer in 15 cases. No infection, fistula, implant exposure, or reconstruction failure was observed. There was 1 major complication (postoperative hematoma) requiring operative reintervention. At the time of writing, no case of local recurrence has been observed.

Conclusions: NSM with immediate reconstruction can successfully be performed through a single periareolar incision. This method maximizes esthetic effects and can be an appropriate surgical option for NSM.

CONSERVING THE LYMPHATIC DRAINAGE FROM THE ARM USING FLUORESCENCE IMAGING IN PATIENTS WITH BREAST CANCER AT HIGH RISK OF POSTOPERATIVE LYMPHEDEMA

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Background: Postoperative lymphedema in breast cancer survivors is a serious complication that develops from axillary lymph node dissection (ALND), chemotherapy, and radiation therapy. Axillary reverse mapping (ARM) has been recently introduced to reduce lymphedema. This pilot study aimed to investigate the feasibility of preserving the ARM node using fluorescence imaging for patients at high risk of lymphedema.

Methods: We prospectively screened patients with breast cancer who had pathologic node-positive disease at diagnosis and are scheduled for neoadjuvant chemotherapy. Sentinel lymph node (SLN) was identified using blue dye and radioisotope, and the ARM node was traced using indocyanine green. In cases in which SLN was negative on the intraoperative frozen section examination, the ARM node and lymphatics were preserved.

Result: Of the 20 patients screened, six patients whose metastatic axillary lymph node converted to clinically node-negative disease after neoadjuvant chemotherapy were enrolled. All patients had no recurrence at 12 months postoperative. Four patients who had preserved ARM node did not develop lymphedema. One patient who underwent ALND without ARM node conservation because of metastatic SLN on frozen section examination developed postoperative lymphedema. One patient whose ARM node was not preserved due to SLN identification failure did not develop postoperative lymphedema.

Conclusions: ARM is oncologically safe, reduces the incidence of postoperative lymphedema, and allows for the early detection of postoperative lymphedema in patients who underwent ALND. Ultimately, ARM may help improve the quality of life in patients with pathologic node-positive breast cancer.

RE-SENTINEL LYMPH NODE BIOPSY FOR BREAST RECURRENCE AFTER BREAST-CONSERVING SURGERY

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Background: The usefulness of re-sentinel lymph node biopsy (re-SLNB) in unclear in the management of patients with ipsilateral recurrent breast cancer.

Methods: We reviewed the cases of re-SLNB conducted in our institute. We found 50 patients with locally recurrent breast cancer who underwent re-SLNB between July 2012 and November 2018. Forty-three patients were after prior SLNB and 7 were after prior axillary lymph node dissection (ALND). All re-SLNB were performed with dual tracer, indocyanine green and radioactive colloid. Preoperative lymphoscintigraphy was used for all cases.

Result: SLNs were successfully visualized by preoperative lymphoscintigraphy in 47 out of 50 cases (94.0%), and 95.3% in cases with prior SLNB, and 85.7% in cases with prior ALND. Thirty-seven cases had SLNs in ipsilateral axilla, 6 cases in contralateral axilla, and 9 cases in parasternal region. SLNs were successfully removed in 43 (86.0%) out of 50 patients. Sentinel node metastases were detected in two women.

Conclusions: Sentinel lymph node identification was possible with high detection rate among patients with recurrent breast cancer after prior breast-conserving and axillary surgery.

RESULTS OF ACELLULAR DERMAL MATRIX USE IN BREAST CANCER SURGERY

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Background: The acellular dermal matrix (ADM) is a dermal matrix from human skin that removed dermal cells that cause an immune response. The purpose of this study is to evaluate the clinical efficacy of ADM implantation after breast surgery.

Methods: This study was prospective, randomized, two-arm assignment controlled trial of application of ADM for breast surgery, assessed 100 patients who underwent breast conserving surgery (BCS) and/or axillary lymph node dissection (ALND) between November 2017 and October 2018. The primary endpoint was to compare the total drainage volume after operation. The secondary endpoint was patient subjective satisfaction and shoulder movement using visual analogue scale score.

Result: The drainage volume was 163.2 ± 210.4 cc in the BCS without ADM group (n = 36) and 163.0 ± 201.3 cc in the BCS with ADM group (n = 36) (p = 0.991). The total drainage volume was 503.9 ± 376.6 cc in the ALND without ADM group (n = 14) and 532.8 ± 363.3 cc in the ALND with ADM group (n = 14) (p = 0.838). There was no difference in satisfaction with pain, discomfort, and cosmetics between two groups with BCS. Satisfaction with the range of shoulder motion in the ALND was also not different between control and ADM group. One case of wound infection occurred in BCS groups using ADM.

Conclusions: The use of ADM did not increase the amount of drainage in both BCS and ALND. The cosmetic effect did not benefit the patient. There was no difference in short-term results although long-term follow-up studies are needed. In addition, further studies are required for larger defect sites.

LONG-TERM OUTCOMES AFTER BREAST-CONSERVING SURGERY PLUS RADIOTHERAPY COMPARED WITH MASTECTOMY IN EARLY BREAST CANCER IN THE KOREA: A LARGE-SCALE, SINGLE-CENTER STUDY

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Background: In some recent studies, breast conserving surgery and radiotherapy have been reported to improve survival rates compared with mastectomy compared with early breast cancer. The purpose of this study was to evaluate the survival rate after breast-conserving surgery plus radiotherapy compared with mastectomy in Korea women with early breast cancer.

Methods: In this population-based study, all women in the Asan medical center who were diagnosed as primary, invasive, breast cancer from January 1, 1991 to December 31, 2008 were selected either breast-conserving surgery plus radiotherapy or mastectomy, regardless of the use of resection or adjunctive systemic therapy.

Result: Of the 10,945 patients included in this study, 4,593 (42%) received breast-conserving surgery plus radiotherapy and 6,352 (58%) received mastectomy. For both unadjusted and adjusted analysis accounting for various confounding factors, breast-conserving surgery plus radiotherapy was significantly associated with improved 10 year overall survival in the whole cohort overall compared with mastectomy (HR 0.38 [95% CI 0.34-0.42]; $p < 0.001$). After adjustment for confounding variables, breast-conserving surgery plus radiotherapy did significantly improve 10 year overall survival compared with mastectomy (HR 0.58 [0.51-0.66]; $p < 0.001$).

Conclusions: Adjustment of confounding variables by breast conserving surgery and radiotherapy improved overall 10-year survival and relative survival rates compared to mastectomy compared with early breast cancer. These results suggest that breast conserving surgery and radiotherapy are at least equivalent to mastectomy in terms of overall survival and may affect treatment decisions in early breast cancer patients.

THE EFFECTIVENESS OF SURGICAL SITE INFECTION (SSI) PREVENTION BUNDLE IN REDUCING THE INCIDENCE OF SSI POST MASTECTOMY AMONG BREAST CANCER PATIENTS IN UNIVERSITY MALAYA MEDICAL CENTRE (UMMC)

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Background: Surgical site infections (SSIs) are one of the commonest healthcare associated infections, & even for mastectomies the incidence varies from 1-30%. This is significantly higher compared to the expected incidence of 2% for clean surgeries. The aim is to reduce the incidence of SSIs among breast cancer patients undergoing mastectomy at UMMC by implementing the SSI prevention bundle & to identify risk factors of SSI.

Methods: The study was conducted from July 2017-June 2018 & it involved the implementation of the SSI prevention bundle on all breast cancer patients undergoing mastectomy at UMMC. The bundle consists of preoperative, intraoperative & postoperative preventive measures adapted from the Global Guidelines for the Prevention of SSI by WHO. Multivariate logistic regression was used to identify independent risk factors for SSI.

Result: Retrospective analysis of SSI rates from July 2015 to June 2016 (pre-bundle) was 23.1%. Following the implementation of the bundle, there was a 65% reduction in the SSI rates to 8.1%. Multivariate logistic regression analysis revealed that undergoing surgery without the bundle (OR 4.55, 95% CI 1.47-14.04, $p = 0.008$) & obesity (OR 4.80, 95% CI 1.06-21.67, $p = 0.04$) were significant risk factors of SSI.

Conclusions: The implementation of the SSI prevention bundle is effective in reducing the incidence of SSIs amongst breast cancer patients undergoing mastectomy, which in turn reduces morbidity and consumption of hospital resources, ultimately improving the quality of care.

PARTIAL BREAST RECONSTRUCTION WITH LATERAL CHEST WALL PERFORATOR FLAPS TO FACILITATE BREAST CONSERVATION IN WOMEN WITH BREAST CANCER: A SINGLE CENTRE EXPERIENCE OVER 7 YEARS AND REPORT ON FOLLOW-UP

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Background: Lateral chest wall perforator flaps (CWPF) offer an excellent option for partial breast reconstruction (PBR) in women undergoing breast conservation surgery (BCS) for laterally placed tumours in small to moderate non-ptotic breasts. We present our experience with PBR in facilitating breast conservation surgery with medium term follow-up.

Methods: A prospective database was maintained to collect information on clinicopathological features, complications and follow-up. Patients were asked to complete an anonymised PROM questionnaire. All patients are followed up annually for 5 years.

Result: One hundred and five patients underwent PBR with CWPF between 2011 and 2018 by a single surgeon. 75% patients underwent cancer resection and PBR as one operation whilst 25% underwent PBR as two-stage approach. The two-stage approach was undertaken for patients with high tumour:breast ratio (expected loss of breast volume > 30%) to avoid mastectomy. The complication rate was low and re-operation rate for close/involved margins was under 10%. The median follow-up is 39 months (ranging from 12 months to 7 years) with no local recurrence reported so far (3 patients presented with distant disease. The presence of flap did not interfere with interpretation of surveillance mammogram in our cohort. PROM states high satisfaction scores in majority of the domains.

Conclusions: Wide excision combined with perforator flap reconstruction provides an effective oncological approach with good cosmesis, as judged by patients. We recommend considering two-stage approach in women with high tumour-breast ratio to ensure successful BCS prior to undertaking PBR. The medium term follow-up data establishes the safety of BCS in women with high-risk tumour characteristics.

SURGICAL TECHNIQUE AND CRITERIA FOR THE BETTER COSMETIC OUTCOME OF BREAST-CONSERVING SURGERY FOR PRIMARY BREAST CANCER PATIENTS

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Background: Since long-term oncological safety of breast-conserving surgery (BCS) has been established to be equivalent to those of mastectomy, BCS is one of the standard procedures for primary breast cancer. Compared to mastectomy with immediate reconstruction using prosthesis, BCS often leads patients to the better cosmetic outcome and improvement of quality of life. However, the surgical technique of BCS considering the cosmetic outcome has not been generalized, especially for patients who received neoadjuvant chemotherapy (NAC). I aimed to show the criteria of BCS and surgical technique for the better cosmetic outcome.

Methods: Primary breast cancer patients with or without neoadjuvant chemotherapy who underwent BCS were included. The following points were considered to choose surgical procedure; 1. tumor size and location in the breast 2. accurate preoperative assessment using MRI and 2nd-look US, 3. necessity of postoperative irradiation therapy, and 4. hereditary breast and ovarian cancer syndrome.

Result: Lumpectomy with < 1 cm of surgical margin were performed to preserve the volume of breast tissue following the preoperative mapping using US, showing low local recurrence rate in ipsilateral breast as 1.7% and low rate of additional resection as less than 2%. The volume replacement using breast and fat tissue around the cavity was performed in a sitting position to assess contralateral symmetry.

Conclusions: The comprehensive knowledge and surgical technique are important for primary breast cancer patients to achieve the best cosmetic outcome together with oncological safety.

SURGICAL INTERVENTION OF REFRACTORY DONOR-SITE SEROMA AFTER IMMEDIATE BREAST RECONSTRUCTION WITH LATISSIMUS DORSI FLAP

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Background: Donor-site seroma, defined as a seroma that persists for more than 3 weeks, is the most common complication of latissimus dorsi (LD) flaps for breast reconstruction after mastectomy. However, conservative treatment is insufficient to resolve refractory seroma. We report the results of surgical intervention for refractory donor-site seroma.

Methods: From January 2012 to April 2018, 319 cases undergoing LD flap were treated with conservative therapy if seroma was found. Five cases (1.6%) developed refractory seroma of more than 3 months. Before surgery, the precise location and extent of the capsule was determined through chest computed tomography. Capsulectomy was performed with en-bloc. Simultaneously, quilting suture, bolster suture and fibrin sealant were applied to prevent recurrence.

Result: The mean age of the patients with refractory seroma was 45.4 years and the mean body mass index (BMI) was 31.0. All patients underwent extended LD flap or extended LD flap with silicone implant after total mastectomy. During the follow-up period of 10.4 months or more, a mean of 34.4 needle aspiration procedures were performed, removing a mean of 12.8 cc of seroma fluid each time. Intraoperatively, the formation of a capsule with a well-defined border was confirmed, and all patients shows complete resolution within 4 weeks after surgical intervention.

Conclusions: Refractory donor-site seroma occurs rarely, about 1.6% of the all cases. We attempted surgical treatment which is not resolved by conservative therapy. Surgical intervention is one of the most effective methods to achieve complete resolution of refractory seroma.

USEFULNESS OF MESHED SURGIMEND IN DIRECT-TO-IMPLANT BREAST RECONSTRUCTION

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Background: Using acellular dermal matrix (ADM) in implant based breast reconstruction shortly after mastectomy for breast cancer is taking center stage gradually in recent times, since it is possible to obtain a good outcome. This paper analyzed the usefulness of meshed SurgiMend, a Bovine dermis-derived ADM in direct-to-implant breast reconstruction.

Methods: For retrospective, single center analysis, 44 one-stage breast reconstructions using SurgiMend were applied. All the patients went through the immediate breast reconstruction after mastectomy. Implant was inserted into the subpectoral plane and SurgiMend was applied to the infero-lateral part that lacked tissues to wrap the silicone implant. Also, patients satisfaction was compared and analyzed using the questionnaire regarding 5 items; shape, texture, symmetry, pain, and overall, on a scale of 1 to 5.

Result: The incidence of major seroma in the control group and in the experimental group was 1/8 patients (12.5%) and 3/36 patients (8.3%) respectively. No infection, complication were found, such as hematoma and linear necrosis were resolved with conservative treatment. Patients' satisfaction in shape, texture, symmetry, pain, and overall was measured at 4.3, 4.1, 4.7, 4.5, and 4.4 respectively.

Conclusions: It is considered that applying the meshing method to SurgiMend, a bovine derived ADM in DTI breast reconstruction is a useful means of surgery, since this results in a better outcome and satisfaction and less complications.

USEFULNESS OF THE LIGASURE SMALL JAW SEALING DEVICE FOR BREAST RECONSTRUCTION WITH EXTENDED LATISSIMUS DORSI FLAP

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Background: Seromas are the most common complication of latissimus dorsi flap breast reconstruction. Electrocautery for flap elevation can cause seromas and injure the lymph or vessels of the surrounding tissues. Positive effects of the LigaSure Small Jaw (Medtronic, Minneapolis, MN, USA) sealing device were examined.

Methods: Forty-three latissimus dorsi flap breast reconstruction patients were included. Twenty-three underwent surgery with electrocautery and 21 underwent surgery with LigaSure. The seroma formation rate, total drain volume, drainage indwelling periods at the breast site and donor site, operative time, and hospital stay duration were retrospectively compared. Associations between patient characteristics and these variables were analyzed.

Result: Seroma incidence rates were 9/22 (40.9%) and 3/21 (33.3%) for the control and experimental groups. One control group patient underwent surgical treatment; the rest underwent conservative treatment. A significant difference in latissimus dorsi flap elevation time was found between the control and experimental groups (135.6 minutes and 107.1 minutes; $p = 0.026$). A significant difference in the drainage indwelling periods of the latissimus dorsi donor site was found (15.1 days and 13 days; $p = 0.006$). Excised breast mass weight, latissimus dorsi flap weight, breast drain total volume/indwelling period, and latissimus dorsi drain volume/indwelling period showed statistically significant associations. Radiation and chemotherapy were not significantly associated with any variables.

Conclusions: The LigaSure device for latissimus dorsi flap breast reconstruction can reduce seromas, operative time, and hospital stay. It is a reliable and useful surgical sealing device that does not cause injury to the surrounding tissues.

VALUE OF BIOMARKERS AND MAMMOGRAPHIC MICROCALCIFICATION IN GUIDING ADJUVANT RADIOTHERAPY AFTER BREAST-CONSERVING SURGERY FOR DUCTAL CARCINOMA-IN-SITU

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Background: To explore role of whole breast radiotherapy (WBRT) in ductal carcinoma-in-situ (DCIS) subtypes with different ipsilateral breast recurrence risk (IBTR).

Methods: We retrospectively reviewed medical records of breast cancer patients with pathologically confirmed pure DCIS and received breast conserving surgery at our institution between January 2009 and December 2015. Time-to-event curves were calculated by Kaplan-Meier methods and compared by log-rank test. Multivariate analyses were performed using Cox regression analysis.

Result: In total, 113 patients were enrolled and 94 out of them received WBRT. After a median follow-up of 4.9 years, 10 (8.8%) IBTR events occurred. By univariate and multivariate analysis, tumor size > 2.5 cm, Ki67 index > 14% and presence of mammographic clustered microcalcifications were found to be independent risk factors for IBTR ($p < 0.02$). Based on three independent risk factors, patients were subdivided into three subgroups as follow: low-risk (no risk factor), intermediate-risk (one risk factor) and high-risk (two or three risk factors). Significant differences in IBRT existed in low-, intermediate- and high-risk subgroups ($p < 0.001$). Among patients with hormonal receptor (HR) negative tumor, 5-year IBTR risk was significantly reduced with use of WBRT (33.3% vs. 14.6%, $p = 0.03$). WBRT was also found to significantly decrease IBRT in HR positive tumor with intermediate-risk (25.0% vs. 0%, $p = 0.03$). No significant reduction of IBTR was observed with delivery of WBRT in HR positive tumor with low-risk ($p = 0.66$) or high-risk ($p = 0.99$).

Conclusions: In modern era, benefit from WBRT varied in large span for DCIS. For HR negative tumor and HR positive tumor with intermediate-risk, WBRT could significantly decrease risk of IBTR.

RISK OF RADIATION PNEUMONITIS CAN BE MINIMIZED WITH ADOPTION OF HYPOFRACTIONATION AND MODERN RADIATION THERAPY TECHNIQUES FOR BREAST RADIATION THERAPY

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Background: The purpose of this study is to investigate the risk of radiation pneumonitis (RP) and identify dosimetrical parameters to predict the risk of RP in women treated with breast radiation therapy (RT).

Methods: We identified 1847 women who received surgery and adjuvant RT for breast cancer between 2015 and 2017. Patients received RT either with conventional fractionation (21.2%) or hypofractionation (78.8%). We applied the individualized RT techniques (e.g deep inspiration breathing hold, arc-therapy and prone technique) to minimize heart dose and target dose inhomogeneity. For dosimetrical analysis, planning data were transferred into MIM software for multiple-plan comparison.

Result: The median follow-up period was 14.5 month and the incidence of RP was 2.1%. In multivariate analysis, ipsilateral lung V20 (percentage of lung receiving 20 Gy) and V30 (percentage of lung receiving 30 Gy) were the most relevant dosimetric factor predicting the development of RP. When stratified with these parameters, patients were divided into 3 groups: V20 $\leq$ 25%, V30 $\leq$ 10%: 0.8% vs. V20 $\leq$ 25% but V30 > 10%: 3.4% vs. V20 > 25%: 6.1%, $p < .001$). Multiple linear regression showed the use of hypofractionation (OR = -7.5), arc-therapy (OR = -7.8), and prone technique (OR = -13.8) significantly reduced the lung V20 and V30, while regional node irradiation (OR = 11.7) significantly increased lung dose.

Conclusions: Lung V20 $\leq$ 25%, V30 $\leq$ 10% can be new dose constraint for RT planning. Adoption of hypofractionation and arc-therapy can play a major role in minimizing lung dose, especially in patients undergoing regional RT.

TUMOR TREAT FIELDS THERAPY IS A NEW MODALITY TO CENTROSOME AMPLIFIED TRIPLE NEGATIVE BREAST CANCER CELLS

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Background: Tumor Treating Fields (TTFields), a promising anti-cancer therapy utilizing alternating electric fields, is approved for glioblastoma therapy, but has not been fully elucidated in the efficacy to breast cancer yet. Triple negative breast cancer (TNBC)s are strongly correlated with amplified centrosomes, considered as a predictive biomarker of aggressive forms of cancers. It remains one of the notorious cancer types defying medical treatments due to absence of representative breast cancer receptors; therefore, development of a new and powerful strategy is highly required to cope with TNBCs.

Methods: The efficacy of TTFields application was investigated in triple negative breast cancer cell lines, BT-549, MDA-MB-231 and ER-positive cell line, MCF7. In addition, MCF7 cells overexpressing PLK4 were developed to examine whether sensitivity of TTFields is specifically dependent on amplified centrosomes. Ionizing radiation (IR) was used to amplify an excessive number of centrosomes in breast cancer cell lines, and then synergistic effect was observed through cell viability, clonogenic, immunofluorescence assay.

Result: We showed that TTFields increased disruption of mitosis and cell death in TNBCs whereas relatively resistant in ER-positive cells. PLK-overexpressing MCF7 cells possessing amplified centrosomes showed enhanced sensitivity of TTFields application and resulted in cell death. Furthermore, centrosome amplification (CA) induced by IR exposure to breast cancer cell lines was related to promoting sensitivity of TTFields treatments.

Conclusions: Our data provides that CA might be a novel predictive biomarker for the improvement of TTFields treatments in breast cancer patients and supports a new strategy for enhancing sensitivity of TTFields by combining with radiotherapy.

DOSE-DENSE DOXORUBICIN AND CYCLOPHOSPHAMIDE (DDAC) FOLLOWED BY TAXANE (T) FOR PATIENTS WITH EARLY BREAST CANCER IN JAPAN: A RETROSPECTIVE STUDY

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Background: The chemotherapy of dose dense AC (doxorubicin 60 mg/m^2 plus cyclophosphamide 600 mg/m^2 on day 1 and pegfilgrastim 3.6 mg/body on day 2 every 2 weeks for 4 cycles) followed by taxane (ddAC-T), one of the global standard regimens for early breast cancer, became available since September 2014 in Japan. The aim of this study is to examine the feasibility and efficacy of ddAC-T in Japanese women with early breast cancer in our institution.

Methods: We retrospectively reviewed data of consecutive patients with early breast cancer (stage I-III), who received ddAC-T or FEC-T as neo-adjuvant or adjuvant chemotherapy in our institute between January 2014 and February 2017. Primary endpoints were adverse events (AEs), and secondary endpoints were completion rate, relative dose intensity (RDI) and pathological complete response (pCR) rate.

Result: We reviewed total of 122 patients who were included in this analysis. Among 122 patients, 89 patients received ddAC-T and 33 patients received FEC-T. The number of ER-positive breast cancer patients were 55 (62%) in ddAC group, 19 (57%) in FEC group. The treatment-related AEs of grade 3 or 4 were as below: neutropenia (4% in ddAC group and 33% in FEC group), febrile neutropenia (1% and 3%). The completion rate was 89% in ddAC group, 88% in FEC group. The grade 3 pneumonia was 4 (4%) in ddAC group including three patients with Pneumocystis jiroveci pneumonia.

Conclusions: Dose-dense AC-T is feasible in Japanese women with early breast cancer.

THE EFFECT OF ADJUVANT CHEMOTHERAPY ON SURVIVAL IN KOREAN PATIENTS WITH NODE NEGATIVE T1C, TRIPLE NEGATIVE BREAST CANCER

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Background: The present study investigated the prognostic role of adjuvant systemic chemotherapy in patients with node negative, T1c triple negative breast cancer (TNBC) from a nationwide cohort. In addition, the prognostic effect between 3 different chemotherapy regimens were compared in node-negative T1c TNBC patients by subgroup analysis.

Methods: From the Korean breast cancer registry database, 1,151 T1c node negative TNBC patients were included in this study. Patients were categorized into four treatment groups according to chemotherapy regimen: (1) no chemotherapy, (2) adriamycin plus cyclophosphamide (AC), (3) adriamycin/epirubicin plus cyclophosphamide plus 5-FU (FAC/FEC), and (4) cyclophosphamide plus 5-FU plus methotrexate (CMF). Overall survival (OS) was evaluated between each patient group.

Result: Of the 1,151 T1c node negative TNBC patients, 1,006 received adjuvant chemotherapy, while 145 received no chemotherapy. Among the patients receiving adjuvant chemotherapy the distribution of regimens was: 586 AC, 168 FAC/FEC (126 FAC, 42 FEC), and 252 CMF. The mean follow-up time of the full study cohort was 87.98 ± 33.56 months (range = 6 ± 192 months). Patients in the no chemotherapy group showed significantly worse OS compared to each chemotherapy regimen group. However, when OS was compared between each chemotherapy regimen, no significant difference was found.

Conclusions: This study showed that adjuvant systemic chemotherapy improved OS in T1c node negative TNBC patients, regardless of chemotherapy between AC, FAC/FEC, and CMF regimens.

PHARMACOLOGICAL INHIBITION OF TFF3 ENHANCES CHEMO-SENSITIVITY

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Background: Dose-dependent toxicity and acquired chemo-resistance are two major challenges in the use of doxorubicin in breast cancer treatment. The activation of AKT has been recognized as a cellular defence mechanism against doxorubicin treatment. Trefoil factor 3 (TFF3), a secreted ligand was shown to activate various oncogenic pathways, hence promoting cancer progression. Here, the role of TFF3 in reduced sensitivity and acquired resistance of breast cancer to doxorubicin was investigated.

Methods: TFF3-knockdown MCF-7, ZR-75-1, and BT474 cells, and doxorubicin-resistant MCF-7 cells generated from pulsatile exposure to doxorubicin, were used as in-vitro models. A novel non-toxic small molecule (AMPC), which specifically binds cysteine-57 residue of dimeric TFF3 to promote its monomerization, was used for pharmacological inhibition of TFF3.

Result: Similar to the siRNA-mediated depletion of TFF3, the inhibition of TFF3 by AMPC increased doxorubicin sensitivity of breast cancer cells. Notably, AMPC combined with doxorubicin in a synergistic manner, enabling doxorubicin dose reduction. Mechanistically, the co-treatment with AMPC inhibited doxorubicin-induced AKT activation, thereby enhancing doxorubicin-induced apoptosis as compared to doxorubicin monotherapy. In MCF-7 cells with acquired doxorubicin resistance, elevated TFF3 expression was observed with increased AKT activity. These were suppressed by AMPC, which re-sensitized the resistant cells to doxorubicin-induced cytotoxicity and apoptosis. Interestingly, AMPC as a single agent also showed efficacious inhibitory effects towards doxorubicin resistant MCF-7 as shown in the cell viability, foci formation and 3D growth assays.

Conclusions: The pharmacological inhibition of TFF3 with AMPC is a potential therapy, in combination with doxorubicin, in naive and doxorubicin resistant breast cancer.

PRECLINICAL EVALUATION ON A THERAPEUTIC MARKER OF RX-5902, A BETA-CATENIN MODULATOR IN TRIPLE NEGATIVE BREAST CANCER

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Background: Despite recent advances in breast cancer therapeutics, mortality of highly metastatic triple negative breast cancer (TNBC) subtype remains high. Therefore, there is a pressing need to identify new therapeutic targets for this group of breast cancers. Aberrant activation of Wnt/β-catenin signaling has been associated with TNBC.

Methods: A series of in vitro and in vivo assays were used in this study.

Result: Herein, we identify DEAD-box RNA helicase DP103 as a novel driver of Wnt/β-catenin pathway and a therapeutic target of a Phase II drug, RX5902 in TNBC. The link between DP103 and Wnt/beta-catenin signaling was validated using cell-based assays and in vivo Drosophila models, where knocking out of DP103 gene resulted in severe early embryonic developmental defects which phenocopies loss of Wnt/beta-catenin signaling, an effect similar to treating wild type Drosophila with RX5902. Interestingly, we show DP103 drives breast cancer stem cell (CSC) formation, a process regulated by the Wnt/beta-catenin pathway. Depletion of DP103 or treatment with RX5902 led to a marked reduction in the percentage of CSC-enriched mammospheres. Mechanistically, we show DP103s role in driving Wnt/beta-catenin pathway is independent of caesin kinase I activity but highly dependent on GSK3β activity abrogated by RX5902. More interestingly, from molecular docking data and follow-up SILAC, we found DP103 protein has to be phosphorylated at threonine residue 552, when it interacts with GSK3β.

Conclusions: Collectively, our data suggest DP103 as a novel therapeutic target of RX5902 and driver of the Wnt/β-catenin signaling pathway in parental and CSC derived TNBC.

COMPREHENSIVE GENOMIC PROFILING OF MALIGNANT AND BENIGN PHYLLODES TUMORS

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Background: Comprehensive genomic profiling (CGP) has enabled to detect cancer-related gene alterations in neoplasms. Phyllodes tumors (PTs) are fibroepithelial neoplasms. Malignant phyllodes tumor is rare but well-known as highly aggressive and resistant to chemotherapy. Genomic profiling of PTs has been revealed and the genomic-profiling difference of malignancy has also been reported. However, these findings in Japanese population have been poorly reported. Here, we evaluated CGP for PTs in Japanese cases.

Methods: We selected 6 PTs (malignant; n = 4, borderline; n = 1, benign; n = 1) which were resected at Aichi Cancer Center from 2014 to 2017. The CGP assay (FoundationOne) was performed for 6 tumors to evaluate the 324 cancer-related gene alterations, microsatellite instability and tumor mutation burden (TMB). DNA samples were extracted from the formalin-fixed, paraffin-embedded surgical specimens.

Result: In the 3 of 4 malignant tumors, gene alterations were detected in BRAF, EGFR, NRAS and PIK3CA as druggable mutations, and in ATRX, BCOR, CDKN2A, CREBBP, KEL, MED12, MLL2, TERT, and TP53 as actionable mutations. In the borderline tumor, gene alterations were detected in EGFR as a druggable mutation, and inCDKN2A/B, MTAP, MED12 and TERT as actionable mutations. In the benign tumor, no druggable mutation and actionable mutations in MED12 and TERT were observed. All cases were microsatellite stable and low-TMB (0-3 mut/Mb).

Conclusions: Malignant and borderline PTs harbored additional druggable mutations. CGP for PTs can lead to targeted-therapies and can be helpful for differentiating malignancy of PTs.

M1 NECK LYMPH NODE POSITIVE WITHOUT DISTANT METASTASIS IN BREAST CANCER: COMPARISON WITH STAGE IIIC

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Background: To analyze the treatment outcomes of ipsilateral cervical lymph node (LN)-positive breast cancer in the absence of other distant metastases, and to compare these outcomes with those of supraclavicular LN (SCL)-positive breast cancer.

Methods: Seventy-nine breast cancer patients with involvement of ipsilateral cervical LN above the supraclavicular fossa (cervical LN(+) group) were treated with curative intent from 2000 to 2014 at 7 institutions. Most patients (n = 75) received systemic chemotherapy (neoadjuvant and/or adjuvant) and breast surgery followed by locoregional radiotherapy. Outcomes of the cervical LN(+) group were evaluated and compared with those of 183 patients with SCL involvement (SCL(+) group) from the KROG 16-14 study.

Result: Median follow-up duration was 51.2 months (range, 5.9-138.0). Twenty-two regional failures were found in 15 patients: axillary LN in 8, SCL in 6, internal mammary LN in 3, involved cervical LN in 4, and uninvolved cervical LN in 1. The 5-year overall survival (OS), disease-free survival (DFS), locoregional relapse-free survival (LRRFS), and distant metastasis-free survival (DMFS) rates were 64.9%, 44.8%, 68.9%, and 55.2%, respectively. Neck dissection failed to improve LRRFS and DFS ($p = 0.901$ and 0.366, respectively). After propensity score matching, survival outcomes of the cervical LN(+) and SCL(+) groups were not statistically different (5-year OS, 62.6% vs. 72.2%, $p = 0.560$; DFS, 45.7% vs. 52.2%, $p = 0.620$; LRRFS, 64.7% vs. 78.1%, $p = 0.110$; DMFS, 57.4% vs. 53.2%, $p = 0.590$, respectively).

Conclusions: Based on comparable clinical outcomes, breast cancer patients with ipsilateral cervical LN metastases without other distant metastases might benefit from aggressive locoregional and systemic treatments as those with N3c disease.

Poster Presentation

PHASE II TRIAL OF CARBOPLATIN+S-1 THERAPY FOR JAPANESE PATIENTS WITH METASTATIC OR RECURRENT TRIPLE NEGATIVE BREAST CANCER

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Background: In a phase III clinical trial, carboplatin (CBDCA) was reported to have a superior response rate for triple negative breast cancer (TNBC) with germline BRCA mutations than docetaxel, but CBDCA has not been approved in Japan. S-1 is already approved for TNBC in Japan. Combination CBDCA+S-1 therapy was tolerable among Japanese patients with lung cancer in a domestic clinical trial. The authors hypothesized that this combination could be tolerable and effective for Japanese patients with TNBC and conducted a phase II trial of CBDCA+S-1 therapy for patients with metastatic or recurrent TNBC in Japan.

Methods: The main inclusion criteria included age > 18 years, PS 0-2, TNBC pretreated with both anthracycline and a taxane, at least one target lesion, and sustained organ function. Patients with symptomatic brain metastasis, marked effusion, and a history of platinum-based treatment were excluded. CBDCA (AUC = 5, day 1) and S-1 (80 mg/m^2, days 1$\sim$14) were given over a 21-day cycle. The expected response rate and threshold response rate were 35% and 15%, respectively, leading to an estimated required sample size of 28 cases.

Result: The trial enrolled 30 patients from February 2013 to July 2017. The overall response rate was 41.3% (95%CI, 24.4-58.2). 63% of the study population had lung or liver metastasis. The major adverse event was neutropenia, which was safely managed by planned dose reduction. No treatment-related deaths occurred.

Conclusions: CBDCA+S-1 therapy is effective for TNBC.

ACTIVE SUPPORT FOR METASTATIC BREAST CANCER PATIENTS RECEIVING ORAL ANTI-CANCER DRUG BY MULTIDISCIPLINARY MEDICAL TEAM

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Background: New molecular target drug significantly prolonged the survival and changed the treatment strategy for ER positive metastatic breast cancer patients from sequential monotherapy of AI, SERD and SERM according to Hortobagyi algorism to combination therapy. On the other hand, the management of adverse events which are not common for hormone therapy are needed. The effective supportive care by multidisciplinary team is very important in order to continue administration with maximum effect of these drugs and keeping patients' QOL.

Methods: We analyzed the adverse events of mTOR inhibitor with AI or SERM for ER positive MBC with active supportive care by multidisciplinary team. 1. The dental hygienist checked the oral situation and do the oral care counseling. 2. The pharmacist checked the total adverse events and compliance. 3. The medical doctor gave the medical examination and decided the treatment.

Result: Forty three patients received the mTOR inhibitor. The rate of oral mucositis was G1 18 (43%), G2 6 (14%), G3 4 (10%). 5 (12%) patients were reduced the amount of drug. There were no patients who stopped the administration of mTOR inhibitor because of mucositis.

Conclusions: The multidisciplinary team including dental hygienists was very effective to continue the mTOR inhibitors safety.

CONDITIONALLY REPROGRAMMED CELL CULTURE OF CIRCULATING TUMOR CELLS IN BREAST CANCER PATIENTS

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Background: Multiple technologies have been developed to detect and isolate circulating tumor cells (CTCs), but the detection of CTCs remained as a main issue of CTCs study. We aimed to verify the efficacy of conditionally reprogrammed cell (CRC) culture method in CTCs detection in breast cancer.

Methods: CTCs were isolated from peripheral blood of breast cancer patients and the collected CTCs were cultured according to the conditional reprogramming protocol. Total RNA was extracted from the blood, and hTERT and MAGE A1-6 genes were amplified using RT-PCR.

Result: CTCs were isolated from 23 out of 34 patients (67.6%). CRC culture was carried out and CTCs were grown in 7 samples (23.3%). The positive expression rates for the hTERT and the MAGE genes in CTCs by RT-PCR only were 44.1% and 23.5%, respectively. When combining the positive expression rates of RT-PCR only and CRC culture for the hTERT and the MAGE genes, CTC detection rates were increased to 56.3% and 30.3%, respectively. Also, when combining the positive expression rates of both genes by either method, CTCs detection rate was highest.

Conclusions: Our study showed a potential of CRC culture method to detect CTCs in breast cancer. Also, we showed that combination of CRC culture methods and RT-PCR of hTERT and MAGE A1-6 gene is useful in enhancing the detection rate of CTCs in the blood.

PLASMA LIPID RELATED METABOLITES AS POSSIBLE BIOMARKERS FOR PREDICTION OF BREAST CANCER

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Background: Metabolomics has been actively studied to demonstrate the possibility of new diagnostic biomarkers in various types of cancers. Especially, it has been well documented that altered lipid metabolism plays an important role in proliferation of cancer cells. In this study, we aimed to explore lipid-related potential biomarkers in breast cancer by plasma metabolic profiling. Futhermore, we analyzed whether these substances had relationships with clinicopathologic characteristics of breast cancer.

Methods: We performed lipid metabolic profiling of a total of 46 plasma samples from 30 patients with breast cancer and 16 healthy controls by liquid chromatography coupled with mass spectrometry (LC with MS). Receiver operating characteristic (ROC) analysis was used to evaluate the lipid-related metabolites as potential biomarkers for the diagnosis of breast cancer.

Result: Among the 41 metabolites related to fat metabolism, there were significant differences in 12 lipid-related metabolites between breast cancer group and healthy group ($p < 0.05$). 9,10,13-TriHOME shows best diagnostic performance with 100% sensitivity. Metabolites such as Octanoic acid, Docosahexaenoic acid, LysoPE (18:1) and LysoPE (18:2) also were demonstrated as a valuable biomarkers with sensitivity greater than 80%. Although there were no significant relationships among lipid-related metabolites in progesterone receptor, HER2-neu status, histologic grade and Ki-67, some substances showed significant correlations with stage, tumor size, lymph node metastasis and estrogen receptor status.

Conclusions: Lipid-related metabolites identified in this study can be considered as potential biomarkers for the prediction of breast cancer. However, the diagnostic performance of lipid-related metabolites in breast cancer still needs to be confirmed by further studies with larger sample sizes.

EFFECTIVE DETECTION OF BREAST CANCER BY THE QUANTITATIVE MEASUREMENT OF THIOREDOXIN 1 FROM BLOOD

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Background: Breast cancer is one of the leading cancers for women worldwide. Mammography is the most widely used to screen breast cancer, although it is inaccurate in young women or women with dense breasts in Korea and Asian countries. We have reported that the level of thioredoxin 1 (Trx1) was increased specifically in breast cancer tissues. Therefore, it would be interesting to examine whether the quantitation of Trx1 from blood could be a tool to detect breast cancer and to complement mammography.

Methods: We have developed an ELISA kit quantitating Trx1. Trx1 levels of bloods from 116 normal healthy women, 140 confirmed breast cancer patients with stage from 0 to 4, and each 30 confirmed patients of lung, ovarian, gastric, colorectal, and cervical cancer have been estimated by the kit. The test results were analyzed by ROC curve, one-way ANOVA test, and unpaired t-test.

Result: The mean value of Trx1 level from normal women was 7.506 (U/mL) and that from breast cancer patients was 37.75. The Trx1 level clearly differentiated breast cancers from normal cases with sensitivity of 96.4% and specificity of 99.1% (AUC 0.990, $p < 0.001$). Each level of Trx1 from lung (16.7), ovarian (15.50), gastric (15.66), colorectal (16.39), and cervical (22.51) cancer was below the cut-off value (22.8 U/mL) for breast cancer detection.

Conclusions: These results indicated that the blood level of Trx1 estimated by the ELISA kit was effective and accurate to detect breast cancer.

CONTRALATERAL AXILLARY SENTINEL LYMPH NODE UPTAKE IN THE INTRA-OPERATIVE EVALUATION FOR COMPLETION MASTECTOMY: FAILED EXAMINATION OR OTHERWISE?

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Background: Breast cancer is the most common malignancy in women, and axillary nodal involvement has been established as an indicator of poor prognosis. Sentinel lymph node biopsy (SLB) has been validated as a standard surgical staging tool. Its application has evolved beyond that of early-stage malignancy, and is considered the current paradigm in the management of regional basin in breast cancer. Positive SLB uptake is classically seen at the ipsilateral axilla.

Methods: Herein, we report a rare case series of four patients with contralateral axillary SLB uptake during completion mastectomy for recurrent breast cancer.

Result: A retrospective review was performed for sentinel lymph node biopsies performed at a tertiary centre over 5 years (2013-2017). The primary inclusion criteria was contralateral axillary SLB uptake. Four female patients with breast carcinoma (mean age: 53 years) were included. These patients had prior breast surgery (two with breast conserving therapy, and another two with modified radical mastectomy and TRAM reconstruction), and had subsequently presented with local recurrence of disease. The authors herein discuss the associations of clinical and biological factors, overall prognosis and the possible clinical implications of contralateral axillary SLB uptake.

Conclusions: In the setting of prior breast surgery, these scintigraphy findings could represent aberrant or new lymphatic drainage at the contralateral breast. Possibility of microscopic metastasis to the contralateral axillary nodal basin should also be considered. Prudent physical examination and screening of the contralateral axilla are hence recommended in these rare situations.

SENTINEL LYMPH NODE BIOPSY WITH NO AXILLARY DISSECTION VS. COMPLETE AXILLARY LYMPH NODE DISSECTION IN EARLY BREAST CANCER: A SYSTEMIC REVIEW AND META-ANALYSIS

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Background: Sentinel lymph node biopsy (SLNB) is a standard procedure in early breast cancer, and surgery is terminated if SLNB is negative. Complete axillary lymph node dissection (ALND) is performed to control and identify nodal metastases when SLNB is positive; however, the efficiency of performing ALND compared to SLNB alone is still unclear. We performed the meta-analysis to compare the outcome of SLNB vs. complete ALND.

Methods: We systematically searched the database and reference lists from January 2000 to December 2018 from Pubmed, Web of Science, The Cochrane Library, and Scopus. We included six randomized controlled trials (RCTs) that compared survival outcomes of 7,249 patients with early breast cancer after SLNB alone and SLNB with ALND.

Result: Evidence on heterogeneity ($I^2 = 3\%$, $p = 0.40$) and publication bias were not observed. Fixed effect meta-analysis showed that there was no statistical difference in overall survival (hazard ratio [HR], 1.02; 95% confidence interval [CI], 0.87 1.20) and disease-free survival (HR, 0.99; 95% CI, 0.88 1.11) between SLNB and ALND group. Moreover, neither sensitivity analysis nor meta-regression showed difference in outcome between SLNB and ALND group.

Conclusions: In conclusion, clinical outcome for patients treated with SLNB alone was non-inferior to those treated with complete ALND. Our results support the current practice of not doing a routine ALND when the tumor burden in the sentinel nodes is minimal or moderate in patients with early breast cancer.

ACCURACY OF PREOPERATIVE ULTRASOUND STAGING OF THE AXILLA A SINGLE INSTITUTE EXPERIENCE IN THE UK

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Background: Axillary node status remains one of the most important prognostic factors in breast cancer. Ultrasound of the axilla is still the only way of accurately staging of the axilla. The aim of this study is to evaluate the accuracy of pre-operative staging of the axilla in patient with suspected or confirmed breast cancer using an ultrasound (USS) machine.

Methods: One hundred forty two female patients have been diagnosed with breast cancer in between March 2018-August 2018. 55 patients (screen detected), 86 (symptomatic) and one patient (family history clinic). All patients subjected to USS and core biopsy of lymph node if suspicious. Ultrasound of the axilla using a 12-16 MHz matrix line array transducer on a Toshiba Aplio ultrasound platform. The nodal morphology was recorded, including whether the outline of the node was smooth, uni or multi-lobulated with normal or absent hilum. If the lymph node was > 10 mm in maximum longitudinal dimension, then a biopsy was taken. If more than one node was identified, the most morphologically abnormal node was selected for biopsy.

Result: Out of 142 newly diagnosed breast cancer, 42 abnormal lymph nodes were identified and patients has had ALND. 100 patients underwent SLNB with normal preoperative axillary USS staging. Sensitivity 70% (56-80), specificity 90% (83-95), PPV 80%, NPV 83%, false positive 17%, and false negative 16%. Positive SNB (18), 6 invasion > 10 mm, 5 between 5-10 mm, and 7 < 5 mm.

Conclusions: In our practice, ultrasound is still the most acceptable modality for preoperative axillary staging with an acceptable false negative rate comparing to meta analysis.

MAMMOGRAPHY AFTER NEOADJUVANT CHEMOTHERAPY IN BREAST CANCER PATIENTS: CORRELATION WITH TUMOR REPONSE GRADE AND COMPARISON WITH LESION EXTENT

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Background: After neoadjuvant chemotherapy (NAC), persistent microcalcifications are often observed in spite of a decrease in the primary tumor size. This study aimed to analyze the changes in microcalcifications after NAC and to evaluate the accuracy of residual microcalcifications in predicting the extent of residual cancer.

Methods: Eighty patients who received NAC and underwent both mammography and magnetic resonance imaging (MRI) before and after the completion of NAC were included. The location of microcalcifications was classified into two types: inside the mass and outside the mass.

Result: The extent of the residual calcifications was larger than the pathologic residual lesion in 14 (74%) of 19 patients with complete response (CR) on MRI, but the discrepancy was < 1 cm in eight (42%) patients. The median value of the discrepancy was significantly higher in patients showing CR with outside calcifications compared to CR with inside calcifications (2.0 cm vs. 0.7 cm, $p = 0.008$). After NAC, the decrease of calcifications was more frequently observed in cancers showing CR on MRI or Miller-Payne grade 5 and the increase of calcifications more frequently occurred in cancers showing progress disease on MRI or Miller-Payne grade 1 ($p < 0.001$ and $p = 0.044$).

Conclusions: The change in microcalcifications after NAC was correlated with the tumor response to NAC. The discrepancy was highest in the group showing CR on MRI with outside calcifications. In tumors with inside calcifications, the discrepancy was relatively low within an acceptable range.

USEFULNESS OF BREAST MAGNETIC RESONANCE IMAGING IN DETERMINING THE SURGICAL PLAN FOR BREAST CANCER PATIENTS WITH DUCTAL CARCINOMA IN SITU AND THOSE WITH INVASIVE DUCTAL CARCINOMA

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Background: Preoperative breast magnetic resonance (MR) imaging provides more information than mammography and ultrasonography for determining the surgical plan in patients with breast cancer. This study aimed to evaluate whether breast MR is more useful in determining the surgical plan for patients with ductal carcinoma in situ (DCIS) lesions than for those with invasive ductal carcinoma (IDC).

Methods: A total of 1,113 patients with breast cancer, ductal origin, underwent mammography, breast ultrasonography, and additional breast MR before surgery in Kyungpook National University Hospital. The patients were divided into DCIS group (n = 199) and IDC group (n = 914), and their clinicopathologic characteristics with oncologic outcomes were compared. The initial surgical plan based on routine mammography and ultrasonography and final surgical plan after additional breast MR were compared between the two groups.

Result: The disease characteristics and prognosis of patients in this study were similar to those of previous studies. Changes in surgical plans more commonly occurred in the DCIS group than in the IDC group ($p < 0.001$). The reasons for these changes were as follows: larger extent of suspicious lesion detected on breast MR, detection of additional daughter nodule, multifocality or multicentricity, or suspicious findings in mammography or ultrasonography but benign in breast MR.

Conclusions: Preoperative breast MR may provide more information for determining the surgical plan for patients with DCIS than those with IDC.

ROLE OF ULTRASOUND FOR THE DETECTION OF SUPRACLAVICULAR LYMPH NODE IN PATIENTS WITH BREAST CANCER

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Background: Neck ultrasound, computed tomography and PET/CT are useful imaging modalities for detection of supraclavicular lymph node metastasis in breast cancer. The aim of this study is to compare US, CT, PET/CT and establish the role of US for the detection of supraclavicular lymph node metastasis in breast cancer.

Methods: Between 2008 and 2013, 1,150 patients with operable breast cancer underwent neck US, CT, and PET/CT for detection of supraclavicular lymph node metastasis in follow up surveillance after treatment. When the suspicious lymph node was detected, the ultrasound-guided fine needle aspiration cytology was performed for confirmation of supraclavicular lymph node metastasis. The sensitivity, specificity, positive and negative predictive value and accuracy were compared.

Result: During 34 cases with suspicious supraclavicular lymph node, 27 patients were diagnosed as supraclavicular lymph node metastasis of breast cancer by US-guided FNAB. The sensitivity of US+CT (100.0%) were higher than that of US (96.3%), CT (92.6%), PET/CT (96.3%) and the accuracy (99.5%) were all same among those modalities. And the false negative rates were lower in order of CT+US (0.0%), US = PET/CT (0.1%) and CT (0.2%).

Conclusions: US, CT and PET/CT, all showed high accurate rate for detection of supraclavicular lymph node metastasis. However, considering the false negative rate, the US+CT would be the effective diagnostic method for supraclavicular lymph node metastasis. And because the confirmation of supraclavicular lymph node metastasis is done by US-guided FNAB, the role of US would be very important for diagnosis of supraclavicular lymph node metastasis in breast cancer.

BENEFIT OF CONTRALATERAL BREAST ULTRASOUND SCREENING IN NEWLY DIAGNOSED BREAST CANCER

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Background: To determine the merit of supplementary ultrasound (US) screen in patients diagnosed with breast cancer.

Methods: Patients with a new breast cancer (BC) diagnosis and bilateral intact breasts who presented to the Singapore General Hospital Department of Radiology from 2008-2016 were reviewed. The number of contralateral breast cancers (CBC) detected by mammogram (MMG) and/or ultrasound (US) screening of the contralateral breast were analysed.

Result: Five hundreds ninety one women presented with breast cancer and 41 (6.9%) had CBC. 359 patients had combined MMG and US screen of the asymptomatic contralateral breast which yielded a CBC detection rate of 9.2% (33/359). Of these, 3 (8.6%) were detected by MMG only, 16 (45.7%) by US only and 14 (40.0%) by both MMG and US. Two (5.7%) were found by MRI only. CBC detection rate of US cases with negative MMGs was 5.0% (16/322). US screening additionally identified 3 cases of contralateral axillary nodal metastases, thereby upstaging to distant metastases. Greater number of US-screened detected CBCs were found in mammographically dense women (13/15) compared to MMG-detected CBCs (8/17, $p = 0.035$). Tumour histology, grade and hormonal receptor status were not significant in multivariate analysis.

Conclusions: Adding US to MMG screening of the contralateral breast almost doubled the number of CBCs detected. US was also useful in detecting contralateral axillary nodal disease which would significantly alter management. Contralateral US breast screening should be considered in newly diagnosed breast cancer cases with dense breasts.

DIAGNOSIS OF BREAST CANCER THROUGH MALDI-TOF-MASS SPECTROMETRY-BASED ANALYSIS OF SERUM N-GLYCANS

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Background: Because of existence of certain links between cancer and altered protein glycosylation, serum N-glycans are frequently used as a tool for cancer diagnosis. Matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF-MS) is a simple, rapid, sensitive, and accurate analytical technique for a wide application, including glycan detection. The present study is aimed to develop a platform for diagnosis of breast cancer (BrC) based on the serum N-glycan profiling using MALDI-TOF-MS.

Methods: Glycans were isolated from the serum of female normal subjects and breast cancer patients using our optimized protocol involving denaturation and enzymatic deglycosylation followed by purification through solid phase extraction and finally analyzed by MALDI-TOF-MS.

Result: Serum N-glycan profiles were studied using MALDI-TOF-MS in non-cancer healthy volunteers (n = 311) and in subjects with IDC (n = 256) which encompasses breast cancer stage 1 (n = 113), stage 2 (n = 102), stage 3 (n = 33), and stage 4 (n = 8). The results showed an efficient pattern recognition of invasive ductal carcinoma (IDC) patients with a very high diagnostic performance reflected by the ROC analysis (AUC: 0.93 and 95% CI: 0.917-0.947). Furthermore, the study exhibited an effective stage-specific differentiation of breast cancer patients from the normal with 82% specificity, 84% sensitivity, and 83% accuracy for the diagnosis of stage 1 breast cancer. Additionally, the current method is also able to recognize hormone receptors (HR/HER) and lymph node invasion ((N-)/(N+)) subtypes based on their N-glycan profile against normal subjects.

Conclusions: Therefore, the technique presented here is advantageous over the currently available methods for breast cancer diagnosis.

ANGIOMOTIN PROTEIN EXPRESSION IN BREAST CARCINOMAS AND ITS PROGNOSTIC SIGNIFICANCE: FROM THE VIEWPOINT OF MOLECULAR SUBTYPE

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Background: Angiomotin (AMOT) is an angiostatin binding protein in regulating angiogenesis, and although the oncogenic and tumor-suppressive roles of AMOT were recently reported, the specific roles of AMOT have not yet been clarified in breast cancer. The aim of this study was to evaluate the relationship between AMOT expression and clinicopathologic characteristics to determine its prognostic implications in breast cancer.

Methods: We enrolled 446 patients with breast cancer in this study and measured the immunoreactivity of AMOT in a tissue microarray. The data were analyzed using a χ^2 test, Cox regression hazards model and log-rank test with Kaplan-Meier curves.

Result: High AMOT expression was found in 23.3% (104/446) patients. High AMOT expression was significantly associated with invasive ductal carcinoma (IDC) histology ($p = 0.027$), high histologic grade ($p = 0.024$), and high Ki-67 proliferating index ($p = 0.018$), but there is no statistical significance for the other clinicopathological parameters. Univariate survival analysis using the Kaplan-Meier method showed that AMOT expression were not associated with disease-free survival (DFS, $p = 0.567$) or overall survival (OS, $p = 0.831$). In intrinsic subtype analyses, high AMOT expression had significantly poor overall survival in luminal A subtype ($p = 0.042$). However, in basal TNBC subtype, high AMOT expression had significantly better overall survival ($p = 0.037$).

Conclusions: Our findings collectively demonstrate that breast tumors with high AMOT expression may have different biological mechanism, according to breast molecular subtype. These findings suggest that AMOT may need to be analyzed to obtain complete prognostic information.

FACTORS AFFECTING SLEEP QUALITY OF PREMENOPAUSAL PATIENTS WITH BREAST CANCER

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Background: Premenopausal women with breast cancer experience severe menopausal symptoms or ovarian insufficiency during or after treatment of their breast cancer. The purpose of this study is to investigate the factors affecting the sleep quality of premenopausal breast cancer patients.

Methods: A total of 110 patients who were premenopausal at the time of being diagnosed with breast cancer were recruited from a university affiliated hospital, Seoul, from September 18, 2017 to December 7, 2018. Sleep quality was evaluated with the Pittsburgh Sleep Quality Index (PSQI). The M.D. Anderson Symptom Inventory Cancer Module (MDASI), the International Physical Activity Questionnaire (IPAQ), the Hospital Anxiety and Depression Scale (HADS), and the Dysfunctional Beliefs and Attitudes about Sleep (DBAS-16) were measured.

Result: The patients with low sleep quality (76.4%) were more likely to be married ($p < 0.049$), have sleep problem before cancer diagnosis ($p < 0.002$), symptom experience ($p < 0.001$), anxiety ($p < 0.001$), depression ($p < 0.002$), illogical beliefs and attitudes about sleep ($p < 0.001$). Low sleep quality was associated with existing sleep disorders before cancer diagnosis, symptom experiences or anxiety and illogical beliefs about sleep.

Conclusions: In premenopausal breast cancer patients, sleep disturbance is common. Thus, screening for sleep disorders at initial diagnosis and treatment of cancer should be implemented in clinical practice. To improve sleep quality of premenopausal breast cancer patients at high risk of sleep disturbance, symptom management and psychosocial approaches to reduce anxiety and illogical beliefs and attitude about sleep are needed.

THE UPDATED MULTIDISCIPLINARY APPROACH TO FERTILITY PRESERVATION FOR BREAST CANCER PATIENTS WITH LOCAL MEDICAL NETWORK.

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Background: Young women diagnosed with breast cancer may have concerns the risk of loss of fertility due to cancer treatment which may influence on the treatment decision. It is important for patients to discuss this issue with health care providers prior to cancer treatment.

Methods: From 2009 April, we have referred younger patients who diagnosed with breast cancer for fertility counseling with a multidisciplinary team including breast oncologist, gynecologist, nurses and counselor, and discuss the fertility issues in our University Hospital. From 2017 April, we have monthly meeting with expanded multidisciplinary team. This expanded multidisciplinary team is composed of hematologist, medical oncologist, urologist in our University Hospital who should also recognize this issue, and reproductive specialists at the local private hospital adding on existing team members.

Result: From the conference with expanded multidisciplinary team, we found that though a lot of young patients who have concern the fertility issue in our local area, the frequency to discuss the issue with health care providers at the appropriate timing is less than we expected except for the University Hospital. So we create the local medical network centered on the University Hospital and opened the webpage easily accessed by patients with local hospital information with experienced specialists for this issue on the local map at a glance.

Conclusions: The multidisciplinary approach with local medical network for young cancer patients is helpful to discuss the issue of fertility preservation even for patients who have difficulty to access the University Hospital.

NIPPLE-AREOLA COMPLEX RECURRENCE AFTER NIPPLE-SPARING MASTECTOMY FOLLOWED BY IMMEDIATE BREAST RECONSTRUCTION FOR INVASIVE BREAST CANCER: A SINGLE-CENTER EXPERIENCE

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Background: This study assessed the incidence, risk factors, treatment, and long-term outcomes of nipple-areola complex recurrence (NR) in a large series of patients with invasive breast cancer who underwent nipple-sparing mastectomy (NSM) and immediate breast reconstruction (IBR) at a single institution.

Methods: We retrospectively analyzed 962 breasts in 944 patients who underwent NSM and IBR for invasive breast cancer between March 2003 and December 2015. Data were analyzed using the Cox proportional hazards model, Kaplan-Meier method, and log-rank test.

Result: During a median follow-up of 85 (range: 14-185) months, we identified 39 cases (4.1%) with NR as the first event after NSM. The 5-year cumulative incidence of NR was 3.5% (n = 34). Multivariate analyses identified multifocality/multicentricity, negative hormone receptor (HR)/positive human epidermal growth factor receptor 2 (HER-2) subtype, high histologic grade, and extensive intraductal component (EIC) as independent factors affecting NR after NSM. All 39 recurrent cases involved wide local excision. Although two patients developed distant metastasis during follow-up, all 39 patients survived with a mean follow-up of 51 months after nipple-areola complex (NAC) removal. Patients who did and did not suffer NR as the first event did not differ significantly in distant metastasis-free ($p = 0.896$) or overall survival ($p = 0.207$).

Conclusions: Patients in our series had a low incidence of NR after NSM and IBR. Multifocal/multicentric disease, HR(-)/HER-2(+) subtype, high histologic grade, and positive EIC were significantly associated with an increased risk of NR. These factors should be considered before determining the NSM procedure. NR had no direct significant negative prognostic impact after appropriate treatment.

Poster Presentation

PROGNOSTIC VALUE OF F-18 FDG PET/CT IN INVASIVE DUCTAL CARCINOMA AT DCUMC

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Background: To determine the prognostic implications of pretreatment F-18 FDG PET/CT (PET/CT) in patients with invasive ductal carcinoma (IDC), we evaluated the relationship between FDG uptake of the primary mass (pSUVmax) and known prognostic parameters of breast cancer. Prognostic significance of pSUVmax for the prediction of progression-free survival (PFS) was also assessed.

Methods: Three-hundred eighty five female patients with IDC who underwent pretreatment PET/CT were enrolled from 2005 to 2016 year. The visual interpretation and pSUVmax of PET/CT was compared with clinicopathological parameters including ER, PR, HER2, axillary lymph node metastasis (LNM) and stage. The prognostic value of pSUVmax, for PFS was assessed using the Kaplan-Meier method.

Result: Positive on tumor and axillary lymph node by visual interpretation of PET/CT can predict recurrence ($p = 0.0052$, $p < 0.0001$). pSUVmax was significantly higher in ERnegative tumors ($p < 0.0001$), PR-negative tumors ($p = 0.0006$), and positive LN metastasis ($p = 0.0001$), but not different according to HER2 status. pSUVmax was significantly higher in patients with progression compared to patients who were disease-free (7.1 ± 5.3 vs. 3.8 ± 3.3, $p < 0.0001$). A receiver-operating characteristic curve demonstrated a pSUVmax of 4.0 to be the optimal cut-off for predicting PFS (sensitivity; 69.4%, specificity; 66.8%). The patients with a high pSUVmax (more than 4.0) had significantly shorter PFS compared to patients with a low pSUVmax ($p < 0.0001$).

Conclusions: PET/ CT before treatment can be useful marker for the prediction of progression in patients with IDC.

Poster Presentation

UTILITY OF 18F-FDG PET/CT FOR PREDICTING PATHOLOGIC COMPLETE RESPONSE OF LUMINAL HER2-NEGATIVE BREAST CANCER PATIENTS RECEIVING NEOADJUVANT CHEMOTHERAPY

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Background: Although pathological complete response (pCR) after neoadjuvant chemotherapy (NAC) is a predictor of better outcome and often used as a surrogate for survival, response of luminal type breast cancer to NAC is variable and mostly limited. This study investigated the predictive relevance of parameters of 18F-FDG PET/CT on the pCR to NAC in patients with luminal HER2negative breast cancer.

Methods: One hundred seventeen hormone receptor-positive and HER2-negative breast cancer patients who were treated with NAC followed by curative surgery were enrolled. Pathologic complete response was defined as the absence of invasive cancer cells in breast and axillary node. 18F-FDG PET/CT maximum standardized uptake value (SUV max) was measured at baseline. Patients received from 6 to 8 cycles of anthracycline and taxane-based NAC.

Result: The median age of the patients was 48 years (range 29-68) and 114 patients (97.4%) showed ductal carcinoma histology. One hundred and four patients (88.9%) were PR-positive, and forty-nine (41.9%) patients showed high ki-67 expression at initial diagnosis. The patients were divided into two groups according to the mean SUVmax of breast tumor on initial 18F-FDG PET/CT for the comparison with pCR rate. After NAC, nine patients (7.7%) achieved pCR, which was remarkably higher in patients who had high initial SUVmax ($\geq$9.09) compared to low initial SUVmax (77.8% vs. 22.2%). In the ROC analysis, the area under the curve for initial SUVmax was 0.638 for pCR

Conclusions: In luminal HER2-negative breast cancer, 18F-FDG PET/CT SUVmax was useful for predicting pathologic complete response after NAC.

RISK OF CONTRALATERAL BREAST CANCER AND IPSILATERAL BREAST TUMOR RECURRENCE IN BRCA1/2 MUTATION CARRIERS AND NON-CARRIERS WITH HIGH RISK OF HEREDITARY BREAST CANCER

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Background: We assessed the risk of contralateral breast cancer (CBC) and ipsilateral breast tumor recurrence (IBTR) among breast cancer patients with BRCA mutation and non-carrier with a high risk of hereditary breast cancer and to determine the predictive factors of CBC and IBTR.

Methods: We analyzed prospectively collected clinical data of 540 patients with a high risk of hereditary breast cancer who got BRCA testing from 2003 to 2013 at Seoul National University Bundang Hospital.

Result: Forty-five patients were BRCA1-positive, 50 were BRCA2-positive, and 445 were negative for BRCA mutations. Median follow-up was 84.5 months. Overall, 61 patients (11.3%) developed a CBC (24.4% for BRCA1 carriers, 20.0% for BRCA2 carriers, and 8.9% for non-carriers). The 10-year cumulative risk for CBC was 23.8% for BRCA1 carriers, 19.1% for BRCA2 carriers, and 9.8% for non-carriers ($p = 0.174$). Twenty-nine patients (5.4%) developed an IBTR (9.1% for BRCA1 carriers, 16.6% for BRCA2 carriers, and 10.1% for non-carriers). The 10-year cumulative risk for IBTR for BRCA1 carriers, BRCA2 carriers, and non-carriers was 8.7%, 14.1%, and 20%, respectively ($p = 0.577$). Negative estrogen receptor status was found to be a significant predictive factor for CBC (RR, 3.77; 95% CI, 1.98 to 7.17), and the tumor size ≥ 2 cm was a significant risk factor for IBTR (RR, 6.11; 95% CI, 2.03 to 18.38).

Conclusions: The risk of CBC in women with a BRCA mutation is 21.1% at 10 years, and that of IBTR is 11%. Non-carriers with high risk have a high risk of CBC and IBTR as well.

THE USE OF A GENE PROFILING ASSAY TO INFORM THE USE OF ADJUVANT CHEMOTHERAPY IN EARLY BREAST CANCER OVER 5 YEARS IN OXFORD

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Background: The decision for adjuvant chemotherapy in breast cancer is traditionally based on clinco-pathological factors; about 34% receive it with potential short and long-term side-effects. Oncotype Dx, Gene expression profiling assay, is now used for patients with ER+, HER2-, LN cancers to predict chemotherapy benefit as recommended by the National Institute for Clinical Excellence (NICE). Our MDT had been using it regularly since then but have also extended the indication for highly-selected node-positive patients. We evaluated the impact of Oncotype-DX usage on treatment recommendations over 5 years (2013-2018).

Methods: Onctoype DX was carried out on 146 women with ER+, HER2-, invasive breast cancer who underwent primary surgery. The treatment recommendations were was noted in the MDT and then compared to the decision after DX testing. The impact on treatment decisions and associated cost impact was assessed.

Result: In the LN negative group (n = 77); 43 were recommended to have chemotherapy and hormone-therapy and 34 hormone-therapy only. The RS (recurrence score) allowed 24 women (58%) to avoid unnecessary chemotherapy and discovered 9 (26%) to benefit from chemotherapy. In the LN positive group (n = 62); all were recommended chemotherapy; RS allowed 52 women (85%) to avoid it. The costs involved were compared using standard chemotherapy cost without taking into consideration the cost incurred by the hospital to manage chemotherapy complications.

Conclusions: Incorporating Oncotype testing into clinical practice for node-negative and highly-selected node-positive patients, predicted to derive were benefit has reduced chemotherapy use. No negative impact has been observed so far by the omission of chemotherapy.

PROGNOSTIC ROLE OF KRAS RNA EXPRESSION IN BREAST CANCER: A STUDY ANALYZING TCGA AND METABRIC DATABASES

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Background: To investigate the prognostic role of KRAS RNA expression in breast cancer using The Cancer Genome Atlas (TCGA) and Molecular Taxonomy of Breast Cancer International Consortium (METABRIC) databases.

Methods: Clinical and biological data of 1,093 breast cancers from TCGA database and 1,904 breast cancers from METABRIC database were analyzed. Overall survival (OS) and breast cancer-specific survival (BCSS) were determined. Biologic data including RNA expression, methylation, copy number alteration (CNA), and mutation were analyzed.

Result: High KRAS RNA expression group showed worse survival than the low KRAS RNA expression group regarding both OS ($p = 0.012$ in TCGA, $p = 0.001$ in METABRIC) and BCSS ($p = 0.001$ in METABRIC). By multivariable analysis, KRAS RNA expression level was an independent prognostic factor in both TCGA (hazard ratio [HR]: 1.570; 95% confidence interval [CI]: 1.026-2.403) and METABRIC (HR: 1.254; 95% CI: 1.087-1.446) databases. Positive correlation was observed between RNA expression and CNA ($\gamma = 0.577$, $p < 0.001$ in TCGA; $\rho = 0.343$, $p < 0.001$ in METABRIC). Methylation showed negative correlations with both RNA expression and CNA ($\gamma = -0.272$, $p < 0.001$ in TCGA). RNA expression had little association with mutation status of having approximately 0.6% of mutation frequencies.

Conclusions: KRAS RNA expression was significantly associated with breast cancer prognosis. It was an independent prognostic factor for breast cancer. RNA expression was positively correlated with CNA but negatively correlated with methylation. RNA expression had little association with mutation status of having approximately 0.6% of mutation frequencies. Further studies are needed to validate the prognostic role of KRAS RNA expression in breast cancer.

Poster Presentation

CLINICAL VALIDATION OF BREAST CANCER TEST SCORES AND THEIR CORRELATION WITH THE KI67 INDEX IN HORMONE RECEPTOR-POSITIVE, HER2-NEGATIVE, CT1N0 BREAST CANCER

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Background: Multigene profiling assays provide strong evidence for predicting the prognosis of breast cancer. In this study, we aimed to evaluate the clinical value of the Breast Cancer Test (BCT) score as a prognostic marker in relation to various clinicopathologic factors.

Methods: One-hundred and thirty-three cases of hormone receptor-positive, HER2-negative, cT1N0 breast cancer were selected for this study. Clinicopathologic variables, including patient's age, body mass index, tumor size, nodal status, overall stage, oncologic outcomes, and immunohistochemical staining results, were reviewed and analyzed according to BCT scores.

Result: Based on BCT scores, patients were separated into low (n = 105) and high risk groups (n = 28). With the exception of pathologic tumor size and lymph node status, which are key factors in BCT score calculation, most clinicopathologic factors did not show significant differences between the two groups. However, the Ki67 index showed strong correlations with risk stratification based on BCT scores, and p53 also showed some degree of correlation.

Conclusions: Risk classification based on BCT scores might have clinical significance as a prognostic marker in hormone receptor-positive, HER2-negative, cT1N0 breast cancer.

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

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Background: Low and high level of tumor-infiltrating lymphocytes (TILs) in triple negative breast cancer (TNBC) are associated with pathological complete response (pCR) rate after neo-adjuvant chemotherapy (NAC) and their prognosis. However, the predictive and prognostic impact of intermediate level of TILs are not well known. We aimed to determine the level of TILs in TNBC associated with the response to NAC and their prognosis.

Methods: Eighty consecutive patients who received NAC between 2001 and 2008 were included. The level of TILs was assessed on biopsy specimen before NAC and was defined as Low; 0-9%, Intermediate; 10-49% and High; 50%. We analyzed the association of these TILs level with clinicopathological factors, pCR rate and RFS.

Result: The level of TILs were low in 25 (31%), intermediate (int) in 39 (49%), and high in 16 patients (20%). Age, clinical T, clinical N, nuclear grade, Ki67 were all balanced in each TILs groups. In multivariate analysis, low-TILs was associated with lower pCR rate than high-TILs (OR = 0.027, $p = 0.002$) and int-TILs had a similar trend (OR = 0.352, $p = 0.094$). At the median follow-up period of 98 months, compared to high TILs, low-TILs was independent factor of short RFS (HR = 12.053, $p = 0.016$) in multivariate analysis. However, int-TILs did not differ from high-TILs in terms of RFS (HR = 2.575, $p = 0.381$). Age under 50 were also independent poor prognostic factor (HR = 2.583, $p = 0.041$).

Conclusions: In TNBC, int-TILs before NAC had a trend of lower pCR rate compared to high-TILs but was not associated with poor prognosis.

ELEVATED NEUTROPHIL TO LYMPHOCYTE RATIO PREDICTS POOR SURVIVAL IN HER2 POSITIVE BREAST CANCER TREATED WITH ADJUVANT TRASTUZUMAB

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Background: The neutrophil to lymphocyte ratio (NLR) has been reported that is associated with response to chemotherapy and prognosis in breast cancer, but its role is unclear in HER2 positive breast cancer. Here, we aimed to evaluate the prognostic significance of NLR in HER2 positive breast cancer patients underwent adjuvant trastuzumab.

Methods: Pre-treatment NLR was assessed in 178 non-metastatic, HER2 positive breast cancer patients who were treated with adjuvant trastuzumab in Gangnam Severance Hospital from January 2009 to December 2014. The cutoff value of NLR was defined as 2.75. We evaluated the disease-free survival (DFS) and overall survival (OS) according to NLR status by Kaplan-Meier method. The Cox regression model was used to evaluate the prognostic value of NLR.

Result: Of all patients, 142 (79.8%) patients were classified as low NLR group (NLR < 2.75) and 36 (20.2%) patients as high NLR group (NLR ≥ 2.75). There were no significant different clinicopathologic parameters between the two groups. During the median follow up of 59.5 months, DFS was significantly poorer in patients with high NLR than in those with low NLR (86.1% vs. 95.1%, $p = 0.045$), but the OS was not different between the two groups (97.2% vs. 99.3%, $p = 0.296$). Multivariable analysis showed that NLR was an independent risk factor for DFS (OR = 3.27, 95% CI: 1.04-10.30, $p = 0.043$).

Conclusions: Elevated pre-treatment NLR predicted low survival outcomes in HER2 positive breast cancer, suggesting that host immune function may enhance the efficacy of trastuzumab.

IS LYMPH NODE RATIO AN ALTERNATIVE TO PN STAGING IN BREAST CANCER, SINGLE INSTITUTION AUDIT

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Background: Axillary lymph node (LN) is the most important prognostic factor breast cancer. Studies have suggested, LN ratio (LNR), may be a superior indicator of LN burden and prognosis. When modest number of LN are removed, LNR performs better than positive LN (pN), while when few LN are removed, LNR worse than pN and may be misleading. We conducted a retrospective review our institution to evaluate LNR and disease free survival (DFS).

Methods: Women treated for operable breast cancer in 2008 with at least 5 year follow-up were included. Clinico-pathological and follow up data was extracted. LNR categories of low, intermediate and high were calculated based on the classification proposed by Vinh Hung Et al. Predicting risk factors for relapse and DFS was estimated.

Result: Of the 587 women whose data was analyzed, median age was 45 years, median pT was 2 cm. The pN staging was pN0 291patients, pN1 [1-3 nodes positive] 157 patients, pN2 [>4 nodes positive] 139 patients. LNR, 482 low risk [LNR ≤0.2], 84 intermediate risk [LNR 0.21 -0.65] and 21 high risk [>0.65]. Median follow-up was 82 months. The 5-year DFS decreased with increasing LNRs and pN. The DFS curves were better aligned to LNR compared to pN. However on multivariate analysis, age ($p=0.007$), presence of lymphovascular emboli ($p=0.001$) and pN ($p=0.004$) were significant, LNR was not ($p=0.652$).

Conclusions: LNR does not define the prognosis in breast cancer more adequately than the pN status, reinforcing the importance of pN as a prognostic variable.

LOCOREGIONAL FAILURE OF BREAST CANCER AND ITS ASSOCIATED FACTORS: A MALAYSIAN EXPERIENCE

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Introduction: According to the Malaysian Cancer Registry, breast cancer is the commonest cancer, constituting 17.7% of all cancers in Malaysia. Given the number of breast cancer patients that Malaysian hospitals diagnose every year, there needs to be more insight into the characteristics of breast cancer patients in Malaysia to improve survival and reduce recurrence rates.

Objectives: To identify factors which affect prognosis, specifically locoregional failure (LRF) and survival duration.

Methods: This was an observational follow-up study of all breast cancer patients who had surgical treatment at Putrajaya Hospital (PH) from 2006 to 2014.

Result: A total of 480 patients were treated between 2005 -2014 at PH. Mean age was 52 years old (range 21-85 years old). PH reported majority of patients being Stage II at diagnosis at 50.6%, followed by Stage III (17.5%), stage I (16.1%) and 12.8% being stage IV at diagnosis. Median follow-up duration was 54 months (range 1-216 months). The overall 5-year and 10-year cumulative incidences of LRF was 7.5% and 9.2%. The median time to develop LRF was 2 years. The overall survival for 5 years and 10 years were 92.5% and 91.9% respectively. Univariate analysis showed estrogen receptor status, cancer stage and subtype as significant predictors for LRF. On multivariate analysis, only estrogen receptor status and cancer stage significantly affect LRF.

Conclusions: Overall cumulative incidence of LRF and overall survival in our centre are comparable to other centre. Negative estrogen receptor and higher cancer stage are strong predictor for locoregional failure.

ASSESSMENT OF CPS+EG, NEO-BIOSCORE AND MODIFIED NEO-BIOSCORE IN BREAST CANCER PATIENTS TREATED WITH PREOPERATIVE SYSTEMIC THERAPY: A MULTICENTER COHORT STUDY

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Background: An accurate prognostic assessment of breast cancer patients after preoperative systemic therapy (PST) is critical for the adjustment of the systemic treatments. This study was to assess CPS+EG, Neo-Bioscore, and a modified Neo-Bioscore system.

Methods: A retrospective multicenter cohort study was conducted from 12 participanting hosipitals' databases from 2006 to 2015. Data were reviewed to meet the inclusion criteria of complete clinico-pathological data required by the study. Five-year disease free survival (DFS), disease specific survival (DSS) and overall survival (OS) were calculated using Kaplan-Meier Method. Area under the curve (AUC) of the three staging systmes was compared. Wald test and maximum likelihood estimates in Cox proportional hazards model was used for multivariate analysis.

Result: A total of 1,077 patients were enrolled. 45% of human epidermal growth factor receptor 2 (HER2)-positive patients received trastuzumab. The CPS+EG, Neo-Bioscore, and modified Neo-Bioscore could all stratify the DFS, DSS and OS (all $p < 0.001$). While in the same stratum of Neo-Bioscore score 2 and 3, the HER2-positive patients without trastuzumab therapy had much poorer DSS ($p = 0.013$ and P values < 0.01, respectively) as compared to HER2-positive patients with trastuzumab therapy and HER2-negative patients. Only the modified Neo-

Poster Presentation

Bioscore had a significantly higher stratification of 5-year DSS than PS (AUC 0.79 vs. 0.65, $p = 0.03$). Multivariate analyses revealed that the menopause status was an independent prognostic factor.

Conclusions: The modified Neo-Bioscore could circumvent the limitation of CPS+EG or Neo-Bioscore. The access of appropriate treatment should be incorporated into the existing staging systems for more refine prognosis prediction.

MENOPAUSAL SYMPTOMS AND QUALITY OF LIFE BETWEEN CHEMOTHERAPY-INDUCED MENOPAUSE WOMEN WITH BREAST CANCER AND NATURAL MENOPAUSE WOMEN WITHOUT CANCER

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Background: The purpose of this study was to investigate a menopausal symptoms and quality of life of chemotherapy-induced menopause women with breast cancer, as compared to natural menopause women without cancer.

Methods: The participants were recruited from the Breast Cancer Center at A hospital from September 2017 to June 2018. A total of 128 women were included; 64 with chemotherapy-induced menopause women with breast cancer and 64 with natural menopause women without cancer. Outcome variables were measured by the Korean version of the Menopause Rating Scale (MRS) and the Short-Form 36 Questionnaire Version 2 (SF-36V2).

Result: A mean score of MRS with chemotherapy-induced menopause women with breast cancer was 17.8 (±8.2), which is higher than that of natural menopausal women [12.9 (±8.4), $p = 0.001$]. There were significant differences in total MRS score between chemotherapy-induced menopause women with breast cancer and natural menopause women without cancer and included three dimension, psychological symptoms, somato-vegetative symptoms, and urogenital symptoms. There were significant differences between chemotherapy-induced menopause women with breast cancer and natural women without cancer in quality of life; role-physical ($p = 0.012$), role-emotional ($p = 0.010$) and general health ($p = 0.019$).

Conclusions: Chemotherapy-induced menopause women with breast cancer are exposed to a variety of severe menopausal symptoms than menopause women without cancer, resulting in decrease of quality of life. Therefore, it is suggested that the development of differentiated guidelines focused on symptoms is necessary, which should be provided continuously not only before treatment but also after treatment is complete.

TREATMENTS OF LYMPH EDEMA IN BREAST CANCER (MODIFIED ACUPUNCTURE, ETC.)

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Background: The goal of lymph edema treatments is to re-route the flow of stagnated lymphatic around blocked areas into more centrally located healthy vessels, which eventually drain into the venous system. If we can be activating on more other lymph pathway than pure axillary lymph pathway at upper extremities. Arm sizes, edema, flush, pain were diminished

Methods: With hyaluronic acid, metallic dry needle techniques, mesotherapy, electric muscle twitching tools. Stimulates on lateral aspect of arm, deep artery vein, pectoral area, neck, clavicular area, posterior of shoulder. Check up pain score, arm size, Grade of lymph edema and their cancer state, etc.

Result: It submitted the report on time even though time, selected patients groups, control groups are very small, statistically. Mean size of affected arm (4 part), grade of lymph edema, Score of pains has be improving. About 3-5 cm in arm size, edema, pains has been marked improved

Conclusions: It is necessary to reroute the flow of stagnated lymph in the subqutaneous tissues around blocked axillary area toward and into the axillary lymph nodes on the opposite side and inguinal, thoracic lymph nodes on same side the surgery was performed. These methods can be solved to lymph edema on breast cancer

DAILY COLLECTION OF PHYSICAL ACTIVITY VIA SMARTPHONE APPLICATION AND SMART BAND FOR DEVELOPMENT OF DISTRESS SCREENING TOOLS IN BREAST CANCER SURVIVORS: A FEASIBILITY STUDY

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Background: Mobile health apps are increasingly gaining attention as opportunities to obtain patient-generated health data without asking for self-report or visiting hospital. Since there are few studies regarding the mobile-based activity trackers in breast cancer patients, we decided to evaluate the feasibility of a mobile walking app and a smart band as a tool for collecting physical activity of breast cancer patients.

Methods: Between June 2017 and March 2018, patients who received surgery for breast cancer at Asan Medical Center were enrolled and asked to access two mobile apps on a weekly basis for six-months. Their daily physical activity was automatically recorded.

Result: A total of 160 participants were analyzed. Despite the fact that both smartphone app and the smart band showed more than 50% of compliance rate during the six-month follow-up period, smartphone walking app demonstrated higher overall compliance rate (88%) than a smart band (52%). The median value of individual compliance rate was 91% for the walking app and 55% for a smart band. Women having other diseases, an anti-hormonal therapy or a targeted therapy showed higher compliance to smartphone walking app. Younger women also reported a higher compliance rate to the app than older women. However, there was no association between any of the patient characteristics and a compliance rate to the smart band.

Conclusions: Smartphone apps or smart bands are feasible tools to collect daily physical activity data in breast cancer survivors.

THE EFFICACY OF SOFTWARE TO HELP PATIENTS UNDERSTAND DRUG COSTS FOR ADJUVANT TREATMENT FOR BREAST CANCER: A PILOT RANDOMIZED CONTROLLED TRIAL

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Background: Although communication of treatment costs is necessary for selecting the treatment for women with breast cancer, barriers such as uncertainty about prices and cost-sharing arrangements, as well as insufficient medical personnel training, make this difficult. To overcome these barriers, we conducted a pilot study on whether ChemoCalc (Nippon Chemiphar, Tokyo, Japan), a freely downloadable software for calculating drug costs, helps patients more easily understand drug costs.

Methods: We randomly assigned, in a 1:1 ratio, 20 women with early breast cancer and who had undergone surgery for the cancer, to discuss adjuvant treatment together with use of ChemoCalc (ChemoCalc group) or without (Usual Explanation group). The participants completed a five-grade evaluation questionnaire after these discussions. The primary endpoint was comparing the two groups questionnaire scores on their understanding of the drug costs for their treatment.

Result: There was no significant difference in median age between the ChemoCalc group and Usual Explanation group (57 vs. 50, respectively; $p = 0.27$). The ChemoCalc group showed significantly higher scores on the patients perceived level of understanding of the drug cost compared with those in the Usual Explanation group (5 [4-5] vs. 2.5 [1-5], respectively; $p = 0.002$). Scores related to patients perception that drug costs are important in treating breast cancer were also higher in the ChemoCalc group than those in the Usual Explanation group (5 [2-5] vs. 3 [1-5], respectively; $p = 0.049$).

Conclusions: ChemoCalc was found useful for helping patients to understand drug costs.

THE DIFFERENCES ACCORDING TO MARRIAGE STATUS DURING ACCESSORY BREAST SURGERY

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Background: Accessory breast is common occurring in 2-6% women and has the same natural changes as the normally located breast tissue such as development, shrinkage and fatty change according to their hormone level. We conducted an analysis of clinical factors according to marriage status in accessory breast patients.

Methods: One hundred patients who have been treated with an excision of accessory breast tissue from September 2017 to December 2018 at the Spring Day Clinic were analyzed retrospectively to clinical factors according to marriage status.

Result: The married group was observed in 47.0% (47 patients) and the unmarried group in 53.0% (53 patients) of all accessory breast patients. The mean age was 38.0 years in married group and 28.2 years in unmarried group. The main symptom for accessory breast treatment was cyclic pain and unwished appearance after delivery in married group, cyclic pain and unwished appearance after puberty in unmarried group. The amount of accessory breast tissue was statistically more observed in married group (40.3 ± 25.7 g) than in unmarried group (30.9 ± 22.5 g). The amount of liposuction during accessory breast surgery showed a significant increase in married group, too (420.6 ± 228.7 mL vs. 275.9 ± 168.8 mL).

Conclusions: From our data, we can observe more amounts of breast tissue and fatty tissue in married group than in unmarried group. Breast surgeon should know that accessory breast has the same natural changes as the normally located breast tissue after delivery and consider this condition during accessory breast surgery.

A PHASE I TRIAL TO ENHANCE CHEMOSENSITIVITY THROUGH THE INDUCTION OF MESENCHYMAL-EPITHELIAL TRANSITION IN METASTATIC TRIPLE-NEGATIVE BREAST CANCER (MTNBC)

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Background: Chemoresistance is mediated by cancer stem cells (CSC) which possess features of epithelial-mesenchymal transition (EMT). By inducing mesenchymal-epithelial transition (MET), chemoresistance of the CSC phenotype may be reversed. Our preclinical study identified a MET inducer which enhanced the chemosensitivity of TNBC in vitro and in vivo to 5-fluorouracil after established taxane resistance. We hypothesize that taxane-resistant mTNBC will be more sensitized to Capecitabine by inducing MET.

Methods: This is a single-arm, single-center phase I study. Twelve patients with histologically or cytologically proven mTNBC which has progressed after prior taxane therapy in the metastatic setting, and who have not received Capecitabine or 5-fluorouracil, will be enrolled. Primary endpoint is the changes in transcriptome (RNASeq) and protein profiling (immunohistochemistry) which are representative of MET through serial tumor biopsies. Secondary endpoints are early safety and tolerability signals of the combination of Capecitabine and MET inducer. The MET inducer is dosed O.D. 2 weeks as lead-in followed by Capecitabine D1-14 q21d from week 3 onwards. The MET inducer is then dosed D15-21 q21d, i.e. weeks 5, 8, 11, 14, 17, 20. A 3+3 design for dose escalation of the MET inducer will be employed. Study treatment is continued until week 20, after which Capecitabine monotherapy may be maintained until PD as per RECIST v1.1. Biopsies are scheduled at the start of weeks 0, 3 and 5, then upon PD.

Result: This trial is in progress.

Conclusions: This is a proof-of-concept study of the effect of inducing MET upon the sensitivity of post-taxane treatment in mTNBC.

EVALUATION THE USE OF FROZEN SOCK TO PREVENT DOCETAXEL-INDUCED PERIPHERAL NEUROPATHY IN BREAST CANCER PATIENTS

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Background: Docetaxel is most commonly used cytotoxic agent for breast cancer and its toxicities include peripheral neuropathy (PN), skin and nail toxicity. Aim of the study is to evaluate role of frozen sock (FS) for preventing docetaxel induced PN by performing nerve conduction study (NCS) and skin/nail toxicities.

Methods: From August 2017 to June 2018, patients with invasive carcinoma and planned for docetaxel administeration (doses 75-100 mg/m^2) as a 90-minutes IV infusion every 3 weeks were included. Patients wore an FS during docetaxel infusion on the right foot. The left foot was not protected by the FS. Motor and sensory NCS, nail and skin toxicities, quality of life scale were assessed before first cycle and 3 months after the end of last cycle.

Result: Forty-eight patients were included. Amplitude and velocity of motor/sensory nerve significantly decreased after 3 months in both foot. However degree of reductions in both amplitude and velocity did not differ between two feet, except peroneal nerve. Before and after 3 months of chemotherapy, the amplitude (CMAP, mV) for right/left peroneal nerve were as follows; before 7.6 ± 2.4 and 7.1 ± 2.4 ($p > 0.05$), after 6.8 ± 2.2 and 5.9 ± 2.2 ($p = 0.047$). Reductions in amplitude of peroneal nerve was significantly lower in right foot compared to left foot (0.8 ± 0.2 vs. -1.2 ± 0.2, $p = 0.029$). Nail and skin toxicities were significantly lower in the right foot compared with the left foot ($p < 0.005$).

Conclusions: Docetaxel induced motor and sensory PN, however FS caused lesser reduction of amplitude in peroneal nerve 3 months after end of chemotherapy.

BILATERAL BREAST CANCER: 13-YEAR EXPERIENCE OF E-DA HEALTH GROUP, KAOHSIUNG, TAIWAN

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Background: Bilateral breast cancer (BCC) is a rare, but increasingly common disease. The aim of this study is to define the epidemiological and tumor characteristics of BCC in E-Da Health Group (EDHG).

Methods: Between April 2004 and June 2017, 2,248 breast cancer patients were treated in EDHG. Of these 2,248, 23 patients met our criteria for this study. Patients with less than a six month interval between the two tumors diagnosis were grouped as synchronous breast cancer (SBC), more than six months interval were metachronous breast cancer (MBC).

Result: The average age was 59.5 in SBC and 57.6 in MBC groups. Eighteen patients were SBC and for 66.7% the contralateral breast cancer (CBC) was detected by mammography. In the five cases of MBC, the CBC was found during routine mammography and the average tumor diagnosis interval was 41.1 months. In SBC, 66.7% of CBC was invasive duct carcinoma, and 80% was in situ carcinoma in MBC. In MBC, 80% of index tumors were found in stage II and 80% of CBC were found in stage 0. Concordance rate of ER, PR, Her2 in SBC was 81.8%, 50.0%, and 78.6% respectively.

Conclusions: CBC is more commonly identified at an earlier stage than index tumors. All the contralateral tumors of MBC were found in mammography follow-up, demonstrating microcalcification. This highlights the importance of CBC screening at the time of primary diagnosis and during follow-up. There is good pathological concordance between the index and contralateral breast cancer in SBC.

MYOID HAMARTOMA OF THE BREAST: A CASE REPORT

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Background: Myoid hamartoma of the breast is an extremely rare benign tumor-forming lesion characterized by the presence of predominant smooth muscle component.

Methods: We describe a case of myoid hamartoma of the breast.

Result: A 44-year-old woman presented with a 2-year history of a mass in her left breast. The mass recently increased in size. Mammography revealed an oval calcified mass that was partly indistinct, and ultrasonography showed a 1.7 cm irregular indistinct hypoechoic mass with calcifications in the left breast. After US-guided staining, a local excision of the mass was performed. Macroscopically, the cut surface of the lesion revealed a yellow-white, non-encapsulated mass with slightly irregular margins. Microscopically, the mass contained glandular and stromal elements in a disorganized pattern. The glandular structures showed cystic changes, apocrine metaplasia, and adenosis. The dominant feature of stromal elements was the presence of a fascicular formation of elongated spindle cells with incursion between some glandular structures. These spindle cells mingled with adipose and fibrous tissues. There was no necrosis and mitosis. Microcalcifications were present inside the stromal elements. Immunohistochemical findings showed smooth muscle differentiation in the spindle cells characterized by actin, desmin, and smooth muscle myosin heavy chain expression. In contrast, both CD34 and S-100 protein expressions were negative. Estrogen receptor showed positive expression in glandular elements and spindle cells. Histological and immunohistochemical findings were consistent with myoid hamartoma of the breast. The patient was well 4 months later without tumor recurrence.

Conclusions: We report the morphologic features of a rare case of myoid hamartoma of the breast.

A CASE REPORT OF BREAST CANCER INCIDENTALLY FOUND DURING HEMATOMA TREATMENT

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Background: A breast hematoma may be caused by trauma, or procedures such as breast biopsy or breast surgery. Generally, breast cancer is not considered as the cause of breast hematoma.

Methods: Here we report a rare case of breast cancer diagnosed in a patient with the breast hematoma.

Result: A 57-year-old woman presented with slowly increase in size and pain on right breast from two months ago. A mixed echoic lesion was observed ultrasonography in the outside primary clinic and it was estimated to be hematoma. She said minor hit about two months ago. On physical examination, she had a palpable soft and non-tender mass sized about 10cm in right breast. The sonographic image has a relatively well-defined margin with internal mixed anechoic and hypoechoic portions. Approximately 300 cc of old blood fluid was aspirated and the hematoma was disappeared. However, hematoma remained the initial state on week later and the surgical treatment was decided. The hematoma were evacuated and histological examination of the surrounding tissues of the hematoma was performed. Unexpectedly, the result of histology was invasive ductal carcinoma. Positron emission tomography (PET) showed only focal hyper-metabolic lesion in the right breast operation site. The Breast MRI showed small nodular enhancing lesion suspected of residual breast cancer in right breast operation site lateral wall. The second surgery was decided by modified radical mastectomy. The final pathologic stage was IIA (T2N0). She is receiving adjuvant chemotherapy.

Conclusions: In the management of breast hematoma, in which trauma history is not clear, biopsy confirmation is essential.

TREATMENT OF LATE SOLIDIFIED HEMATOMA IN BACK DONOR SITE AFTER BREAST RECONSTRUCTION WITH LATISSIMUS DORSI FLAP: THREE CASES REPORT

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Background: Late solidified hematoma is a rare complication of breast reconstruction with latissimus dorsi (LD) flap. The majority of hematomas occur in the immediate postoperative period; however, some cases can occur at a distant point in time after surgery and do not have a definitive mechanism of injury or develop symptoms immediately after the triggering event. Moreover, treatment of hematoma has not yet been established.

Methods: Breast reconstruction with LD flap has been performed between January 2014 and June 2018 in more than 275 cases. We report 3 cases of late solidified hematoma at the back-donor site that have developed years after breast reconstruction with LD flap, in which a surgical approach was performed because the solidified hematomas could not be treated with percutaneous aspiration. They were planned for a surgical excision. Preoperative computed tomography (CT) and a biopsy were performed to confirm late hematoma.

Result: Preoperative CT detected a cystic mass. During surgical excision, we observed a capsule-enveloped hematoma, and inside, a solidified hematoma with semisolid blood clots was identified. A definitive diagnosis was made based on the results of the pathological examination. Biopsy revealed that the capsule consisted of fibrous tissue, and the content of the cyst comprised some blood and fibrinoid material. The three patients were followed-up and there were no complications nor recurrence in either patient.

Conclusions: We report successful surgical treatment and histological findings of late-onset solidified hematoma as a rare complication of Breast reconstruction with LD flap.

HIGH-GRADE, HORMONE RECEPTOR-LOW, INVASIVE ENCAPSULATED PAPILLARY CARCINOMA OF THE BREAST: A CASE REPORT

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Background: Encapsulated papillary carcinoma (EPC) is conventionally considered a variant of ductal carcinoma in-situ (DCIS); collagen type IV immunoreactivity studies support the notion that EPCs are confined within an intact basement membrane. Negative axillary lymph nodes were found in over 70 previously reported cases, while rare reports of metastases were flawed by not submitting entirely the lesion for histologic evaluation thus not excluding the possibility of associated occult invasive carcinoma. EPCs are also characterized by low grade nuclei and mitotic activity, with estrogen receptor (ER) and progesterone receptor (PR) positivity.

Methods: We report a case of high grade, hormone receptor-low pure EPC, with isolated tumor cells in one sentinel lymph node.

Result: A 76-year-old woman underwent mastectomy for left subareolar mass which was entirely submitted for histologic evaluation. Pathology showed 2.7 cm grade 3 EPC with no evidence of invasive carcinoma but adjacent foci of conventional low grade DCIS. The tumor showed no lymphovascular invasion. Immunohistochemical staining demonstrated focally absent myoepithelial layer around the encapsulated component, although it was preserved around the DCIS. ER score was 15/300, PR score 0, and Ki67 index high at 35%. One sentinel lymph node was found to contain isolated tumor cells.

Conclusions: On rare occasions, EPC may possess adverse histopathological features and metastatic potential. Sentinel lymph node sampling and comprehensive histologic evaluation are essential.

TRASTUZUMAB-INDUCED REVERSIBLE ACUTE SINUS NODE DYSFUNCTION: A CASE REPORT

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Background: Cardiomyopathy is the most common cardiotoxicity of trastuzumab, while arrythmogenic potential of the drug is much less described.

Methods: We report a case of trastuzumab-induced reversible acute sinus node dysfunction.

Result: A 42-year-old woman with T2N2 HER2-positive right breast cancer, but otherwise good health, was treated with adjuvant docetaxel, carboplatin, trastuzumab and pertuzumab. Approximately 4 hours after the first dose of subcutaneous trastuzumab, asymptomatic gradual deceleration of apical heart rate from a baseline of 70 to a nadir of 35 beats per minute (bpm) was noted. Electrocardiogram and holter showed sinus bradycardia. Electrolytes, thyroid function and echocardiogram were normal. The period of bradycardia lasted for 3 days and was fully reversible. In the second cycle, pertuzumab was omitted and subcutaneous trastuzumab led to a similar pattern of bradycardia. In the third cycle, pertuzumab was uneventful but intravenous trastuzumab on the next day resulted in infusion rate-dependent sinus bradycardia.

Conclusions: Sinus node dysfunction is a rare complication of trastuzumab; the route of administration and infusion rate may affect its onset. Clinical awareness and close monitoring are called for.

A CASE OF AXILLARY EXTRAMAMMARY PAGETS DISEASE: IS IT REALLY DIFFERENT FROM MAMMARY PAGETS DISEASE?

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Background: Extramammary Pagets disease (EMPD) is an uncommon intraepithelial adenocarcinoma that usually arise at anatomic sites rich in apocrine glands and axillary location of EMPD is very rare. We present a case of axillary EMPD of a Korean postmenopausal woman.

Methods: A 55 years old woman visited our hospital due to 5×5 cm sized red pigmented plaque with erosion and scale on left axilla. Punch biopsy of the lesion showed hyperkeratosis and acanthosis of epidermis with proliferation of large cells with clear cytoplasm which is appropriate for diagnosis of Pagets disease. There was no evidence of other primary invasive carcinomas including breast cancer on full diagnostic workup. She underwent wide excision of left axilla with local flap reconstruction surgery. Sentinel lymph node biopsy was performed concomitantly.

Result: Pathologic review of surgical specimen confirmed invasive mammary-type ductal carcinoma with intraepidermal Pagetoid spread. Tumor was involving apocrine gland and peri follicular structures. There were also focal ductal carcinoma in situ lesions in skin adnexal ducts. Immunohistochemistry and special stain for the specimen showed positive for CK7, PAS, GCDFP-15, ER and HER-2/neu. The patient received postoperative adjuvant radiotherapy. Until now, the patient is alive healthy and no sign or symptoms of recurrence have been noticed after 6 months.

Conclusions: EMPD of axilla is a very rare disease. Histologic diagnosis can be confusing especially when immunohistochemical profile is similar with that of mammary Pagets disease. Thorough preoperative systemic examination for underlying malignancy is essential.

USEFULNESS ABNOBA VISCUM TO TREAT REFRACTORY SEROMA AFTER BREAST RECONSTRUCTION WITH LATISSIMUS DORSI FLAP: A CASE REPORT

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Background: Despite the increasing latissimus dorsi (LD) flap, long-term seroma is still difficult to solve. The following methods have been widely used to solve this problem: aspiration, compression, immobilization arm, injecting triamcinolone, and surgery capsular removing. Capsulectomy is aggressive so that the patients can feel uncomfortable before and after surgery. Therefore, using abnoba viscum to solve the long-term seroma can be used as a breakthrough in the field of breast reconstruction.

Methods: The study was carried out by a single surgeon. The total number of subjects was 3. Abnoba viscum was adopted. Old & refractory seroma patients take aspiration, elastic band (EB) dressing, fixed arm treatment injecting triamcinolone. If the aforementioned treatment and if failed, finally they take injection Abnoba viscum.

Result: The results were assessed by the fluid collection in back and it turned out that Abnoba viscum was very effective to all three patients in treating seroma. Even after about 6 months, a seroma was not detected. Some side effects occurred but they were not threatening.

Conclusions: Many methods have been discussed to treat back seroma, and many preventative measures have been used. In the case of uncontrolled seroma, repeated use of Abnoba viscum is effective in reducing seroma. It can be one of good options.

STOMACH METASTASIS OF INVASIVE LOBULAR CARCINOMA; CASE REPORT

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Background: The stomach metastasis from breast cancer is rare. The main organs of metastasis from breast cancer is different depending on the cancer subtypes.

Methods: February 2016, a 49-year-old woman who had no past history, visited our hospital with a palpable mass of the left breast. The patient was diagnosed with invasive lobular breast cancer and underwent modified radical mastectomy. Stage was IIIC (pTN3M0), positive for ER and PR, negative for C-erbB2. She was administered chemo- radiation and endocrine therapy. In June 2018, the patient was performed endoscopic biopsy due to dyspepsia and poor oral intakes. And the results were invasive lobular cancer metastasis to stomach. We reviewed the patient's clinical records, diagnostic methods and pathologic reports.

Result: The immunohistochemistry stain of stomach biopsy presented Positive for ER (total score: 8 by Allred score), negative for PR (total score: 0 by Allred score), and negative for E-cadherin and CDX2, positive for GCDFP- 15. These findings mean metastasis from breast cancer. She received a total gastrectomy and transverse-colon segmental resection due to incidentally observed T-colon invasion at the time of surgery. The patient underwent a follow-up systemic examination in December 2018, and there was no evidence of metastasis or recurrence.

Conclusions: The stomach metastasis of breast cancer is rare and diagnosis is difficult. Follow-up study guidelines according to subtypes of breast cancer need to be established. We suggest that appropriate GI tract evaluation should be performed for advanced lobular carcinoma of breast.

GIANT LIPOMA OF BREAST

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Background: Lipoma is one of the most common benign neoplasms derived from fatty tissue. The incidence accounts for approximately 16% of all mesenchymal tumor.

Methods: We reported a case of a 50-year-old female with giant lipoma of the right breast. Because asymmetry, mammoplasty are encountered. Reconstruction proceeded with reduction of redundant skin and reposition of breast tissue.

Result: Symmetry and viability of the nipple areolar complex were achieved.

Conclusions: Severe asymmetry causing giant lipoma can be corrected with reconstruction.

A CASE REPORT OF FIBROADENOMA WITH COMPLETE REPLACEMENT OF FLORID LOBULAR CARCINOMA IN SITU, AND ITS CLINICAL SIGNIFICANCE

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Background: Case History; The authors describe the case of a 44 year old female who presented two breast masses for one month. Mammograms show a 1.2 cm sized hypodense fibroadenomatoid nodule and the other one 1.3 cm sized ill defined microcalfied mass. Microscopically, one nodular tumor composed of totally replacement of florid lobular carcinoma cells in fibroadenoma. The other mass shows mixed with invasive lobular carcinoma, diffuse ductal and lobular cancerization with lobular carcinoma in situ, ductal carcinoma in situ with microcalcifications.

Methods: A case report with review.

Result: Discussion; The natural history and optimal treatment of pleomorphic and florid lobular carcinoma in situ (LCIS) variants remains uncertain. Usually, classic LCIS was multifocal with wider distribution. Pleomorphic (LCIS) is distinguished by marked nuclear pleomorphism. Florid LCIS has nuclear features of classic LCIS, but differs from classic LCIS in showing marked distention of ducts and lobules with little residual stroma between the expanded spaces. Classic LCIS has long been considered a risk factor for invasive carcinoma, and treatment often consists of lifelong follow-up with risk-reduction rather than surgery. Florid LCIS is considered to be more aggressive than classic LCIS, but management remains controversial due to a limited understanding of their biology and natural history.

Conclusions: In summary, florid LCIS demonstrate features of direct precursor lesions warranting surgical excision.

INFECTION FOLLOWING IMPLANT-BASED BREAST RECONSTRUCTION: SUCCESSFUL SALVAGE OF 12 CONSECUTIVE PATIENTS

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Background: Implant-based breast reconstruction has been performed in recent years because of its simplicity and short operation time, rapid recovery of the patient, lack of donor site, and fewer scars. However, it can lead to complications such as infection, capsular contracture, malposition of implant, hematoma or seroma. Several studies have been conducted on the treatment of infection of implant, which is a serious complication. The purpose of this study is to evaluate the effective method in salvage of implant infection.

Methods: A retrospective study of 132 patients from January 2012 to December 2018 underwent implant-based breast reconstruction. Age, BMI, history of chemotherapy, radiation exposure, and smoking history were evaluated as potential factors of infection after the surgery. Also, infection symptom, culture result, complication were evaluated. In addition, mastectomy type, ADM use, duration of drain removal, underlying disease, axillary node dissection were evaluated.

Result: The total infection rate was 9.1% (12 of 132) and the total salvage rate was 91.7% (11 of 12). One patient with Pseudomonas aeruginosa did not respond to drainage and antibiotic treatment and explantation was performed. The other patients were treated with antibiotic therapy and USG guided aspiration.

Conclusions: In implant-based breast reconstruction, prevention of infection is the most important. However, in the case of infection, it is necessary to confirm the infection symptomatically. The status should be confirmed through ultrasound examination, drainage, and bacterial cultures. Through this, accurate diagnosis of the causative bacteria and symptoms should be made and swift and appropriate salvage should be performed.

MALIGNANT PHYLLODES TUMOR IN A GIRL: A CASE REPORT

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Background: Malignant phyllodes tumor is a rare fibroepithelial neoplasm of the breast . We report a case of malignant phyllodes tumor in a 14 years old girl. To explore the clinicopathological characteristics and diagnostic criteria of breast malignant phyllodes tumors in young female patient.

Methods: Clinical data, pathomorphology and immunohistochemical staining of breast malignant phyllodes tumor in the girl patient were analyzed, and related literature were reviewed.

Result: In March 2018, the patient found the left breast mass was about 3.5 cm × 4 cm × 3 cm in the areola area. There was no significant past or family history. By June 2018, the tumor rapidly grew, physical examination revealed a 18 cm × 16 cm × 14 cm mass which involved the entire left breast. There was no axillary or supraclavicular lymphadenopathy. Core needle biopsy was advised to undergo and on histopathological examination a possibility of malignant phyllodes tumor was rendered. Following this, lumpectomy was performed and microscopic examination showed that tumor cells were obviously atypia and mitotic count was more than 20/10HPF,a diagnosis of malignant phyllodes tumor was confirmed. Within three months of surgery patient had a recurrence of a breast lump about 5cm × 4cm × 4cm and underwent a left simple mastectomy. Patient is currently under follow up period and free of disease.

Conclusions: Breast malignant phyllodes tumor in young female patients is rare. A definitive diagnosis is of utmost importance in correct surgical management of the patient.

IMPROVING COMPLETION OF TRIPLE ASSESSMENT FOR BREAST CANCER IN A NATIONAL SCREENING PROGRAM

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Background: Breast cancer accounts for 1 in 3 incident cancers in Singaporean women and has been on an upward trend. Despite a National Screening Program (BSS), the number of women diagnosed at later stages is proportionately higher in Singapore than other comparative countries. This is reflected in low participation rates in BSS and even lower number of patients completing their triple assessment.

Methods: The National University Cancer Institute, Singapore (NCIS), together with BSS, intervened with a prospective study aiming to determine if the addition of a phone call made to defaulters by a trained staff would decrease the rate of drop-outs during triple assessment. Reasons for defaulting were also studied. Defaulters were defined as patients with abnormal mammogram results who failed to make an appointment at NCIS for additional required scans or biopsies after being notified by BSS.

Result: Three hundred thirteen defaulters were identified between December 2017 to September 2018. One hundred ten (35%) scheduled an appointment after the intervention call and 89 (81%) completed triple assessment. Fifty one (25%) were uncontactable despite 3 interval calls. Of those who did not schedule appointments, 33 (16%) were seen at other hospitals, 32 (15%) patients declined follow up, 11 (5%) had made earlier appointments to see a surgeon in NCIS. Other patients quoted financial difficulty, fear and inability to find time as reasons for rescheduling appointments to a later date.

Conclusions: Targeted calling of patients with abnormal screening results is an efficient, effective and sustainable method of increasing earlier diagnosis of breast cancer. It also provides an opportunity for health education.

A NATURAL PROGRESSION AUSTRALIAN WOMENS ATTITUDES ABOUT AN INDIVIDUALISED BREAST SCREENING MODEL

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Background: Population breast screening has been credited with a 20% reduction in breast cancer mortality since its introduction in the 1990s. There is international interest in improving this one-size-fits-all approach by offering an individualised regime. We aimed to explore women's attitudes to our current program, gauge their understanding of individual risk and assess their openness to change toward individualised screening.

Methods: Qualitative approach was taken using focus groups facilitated in community settings in Melbourne, Victoria. Women were recruited from a population-based breast screening cohort and group discussion was facilitated following three main themes: 1) experience of breast screening; 2) breast cancer risk perception, and 3) views on individualised screening.

Result: A total of 52 women participated in one of 4 focus groups, and were experienced with screening with 90% of participants having had more than 3 mammograms. They had strong, positive, emotional ties to breast screening in its current structure but were supportive, with some reservations, of the idea of individualised screening. There was good understanding about the factors contributing to personalised risk and a wide range of opinions about the inclusion of genetic testing with genetic testing being considered a foreign and evolving domain.

Conclusions: Individualised breast screening that takes account of risk factors such as mammographic density, lifestyle and genetic factors would be acceptable to a population of women who are invested in the current system. Reservations may be had in regards to uptake of genetic testing, motivations behind the change and management of the women allocated to a lower risk category.

EFFECTS OF STEADY LOW INTENSITY PHYSICAL ACTIVITY ON BREAST CANCER PROGRESSION

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Background: In which process physical activity would affect breast cancer initiation to progression has limited evidence and relevant topic. We examined how physical activity and dietary habits influence breast cancer latency and outcome throughout the cancer progression with different timing and intensity intervention.

Methods: In Model 1, mice started low or moderate intensity of exercise(HFLE, HFME) with the study initiation, then 4T1 mouse mammary tumor cells (1×10^3) were transplanted into mammary fat pad at 8 weeks. Otherwise in Model 2, mice started low or moderate intensity of exercise at the same time of tumor cell transplantation at 8 weeks. Latency was calculated as the time for the injected tumor cells to reach a size of 8 mm^3. Tumor volumes were measured twice per week and calculated until tumor volumes were reached at 600 mm^3.

Result: The Model 1 showed the HFLE mice had longest latency to tumor growth (12 days), and lowest volume of final tumor assessment. In the Model 2, HFDC and HFME mice showed relatively shorter latency (8.5 days) compared to HFDR or HFLE mice (10.5 days). And probably due to the shorter duration, HFDR mice achieved lowest tumor volume finally. In the myokine analysis, PGC1-a, iL-15, Irisin, and Oncostatin-M were detected highest in HFME mice. However, high serum myokine level didnt result in favorable tumor latency and final tumor volume.

Conclusions: Steady low intensity exercise at ordinary time could delay breast cancer growth and result in smallest tumor volume. After initiation of breast cancer occurrence, short term high fat restricted diet could affect tumor volume favorably.

CANCER WORRY, GENETIC KNOWLEDGE, AND ATTITUDES TOWARDS NGS MULTIGENE PANEL TESTING AMONG KOREAN BREAST CANCER PATIENTS WITH HIGH RISK FOR HEREDITARY BREAST CANCER

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Background: Although recent advances in NGS helped us to test multiple germline genetic mutations simultaneously, clinical application of NGS multiple panel test still has many limitations.

Methods: In this study, we provided sequential genetic testing and counselling programs for BRCA1/2 mutation tests and multigene panels beyond BRCA, and investigated cancer worry, genetic knowledge, and attitude towards gene panels among the patients.

Result: As of 31 January 2019, we prospectively enrolled 132 Korean BRCA1/2 mutation-negative female breast cancer patients with high risk for hereditary breast cancer. Among the patients, we identified 14 cases with pathogenic/likely pathogenic variants. After genetic counselling about multigene panel, patients showed slightly decreased concern about the possibility of cancer in the future (average score of pre-, 4.31 to post-, 4.08; $p = 0.009$) and lower influence on mood (average score of pre-, 3.31 to post-, 3.19; $p = 0.009$). However, there were no changes in the average score of genetic knowledge (pre-, 0.68 to post-, 0.68; $p = 0.968$), and the impact of cancer worries on daily activities (pre-, 3.04 to post-, 2.98; $p = 0.298$). In the survey on multigene panel, 126 (95.5%) patients reported that genetic testing and counseling about multigene panel were very much (55.3%) or much (40.2%) helpful for the patients and family. Fifty two (39.4%) patients wanted concurrent application of BRCA1/2 mutation testing and multigene testing beyond BRCA, and 66 (50%) patients wanted sequential application of the tests.

Conclusions: Multigene panel testing and genetic counselling may help to decrease cancer worry of BRCA1/2 mutation-negative patients with high risk for hereditary breast cancer.

VARIANT OF UNCERTAIN SIGNIFICANCE IN BRCA 1/2 GENETIC MUTATION TEST WITH POSSIBILITY OF PATHOGENICITY IN HEREDITARY BREAST AND OVARIAN CANCER

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Background: Variant of unknown significance (VUS) is a term that describes gene sequence variants that are not confirmed nor excluded for disease risk. VUS result in BRCA 1/2 genetic mutation test (BRCA test) makes it difficult for clinicians and patients to interpret. Therefore, more cases of patients should be actively reported to find a relationship between VUS and pathogenicity.

Methods: We retrospectively analyzed data from a total of 108 patients who were diagnosed with breast cancer and underwent BRCA test from March 2015 to October 2018 in Pusan National University Yangsan Hospital. BRCA test results were reported according to American College of Medical Genetics and Genomics standard and guidelines.

Result: A total of 15 patients were reported as VUS by BRCA test. Four cases were detected in BRCA1 gene and 11 cases were detected in BRCA2 gene. Three patients had family history of breast or ovarian cancer, and 2 patients had both breast and ovarian cancer. Total of 9 different variants were identified among these patients. Variants reported in multiple cases include c.68-7delT, c.1909+12delT, c.5339T>C (p.Leu1780Arg), c.5969A>C (p.Asp1990Ala), and c.8187G>T (p.Lys2729Asn).

Conclusions: We reported 5 variants of VUS that may be pathogenic in hereditary breast and ovarian cancer. Because of the limited number of patients in this study, more cases of VUS should be actively reported in order to find the pathogenicity of each VUS variants.

THE RISK ANALYSIS OF BRCA 1/2 MUTATION IN BREAST CANCER PATIENTS ACCORDING TO KOREAN INSURANCE GUIDELINES

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Background: Interest in the BRCA 1/2 genetic mutation test (BRCA test) after the "Angelina Jolie" effect increased in Korea. It is expected that medical expenses will increase as clinicians in Korea actively perform BRCA test. In this study, we analyzed the risk of BRCA1/2 genetic mutation based on the criteria of the Health Insurance Review & Assessment Service (HIRA) in Korea.

Methods: We retrospectively analyzed data from a total of 108 patients who were diagnosed with breast cancer and underwent BRCA test from March 2015 to October 2018 in Pusan National University Yangsan Hospital. BRCA test was performed according to HIRA guidelines.

Result: Of the 108 patients, 20 patients (18.5%) had BRCA 1/2 genetic mutations. Of the breast cancer patients who underwent BRCA test, 40 (37.0%) had a family history of breast cancer or ovarian cancer, 60 (55.6%) had breast cancer before the age of 40, 5 (4.6%) had ovarian cancer, 17 (15.7%) were bilateral breast cancer, and 3 (2.8%) were male breast cancer. In the risk analysis for BRCA mutation positiveness, family history (OR 6.27; 95% CI, 1.61 24.47), ovarian cancer (OR 8.89; 95% CI, 1.359 58.19), and bilateral breast cancer (OR 9.83; 95% CI, 2.08 48.36) were correlated as risk factors.

Conclusions: In this study, family history, ovarian cancer, and bilateral breast cancer showed as strong risk factors of BRCA mutation positiveness. On the other hand, age below 40 years did not act as a risk factor. A study on the age standard suitable for Koreans should be carried out in the future.

NEXT-GENERATION SEQUENCING FOR BREAST CANCER IN SINGLE CENTER DATA

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Background: The next generation sequencing technology has the advantages of high speed, high throughput and high accuracy. Because of these advantages, it is used in various cancer fields. Several gene pannels have been applied to breast cancer to assess risk and determine treatment direction accordingly. The purpose of this study was to improve the prognosis and future treatment of patients with breast cancer by applying NGS.

Methods: In 2018, 158 patients who underwent surgery at Kosin Gospel Hospital were enrolled. Neo-adjuvant chemotherapy patients were included. The panel we used was able to analyze 143 genes.

Result: Of the 158 patients, 54 were luminal A, 38 were luminal B, 33 were HER2, and 33 were TNBC. In the NGS results, 121 patients were positive and 37 patients were negative. The following gene mutations have been found. There were PIK3CA TP53 GATA3 BRCA2 AKT1 CDH1 BRCA1 CCND1 CCNE1 ERBB2 FGFR1 FGFR2 MCL1 MYC RB1 RPS6KB1 CD44 FGFR3 FGFR4 MAPK1 MDM2 MED12 PIK3R1 PTCH1 PTEN SF3B1 SOX2 TSC1 VHL and ZNF217. There were two or more mutations in 48 cases. There were 178 gene mutations in total. PIK3CA was the largest with 56 cases, followed by TP53 with 54 and GATA with 15.

Conclusions: Analysis by next-generation sequencing revealed that various gene modifications were expressed in breast cancer patients. Additional large-scale studies are needed to determine the effect of gene mutation detected through NGS on the prognosis of patients.

THE EFFECT OF BMI ON INITIAL BREAST CANCER STAGE: ANALYSIS USING CLINICAL DATA WAREHOUSE

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Background: The relationship between obesity and breast cancer stage is not well-known in Korean population. The aim of this study was to identify the effect of BMI on initial breast cancer stage.

Methods: Among the patients who underwent surgery for breast cancer (stage 0-III) from June 2003 to December 2018 in Seoul National University Bundang Hospital, 4,672 patients who were able to identify BMI data from clinical data warehouse were analyzed.

Result: The average BMI of our subjects was 23.6 (range 14.2-44.9). In total, 4.7% and 24.1% of patients had a BMI ≥ 30 (obese) and BMI 25-29.9 (overweight), respectively. In patients with obesity, the proportion of T2-4 was 39.7%, which was higher than that in patients with BMI 25-29 (27.1%, $p < 0.001$) or BMI < 25 (21.8%, $p < 0.001$). There was no difference in the distribution of hormonal receptors by BMI. Patients with higher stage were more likely to have higher BMI. The effect of BMI on stage was stronger in patients younger than 50 years (OR 2.48, 95% CI 1.82-3.40). The proportion of patients with BMI ≥ 27.3 was higher in patients with stage II-III (17.19%) compared to patients with stage 0-I (11.18%).

Conclusions: Our study suggests that obesity is associated with advanced breast cancer stage which represents a poor prognosis.

TREATMENT INTENSITY DIFFERENCES AFTER EARLY STAGE BREAST CANCER DIAGNOSIS DEPENDING ON PARTICIPATION IN A SCREENING PROGRAM

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Background: While population mammographic screening identifies early stage breast cancers (ESBC) (DCIS and invasive disease Stages 1 to 3A), commentaries suggest that harms from overdiagnosis and overtreatment may outweigh the benefits. Apparent benefits to patients with screen-detected cancers may be due to selection bias from exclusion of interval cancers. Treatment intensity is rarely discussed, with an assumption that all ESBC is treated similarly. We hypothesised that women diagnosed while in a screening program would receive less intense treatment than those never or not recently screened.

Methods: Retrospective analysis of all women aged 50-69 managed for ESBC (invasive or DCIS) during 2007-2013 within a single service, comparing treatment according to screening status. Data on demographics, detection, pathology, and treatment were derived from hospital, cancer registry and screening service records.

Result: Six hundred twenty two patients were active screeners (AS) at diagnosis (569 screen-detected and 53 interval cancers) and 169 patients not recently screened (NRS). AS cancers were smaller (17 mm vs. 26 mm, $p < 0.0001$), less likely to involve nodes (26% vs. 48%, $p < 0.0001$) and lower grade. For invasive cancer, NRS patients were more likely to be recommended for mastectomies (35% vs. 16%, RR = 2.2, $p < 0.0001$), axillary dissection (43% vs. 19%, RR = 2.3, $p < 0.0001$), adjuvant chemotherapy (65% vs. 37%, RR = 1.7, $p < 0.0001$), and post-mastectomy radiotherapy (58% vs. 39%, RR = 1.5, $p = 0.04$).

Conclusions: Participants in population screening diagnosed with ESBC receive substantially less intense treatment than non-participants. Differences persist when potential overdiagnosis is taken in to account. These differences should be factored into debates around mammographic screening.

Poster Presentation

OPTIMAL TREATMENT OF BREAST CANCER IN WOMEN OLDER THAN 75 YEARS: DATA FROM KOREA BREAST CANCER REGISTRY DATABASE

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Background: It is challenging for the clinicians to manage these old age breast cancer patients because there is no standard therapeutic guidelines for elderly patients. In this study, we investigated therapeutic efficacy of adjuvant modalities for the old age breast cancer women according to nationwide registry data.

Methods: In this retrospective study, we analyzed data from the Korean Breast Cancer Society registry which is a nationwide multicenter registry of data collected from January 2005 through December 2010. Patients survival data, including dates of death, were obtained from the Korea Central Cancer Registry, Ministry of Health and Welfare, Korea until December 2014. The cut off age of elderly patents in our study was set 75 years old.

Result: The median follow-up was 67 (range, 1-134 months) months. Elderly patients had higher pathological stage than control group ($p < 0.001$). The tumor size was also larger in elderly group than control group. From our registry data, Elderly group showed significant overall survival gain for hormonal treatment in HR positive breast cancer (Log-rank $p = 0.002$). Chemotherapy yielded statistically improved overall survival in younger patients elderly patients. In multivariate analysis revealed type of breast surgery, TNM stage, chemotherapy and hormonal therapy were found to be the independent factor for overall survival.

Conclusions: The management of breast cancer in elderly might be complex. The clinicians should be consider life expectancy, potential risks and benefits of treatment, and quality of life.

BREAST CANCER INCIDENCE FROM 2000 TO 2014 IN KAMPALA, UGANDA

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Background: Little information is available on the burden of breast cancer from sub-Saharan Africa. To help rectify this situation, we examined breast cancer incidence trends over a 15-year period in Uganda using data from the population-based Kampala Cancer Registry

Methods: Breast cancer cases were defined as tumors with ICD-O code C50. Population data was obtained from Uganda Bureau of Statistics. We performed a join point regression analysis to study the trend and presented results using, age specific rates, age-standardized rates (ASRs), Crude rates (CRs) and Annual percentage change (APC). Incidence rates were standardized using the world standard population (WHO 2000-2025) and expressed as per 100,000 persons.

Result: From 2000 to 2014, a total of 1,662 females with breast cancer were registered. The most observed histological types were malignant neoplasm (46.7%) and ductal carcinoma (23%). The number of cases almost doubled from 76 in 2000 to 134 cases in 2014. CRs increased from 8.9 to 11.7 per 100,000 persons with a statistically significant APC of 1.92%. Age specific rates gradually increased from age group 25-29 and were highest among females aged between 65-69 years. ASRs were somewhat consistent from 31.3 to 33.1 per 100,000 persons compared to the previous study where they increased from 18 in 1991 to 31.2 per 100,000 persons in 2010.

Conclusions: The results show that the incidence rates increase with age however more studies need to be conducted to find other associated risk factors and strategies to control the burden of breast cancer.

POST-TRANSLATIONAL MODIFICATION OF RNA-EDITING ENZYME, ADENOSINE DEAMINASE ACTING ON RNA, AND ITS FUNCTIONAL REGULATION IN BREAST CANCER (BRCA)

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Background: Adenosine deaminase acting on rna (ADAR1) catalyses adenosine-to-inosine (A-to-I) changes on RNA, generating transcriptome diversity. Dysregulated A-to-I editing has been implicated in cancer. We investigate the role of post-translational modification (PTM) in regulation of BrCa.

Methods: ADAR1 expression in BrCa patients (pts) was analysed from TCGA database. In -vitro overexpression of estrogen receptor (ER) and ADAR1 in MB231 ER- cell line and tumorigenicity assays were performed. Immunoprecipitation-Stable Isotope Labeling with Amino acids in Cell culture-mass spectrometric analysis(IP-SILAC-MS) was done to identify ADAR1 phosphorylation sites, and phosphomimetics and mechanistic studies completed to study its role.

Result: TCGA analysis suggests high ADAR1 expression correlated with improved overall survival (OS) ($p = 0.046$) in ER- pts, but lower OS ($p = 0.007$) in ER+ pts. Over-expression of ADAR1 alone in ER- cell line conferred lower tumourigenicity, whereas overexpression of both ADAR1 and ER caused increased tumourigenicity. A novel ADAR1 phosphorylation site at Threonine-601 (T601) was identified, and ADAR1 phospho-T601 (pAR1-T601) expression decreased with ER over-expression. Western blot showed higher pAR1-T601 expression in ER- vs. ER+ disease (86% vs. 33%), suggesting phosphorylation at T601 may account for opposing functional role of ADAR1 in ER-/ER+ BrCa. Phosphorylation-inhibitory (T-to-A) mutant of ADAR1 conferred higher tumourigenicity compared to phosphomimetic (T-to-D) mutant, suggesting tumourigenicity in ER+ BrCa resulted from un-phophosphorylated ADAR1. Mechanistic studies showed partial translocation of T-to-A mutant from nucleus to cytoplasm, whereas T-to-D mutant had exclusive nuclear localisation, akin to ADAR1 wild-type.

Conclusions: We describe the presence of phosphorylation modification of ADAR1 in BrCa, leading to an inverse tumourigenic/tumour suppressive phenotype between high ADAR1 expression and the presence or absence ER expression respectively.

Poster Presentation

INVERSE ASSOCIATION BETWEEN NATURAL KILLER CELL ACTIVITY AND BREAST CANCER STAGE

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Background: Natural Killer (NK) cells are cytotoxic lymphocytes critical to the innate immune system and they recognize and lyse malignant transformed cells through early defense against tumors. We aimed to investigate the association between NK cell activity and tumor characteristics, especially TNM stage, in patients with breast cancer.

Methods: We collected and analyzed the data of patients diagnosed with breast cancer between July 2015 and December 2017. Cytotoxic activity of NK cells was determined using the NK Vue-Kit (ATgen, Sungnam, Korea). We transformed IFN-γ levels into natural logs (lnIFN-γ) and analyzed them by using Student t-test or ANOVA.

Result: The mean age of 158 patients at diagnosis was 55.5 ± 12.4 years. The mean level of lnIFN-γ in group A (stage 0), B (stage I, II) and C (III, IV) were 6.48 ± 1.18, 6.14 ± 1.22, and 5.39 ± 1.45 pg/mL, respectively and *p*-value was 0.0061. However, there were no differences of lnIFN-γ level according to histologic grade and invasion to basement membrane, HR status, HER2 status and molecular subtypes.

Conclusions: There was an inverse association between lnIFN-γ level and stage group. Measurement of IFN-γ level released from NK cell can be a useful method of surveillance for breast cancer patients.

CANNABIDIOL INDUCED APOPTOTIC CELL DEATH VIA ENDOPLASMIC RETICULUM STRESS-REGULATED NOXA ACTIVATION IN TAMOXIFEN RESISTANT ER POSITIVE BREAST CANCER CELL

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Background: Tamoxifen remains crucial hormonal treatment for endoplasmic reticulum (ER)-positive breast cancer; however, development of resistance is a disturbance in the treatment or an aggravation of cancer. There were preclinical and clinical studies that Cannabis and cannabidiol have a therapeutic potential for breast cancer. Here, we aimed to identify the effects of on the novel pro-apoptotic Noxa activation in tamoxifen resistant breast cancer cells.

Methods: CBD experiments were performed using the tamoxifen resistant breast cancer cell lines MCF-7. Several pro- and anti-apoptotic proteins expression were identified. To understand the relationship of apoptosis and related proteins, their levels were investigated by using siRNA and the expression of apoptosis markers were identified.

Result: CBD induced apoptosis by regulating pro- and anti-apoptotic proteins, of which Noxa showed significantly higher expression. Noxa levels were downregulated using siRNA, and the expression of apoptosis markers decreased. After ROS was knock-downed, the level of Noxa also decreased, suggesting that ROS is involved in the regulation of Noxa.

Conclusions: CBD induced apoptosis in a Noxa-and-ROS-dependent manner in tamoxifen resistant breast cancer cell.

TRAIL OVERCOMES RESISTANCE OF CYSTINE DEPRIVATION-INDUCED CELL DEATH IN HYPOXIC TNBC CELLS

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Background: Triple negative breast cancer (TNBC) which lacks estrogen receptor, progesterone receptor and HER2 is very aggressive and malignant and has a high recurrence rate and poor prognosis. Tumors frequently encounter hypoxic stress that confers resistance to therapy. Recently, cancer metabolism including glucose degradation and amino acid transportation is emerging as a new target of cancer therapy. xCT, a Cystine transporter, has been reported to be over-expressed in breast cancer. In the present study, effects of amino acid deprivation in TNBC cell line MDA-MB-231 were investigated in hypoxic condition.

Methods: Cell viability was measured using MTT assay and cell death was evaluated using the Annexin V-FITC Apoptosis Detection kit I according to manufacturers instructions (BioVision), and analyzed using a FACScan flow cytometer (BD Science). The protein expression levels were detected by Western blot.

Result: MDA-MB-231 breast cancer cells were treated with medium of individual amino acid deprivation for 48 hours. Cystine deprivation for 48 hours in MDA-MB-231 cells significantly increased cell death by 80%. Sulfasalazine, a potent inhibitor of cystine transporter (xCT), also increase the cell death in MDA-MB-231 cells. However, cystine deprivation- and sulfasalazine-mediated cell death was significantly reduced in the cells under hypoxic condition. Tumor necrosis factor-related apoptosis-inducing ligand (TRAIL) reverses hypoxia-induced resistance to cell death by cystine deprivation- and sulfasalazine.

Conclusions: Taken together, TRAIL overcomes resistance of cystine deprivation- and sulfasalazine-induced cell death in the hypoxic TNBC cells.

THE CLINICAL SIGNIFICANCE OF ENDOTROPHIN EXPRESSION IN BREAST CANCER PATIENTS WITH OBESITY

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Background: Obesity is associated with an overall increase in morbidity and mortality in breast cancer patients. However, the mechanism of this correlation is poorly understood. Endotrophin has been found to be an adipokine with potent tumour-promoting effects in vitro studies. In this study, we investigated the association between endotrophin and the clinical outcomes of breast cancer patients with obesity.

Methods: Formalin-fixed, paraffin-embedded tumor samples from breast cancer patients who underwent surgery from 2012 to 2013 at Seoul National University Hospital was examined immunohistochemically and assessed using histological scores. We classified 59 patients into either obesity (BMI ≥ 25 kg/m^2) or control (BMI < 20 kg/m^2) groups, and clinical outcomes were analyzed including endotrophin expression.

Result: There were no significant differences between the obesity group and control group with regard to invasive tumor size (2.3 ± 1.1 vs. 2.4 ± 1.6 cm; $p = 0.473$), pathological diagnosis, molecular subtypes, histologic grade. The mean age was significantly higher in obesity group compared to control group (56.4 ± 14.2 vs. 44.7 ± 11.1 years; $p = 0.004$). The mean BMI was significantly higher in obesity group compared to control group (26.4 ± 2.2 vs. 19.3 ± 1.3; $p = 0.001$). Endotrophin was highly expressed in obesity group compared to control group (mean IHC score 19.9 vs. 16.5, $p = 0.026$). There were 3 recurred patients in both groups, respectively.

Conclusions: Endotrophin expression is increased in tumor cells and microenvironment of breast cancer patients with obesity. Further studies of large populations are warranted to elucidate the role of endotrophin in clinical outcome.

FEASIBILITY STUDY TO DIAGNOSE PATHOLOGICAL COMPLETE RESPONSE BY NEOADJUVANT CHEMOTHERAPY IN BREAST CANCER ADDING CORE NEEDLE BIOPSY (KBOG1301 SUPPORTED BY JONIE)

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Background: Neoadjuvant chemotherapy (NAC) for breast cancer has been improved and about 50% of Her2 positive tumor and over 30% of triple negative tumor could be achieved pathological complete response (pCR). This study aimed to improve diagnostic accuracy of pCR by NAC with core needle biopsy (CNB) for the location where the cancer had existed. Accurate diagnosis of pCR would make surgery be unnecessary.

Methods: In this study, we registered breast cancer patients who were diagnosed as clinical complete response (cCR) after NAC. All patients were classified as cCR by contrast-enhanced magnetic resonance imaging (MRI) after NAC. Under general anesthesia for planned surgery, ultrasound guided CNB was performed targeting the lesion where the cancer existed just before the surgery. Tissues biopsied with CNB and surgical specimens were evaluated by pathologists and diagnosed to i) no remnant carcinoma (= pCR), ii) carcinoma in situ and iii) invasive carcinoma.

Result: The study included 86 women. Seventy patients (81%) underwent NAC containing anthracycline and taxane and trastuzumab was administered in combination with 35 patients. For breast surgery, partial resection was 53 cases, whereas 33 cases underwent mastectomy. Pathological diagnosis of surgical specimen was diagnosed as pCR in 41 cases (48%), carcinoma in situ in 17 cases (20%) and invasive carcinoma remained in 28 cases (32%).

Conclusions: It was not enough to diagnose pCR by NAC accurately adding CNB to contrast-enhanced MRI classified cCR. In order to obtain an accurate diagnosis to omit surgery, method of imaging diagnosis should be improved and more accurate method of biopsy may be necessary.

RETROSPECTIVE AND PROSPECTIVE STUDIES TO TREAT WITHOUT SURGERY FOR BREAST CANCER CASES WHO ACHIEVED CLINICAL COMPLETE RESPONSE BY NEOADJUVANT CHEMOTHERAPY

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Background: Neoadjuvant chemotherapy (NAC) has been increasing the pathological complete response (pCR) rate (approaching to 50%) in patients with hormone-receptor negative breast cancer. Accurate pCR diagnosis is warranted to reduce unnecessary surgery after NAC.

Methods: We retrospectively evaluated outcomes of 395 patients with pCR to NAC (median follow-up: 41 months). In addition, diagnostic accuracy of pCR based on ultrasound-guided core needle biopsy (CNB) in 86 cases diagnosed as clinical CR with MRI was assessed in comparison with the results from surgical specimens.

Result: The pCR cases included 50 Luminal (7.2%), 98 Luminal-HER2 (32.1%), 116 HER2 (52.5%), and 131 triple negative (TN) types (34.2%). Recurrence was rare (5.82% [23/395]), especially local recurrence (1.2% [5/395]). The highest recurrence was observed in HER2 type (10.3% [12/116]) followed by TN (4.58% [6/131]), Luminal-HER2: (4.08% [4/98]), and Luminal (2.00% [1/50]). The initial univariate analysis revealed clinical stage before NAC and nodal status after NAC as risk factors of recurrence, followed by only clinical stage in the multivariate analysis. Pathology of surgical specimen revealed 41 pCR (48%), 17 carcinoma in site (CIS) (20%) and 28 invasive carcinoma (INV) cases (32%). CNB misdiagnosed 24 cases (14 CIS and 10 INV) as pCR, resulting in false negative rate (FNR) and accuracy of CNB to predict INV of 22.2% and 88.4%, respectively.

Conclusions: Local recurrence was rarely observed in any subtypes, especially in early clinical stage. Further improvement of diagnostic accuracy of ultrasound-guided CNB following cCR with MRI is warranted to reduce the number of unnecessary surgery after NAC.

PATTERNS OF RELAPSE AFTER NEOADJUVANT CHEMOTHERAPY IN BREAST CANCER-IMPLICATIONS FOR SURVEILLANCE IN CLINICAL PRACTICE

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Background: Breast cancer patients treated with neoadjuvant chemotherapy (NAC) remain at significant risk of relapse. This study aims to identify the patterns of relapse in patients treated with NAC to refine follow-up recommendations.

Methods: Retrospective analysis on 523 breast cancer patients treated with NAC at 2 public hospitals in Singapore between 2000 and 2014.

Result: Majority of patients (71.9%) had locally advanced disease. Median follow-up was 55 months. Five-year recurrence rate was significantly higher in triple negative breast cancer (TNBC) than non-TNBC subtypes (38.4% vs. 29.5%, $p = 0.042$); 85% of recurrences involved distant sites. Among TNBC and HR (hormone receptor)-/HER2+ subtypes, 97.0% and 95.0% of relapses occurred within 3 years from diagnosis respectively while 10.6% of relapses among HR+ subgroup occurred beyond 5 years. Recurrence risk in high-grade tumours decreased with time. Higher stage at diagnosis (hazard ratio, hr = 2.95; $p < 0.001$), high tumour grade (hr = 1.99; $p = 0.001$), not achieving pathologic complete response (pCR) (hr = 8.73; $p = 0.003$) and not receiving adjuvant radiotherapy (hr = 3.24; $p < 0.001$) were independent predictors of inferior recurrence-free survival. Serum CA 15-3 was raised in 49% of patients upon relapse; it correlated with inferior post-relapse survival (median 11 m vs. 22 m, $p = 0.019$).

Conclusions: There are differences in patterns of relapse and survival outcomes after NAC. We propose 3-monthly follow up for the first 3 years from diagnosis for patients who do not achieve pCR, especially those with TNBC and HR-/HER2+ tumours. Patients who are HR+ and have lower grade tumours will need longer follow up. However, the benefit from blood tests such as CA 15-3 appears limited.

TUMOR-INFILTRATING LYMPHOCYTES AND PATHOLOGIC COMPLETE RESPONSE AMONG THE PATIENTS WITH HER2 POSITIVE BREAST CANCER RECEIVING NEOADJUVANT DOCETAXEL, CARBOPLATIN, TRASTUZUMAB AND PERTUZUMAB

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Background: Dual anti-HER2 blockade increased the rate of pathologic complete response (pCR) in the neoadjuvant chemotherapy. Tumor-infiltrating lymphocytes (TILs) are correlated with prognosis in patients with early breast cancer. We investigate the associations between TILs and pCR rate in HER2(+) breast cancer treated with dual anti-HER2 therapy.

Methods: Ninety-four patients with HER2(+) breast cancer who received neoadjuvant treatment with docetaxel, carboplatin, trastuzumab and pertuzumab (TCHP) were included in this retrospective analysis. Associations between TILs and pCR were assessed in both HR positive(+) and negative(-) populations. We classified subgroups with a cutoff value of stromal TILs ($\leq$ 20% TILs vs. $>$ 20% TILs) based on ROC curves.

Result: Of the 94 cases, 50 (53.2%) tumors achieved pCR (ypT0/is N0) and median TILs was 17.07% [13.81-20.65]. pCR was 46.2% (n = 24/52) in HR(+) group and 62.0% (n = 26/42) in HR(-) group (p = 0.151). The pCR rate was higher in the high TILs group than in the low TILs (69.2% vs. 45.5%, p = 0.042). In HR(-) group, high TILs and low TILs achieved 88.9% (n = 8/9) and 53.1% (n = 17/32) of pCR, respectively. In HR(+), pCR rates of high TILs and low TILs subgroups were 58.8% (n = 11/17) and 38.2% (n = 13/34).

Conclusions: In HER2(+) breast cancer, HR(-) with high TILs showed higher pCR than HR(+) with low TILs. TILs have predictive value in HER2(+) breast cancer. T cell population analysis by sequencing the T cell receptor repertoire will be assessed to predict the anti-HER2 therapy response.

CLINICAL OUTCOME OF HER2 POSITIVE BREAST CANCER PATIENTS WITH PATHOLOGICAL COMPLETE RESPONSE AFTER NEOADJUVANT CHEMOTHERAPY

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Background: Neoadjuvant chemotherapy (NAC) is the accepted approach for women with selected operable breast cancer. High Pathological complete response (pCR) rate after NAC in HER2 positive breast cancer has been reported. The clinical outcome after pCR was less discussed in literature. The aim of this study is to analyze clinicopathological factors influencing recurrence in pCR patients with HER2 positive breast cancer.

Methods: A retrospective study was analyzed from 2005/1 to 2017/12, and a total of 466 invasive HER2 positive breast cancer patients underwent mastectomy or breast conserving surgery (BCS) after neoadjuvant chemotherapy at Linkou Chang Gung Memorial Hospital were enrolled.

Result: The median age was 50 years-old (range 18-93). The pCR was achieved in 151 (32.4%) patients. Median follow up time was 36 months. In 151 patients with pCR, the 3-year DFS rate was 71.4% in chemotherapy alone group, 91.0% in chemotherapy with trastuzumab group and 85.7% in dual blockade group, respectively ($p = 0.44$). In 3-year distant metastasis free survival analysis of pCR patients, the rate was better in chemotherapy with trastuzumab therapy group (95.7%) than chemotherapy alone group (71.4%) ($p = 0.04$). In total pCR patients, 12 patients (7.9%) developed distant metastasis while 6 patients (4.0%) occurred locoregional recurrence. Any recurrence rates of initial clinical stage II and stage III were 5.7% and 18.3%, respectively ($p = 0.01$).

Conclusions: Our findings suggested that pCR was associated with better long-term outcomes in HER2 positive breast cancer but pCR by different regimens may lead to different clinical outcome. Initial clinical stage status was still an important prognostic factor after pCR.

CHEMOTHERAPY IN NONMETASTATIC MALE BREAST CANCER: A POPULATION-BASED OBSERVATIONAL STUDY

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Background: Male breast cancer is a rare malignant disease accounting for less than 1% of all breast cancers. The treatment of male breast cancer is mainly extrapolated from the enormous literature and clinical experience in women. This study was to assess the relationship between adjuvant chemotherapy use and survival in a large population-based cohort of early stage male breast cancer patients.

Methods: Male patients diagnosed with invasive stage I-III breast cancer were identified in the Surveillance, Epidemiology, and End Results (SEER) cancer database from 1973 to 2014. The survival effect of chemotherapy was determined using multivariable Cox regression.

Result: A total of 2,878 male patients were enrolled. Of these patients, 1,936 (67.3%) did not receive chemotherapy. Age, T stage, N status, tumor grade and PR status were strong predictors for chemotherapy use. For men with PR negative breast cancer, chemotherapy use was associated with improved BCSS (HR, 0.47; 95%CI, 0.24-0.93; $p = 0.03$) and OS (HR, 0.43; 95% CI, 0.29-0.65; $p < 0.001$) using multivariable Cox regression analysis. However, chemotherapy use did not improve BCSS for men with PR positive (HR, 0.99; 95% CI, 0.72-1.35; $p = 0.943$), while chemotherapy was associated with improved OS (HR, 0.77; 95% CI, 0.63-0.94; $p = 0.011$) for men with PR positive stage II/III breast cancer, but not PR positive stage I breast cancer.

Conclusions: Chemotherapy should be performed to PR negative nonmetastatic male breast cancer patients, and should be considered for men with PR positive stage II/III breast cancer. Future prospective studies are still needed to confirm our results.

A NEW DEVELOPED PREDICTED PROGNOSTIC SCORE (GENESWELLTM BCT) AS A PREDICTOR OF RISK OF RECURRENCE IN HR+/HER2- EARLY BREAST CANCER IRRESPECTIVE OF AGE

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Background: Multi-gene panels are impact on the 8th AJCC staging system for breast cancer (BC) irrespective of their age. However, the prognostic value of the panels in pre-menopausal patients still remains unclear because most of the panels were validated in postmenopausal Western women. We validated a new developed molecular signature (GenesWell™BCT) for predicting the risk of recurrence in Asian patients with early HR+/HER2- BC including young breast cancer (YBC).

Methods: Among early BC patients with available clinical data at Samsung Medical Center (SMC), 800 patients were randomly selected by age group (31-60 years) and lymph node (N0 vs. N1. 2:1) status between 2005 and 2011. We enrolled YBC patients at Kyungpook National University Hospital and SMC, and excluded inadequate samples for GeneWell™ BCT.

Result: Of the 718 patients who were eligible for the study, 376 (52.7%) and 342 (47.6%) were categorized as BCT low and high risk group. Median follow up duration was 80.0 months. Mean age was 49.1 years, and 96 (13.4%) were less than 35 years. Of those, 189 (50.3%) with BCT low risk underwent CTx while as, 57 (16.7%) with BCT high risk did not. There were significantly worse distant metastasis free survival (DMFS) and disease free survival (DFS) in the BCT high risk group ($p = 0.0003$ and $p < 0.0001$, irrespectively). In addition, the prognostic value was statistically significant regardless of their age

Conclusions: Our results suggest that GenesWell™ BCT is an effective prognostic panel for predicting risk of recurrence in patients with early HR+/HER2- BC irrespective of their age.

COMPARISON OF COMPLICATION ACCORDING TO INCISION TYPES IN NIPPLE-SPARING MASTECTOMY AND IMMEDIATE RECONSTRUCTION

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Background: Nipple-sparing mastectomy (NSM), followed by immediate breast reconstruction (IR), has become the preferred surgical procedure with good results in cosmesis and patient satisfaction. However, nipple-areolar complex (NAC) ischemia and necrosis remains the main problem after NSM and IR.

Methods: We retrospectively analyzed patients who received NSM and immediate reconstruction in Gangnam Severance Hospital from January 2009 to June 2018. We compared patient characteristics and complication rate among three different incisions (inframammary fold, radial, periareolar). Additionally, we evaluated risk factors of NAC necrosis.

Result: The data from eligible 290 breasts of 275 patients were analyzed. Patients with inframammary fold (IMF) incision had relatively smaller breast weight. Overall complication rate was highest in periareolar incision (42.6%) and lowest in IMF incision (18.8%) ($p < 0.001$). Rate of NAC ischemia or necrosis was significantly different among three incisions (9.7%, 17.0%, 31.1% in IMF, radial, and periareolar, respectively). In addition, surgical treatments were more frequently needed in patients with periareolar incision. Neoadjuvant CTx, tumor location of lower inner quadrant, distance from tumor to nipple base, periareolar incision, breast weight and large implant volume were related to NAC necrosis in univariable analysis. Lower inner tumor location, periareolar incision, shorter distance from tumor to nipple base and large breast weight remained as significant risk factor in multivariable analysis.

Conclusions: Periareolar incision showed higher incidence of overall complication and NAC necrosis in our data. Inframammary incision could be an acceptable choice with superior aesthetic outcome and less complication. Risk factors of NAC necrosis should be considered when planning nipple-sparing mastectomy.

OUTCOMES OF SENTINEL LYMPH NODE BIOPSY WITHOUT RADIOTHERAPY AFTER SKIN-SPARING OR NIPPLE AREOLAR COMPLEX-SPARING MASTECTOMY

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Background: There is little known about the prognosis for early breast cancer patients who are not receiving adjuvant radiotherapy after mastectomy with sentinel lymph node biopsy. The purpose of this study were to evaluate the characteristics and outcomes of early breast cancer patients who underwent skin-sparing mastectomy or nipple areolar complex-sparing mastectomy with sentinel lymph node biopsy.

Methods: A total 83 patients with early breast cancer who underwent skin-sparing mastectomy or nipple areolar complex-sparing mastectomy with sentinel lymph node biopsy were identified in Korea Ansan University Hospital between 2002 and 2017. We retrospectively collected clinitopathologic data for these patients. Local recurrence rate, regional recurrence rate, distant recurrence rate, disease free survival, and overall survival were determined.

Result: Nine patients (10.8%) underwent nipple areolar complex-sparing mastectomy with sentinel lymph node biopsy. Most patients had stage I to IIA, estrogen receptor-positive, Her2-negative invasive ductal carcinoma. At a median follow-up of 40.8 months, the 3-year local, regional and distant recurrence rates were 1%, 0.8%, and 0.5%. The 3-year disease free and overall survival rates were 96.9% and 98.9%.

Conclusions: Early breast cancer petients who underwent skin-sparing mastectomy or nipple areolar complex-sparing mastectomy with sentinel lymph node biopsy had excellent outcomes without additional axillary surgery or radiotherapy.

BREAST CONSERVING SURGERY AFTER NEOADJUVANT CHEMOTHERAPY-A SINGLE CENTER ANALYSIS IN SAFETY MARGIN AND EXCISION SIZE

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Background: Neoadjuvant chemotherapy (NACT) provides an opportunity to de-escalate the surgery in patients who need total mastectomy or axillary lymph node dissection and to have a better cosmetic effect in breast conservation surgery (BCS). This single-center retrospective study was performed to evaluate whether the size of the resected breast tissue was reduced after NACT, ensuring the primary goal of breast conserving surgery, the negative resection margin.

Methods: All patient who underwent BCS after NACT in 2015-2016 for invasive breast cancer in Asan Medical Center were included. Patient characteristics, pathology findings, size of specimen, pre- and post-NACT MRI findings were analyzed.

Result: Total 347 patients were analyzed. 110 patients (30.6%) had pCR including Tis. 35 patients (10.1%) had positive resection margin. Average distance from tumor to specimen margin was 1.6cm. Only 19 (5.5%) patients had smaller specimen size in longest diameter compared to pre-NACT MRI.

Conclusions: A relatively low rate of positive tumor was seen in the margin, but in most cases the wider breast tissue tended to be removed than the original tumor size. Techniques are needed to accurately determine changes in tumor area in patients receiving NACT.

THE CLINICAL VERIFICATION OF INTERNAL MAMMARY SENTINEL LYMPH NODE BIOPSY GUIDED BY THE MODIFIED RADIOTRACER INJECTION TECHNIQUE OF THE BREAST

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Background: A modified radiotracer injection technique (periareolar intraparenchymal, high volume and ultrasound guidance) was first produced in Shandong Cancer Hospital & Institute, which had a relatively high visualization rate of internal mammary (IM) sentinel lymph node (SLN) of the breast. A prospective study was designed as a clinical verification of internal mammary sentinel lymph node biopsy (IM-SLNB) guided by the new technique (Clincaltrial No: NCT03024463).

Methods: From August 2017 to January 2019, 45 consecutive patients scheduled for mastectomy with the pathology confirmed invasive breast cancer were involved (included 29 clinical positive axillary lymph node patients and 16 clinical negative axillary lymph node patients with positive axillary SLN intraoperative diagnostic result). Internal mammary lymph node (IMLN) dissection was performed immediately after IM-SLNB to verify the accuracy of IM-SLNB.

Result: The median number of IM-SLN and IMLN removed was 2 (1-4) and 3 (1-9), respectively. The positive rate of IM-SLN was 40% (18/45) and the positive IM-SLN of 12 patients was the only positive IMLN identified. The accuracy of IM-SLNB was 97.8% (44/45). Of 27 patients classified as IM-SLN negative, 26 (96.3%) were confirmed to be IMLN negative by IMLN dissection. Only one patient classified as node negative by IM-SLNB were node positive on IMLN dissection, yielding a false-negative rate of 5.26% (1/19).

Conclusions: IM-SLNB guided by the modified radiotracer injection technique has a high accuracy. We recommend IM-SLNB should be performed in all patients, especially in patients with clinically positive axillary lymph node. IMLN radiotherapy should be tailored and balanced based on the statues of IM-SLN.

ACCURACY OF CORE BIOPSY IN PREDICTING PATHOLOGIC COMPLETE RESPONSE IN THE BREAST IN PATIENTS WITH COMPLETE/NEAR COMPLETE CLINICAL AND RADIOLOGICAL RESPONSE (COMPLETE RESPONDERS IN THE BREAST CRBR)

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Background: With the advent of taxanes and targeted agents in neoadjuvant chemotherapy (NACT) for breast cancer, the rates of pathologic complete response (pCR) have been steadily increasing. The role of surgery in these patients serves the purpose of a biopsy to confirm or negate a pCR.

Methods: We conducted a prospective validation study. Women who had undergone a titanium clip placement followed by neoadjuvant chemotherapy (NACT), and achieved a complete/near complete clinical and radiological response were included. Eligible women underwent an MRI of the breast followed by a US guided core biopsy (CNB) of the tumor bed. The CNB was compared with the final histopathology report.

Result: At the time of this abstract, 50 patients were recruited in the study. 20/50 had triple negative tumors and 10/50 were of the HER2 enriched subtype. The overall pCR rate was 38%. The mean number of cores taken was 6. US guided CNB had an accuracy of 68% in predicting pCR. There were 13 false negative results, giving an FNR of 41.9%. Among the 3 false positive results, two were pure DCIS and one had invasive carcinoma. No untoward side effects were observed in any of the patients.

Conclusions: Additional patients are being accrued to the study and the final analysis will be available during the presentation. At the time of this analysis, US guided CNB of the tumor bed had a high FNR of 41.9%. An increase in the amount of tissue examined or a change in the imaging modality could improve the results.

DIRECT-TO-IMPLANT BREAST RECONSTRUCTION FOLLOWING NIPPLE SPARING MASTECTOMY WITHOUT THE USE OF ACELLULAR DERMAL MATRIX: THE PREDICTIVE FACTORS OF ADVERSE SURGICAL OUTCOMES IN ASIAN BREASTS

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Background: Nipple sparing mastectomy (NSM) and direct-to-implant (DTI) immediate breast reconstruction with the use of acellular dermal matrix (ADM) is growing in numbers and provides reliable oncological and aesthetics outcomes. Despite the proven benefit, ADM significantly increased the cost of procedures. This study is aimed to compare the reconstruction methods between DTI and tissue expander (TE) without ADM following NSM; and evaluate the predictors of post-DTI adverse outcomes.

Methods: The patients undergoing NSM and immediate breast reconstruction with DTI or TE without the use of ADM were enrolled. Age, BMI, medical history, tumor characteristics, neoadjuvant/adjuvant therapy, short/long-term complications and secondary operation were recorded. Primary outcomes included short/long-term complications, removal of implants and aesthetic revision surgeries.

Result: The case numbers of DTI and TE were 70 and 14, respectively. Baseline and tumor characteristics had no significant difference between DTI and TE. TE group had larger final implant size (mL) (393.3 ± 81.1 vs. 294.4 ± 77.8, $p < 0.001$) and more frequent implant/TE removal rate (28.6% vs. 7.1%, $p = 0.038$). In DTI reconstruction, age over 50 (OR: 3.347, 95% CI: 1.03-10.91, $p = 0.045$) and higher mastectomy weight (per 100 gm) (OR: 1.498, 95% CI: 1.01-2.23, $p = 0.046$) presented higher risks for short-term complications. Intra-operative radiotherapy (IORT) on the nipple-areolar complex (OR: 5.714, 95% CI: 1.21-26.93, $p = 0.028$) increased the risks of secondary revision surgeries.

Conclusions: DTI immediate breast reconstruction without ADM after NSM did not increase risk of early complications and showed even better surgical outcomes in comparison to two-stage reconstruction with TE.

COMPARISON OF POSTOPERATIVE OUTCOMES BETWEEN BREAST CONSERVING SURGERY AND TOTAL MASTECTOMY

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Background: The aim of the present study was to evaluate the survival rate of the patients according to 4 surgical methods without distant metastasis of patients.

Methods: A total of 3,020 patients were diagnosed as pathologically as distant metastasis-free breast cancer from 2010 to 2018. The patients were divided into four groups 1) total mastectomy (TM), 2) total mastectomy+reconstruction (TM+R), 3) Breast Conserving Surgery+ Reconstruction (BCS+R), 4) Breast conserving surgery (BCS). The 5-year survival rate and the survival rate according to the neoadjuvant, adjuvant chemotherapy and no received chemotherapy were observed by univariate analysis in each group.

Result: A total of 3,020 patients were included: 774 in the TM group, 308 in the TM+R group, 14 in the BCS+R group, 1924 in the BCS group. After adjusting for patient and treatment characteristics, the relative risk (RR) was 1.39 (95%CI: 1.11-1.75) after TM as compared to BCS. When the 4 groups were classified according to the chemotherapy method-neoadjuvant, adjuvant and no chemotherapy arms. The multivariate analysis performed after age and stage corrections, the relative risk was 1.84 (95%CI: 1.13-3.00) after TM as compared to BCS in neoadjuvant arm. 1.35 (95%CI: 1.01-1.80) after TM and 0.26 (95%CI: 0.08-0.83) after TM+R as compared to BCS in adjuvant arm.

Conclusions: Multivariate analysis of this study showed a interesting conclusion is that TM+R patients showed a difference in survival compared to BCS in patients receiving adjuvant chemotherapy arm. This conclusion is likely to require more research in the future.

ONCOPLASTIC ROUND BLOCK TECHNIQUE OF BREAST CONSERVATION SURGERY

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Background: Round block technique is a volume displacement technique to reshape breast after breast-conserving surgery (BCS) especially with tumor in the superior or lateral side of nipple-areola-complex (NAC). Generally, when the tumor is located inferior or medial side of the NAC, flap surgery or tennis racket method have been required. The purpose of this study is to evaluate the usefulness of round block technique for at all location of tumor.

Methods: A total of 37 patients underwent round block technique after BCS at Kosin University hospital from February 2018 to July 2018. Preoperative designs were made on the peri-areolar and the outer line for incision line. Outer line varies the width according to the tumor location. After the wide excision from GS department, the remnant glandular tissue was lifted off from pectoralis muscle for approximation. After that we dissected skin from glandular tissue to release dimpling. The skin between the two circles was de-epithelialized and closed. Cosmetic results were assessed for 1-6 months follow up.

Result: The median weight of tumor was 24 g (range from 5.0-50 g). The average distance of tumor from nipple was 5.4 cm (range from 2.0-10 cm). There were 4 cases with tumor in the medial side of NAC, and 4 cases with tumor in the inferior side of NAC, and the rest were superior and lateral located tumor (29 cases).

Conclusions: Round block technique is an excellent cosmetic option for patients undergoing BCS, regardless of the locations of tumors.

COMPARISON OF OUTCOMES OF DIRECT-TO-IMPLANT BREAST RECONSTRUCTION BETWEEN THE ELDERLY AND YOUNG ADULTS IN BREAST CANCER

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Background: Breast cancer is the most prevalent female cancer worldwide, occurring in about half of all women over the age of 60. However only a small number of elderly patients (about 4-14%) undergo breast reconstruction. Direct-to-implant reconstruction is a good choice for elderly women because it requires only one operation and shortens the length of hospital stay and operation time.

Methods: From January 2016 to July 2018, we retrospectively analyzed 190 breast cancer patients who received direct-to-implant at a single center. Patient demographics, surgical details, complications, and follow-up were recorded and analyzed.

Result: Twenty five patients were ≥ 60 years old and 165 were younger, < 60 years old. There were no significant differences in baseline characteristics between the two groups. The rate of overall complication was higher in the elderly group (60.0%) than in the control group (33.9%). ($p = 0.022$). However, no significant difference was observed between the two groups in major complication and implant removal rates. Periareolar incision showed higher complication rate than inframammary fold (IMF) incision or lateral incision ($p < 0.001$).

Conclusions: As the age of patients increases, the rate of complications could increase but this does not necessarily mean the rate of major complication is proportionately higher. Moreover, incision type is more significant as a risk factor of complication. Therefore, if there is no other large comorbidity in elderly patients, it may be a good alternative to attempt a direct-to-implant in mastectomy.

P-Z INCISION

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Background: Breast-conserving surgery (BCS) is performed in patients with small tumors because the breast is cosmetically an important organ for women. Several incisional techniques have been performed depending on the location of the tumor in order to improve the cosmetic result by performing incisional scar in an inconspicuous place. The periareolar incision is superior in cosmetology but difficult to use in tumors far from the nipple. We report our experience with periareolar zigzag (P-Z) incision at BCS.

Methods: We reviewed the characteristics, surgical findings, and histopathological findings of patients who underwent P-Z incision among patients who received BCS for breast cancer from January 2016 to December 2017.

Result: Three hundreds ninety seven patients underwent BCS using the P-Z incision at the Asan Medical Center. The median age of the patients in the study was 52 years (range: 20-96 years). 312 patients (78.4%) had invasive cancer and 85 patients (21.4%) had carcinoma in situ. Frozen biopsy of the resection margin during surgery revealed tumor positive in 69 (17.2%) cases and re-excision was performed. median time of operation was 72 minutes in patients who did not undergo axillary surgery or sentinel node biopsy only, and 83 minutes in patients who underwent axillary node dissection or supraclavicular node dissection

Conclusions: Partial resection using P-Z incision in breast cancer patients has a relatively short operation time and a low rate of margin positivity. Therefore, it can be used safely and effectively even in the removal of relatively large tumors.

TWO-YEAR EXPERIENCE WITH THERAPEUTIC MAMMOPLASTY IN TREATMENT OF BREAST CANCER IN REGIONAL AUSTRALIA

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Background: Wide local excision followed by radiotherapy has long been established as a treatment option for early breast cancer. However, patients may require multiple operations to achieve clear margins. Re-excision can result in large volume loss and poor cosmesis, particularly in women with fatty breasts or those with lower pole and inner quadrant cancers. This study evaluates therapeutic mammoplasty (TM) as an extension of breast-conserving surgery (BCS).

Methods: Two-year review of a prospectively collected database of 12 patients undergoing TM was performed. Patients demographics, clinical findings and long-term outcome was evaluated.

Result: Of the 12 patients (17 breasts), 5 (41.67%) underwent bilateral mammoplasties for concurrent lesions (2) or as symmetrizing procedure (3). Average age was 59 (44-72). All patients were non-diabetic and only one was a smoker. Median weight of specimen was 320.97 grams. Superio-medial pedicle was used more frequently than inferior pedicle (ratio 9:8). Of the 17 breasts resected, 4 required further re-excision with one due to occult lesion. Two subsequently required mastectomies to achieve oncological clearance upon completion of adjuvant treatment. Rate of wound infection was 17.65% Adjuvant treatment were commenced without delay in all patients.

Conclusions: TM is a safe extension of BCS when performed by oncoplastic breast surgeon. This is used to achieve better aesthetic results without delay to adjuvant treatment, particularly for patients with high BMI, fatty breasts or those with cancers in undesirable locations. However, careful pre-operative assessment is crucial to minimize need for re-excision or conversion to mastectomy.

TWO-YEAR EXPERIENCE OF IMMEDIATE DIRECT-TO-IMPLANT BREAST RECONSTRUCTION USING TILOOP BRA MESH FOLLOWING MASTECTOMY IN REGIONAL AUSTRALIA

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Background: Single-stage direct-to-implant (DTI) breast reconstruction presents an ideal reconstructive option as it allows for shorter operative and recovery time with no donor site morbidity. However, prior to the introduction of acellular dermal matrix (ADM) or synthetic mesh products, this was abandoned due to complications including implant extrusion, malposition and capsular contraction. This multi-center study analyses outcome of DTI in regional center since the introduction of TiLoop Bra mesh (titanium coated polypropylene).

Methods: Audit from a prospectively collected database of women undergoing mastectomy and DTI reconstruction with TiLoop Bra mesh performed during a period of 24 months in 2 regional Australian centers by 2 oncoplastic breast surgeons. Patient demographics and co-morbidities along with short-term outcomes were analyzed.

Result: A total of 24 mastectomies (17 nipple sparing and 7 skin sparing) were performed on a group of 16 patients. Median size of implant was 388.63 cc (range 111 cc-615 cc). One woman developed nipple necrosis requiring implant removal while 2 others had explantation due to infection. Another patient developed non-infected seroma requiring percutaneous drainage due to pain. Re-excision rate was low at 4.2% with 1 woman requiring subsequent nipple resection due to an incidental finding of DCIS on risk-reducing mastectomy. 50% of the women with post-operative complications, were ex-smokers with < 4 weeks history of abstinence.

Conclusions: Single stage DTI reconstruction with TiLoop Bra mesh is a safe procedure with a low overall complication rate (16.7%). Attention to co-morbidities when selecting patients is crucial to optimize results.

TWO YEAR EXPERIENCE OF SINGLE-STAGE VS. 2-STAGE BREAST RECONSTRUCTION IN REGIONAL AUSTRALIA

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Background: Single-stage direct-to-implant (DTI) breast reconstruction offers expedited recovery with improved psychosocial well-being over the more conservative two-stage approach of insertion of temporary tissue expander (TE) prior to definitive exchange to implants or autologous reconstructions. However, concern over its potential complications remains a limiting factor. This study seeks to review and compare the 2-year outcomes of aforementioned procedures performed by 2 oncoplastic breast surgeons.

Methods: Multi-center analysis on prospective cases of DTI and insertion of TE performed between January 2017 and December 2018. Short term outcomes and immediate complication rates were compared adjusting for patients demographics and co-morbidities.

Result: Of the 36 patients (51 breasts), 16 underwent DTI and 20 had insertion of TE. Infection rates were low in both groups (8.3% DTI vs. 14.8% TE). However, 3 women in the TE group developed infection requiring further debridement. The explantation rate was 12.5% in DTI and 7.4% in TE. Overall complication rates were similar between the 2 groups (16.7% DTI vs. 18.5% TE). 50% of the complications in the DTI group occurred in ex-smokers with < 4 weeks of abstinence while both patients in TE group who had expanders removed were active smokers undergoing chemotherapy.

Conclusions: There are no significant differences in complication rates between single-stage and the traditional 2-stage reconstruction in our series. However, not every patient is a candidate for DTI and the potential benefits must still be weighed against the associated risks to prevent delay to adjuvant treatment.

COMPARISON OF ACCURACY BETWEEN MAMMOGRAPHY AND BREAST-SPECIFIC GAMMA IMAGING FOR RESIDUAL CALCIFIED LESIONS IN BREAST CANCER PATIENTS UNDERGOING NEOADJUVANT SYSTEMIC THERAPY

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Background: Neoadjuvant systemic therapy (NST) aided in increasing breast-conserving surgery (BCS) in advanced cases. Current practice recommends resecting remnant suspicious looking calcification on MMG after NST. A new functional breast imaging modality called breast-specific gamma imaging (BSGI) is used in detecting breast tumor, and many studies presented BSGI to have higher diagnostic efficacy than MRI. This study aimed to evaluate and compare the accuracy of diagnostic performance of BSGI and MMG in correlation to pathologic result in assessing residual calcified lesion after NST.

Methods: This is a single-center, retrospective study. Breast cancer patients who underwent NST with suspicious looking microcalcifications in post-NST MMG, have both post-NST MMG and BSGI, and underwent surgery from January 2013 to December 2014 at Asan Medical Center were included. Final pathologic tumor size with histopathology and biomarker status were obtained postoperatively.

Result: A total of 139 patients were included. Tumor size measured on MMG was greater than BSGI. In overall, BSGI correlated better than MMG in predicting the tumor size [intraclass correlation coefficient (ICC) = 0.748 vs. 0.651]. Except for HR+/HER2- subtype, BSGI correlated better than MMG in all other 3 subtypes (HR+/HER2+, HR-/HER2+, TN ICC BSGI vs. MMG = 0.733, 0.902, 0.776 vs. 0.570, 0.555, 0.467). Especially in HR-/HER2+ subtype, BSGI showed almost perfect reliability (ICC = 0.902).

Conclusions: BSGI is more accurate in estimating residual tumor size than MMG in post NST evaluation of tumor size in lesions with diffuse suspicious looking microcalcifications, especially in hormone receptor negative breast cancer. However, in HR+/HER2- subtype, the accuracy of BSGI is reduced therefore efforts to excise the extent of suspicious calcifications is suggested.

A NEW ONCOPLASTIC VOLUME REPLACEMENT TECHNIQUE FOR BREAST CANCER IN THE LOWER QUADRANTS, MINIMIZING VISIBLE SCAR

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Background: As for breast cancers located in the lower quadrants, deformity is likely to occur after breast conserving surgery. Herein, we present our experience of a new volume replacing oncoplastic technique using abdominal advancement flap.

Methods: Preoperatively, a neo-inframammary fold (IMF) is drawn 3-4 m below the original IMF in the standing position. The level may vary, depending on the volume expected to be excised. Incision is then made on the original IMF and partial resection of the breast tissue including cancer, is performed cranially. Next, subglandular plane between the original IMF and neo-IMF is dissected and de-epithelialization of the overlying skin is performed, generating a flap. This flap further provides sufficient volume to fill the defect. Absorbable interrupted sutures (1-0 vicryl) are then applied on the neo-IMF from the inside of the breast cavity to anchor dermis and breast tissue on one side. The other side is then sutured to the breast tissue remaining in the upper quadrants. Next, the sutures are tightened carefully so that the flap is elevated until the neo-IMF is naturally positioned at the level of the original IMF. Then the flap is fixed and secured onto the surrounding tissue to model breast mound. Finally, the overlying skin of the breast is brought down to cover the de-epithelized flap and is closed at the IMF.

Result: The technique proposed here enables achievement of good cosmetic outcomes, minimizing visible scar.

Conclusions: This technique is feasible and effective in supplementing large defects remaining in the lower quadrants after breast conserving surgery.

SURVIVAL OUTCOME OF ASIAN WOMEN TREATED WITH GRISOTTI'S FLAP FOR CENTRAL RETRO-AREOLAR BREAST CANCERS: 5-YEARS SINGLE INSTITUTIONAL EXPERIENCE

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Introduction: Breast conserving surgery used to be contraindicated for central retro-areolar tumors. Oncoplastic techniques brought along a paradigm shift. Grisotti's flap is a breast conserving surgery for central retro-areolar cancers. We present our experience and outcome from Breast Surgery Unit, University Malaya Medical Center (UMMC).

Methods: A prospective analysis of 11 patients with central retro-areolar breast cancer operated from 2012 to 2017 in UMMC. We assessed post-operative complication, margins, loco-regional recurrence and survival outcome. All patients received postoperative radiotherapy. Patients were followed-up one week, one month, three monthly for 1 year and 6 monthly for 5 years.

Result: Mean age of patients is 64-year-old. Mean follow up is 36.9 months. All tumors less than 5 cm. Majority of patients are stage 1 (36.4%) and 2 (45%). One patient had surgical site infection resolved with antibiotics. One patients had hematoma. None require re-operation. Tumor margins were clear in all patients. No loco-regional recurrence. Overall survival is 100%. All are please with their cosmetic outcomes.

Conclusions: Grisotti's flap is a volume displacement technique which provides satisfactory cosmetic outcome for centrally located breast cancer. Our 5 years' experience showed that this is oncologically safe and could be used selectively. It provides a good alternative in patients whom are otherwise subjected for mastectomy.

TREATMENT OUTCOMES OF BREAST CANCER WITH SUPRACLAVICULAR AND/OR INTERNAL MAMMARY LYMPH NODE INVOLVEMENT: A MULTICENTER, RETROSPECTIVE STUDY (KROG 16-14)

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Background: The purpose of this study was to evaluate the treatment outcomes of radiotherapy (RT) for breast cancer with ipsilateral supraclavicular (SCL) and/or internal mammary (IMN) lymph node involvement.

Methods: A total of 158 patients from 11 institutions were included in this study. 91 patients had SCL involvement, 54 had IMN involvement, and 13 had both. All patients underwent breast-conserving surgery (n = 74) or mastectomy (n = 84) followed by adjuvant systemic therapy and postoperative RT to whole breast/chest wall with or without regional nodal RT up to a median dose of 60 Gy (range, 45-66.4). Regarding managements for SCL and IMN, SCL excision was performed in 59 patients (37.3%), IMN excision in 10 (6.3%), SCL RT in 143 (90.5%), and IMN RT in 68 (43.0%).

Result: The median duration of follow-up was 72 months (range, 7-182). There were 20 locoregional recurrences and 45 distant metastases. In-field progression was present only in SCL (n = 8), and 6 of them initially underwent SCL excision. The 5-year loco-regional progression-free, disease-free survival (DFS) and overall survival rates were 87.3%, 71.6%, and 89.7%, respectively. Neither SCL excision nor SCL RT dose ≥ 54 Gy improved locoregional control ($p = 0.927$ and 0.693, respectively) and DFS ($p = 0.394$ and 0.686, respectively). On multivariate analysis, number of axillary lymph node ≥ 10 was the only independent prognosticator for DFS ($p = 0.003$).

Conclusions: Upfront surgery followed by systemic therapy and postoperative RT achieved an acceptable in-field regional control rate in patients with SCL and/or IMN involvement. More aggressive regional therapy did not improve locoregional control and survival.

PATTERNS OF CARE AND OUTCOMES FOR BREAST CANCER PATIENTS WITH BRAIN METASTASES: A MULTICENTER RETROSPECTIVE STUDY IN KOREA (KROG 16-12)

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Background: The purpose of this study was to investigate the patterns of care for breast cancer patients with brain metastases (BM), and to evaluate the prognostic factors affecting overall survival (OS).

Methods: Between 2000 and 2013, 730 breast cancer patients with BM were included from 20 institutions in Korea, and retrospectively analyzed. OS was calculated from the time of BM diagnosis.

Result: Median age at BM diagnosis was 50 years. There were 194 patients with hormonal receptor(HR)-positive/HER2-negative tumors, 126 HR-positive/HER2-positive, 193 HR-negative/HER2-positive, and 217 HR-negative/HER2-negative. Most patients had extracranial metastases (84.2%), but controlled primary tumor (74.2%). Initial local treatments for BM were as follows: whole brain radiotherapy alone in 430 patients (58.9%), stereotactic radiosurgery in 160 (21.9%), surgery alone in 27(3.7%), and combined treatments in 113 (15.5%). Median OS was 15 months. Poor performance status, number of BM >3, triple negative subtype, and presence of extracranial metastases were significantly correlated with inferior OS on multivariate analysis ($p=0.008$, <0.001, <0.001, and <0.001 respectively). Given these results, a nomogram predicting OS was developed and the bootstrap-corrected concordance index was 0.66.

Conclusions: Whole brain radiotherapy is still the mainstay of local treatment for BM from breast cancer in this patient population. We developed a nomogram predicting OS, which may help to tailor local treatment for these patients. OS seems to be improved compared with historical control. However, close surveillance of high risk group for early detection of BM and more effective local and systemic treatment strategies according to molecular subtype are needed to improve clinical outcome.

CARDIAC, LUNG AND LEFT ANTERIOR DESCENDING ARTERY DOSIMETRIC STUDY USING DEEP INSPIRATION BREATH HOLD IN LEFT BREAST CANCER IRRADIATION

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Background: This study was done to assess heart, lung and left anterior descending (LAD) dose using deep inspiration breath hold (DIBH) comparing with free breath (FB) in left breast cancer irradiation with or without internal mammary lymph node (IMN) irradiation.

Methods: A 25 left breast cancer who had breast conserving surgery were prospectively included.CT simulation were acquired in FB and DIBH. Respiratory management using Varian Real-time simulation and Vision RT during treatment were performed. Four planning in each patient were done in tangential direction,covering breast or chest wall plus IMN. Dosimetric parameters including heart (mean heart dose (MHD), V25 and V40), lungs (mean left lung, left lungV20, mean bilateral lung,bilateral lung V40) and mean LAD were compared using two tailed unpaired t test. In-field maximum heart distance, heart volume and breast size were analyzed using Pearson correlation test to show correlation with MHD.

Result: Comparing FB and DIBH in whole breast RT,there is significant reduction in MHD (5.3 vs. 2.9 Gy respectively, p 0.006) and Heart V25 (8.2 vs. 3.3% respectively, p 0.005).LAD dose has trend of reduction in DIBH, 18.3 vs. 12.5 Gy, p 0.057. In wide tangent, there were non-significantly better in MHD and LAD. Heart V40 and all lung parameters didn't show significant difference. MHD reduction significantly correlated with in-field maximum heart distance, heart volume and breast size. In-field maximum heart distance < 1 cm, MHD was within acceptable dose range.

Conclusions: DIBH in left breast cancer RT reduce radiation to the heart and LAD while achieving adequate target volume coverage. There were no significant different in lung dose. Optimal in-field maximum heart distance will help keeping acceptable MHD.

ANTI-HORMONE THERAPY ONLY IN THE YOUNGER AGE GROUP UNDER 50 YEARS: N1 STAGE, HORMONE RECEPTOR-POSITIVE AND HER-2 NEGATIVE

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Background: Younger patients under the age of 50 have a higher risk of recurrence of breast cancer than old age patients. The prognosis of hormone receptor-positive and HER2-negative breast cancer is better than that of other subtypes. The purpose of this study was to evaluate the efficacy of anti-hormonal therapy alone in younger patients under than 50 years.

Methods: This was a retrospective study if young patients under 50 years who were surgically treated for invasive breast cancer at Single Center between January 1993 and December 2012. 1:1 case-control matching was performed with anti-hormonal only group (N = 33) and with chemotherapy group (N = 37). Lymph-node-positive, Hormone-receptor-positive and HER2-negative breast cancer patients were compared between anti-hormonal therapy group and with chemotherapy group.

Result: In survival analysis, the survival parameters of the endocrine therapy-only group and the chemotherapy with endocrine therapy group were respectively 90.6% and 90.2% for 5-year recurrence free survival (RFS), 73.3% and 87.7% for 10-year RFS, 90.2% and 87.7% for 5-year distant metastasis-free survival (DMFS), 90.2% and 87.7% for 10-year DMFS, 100.0% and 97.0% for 10-year breast cancer-specific survival (BCSS), and 100.0% and 97.0% for 10-year overall survival (OS). There were no significant differences in RFS ($p = 0.56$), DMFS ($p = 0.33$), BCSS ($p = 0.18$) and OS ($p = 0.18$) between the two groups.

Conclusions: Even younger patients under the age of 50 may not benefit from chemotherapy. Gene assays may be useful for patients under 50 years of age.

REAL INCIDENCE AND IMPACT ON PROGNOSIS OF FEBRILE NEUTROPENIA AMONG ADVANCED BREAST CANCER PATIENTS RECEIVING ADJUVANT TAC (DOCETAXEL-DOXORUBICIN-CYCLOPHOSPHAMIDE) CHEMOTHERAPY IN KOREAN

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Background: The concurrent regimen of docetaxel, doxorubicin, and cyclophosphamide (TAC) has been categorized into the high risk group for febrile neutropenia (FN) by all guidelines. The incidence of FN was 17-26% in studies conducted in Western countries. However, this incidence may be different between ethnic groups. This study aimed to evaluate the real incidence of FN and its effect on prognosis after adjuvant TAC chemotherapy and in Korean patients with advanced breast cancer

Methods: We analyzed data from 187 received 6 cycles of adjuvant TAC chemotherapy between Jul 2005 and December 2014. All patients did not received long acting G-CSF as primary prophylaxis for FN because of disapproval of reimbursement. The incidence of FN, dose reduction and relative dose intensity (RDI), relapse-free survival (RFS) and overall survival (OS) were investigated.

Result: One hundred two (54.5%) of all the patients experienced FN. FN was more frequently observed in patients with older age (49 yeas vs. 51 years, $p = 0.0458$). RDI was lower in patients who experienced FN (99.5% vs. 96.4%, $p = 0.001$). Relapse rates were for the patients who not experienced FN (9.41%) and the patients who experienced FN (14.70%) [hazard ratio (HR): 2.19; 95% confidence interval (CI): 0.83 to 5.78; $p = 0.111$]. FN was significant associated with poor OS (2.35% vs. 9.80%, HR: 6.64; 95% CI: 1.28 to 34.36; $p = 0.024$).

Conclusions: The incidence of FN during adjuvant TAC chemotherapy in Korea was much higher than most studies conducted in Western countries. Needless to say, FN was significant associated with poor outcomes.

A CONCORDANCE STUDY ON WATSON FOR ONCOLOGY RECOMMENDATIONS FOR BREAST CANCER TREATMENT

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Background: While the demand for physicians to treat cancers is gradually increasing, the supply is insufficient. Therefore, clinical decision support systems (CDSS) have emerged as key elements that may solve this challenge; Watson for Oncology (WFO) is a representative CDSS. In this study, we compared the treatment recommendations of WFO and those of the tumor board of the Gil Medical Center and investigated the concordance rate.

Methods: Patients with breast cancer were selected by applying the patient selection criteria of WFO. In the final analysis, we included the data of 360 patients with breast cancer attending the Gil Medical Center, between January 2013 and June 2017. This study analyzed the number of patients, cancer stage, receptor status and menopausal status as cancer characteristics. Concordance rates were based on three groups: 'recommended', 'for consideration', and 'not recommended. Not recommended' included treatment plans that were either not recommended or corresponded to contraindications. A logistic regression was used to analyze statistical significance of concordance rate in cancer characteristics.

Result: The concordance rate of the treatment recommendations between WFO and the tumor board of the Gil Medical Center was 81.4%. Logistic regression analysis found no effects of the tumor stage, receptor status, menopausal status, and patient age on the concordance rate.

Conclusions: WFO and the tumor board of the Gil Medical Center showed a high concordance rate. We found no significant differences in the tested variables. This study suggests that WFO can recommend appropriate breast cancer treatments to oncologists.

CLINICAL STUDY OF LOUCI NODULE-DISSIPATING DECOCTION ON THE PREVENTION OF RECURRENCE AND METASTASIS OF TRIPLE-NEGATIVE BREAST CANCER

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Background: Triple negative breast cancer (TNBC) is characterized by poor prognosis and lack of effective treatment. The prevention of recurrence and metastasis of postoperative TNBC patients is important. In China, herbal medicine has been widely used to prevent recurrence and metastasis as a mild therapy. Louci Nodule-dissipating Decoction has obtained good clinical effect as a compound decoction.

Methods: Our study reviews the data of 132 postoperative TNBC patients who took Louci Nodule-dissipating Decoction in recent 2 years. We summarized disease-free survival (DFS) rate of TNBC patients in the first two years, and investigated their behavior abilities, sleep conditions, anxiety and depression by ECOG, Pittsburgh Sleep Quality Index and Hospital Anxiety and Depression Scale, observing adverse reactions of the decoction.

Result: The first two years of DFS rates were 99.24% and 90.2%, respectively. ECOG score and sleep quality were significantly improved in the 4th, 8th and 12th months after taking the decoction compared with the baseline score ($p < 0.05$). Scores of anxiety and depression in the 4th, 8th and 12th months were significantly lower than the baseline scores ($p < 0.05$). No side effects over grade 3 (WHO) were observed.

Conclusions: Louci Nodule-dissipating Decoction could improve DFS rate of the first two years, and enhance the quality of life.

FLUORESCENCE IN SITU HYBRIDIZATION ANALYSIS OF HER2 IHC 3+ BREAST CANCER PATIENTS WITH NEOADJUVANT THERAPY USING PERTUZUMAB AND TRASTUZUMAB

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Background: HER2 is amplified approximately 20% of breast cancers and HER2 targeting therapy is associated with a significant improvements in disease-free and overall survival. In previous clinical trials, the pathologic complete response (pCR) rate was significantly increased when combining pertuzumab and trastuzumab treatment. Although the efficacy and safety of anti-HER2 dual blockade therapy has been reported, the markers that predict the response are still unclear. Particularly, HER2 IHC 3+ patients do not perform fluorescence in situ hybridization (FISH) analysis, so there is limited information available. This study aimed to investigate the relationship between FISH result and the pCR to neoadjuvant therapy based on trastuzumab and pertuzumab of HER2 IHC 3+ patients.

Methods: Nineteen HER2 IHC 3+ breast cancer patients who had received neoadjuvant docetaxel, carboplatin, trastuzumab, and pertuzumab chemotherapy were included in this study. HER2/CEP17 ratio was measured by FISH analysis. The relationship between HER2/CEP17 ratio and tumor pCR status (ypT0 ypN0) was investigated.

Result: The Median age was 48 years (range: 33-62). 26.3% of the patients were hormone receptor (HR) positive and 73.6% of the patients were HR negative. The pCR rate was 73.6%. The patients who experienced a pCR had a mean HER2/CEP17 ratio of 6.9 ± 2.3 (range: 3.16-10.40) in comparison with median ratio of 4.7 ± 1.5 (range: 2.14-6.15) if they did not ($p = 0.068$).

Conclusions: PCR was highly correlated with HER2/CEP17 ratio in the neoadjuvant setting with anti-HER2 dual blockade. This suggests that the HER2/CEP17 ratio can be used as a predictive marker to predict pCR in neoadjuvant therapy based on trastuzumab and pertuzumab of HER2 IHC 3+ patients.

THE EFFICACY OF TRASTUZUMAB-EMTANSINE AFTER PRIOR USE OF PERTUZUMAB AMONG PATIENTS WITH HER2 POSITIVE METASTATIC BREAST CANCER

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Background: Trastuzumab-emtansine (T-DM1) showed overall survival benefit in clinical trials and now T-DM1 is widely used for patients with HER2 positive metastatic breast cancer. But several clinical data showed limited efficacy of T-DM1 after prior use of pertuzumab. The purpose of this retrospective study is to evaluate the influence of prior pertuzumab on the efficacy of T-DM1.

Methods: We found 59 patients who were treated with T-DM1 in our institute between 2014 May and 2017 Dec, and 45 cases were available for this analysis.

Result: Thirty-two patients had prior use of pertuzumab. Median line of T-DM1 was 2 (1-8) among patients with prior pertuzumab, and 2 (0-8) without prior pertuzumab. Overall response rate (ORR) were 25% and 38.5% respectively (Fisher's exact test, $p = 0.47$, 95%CI 0.11-2.73) and clinical benefit rate (CBR) were 31.3% and 38.5% ($p = 0.732$, 95%CI 0.16-3.60). The median time to treatment failure (mTTF) were 4.3 months and 6.3 months respectively (log-rank test, $p = 0.25$). We didn't find any statistical significance in this analysis, but the duration of mTTF was numerically shorter in prior pertuzumab group and was similar to the previous reports.

Conclusions: There is a possibility that the efficacy of T-DM1 would be weakened after prior use of pertuzumab.

DEVELOPMENT OF A NOVEL SFK INHIBITOR IN PRECLINICAL MODELS OF TRIPLE NEGATIVE BREAST CANCER

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Background: The Src Family Kinases (SFKs) are key mediators in various oncogenic pathways and are commonly activated in cancer. Of the nine members of SFKs, increasing reports suggest aberrant activation of Lyn in breast cancer. Bioinformatics analysis reveals that Lyn expression is strongly associated with the TNBC patient group. Due to the current lack of targeted therapy for the TNBC subtype, it becomes worthwhile to investigate the potential of Lyn as novel therapeutic targets. In this project, we developed a novel SFK inhibitor that specifically targets Lyn.

Methods: Patient data analysis, Ligand-based computation, Proteome Profiler Array, in vivo mouse Pharmacokinetics and Pharmacodynamics studies, Bioinformatics analysis, Affymetrix Microarray, Secretome Analysis, Cell viability assays, Flow cytometry, Western blot, qPCR, Immunofluorescence, Transwell assays, 3D Matrigel Assays, and Tube-formation assay.

Result: Proteome Profiler Array results validated the ligand-based target prediction analyses of Drug X in vitro. Mouse studies show that Drug X is well-tolerated and exhibited significant tumor burden load reduction. Downstream functional studies were performed, and Drug X was found to induce apoptosis via the intrinsic pathway. Also, Drug X could down-regulate the mesenchymal properties of TNBC cell lines via the modulation of key EMT-related genes. Preliminary in vitro and in vivo rat aortic ring assay data also suggested that Drug X could harbor potent anti-angiogenic effects.

Conclusions: Preliminary findings have supported that Drug X could potentially be a promising novel drug candidate for TNBC treatment and on-going efforts are being made to further elucidate the underlying mechanisms of Drug X in modulating the key oncogenic processes

EXPRESSION OF PHOSPHORYLATED S6K1 IS A MARKER FOR ADJUVANT AROMATASE INHIBITOR THERAPY IN MENOPAUSAL OR OVARIAN FUNCTION SUPPRESSED PATIENTS WITH HORMONE SENSITIVE BREAST CANCER

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Background: Phosphorylated ribosomal S6 Kinase 1 (pS6K1), a major downstream regulator of the mTOR pathway, is a marker of proliferation in cancer development. Recent investigations have addressed the role of S6K1 in adipogenesis. Theoretically, as pS6K1 is associated with adipogenesis and increased local estrogen level, pS6K1 may affect the outcomes of estrogen depletion therapy. The purpose of this study was to investigate the potential of pS6K1 as a predictive marker for adjuvant aromatase inhibitor (AI) therapy in menopausal or ovarian function suppressed patients with hormone sensitive breast cancer.

Methods: Medical records were retrospectively reviewed for menopausal or ovarian function suppressed patients with estrogen receptor positive, node positive primary breast cancer patients who received adjuvant endocrine therapy. pS6K1 status was dichotomized at 0 as negative, and from 1+ to 3+ as positive expression based on an immunohistochemical analysis.

Result: Four hundred twenty eight patients were eligible for this analysis. Median follow up period was 44 months (range, 1-90). In patients with positive pS6K1 expression, disease-free survival (DFS) was significantly longer in patients treated with AI compared to tamoxifen (25.6 vs. 40.6 months, $p = 0.016$). However, there was no benefit of AI on DFS in pS6K1 negative group (mean 36.9 vs. 31.5 months, $p = 0.630$). In multivariate analysis, AI therapy remained as a significant predictor for DFS in pS6K1 positive group (HR 0.39, 95% CI 0.184-0.825, $p = 0.014$).

Conclusions: PS6K1 might be a potential marker for adjuvant AI therapy. AI is preferred in pS6K1 positive patients, while AI or tamoxifen could be freely chosen in pS6K1 negative patients, considering individual preferences and risks for adverse effects.

FACTORS ASSOCIATED WITH CLINICAL RESPONSE TO ERIBULIN IN PRETREATED METASTATIC BREAST CANCER PATIENTS: MULTI-CENTER, REAL-WORLD SITUATION

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Background: Eribulin mesylate has been approved for second or later-line treatment in metastatic breast cancer (MBC) patients who previously received anthracycline and taxane chemotherapies. Here, we review the efficacy and safety of eribulin and to determine factors correlated with clinical outcomes in real world practice in Thailand.

Methods: Two-hundred and three MBC patients who received eribulin as second or later-line of chemotherapy at three academic hospitals were retrospectively reviewed. Clinico-pathologic features, lines of therapy, dose intensity of eribulin, clinical response, survival outcomes and safety were evaluated. The clinical features that associated with outcomes were also analyzed.

Result: Median age was 57 years (24-88). In 203 patients, 56.6% had hormonal receptor positive and HER2 negative, 23.2% had HER2 positive whereas 18.7% had triple-negative. Most of patients previously received anthracycline and taxane chemotherapy and pretreated capecitabine was identified in 84.7%. More than two lines of chemotherapy were reported in 46.3%. A dose of 1.4 mg/m^2/wk intravenous was given in 69.5%. Median cycles of eribulin were 5 cycles (1-25). Overall response rate and disease control rate were 18% and 52%. At the time of analysis, median progression-free survival and overall survival in overall population were 4 months and 7 months, respectively. No statistically significantly difference in survival outcomes between subtypes of breast cancer, lines of treatment and dose of eribulin was demonstrated. About safety profile, grade III-IV neutropenia was reported in 26% but only 5.5% had febrile neutropenia.

Conclusions: Eribulin mesylate showed benefit in term of efficacy and well tolerability in MBC patients in real world practice in Thailand.

TARGETING AMP-ACTIVATED PROTEIN KINASE AS AN ANTI-TNBC STRATEGY IN WILD-TYPE AND CHEMO-RESISTANCE CANCERS

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Background: AMPK (AMP-activated protein kinase) is one of the central regulators of cellular and organismal metabolism. Higher expression of AMPK has been linked to the inhibition of progression breast tumor; however, its biological functions and signaling cascades remain unclear in triple negative breast cancer (TNBC). Recently, there are many AMPK activators, including metformin, phenformin, and nilotinib, show anti-cancer efficacy. Nilotinib is a small-molecule tyrosine kinase inhibitor approved for the treatment of imatinib-resistant chronic myelogenous leukemia. Previously, nilotinib increased AMPK phosphorylation and lead to autophagic cell death in human hepatocellular carcinoma (HCC) cells.

Methods: We designed the novel small molecules, with similar structure of nilotinib but without hinge binding activity in the ATP binding pocket of kinases to understand the importance of AMPK activators in suppressing TNBC progression. We also performed in silico analysis using a publically available database Kaplan-Meier Plotter to investigate the importance of AMPK clinically.

Result: Kaplan-Meir survival analysis of AMPKα1 mRNA in TNBC patients revealed that DFS was shorter in the AMPKα1 mRNA low expression group than in the AMPKα1 mRNA high expression group, clinically supported AMPK showed tumor suppressor role in TNBC patients. We found one of the nilotinib derivative, SCT-1015, showed greater anti-cancer property and strongly activated AMPK in cell-base and cell-free model without inhibiting bcr-abl kinase. Strikingly, SCT-1015 exhibited the therapeutic potential in long-term training Taxol or doxorubicin resistant HCC1806 cells. Notably, SCT-1015 displayed a significant growth inhibition in TNBC-bearing orthotopic models.

Conclusions: Our results suggested that the further study of SCT-1015 for clinical investigations should be warranted.

GENETIC AND CLINICAL PREDICTORS OF DURABLE RESPONSE FOR CAPECITABINE AFTER ANTHRACYCLINE AND TAXANE FAILURE IN METASTATIC BREAST CANCER

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Background: Capecitabine is one of a treatment option in anthracycline and taxane pre-treated metastatic breast cancer (MBC) patients. Oral administration with relatively low toxicity profile has made capecitabine as one of a maintenance regimen in MBC. In this study, we analyzed the clinicopathologic and genetic differences between durable responder (partial response or stable disease for more than 10 cycles of chemotherapy) and poor responder during capecitabine treatment.

Methods: Between January 2006 to December 2016, 66 patients who were treated with capecitabine monotherapy after anthracycline and taxane failure were enrolled. Clinicopathologic features associated to survival outcomes were analyzed. For analysis of miRNA expression between durable responder and poor responder, 12 archival tumor tissues (6 durable responder and 6 poor responder, each) were collected and went through nCounter miRNA expression assay.

Result: Median TTP in total population was 4.32 months (range 0.87-35.07). Triple negative breast cancer (TNBC) patients showed inferior TTP compared to hormone receptor (HR) positive MBC (median 3.07 vs. 5.47 months, $p = 0.038$). Among HR positive patients, patients who received hormonal treatment before administration of capecitabine showed better PFS (median 7.7 vs. 4.03 months, $p = 0.006$). In durable responders, miR-181a-5p and miR-361-5p were significantly upregulated.

Conclusions: HR positive patients showed superior survival compared to TNBC patients, and prior hormonal treatment were associated to better survival in HR positive patients. In durable responders, miR-181a-5p and miR-361-5p were upregulated compared to poor responders. We are planning to carry on breast cancer cell line study to analyze the target gene associated to durable response to capecitabine.

SENSITIVE DETECTION AND ISOLATION OF CIRCULATING TUMOR CELLS USING SMALL VOLUME OF PERIPHERAL BLOOD IN BREAST CANCER

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Background: Circulating tumor cells (CTCs) has been known as a non-invasive biomarker of breast cancer. However, CTCs have the limitations with low detection rates and low sensitivity. This study is aimed to evaluate the sensitivity and specificity of the isolation of CTCs from the small volumes of blood in breast cancer patients using multifunctional magnetic nanowires.

Methods: This study consisted of 26 breast cancer patients who diagnosed at National Cancer Center, Korea and 50 healthy donors as control. We isolated CTCs from 3 mL of the peripheral blood using multifunctional magnetic nanowires and analyzed sensitivity and specificity of CTCs for breast cancer.

Result: Of the 26 breast cancer patients, 23 (88.5%) found CTCs. Among healthy donors, 1 out of 50 (2%) showed identifiable CTCs and one CTC was isolated. The number range of isolated CTCs in breast cancer patients was at least 1 to maximal 9 cells per 3 mL of blood. CTCs were isolated from breast cancer patients at various stages from Tis to III. There was no correlation between the number of CTCs and the stage of breast cancer. Comparing detection rate of CTCs by subtype, triple negative breast cancer (TNBC) was significantly lower (luminal A = 94.7%, luminal B = 100%, HER2 = 100%, TNBC = 33.3%, $p = 0.009$).

Conclusions: This study found high rate of detection and isolation of CTCs in breast cancer patients through small volumes of blood. The result might be clinical availability of CTCs as a biomarker for the initial screening method of breast cancer.

RE-ANALYSIS OF AXILLARY REGIONAL RECURRENCE IN NO AXILLARY DISSECTION GROUP FROM IBCSG 23-01 STUDY

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Background: We aim to analysis the difference of axillary regional recurrence between patients with axillary management and without in the no axillary dissection group from IBCSG 23-01 study, and explore the significant of axillary management in patients with sentinel lymph nodes (SLNs) micrometastases.

Methods: In patients with one or more micrometastatic (≤ 2 mm) SLNs, whole breast irradiation (WBI) after breast conserving surgery (BCS) was considered as a management of axilla, but partial breast irradiation (PBI) during BCS or no axillary dissection after mastectomy was regarded as no axillary management. The rate of axillary regional recurrence was compared between the two subgroups. The χ^2 test was used for evaluation of all binary variables. $P < 0.05$ was considered statistically significant.

Result: In no axillary dissection group, there were 333 patients with axillary management, and 134 patients without axillary management which included 42 cases receiving mastectomy without axillary dissection, 12 cases BCS without radiotherapy, and 80 cases BCS with intraoperation PBI. The ten-year follow-up date showed that the total axillary recurrence rate was 1.7% (8/467), but the axillary recurrence rate was 4.5% (6/134) in the no axillary management subgroup which was significantly higher than that of 0.6% (2/333) in the axillary management subgroup ($p = 0.0024$). In patients with axillary recurrence, 75% were no axillary management.

Conclusions: In patients with SLNs micrometastases, no axillary management could not control the residual tumor burden and would lead to recurrence in axilla. Currently, axillary management should still be required for these patients.

SENTINEL LYMPH NODE BIOPSY IN AXILLA WITH NEGATIVE EVALUATING BY PHYSICAL EXAMINATION BUT SUSPICIOUS FINDING ON PREOPERATIVE IMAGING AND METASTASIS PROVING WITH BIOPSY

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Background: With the increasing sensitivity of axillary imaging and ultrasound guided biopsy, some clinically axillary negative patients were upstaged to axillary positive (cN1) and received axillary lymph node dissection (ALND). This study was to assess the feasibility of sentinel lymph node biopsy (SLNB) in patients with axilla lymph node (ALN) negative evaluating by physical examination but suspicious lymph nodes finding on preoperative imaging and metastasis proving with a fine-needle aspiration/core biopsy.

Methods: This retrospective cohort study included patients with early breast cancer who had ALN negative evaluating by physical examination but suspicious lymph nodes finding on preoperative imaging and metastasis proving with a fine-needle aspiration/core biopsy from October 2012 to December 2018 in the Breast Cancer Centre of Shandong Cancer Hospital Affiliated to Shandong University. All patients received ALND.

Result: A total of 129 patients were eligible, 42 (42.9%) of them identified only one ALN metastasis after ALND, 15 (15.3%) identified only two ALNs metastases after ALND, 41 (41.8%) identified more than two ALNs metastases after ALND. Among these cases, 40 patients received SLNB followed by ALND, and the false-negative rate of SLNB was 0% with 1-3 positive SLNs detected. Positive non-SLNs were 0, one, two, three and more than three in 65% (26/40), 7.5% (3/40), 2.5% (1/40), 5% (2/40), and 20% (8/40) patients, respectively.

Conclusions: SLNB is accurate and might be feasible in patients with ALN negative evaluating by physical examination but suspicious lymph nodes finding on preoperative imaging and metastasis proving with biopsy.

LONG-TERM ONCOLOGICAL OUTCOME COMPARISON BETWEEN USE OF DYE ONLY AND DUAL USE OF DYE AND RADIOISOTOPE FOR SENTINEL LYMPH NODE MAPPING IN EARLY BREAST CANCER

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Background: It has been shown that dual use of mapping method could decrease the false-negative rate of sentinel lymph node biopsy (SLNB) in early breast cancer. However, a comparison of long term outcome between dual mapping vs. single use of dye method has not been performed appropriately.

Methods: We identified a total of 5,030 women with Stage I-III breast cancer who underwent primary surgery with SLNB between 2005 and 2013. For sentinel lymph node mapping, indigocarmine was used for dye method and Tc99m-antimony trisulfate was used for isotope. Patients who underwent neoadjuvant therapy were excluded. Kaplan-Meier method and log rank test were used for survival analysis.

Result: Among all patients, dye mapping only was used in 1,959 patients and dual mapping of dye and isotope was used in 3,071 patients. Median follow-up period was 7.4 years. The median number of harvested sentinel nodes was 3.15 in dye only group and 3.1 in dual mapping group ($p > 0.05$). There was no significant difference in lymph node-positivity rate between dye only group (17.5%) and dual mapping group (18.2%) ($p = 0.551$). 5-year axillary recurrence rate was 0.7% in dye only group and 0.3% in dual mapping group without statistical significance ($p = 0.083$). 5-year DFS was 96.5% and 95.3% in dye only and dual mapping group, respectively. ($p = 0.326$).

Conclusions: Among women who received SLNB without neoadjuvant chemotherapy for early breast cancer, the use of dye alone for sentinel lymph node mapping is not inferior to dual use of dye and radioisotope in long term oncological outcome of the patients.

UPPER OUTER QUADRANT BREAST CANCER IS ASSOCIATED WITH HIGHER NON-SENTINEL LYMPH NODE METASTASIS IN PATIENTS WITH TUMOR FREE SENTINEL LYMPH NODES USING RADIO-ISOTOPE SINGLE TRACER METHOD

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Purpose: Sentinel lymph node (SLN) biopsy is the current standard for axillary staging in early breast cancer. Notebly, surgeons' experience critically determines the accuracy in addition to various important factors. We aimed to investigate how clinicopathological factors impact on the metastasis in non-hot sentinel lymph node using single radioisotope tracer, and to propose a more delicate intraoperative judgement.

Methods: Our study analyzed stage I and II breast cancer from 2013 to 2017 in our hospital. Totally 696 patients underwent singe probe detection for sentinel lymph node with Technetium-99 colloid lymphoscintigraphy were recruited. Hot nodes and non-hot nodes that were palpable, gritty or significantly enlarged were both biopsied. Cancer metastasis of hot nodes and non-hot nodes were analyzed separately. Factors related to non-hot node metastasis were explored.

Result: In the 47 cases with non-hot SLN metastasis, the hot-nodes were pathologically negative in 18 (38.3%) cases; among which 11 cases (61.1%, $p = 0.019$) were located in upper outer quadrant, 4 cases and 3 cases in lower outer quadrant and center of breast respectively, while no case were found in upper inner and lower inner quadrants. Tumor size also significantly related to non-hot SLN metastasis particularly for T2 (OR 5.82, $p = 0.007$). Receiver operating curve analysis showed 2 cm (AUC = 0.726) warrant careful exploration of non-hot nodes.

Conclusions: In patients with tumor free SLNs, those with larger tumor size and located at the upper outer quadrant have a higher chance of tumor metastasis to non-sentinel nodes.

COST-EFFECTIVENESS OF STEREOTACTIC VACUUM-ASSISTED BIOPSY FOR NONPALPABLE BREAST LESIONS: COMPARISON WITH OPEN SURGICAL BIOPSY

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Background: Several studies had confirmed that stereotactic vacuum-assisted biopsy (SVAB) is a reliable and lower-cost alternative to open surgical biopsy (OSB). However, the cost-effectiveness of SVAB for different category of lesions remains unclear. The purpose of this study was to compare the cost-effectiveness of SVAB and OSB for lesions of different likelihood of malignancy.

Methods: A retrospective review of 276 (33.8%) SVAB and 541 (66.2%) OSB was performed. Direct cost was calculated using patient charges and national health insurance payment. Indirect cost was calculated using sick leave days, average salary, and age-adjusted employment rate.

Result: Comparing with OSB, SVAB decreased the direct cost of diagnosis by $89 (9.9%) and indirect cost by $556.7 (95.2%) per case. SVAB obviated 92.3% benign surgeries. OSB obviated 52% surgical treatments for malignancies, and therefore, had lower total cost (including diagnosis and treatment) than that of SVAB. Cost saving was $795.3 per case. Lower total cost can be attained if SVAB is the diagnostic method for any lesion with likelihood of malignancy lower than 18%. Any lesion with higher likelihood of malignancy, cost saving can be made by OSB when a malignancy has no need of subsequent surgery. BI-RADS category used at the study correlated well with the percentage of malignancy and can thus be used to assess malignant risk before biopsy.

Conclusions: For lesions of BI-RADS category 3 and 4A, SVAB is the more cost-effective diagnostic method. For lesions of category 4B-5, using SVAB may bring about higher medical resource utilization; therefore, a more complete consideration is needed.

OUTCOMES OF DIAGNOSTIC SURGICAL BIOPSY IN A BREAST SCREEN SETTING

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Background: Screening mammography allows earlier diagnosis of breast cancer resulting in reduced breast cancer specific mortality, and potentially reduced morbidity from less intense treatment. Abnormalities detected on screening mammograms are recalled for further assessment. In cases when workup has neither diagnosed malignancy nor excluded its possibility, diagnostic surgical biopsy (DSB) is recommended. DSB of a lesion where final pathology is clearly benign is a harm from a screening program, and the benefit of DSB where a core needle biopsy (CNB) has shown a high-risk lesion is dependent on its identifying more significant pathology than that in the CNB. We aimed to review outcomes of DSB in a population-based mammographic screening program in order to identify situations in which this may be omitted.

Methods: Registry data was extracted including all patients where recommendation for DSB was made over a ten-year period (January 2004-December 2013). Patient demographics, imaging characteristics, core biopsy & DSB pathology were reviewed.

Result: The overall upgrade rate to malignancy on DSB after non-malignant finding on CNB was 21.6%. Of these, 14% were upgraded to DCIS and 7.6% to invasive cancer. Atypical ductal hyperplasia (ADH) was the most common pathology identified on CNB generating recommendation for DSB.

Conclusions: A minority of patients with high-risk lesions were upgraded to malignancy on DSB in this cohort. The psychological and cost-effectiveness implications of this low upgrade rate to significant, life-threatening pathologies warrants further investigation. Our data may therefore allow identification of groups of women who could be safely managed with less intensive treatment.

CORRELATION BETWEEN ULTRASONIC IMAGING FEATURES IN BREAST CANCER AND MRNA EXPRESSION LEVELS OF HER2 AND NGX6

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Background: Breast Cancer is the most malignant tumor among women worldwide. There is limited study on correlation of ultrasound characteristic with human epidermal growth factor receptor 2 (HER2) and nasopharyngeal carcinoma-associated gene 6 (NGX6) expression. To investigate the ultrasonographic features of breast cancer and its correlation with HER2 and NGX6 mRNA expression levels.

Methods: A cross sectional study. Ultrasound imaging results were retrospectively recorded and analyzed among breast cancer and benign breast lesions according to the inclusion criteria. The RT-PCR was used to measure the expression levels of HER2 and NGX6.

Result: Most malignant lesions have classic characteristics, single, irregular, not circumscribed, hypoechoic, posterior shadows, intra-lesion calcification, architectural distortion, skin thickening/retraction, edema, and lymph node abnormalities. In this study, we found significant differences, showing higher level of HER2 mRNA expression and lower level of NGX6 expression in malignant lesion compared to benign lesions ($p < 0.05$). The mRNA expression of HER-2 in the patients with solitary lesion, irregular, microcalcification and axillary node involvement in the lumps was significantly higher than that multiple, circumscribed and without calcification ($p < 0.05$). The mRNA expression of NGX6 in the patients with irregular, no parallel, skin retraction, edema and axillary node involvement was significantly lower than that circumscribed, parallel, without skin retraction, edema and axillary node involvement ($p < 0.05$).

Conclusions: The classical appearances of a malignant breast mass were significantly associated with high level of HER2 mRNA expression but also correlate with low level of NGX6 mRNA expression. NGX6 is a novel biological biomarker of breast cancer.

ASSOCIATION BETWEEN TUMOR METABOLISM ASSESSED BY 18F-FDG PET-CT AND MOLECULAR BIOLOGICAL MARKERS IN LUMINAL B TYPE BREAST CANCER

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Background: Most studies on breast cancer relapse and metastasis have focused on non-luminal breast cancers (including the basal-like and HER-2 subtypes) because of their poor prognosis. Luminal B breast cancer is also defined by aggressive clinical behavior and has a prognosis similar to that of non-luminal cancers. The luminal B subtype is more common however this type has not been investigated as thoroughly. Therefore, the purpose of the study was to determine whether a correlation exists between FDG uptake on PET/CT, expressed as the maximum standardized uptake value (SUVmax), and the luminal subtype of breast cancer, and whether primary tumour SUVmax can predict the molecular subtype.

Methods: This retrospective study involved 171 patients with luminal type invasive breast carcinoma who underwent 18F-FDG PET/CT before therapy. The correlations between primary tumor 18F-FDG uptake on PET/CT, expressed as SUVmax, and clinicopathological findings and histologic factor, i.e. histology (ductal, luminal, etc), axillary lymph node metastasis, extensive intraductal component (EIC), lymphovascular invasion, nuclear grade, T,N,M stage, molecular marker and Ki-67 were analysed.

Result: Among the subtypes of the 171 tumors, 37 (21.6%) were luminal A, 134 (78.4%) were luminal B (HER2-negative), and the corresponding mean SUVmax were 4.25 ± 2.55 (range 1.211.8), 6.12 ± 3.56 (range 0.921.3), respectively ($p = 0.003$). A higher Ki-67 and nuclear grade, a larger tumour size, a positive lymphovascular invasion were all significantly associated with a higher SUVmax and luminal B breast cancer.

Conclusions: SUVmax, a metabolic semiquantitative parameter, shows a significant correlation with the molecular subtype of breast cancer, and is useful for predicting the luminal B subtype.

THE NEW PERSPECTIVE OF PET/CT FOR AXILLARY NODE STAGING IN BREAST CANCER PATIENTS ACCORDING TO ACOSOG Z0011 TRIAL

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Background: According to the results of the ACOSOG Z0011 trial, the use of SLND alone did not result in inferior survival compared with ALND in patients with limited SLN disease treated with BCS. We investigated the diagnostic performance of FDG PET/CT with respect to negative or 1-2 ALN metastasis from three or more.

Methods: We retrospectively analyzed preoperative contrast enhanced PET/CT images taken from January 2010 to June 2012. The patients had clinical T1-2 primary invasive breast cancer without palpable adenopathy and underwent BCS with axillary staging within 2 weeks from the scan. Image analysis was as follows: FDG PET evaluation for any focally increased PET signal, then a morphologic evaluation was done. We compared our PET/CT results with histology reports.

Result: Total 222 women with 225 axilla were enrolled and their mean tumor size was 1.66 ± 0.72 cm (0.2-4.2 cm). 214 cases had limited metastasis (0-2), and 11 had extended metastasis (3 or more). 23 women had recurrence during follow up period. The mean SUVmax for tumor was 5.16 in limited group and 7.16 in extended group ($p = 0.073$). The sensitivity, specificity, NPV and PPV of PET/CT for extended metastasis was 72.7%, 100%, 100%, and 98.6% respectively. Regarding 23 recurred patients, 7.56 in tumor SUVmax and 1.95 cm in tumor size, they had higher SUVmax and larger tumor size than those who did not($p = 0.005$ and $p = 0.046$).

Conclusions: Preoperative PET/CT scan predict 3 or more positive ALN metastasis with high specificity and have evolving role to treat plan in patients with clinical T1-2 IDC and no palpable adenopathy.

THE IMPACT OF PRE-OPERATIVE MRI ON SURGICAL MANAGEMENT OF PATIENTS WITH DCIS PLANNING FOR BREAST CONSERVATIVE THERAPY

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Background: Ductal carcinoma in-situ (DCIS) accounts for 20-40% of all breast cancers detected in western countries. Breast conserving therapy (BCT) is offered to patients with small DCIS as curative treatment. However, DCIS is notorious for indistinctive clinical and radiological features. It has been proposed that MRI may improve the pre-operative assessment of tumour extent.

Methods: We performed a retrospective analysis of the prospectively collected data. Between 2013 and 2016, all consecutive patients with a confirmed histological diagnosis of DCIS who were initially intended for BCT after mammographic and ultrasonographic assessment at Queen Elizabeth Hospital were included. All of them underwent a pre-operative MRI assessment. As a result, there might be a change in the surgical plan. Their clinical data were analysed.

Result: There were a total of 33 DCIS patients who had undergone an MRI assessment. With regard to the performance in assessment of tumour extent, MRI had a correct assessment in 21 patients. It underestimated the tumour extent in 8 patients (24%), who required subsequent re-excision surgery. In another 4 patients, it overestimated the tumour extent, leading to unnecessary mastectomies. Patients with intermediate or high grade DCIS on initial core biopsy were more likely to have concordant MRI and final histological asesssments of tumour size ($p = 0.01$).

Conclusions: Our data did not provide a strong evidence on the use of routine pre-operative MRI in DCIS patients, with over and underestimation of tumour size in our cohort. Further studies are needed to define its role in the pre-operative assessment of DCIS.

PRELIMINARY MICRODOSE CLINICAL TRIAL: COMPARISON OF BIODISTRIBUTION OF 64CU-NOTA-TRASTUZUMAB WITH 64CU-DOTA-TRASTUZUMAB IN BREAST CANCER PATIENTS

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Background: It was reported that PET/CT using 64Cu-1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid (DOTA)-trastuzumab reflects human epidermal growth factor receptor 2 (HER2) expression in breast cancer patients. In this study, we evaluated the bio-distribution of 64Cu-1,4,7-triazacyclononane-1,4,7-triacetic acid (NOTA)-trastuzumab, a novel PET tracer for the HER2, by comparing it with the 64Cu-DOTA-trastuzumab.

Methods: PET was performed on 6 patients with breast cancer at 24 and 48 hours after injection of 296 MBq of 64Cu-NOTA-trastuzumab. PET for 64Cu-DOTA-trastuzumab was performed on 8 patients with breast cancer at 24 and 48 hours of 370 MBq of the tracer. The mean of maximum standardized uptake value (SUVmean) was evaluated from the blood, liver, kidney, muscle, spleen, bladder, lung, and bone.

Result: On both PET images, SUVmean in each tissue decreased with time except for the bladder and kidney that showed an increasing pattern. In the liver, NOTA PET showed SUVmean of 4.64 ± 0.28 at 24 hours and 4.26 ± 0.50 at 48 hours, values of which are less than that of DOTA PET (6.66 ± 1.57 at 24 hours and 7.05 ± 1.72 at 48 hours). In the blood pool of PET image, the SUVmean of NOTA PET (9.32 ± 1.23 at 24 hours and 7.42 ± 1.85 at 48 hours) was greater than that of DOTA PET (7.85 ± 1.76 at 24 hours and 6.25 ± 1.64 at 48 hours). Other tissues showed similar values of SUVmean on both NOTA and DOTA PET.

Conclusions: 64Cu-NOTA-trastuzumab may be superior in detecting metastasis in the liver due to lower uptake of normal liver tissue than 64Cu-DOTA-trastuzumab. The biodistribution results of 64Cu-NOTA-trastuzumab were comparable with that of 64Cu-DOTA-trastuzumab.

CONCORDANCE BETWEEN NEXT GENERATION SEQUENCING AND IMMUNOHISTOCHEMISTRY FOR HER2 STATUS IN BREAST CANCER PATIENTS

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Background: Accurate assessment of human epidermal growth factor receptor 2 (HER2) status is important for the breast cancer treatment decision making. Immunohistochemistry (IHC) and silver in situ hybridization (SISH) have been two standard diagnostic tools to determine HER2 status. Now, in the era of precision medicine, we can directly get information about copy number variation (CNV) of ERRB2 gene. We investigated the concordance between ERBB2 CNV in targeted gene sequencing and HER2 IHC/SISH results.

Methods: By analyzing formalin-fixed, paraffin-embedded (FFPE) tumor tissues of breast cancer, we compared tumor HER2 status confirmed by IHC/SISH and ERRB2 gene amplification detected by CancerSCAN panel v2.2.

Result: From December 2017 to November 2018, 134 patients with breast cancer were enrolled in K-MASTER screening protocol. Of the 134 patients, 120 patients had adequate tumor tissue specimens for DNA extraction. ERBB2 amplification was not detected (ND) in 93 samples, while 27 samples showed meaningful CNV. Within the ND group, 80 samples were confirmed as HER2 negative by IHC/SISH (32 IHC negative, 29 IHC 1+, 4 IHC 2+ and SISH negative), but 13 samples were reported as HER2 positive (9 IHC 3+, 4 IHC 2+/SISH+). All the detected CNV patients were IHC 3+, except for 1 case of IHC negative. Assuming the IHC/SISH as the gold standard, CancerSCAN panel showed a sensitivity of 66.67%, specificity of 98.77%.

Conclusions: There was a fair level of concordance between CancerSCAN CNV assay and IHC/SISH for the diagnosis of HER2 status in breast cancer patients. We will present more data on the day of conference.

MIR-34A AND NOTCH1 EXPRESSION IN TUMOR MICROVASCULAR ENDOTHELIAL CELL AS A PROGNOSTIC MARKER IN LOCALLY ADVANCED TRIPLE NEGATIVE BREAST CANCER

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Background: Triple-negative breast cancer (TNBC) shows poor prognosis with limited treatment options. Angiogenesis is one of a major mechanism of carcinogenesis and cancer progression. Targeting angiogenesis in breast cancer have shown modest clinical benefit, especially in TNBC. We analyzed the expression of miR-34a in breast cancer cell line and human TNBC tissue. The predictive role of tumor microvascular endothelial NOTCH1 expression and miR-34 was analyzed in TNBC patients.

Methods: Between January 2009 to December 2014, 114 TNBC patients with archival tumor tissues were enrolled. Expression of miR-34a was analyzed using MCF-10A, MCF-7, MDA-MB-231 and archival tumor tissues. Archival tumor tissues were immunostained for CD34, NOTCH1 and the ratio of NOTCH1 and CD34 expression in microvessel was defined as endothelial-NOTCH1 (EC-NOTCH1).

Result: In overall patient population, low expression of EC-NOTCH1 (≤ 0.15) was associated to superior overall survival (OS) (median 66.1 vs. 54.3 months, $p = 0.041$), but showed borderline benefit in metastasis-free survival (MFS) and disease free survival (DFS) (data not shown). In locally advanced TNBC with lymph node involvement, high level of miR-34a (> 0.90) and low level of EC-NOTCH1 showed statistically superior survival benefit in OS (median 77.7 months in miR-34a high & EC-NOTCH low vs. 59.1 months in miR-34a high & EC-NOTCH1 high or miR-34a low & EC-NOTCH1 low vs. 52.0 months in miR-34a low & EC-NOTCH high, $p = 0.026$), DFS (median 77.7 vs. 59.1 vs. 39.8 months, $p = 0.009$) and MFS (median 77.7 vs. 59.1 vs. 39.8 months, $p = 0.038$) compared to other patients.

Conclusions: Decreased EC-NOTCH1 expression and increased miR-34a showed survival benefit in locally advanced TNBC.

LOBULAR CARCINOMA IN SITU-UPGRADING RATES IN PREOPERATIVE BIOPSY AND CLINICOPATHOLOGIC FEATURES

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Background: According to the revised American Joint Committee on Cancer (AJCC) staging system of breast cancer, lobular carcinoma in situ (LCIS) is no longer a malignant disease. The treatment of LCIS is risk management, not surgical excision. However, there is a potential risk that diagnosis of LCIS in preoperative biopsy could be changed to ductal carcinoma in situ (DCIS) or invasive carcinoma in the final pathology.

Methods: This study was conducted retrospectively with patients who had been diagnosed with LCIS at core needle biopsy and underwent breast surgery at Severance hospital in Seoul, Korea from 1991 to 2016. We analyzed the clinicopathological features, prognosis and the upgrading rate of LCIS and compared the upgraded group and not-upgraded one.

Result: There were 49 cases of postoperative LCIS. There was no recurrence or mortality from LCIS with the median 57 months follow-up. Among 55 cases of preoperative LCIS, 9 cases were switched to DCIS or invasive carcinoma postoperatively and the upgrading rate was 16.4%. Only the calcification on mammographic findings was marginally different in the comparison of upgraded and not-upgraded groups (p value = 0.05).

Conclusions: In this study, the prognosis of pure LCIS was excellent but there were relatively high rates of upgrading to DCIS or invasive cancer in preoperative LCIS. Because there was no known significant indicator that identifies upgrading of preoperative LCIS, it may be recommended to perform a surgical excision for LCIS to find hidden malignancy.

THE BRCA1 PROMOTER HYPERMETHYLATION IN THE BLOOD DNA OF STAGE I/II NON-BRCA1/BRCA2 PATIENTS

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Background: BRCA1 promoter methylation has been reported for over a decade, and the majority of them were found in sporadic cases. The role in genetic predisposition is awaiting to be elucidated.

Methods: Of the case without a germline BRCA1 or BRCA2 mutation, and with/without paired tumour tissue was available for analysis, blood leukocyte (n = 192) and corresponding tumour (n = 87) DNA were subjected to bisulfite DNA modification. Methylation specific PCR (MS-PCR) was used to detect the presence of hypermethylation in the promoter of BRCA1. Control group from normal individual without BRCA1 and BRCA2 mutation were also investigated in the similar way.

Result: Among blood DNA from the breast cancer patients, 15.6% was BRCA1 promoter hypermethylated. Hypermethylation was also detected in 9.2% cases with paired tumour (n = 87). It implied that 50% of the hypermethylation in blood DNA can be identified in the corresponding tumour.

Conclusions: BRCA1 promoter hypermethylation can be a frequent event in the high-risk breast cancer patients. The methylation can either be a germline predisposition or from the tumour cells that leak into the bloodstream. This hypermethylation event can be exploited as early detection of breast cancer due to the fact that all of them are classified as stage I/II. Meanwhile, it is important to confirm the origin of the BRCA1 promoter methylation in the patients.

THE INFLUENCE OF COGNITIVE EMOTION REGULATION STRATEGIES ON DEPRESSIVE SYMPTOMS IN BREAST CANCER PATIENTS

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Background: Depression is highly prevalent in breast cancer patients. Therefore, regulation strategy for cognitive emotion, the way how cancer patients regulate their emotions, is important to cope well with their stressful events. This study aims to investigate the influence of cognitive emotion regulation strategies on depressive symptoms of breast cancer patients.

Methods: We have reviewed medical records of 119 breast cancer patients retrospectively. Psychiatric assessment was done using Patient Health Questionnaire-9 (PHQ-9), Insomnia Severity Index (ISI), State subcategory of State and Trait Anxiety Inventory (STAI-S), Cancer-related Dysfunctional Beliefs about Sleep (C-DBS), Fear of Progression (FoP), and Cognitive Emotion Regulation Questionnaire (CERQ).

Result: Significant differences in C-DBS, ISI, FoP and regulation strategies of CERQ were observed between depressed groups (PHQ-9 ≥ 10, n = 60) and non-depressed groups (PHQ-9 < 10, n = 59, $p < 0.05$). The PHQ-9 score correlated with C-DBS, ISI, FoP, all maladaptive strategies except blaming others, and negatively correlated with most adaptive strategies excluding refocus on planning ($p < 0.05$). Logistic regression analysis revealed that patients' depression was predicted by high score of ISI, FoP, low acceptance and high catastrophizing item scores.

Conclusions: This study demonstrated that depression of cancer patients was associated with their cognitive emotion regulation strategies. It is helpful to discuss with patients about their coping strategies to improve cancer patients' depression.

TIME TO TAKE SLEEPING PILLS AND SUBJECTIVE SATISFACTION AMONG CANCER PATIENTS

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Background: Cancer patients suffer from fatigue and often have impaired sleep-wake cycle. We investigated the influence of the time to take hypnotics and daytime activity on patient satisfaction with sleeping pills.

Methods: Ninety-six cancer patients who were currently taking benzodiazepine or non-benzodiazepine gamma-aminobutyric acid (GABA) agonists as hypnotics were grouped into satisfied and dissatisfied groups. The subjects' symptoms, time to take sleeping pills, bedtime, sleep onset time, wake up time, and time in bed within 24 hours (TIB/d) were obtained from the medical records.

Result: Compared with the dissatisfied group, the satisfied group had significantly late sleeping pill ingestion time ($p = 0.04$); significantly early wake up time ($p = 0.01$); and significantly shorter sleep latency, TIB/d, duration from administration of pills to sleep onset, and duration from administration of pills to wake up time (PTW). Logistic regression analysis revealed that the significant predictors of patient satisfaction to hypnotics were less severity of insomnia [odds ratio (OR) = 0.91] and the time variables, including late sleeping pill administration time (OR = 1.53) and early wake up time (OR = 0.57). Among the duration variables, short PTW (OR = 0.30) and short TIB/d (OR = 0.64) were significantly related with the satisfaction to hypnotics.

Conclusions: Taking sleeping pills late and waking up early were helpful in enhancing patient satisfaction to the sleeping pills. Moreover, reducing the duration from administration of hypnotics to wake up time and TIB/d can influence the satisfaction to sleeping pills.

EFFECT OF UNCERTAINTY AND RESILIENCE ON PERCEIVED STRESS FOR BREAST CANCER PATIENTS

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Background: This study was conducted to identify factors affecting perceived stress for breast cancer patients.

Methods: A total of 82 breast cancer patients in a university hospital located in J province were participated. After IRB approval, the study period was between April and September, 2018, and the data were collected using by structured questionnaires. Collected data were analyzed by descriptive analysis, t-test, ANOVA, Pearsons correlation, and multiple regression using SPSS 22.0 statistical program.

Result: : The average score of uncertainty, resilience, and perceived stress were 94.27 ± 14.46, 88.74 ± 10.57, and 16.99 ± 4.42. As stress perceived, there were significantly positive correlations stress and uncertainty ($r = 0.258$, $p = 0.019$). There were significantly negative correlation between stress and resilience ($r = -0.265$, $p = 0.016$). In additions there were no differences by breast cancer characteristics except period of cancer treatments. Specially, it was also significantly negative correlation between stress and period of breast cancer treatment ($r = -0.238$, $p = 0.032$). In this study factors affecting stress perceived were resilience ($\beta = -0.285$, $p = 0.007$), and uncertainty ($\beta = 0.218$, $p = 0.041$). The factors explained 15% of perceived stress.

Conclusions: It doesn't matter period of treatment for breast cancer, it is more important to enhance cancer resilience by themselves to clarify cancer prognosis by physicians. It is suggested that strategies of clinical intervention for strengthening emotional support and patients-health professionals communication including uncertainty and resilience management for breast cancer patients

THE POOR PROGNOSTIC EFFECT OF ESTROGEN RECEPTOR IN NODE NEGATIVE BREAST CANCER

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Background: This study analyzed the association of recurrence patterns and prognostic factors with initial lymph node (LN) status. Especially we focused on the prognostic effect of estrogen receptor(ER) in patients with LN negative breast cancer.

Methods: The medical records of 715 breast cancer patients who underwent curative surgery between 2005 and 2015 at a single institution were retrospectively evaluated. We evaluated the prognostic factors of metastasis-free survival (MFS) according to the LN status.

Result: Of the 715 patients, 257 (35.9%) patients had axillary lymph node metastasis. Tumor size and histologic grade were greater in patients with than without LN metastasis. We analyzed the effect of the tumor characteristics on the MFS according to the initial LN status. In patients who had no LN metastasis, the ER positive revealed the poor prognostic effect (mean survival (months), ER negative vs. ER positive: 146.99 vs. 138.90). Although the 5 years MFS rate of ER positive in LN negative patients was 91.7%, 10 years MFS rate for ER positive in LN negative patients was 74.5%. The patients with LN negative who had larger tumor size (≥ 2 cm, *p*-value 0.030) or old age (≥ 50 years, *p*-value 0.030) were showed significantly poor prognosis in ER positive group.

Conclusions: Our study confirmed that the risk of metastasis increases with time constant in patients with LN negative and ER positive breast cancer, especially among older patients or those with larger tumors.

ASSOCIATION BETWEEN LYMPHOVASCULAR INVASION EXPRESSION AND VARIOUS FACTORS IN BREAST CANCER PATIENTS

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Background: Breast cancer is the second most common cancer in Korea, and the number of cases is increasing. We have found various histopathologic differences in breast cancer. We will investigate the relationship between lymphovascular invasion expression and various factors.

Methods: Data from 287 patients with lymphovascular invasion were collected from patients with breast cancer who underwent surgery by 2006-2013. We compared the patients with and without lymphovascular invasion expression. Statistical analysis was performed using SPSS25.0.

Result: In 287 patients, the age of the patients was 51.7 ± 11.7 (29-83) and the mean follow up duration was 74.4 months (3-125). Pathologic types were IDC 268 (93%), ILC 8 (3%), and 11 (4%) others. Stage I to IV were 133 (46.7%), 113 (39%), 40 (14%), 1 (0.3%), respectively. IHC results we as follows, ER+183 (64%), PR+146 (51%) and HER2 3+ were 78 (27%). 29 patients had recurrence or distant metastasis, There were 51 patients with lymphatic or vascular invasion expression, 6 patients with both lymphatic and vascular invasion expression, 40 patients with lymphatic invasion and 5 patients with vascular invasion. The relationship between breast cancer stage and lymphovascular invasion was correlated with lymphovascular invasion expression ($p < 0.001$), and there was no strong correlation with ER ($p = 0.438$). PR and HER2 expression ($p < 0.05$). Survival rate was significantly higher in the absence of lymphovascular invasion. ($p < 0.001$).

Conclusions: Lymphovascular invasion is associated with stage and PR/HER2, and is directly related to survival. Therefore, a more careful observation of patients with lymphovascular invasion appears to be necessary.

FACTORS THAT AFFECTED CHEMOTHERAPY-INDUCED NEUTROPENIA AT THE FIRST CYCLE CHEMOTHERAPY IN PATIENTS WITH BREAST CANCER IN YOGYAKARTA, INDONESIA

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Background: Chemotherapy-induced neutropenia (CIN) is the most apparent myelosupression effect of chemotherapy in patients with breast cancer (BC). CIN occurs most frequently during the first cycle. We aimed to identify cases with CIN at the first cycle of chemotherapy and determine the affecting factors.

Methods: This study was a part of the ongoing prospective cohort study on chemotherapy toxicity. Sixty-one BC cases were recruited. Blood taking was done on day 7 and 14 after first chemotherapy. Neutropenia was graded in accordance with NCI-CTC version 4.0 and the lowest neutrophil counts were recorded. Socio-demographic, clinicopathological, and treatment data were compared between the CIN group and non-CIN group using Chi-square or Fisher exact test.

Result: Among 61 patients, 29 (47.5%) met the criteria for CIN, including 9 of grade 1, 4 of grade 2, 7 of grade 3, and 9 of grade 4. The rates of CIN were higher in cases with good performance status ($p = 0.026$) and normal pretreatment neutrophil count ($p = 0.001$) than those with poor performance and pretreatment neutrophilia. A trend of CIN was also observed in cases with normal pretreatment leukocyte count ($p = 0.061$) and those receiving anthracycline-based therapy ($p = 0.054$) compared with their counterparts. There were no statistically significant differerences between both groups in terms of age, marital status, education level, occupation, body surface area, disease laterality, stage, ER/PR/HER2 status, histology grade, and other baseline laboratory parameters.

Conclusions: CIN at the first cycle was correlated with performance status, baseline neutrophil and leukocyte counts, and chemotherapy regimen.

Poster Presentation

CLINICOPATHOLOGICAL CHARACTERISTICS AND PROGNOSIS OF THE ANDROGEN RECEPTOR EXPRESSION TRIPLE NEGATIVE BREAST CANCER

Ayuha Yoshizawa, Misaki Matsuyanagi, Haruna Sakai, Yuki Matsunaga, Sayuka Nakayama, Kanae Taruno, Rikako Hashimoto, Hiroko Masuda, Yoshimi Ide, Takashi Kuwayama, Terumasa Sawada, Sadako Akashi-Tanaka, Seigo Nakamura

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Background: The androgen receptor (AR) is highly expressed in triple-negative breast cancer (TNBC). Here, we report the characteristics of AR expression in TNBC cases.

Methods: There were 138 cases of which we performed a surgical operation on the primary TNBC (excluding DCIS) from January 2011 to June 2017 in our department, and the AR status was assessed. The relationship between the AR status and clinicopathological features and prognosis was retrospectively examined.

Result: The median age of the patients was 56.5 (46.3-67.0) years. Forty-two (30.4%) and 96 (69.6%) patients were AR positive (AR+) and negative (AR-), respectively. Sixty-nine (50.0%) patients underwent neoadjuvant chemotherapy (NAC), 36 (26.0%) underwent adjuvant chemotherapy, and 32 (24.0%) did not undergo either therapy. The univariate analysis revealed that the AR status was strongly collected with age ($p = 0.002$), Ki-67 index ($p < 0.001$), pathological diagnosis of apocrine carcinoma ($p < 0.001$), and nuclear grade > 3 ($p < 0.001$). The multivariate analysis showed apocrine carcinoma and Ki-67 index $< 35\%$ were significant independent factors. There was no difference in the pCR rate between the two groups ($p = 0.67$) in NAC-treated patients. No significant difference was observed in relapse-free survival (RFS) ($p = 0.14$) and overall survival (OS) ($p = 0.35$).

Conclusions: AR-positive TNBC was significantly collected with apocrine carcinoma and Ki-67 index. Although there was no significant difference in prognosis, both RFS and OS tended to be better in AR-positive TNBC cases.

EFFECT OF YOUNGER AGE ON SURVIVAL OUTCOMES IN T1N0M0 BREAST CANCER: A PROPENSITY SCORE MATCHING ANALYSIS

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Background: We evaluated the effect of younger age on recurrence risk in Chinese women diagnosed with T1N0M0 breast cancer (BC), using propensity score matching (PSM) analysis.

Methods: We included 365 women who were diagnosed with T1N0M0 BC between 2003 and 2016, and who received systematic therapy at Sun Yat-sen Memorial Hospital. They were classified as younger (≤ 40 years old) and older (> 40 years old). We used PSM to balance clinicopathologic characteristics between the two age groups. Survival was analyzed by the Kaplan-Meier method, before and after PSM.

Result: Over a median follow-up period of 79 months, 54 patients developed recurrences. The total cohorts 5-year recurrence-free survival (RFS) was 87.6%. Before PSM, younger patients had worse RFS than older patients ($p = 0.049$). Significantly worse RFS was seen in younger patients with HER2+ BC compared with their older counterparts ($p = 0.006$). Younger patients had higher rates of loco-regional recurrence rather than metastasis ($p = 0.004$), especially in the first 5 years after diagnosis. After PSM, the two age groups still significantly differed in 5-year RFS (80% vs. 96.7%, $p = 0.015$).

Conclusions: Among PSM pairs with T1N0M0 BC, with equal baselines and treatment conditions, we found that patients who presented at younger ages had worse outcomes, independently of other pathological features. Younger patients with BC may require more individualized therapy to improve their prognosis.

PROGNOSTIC AND PREDICTIVE VALUE OF COMBINATION OF TOP2A AND HER2 IN NODE-NEGATIVE TUMORS 2 CM OR SMALLER (T1N0) BREAST CANCER

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Background: We aim to evaluate the prognostic and predictive value of the expression of TOP2A and HER2 at both mRNA and protein level in T1N0 breast cancer patients.

Methods: A total of 299 cases of T1N0 downloaded from Oncomine database (Cohort 1) and 963 of T1N0 breast cancer patients who underwent surgery in our center between 2002 and 2017 (Cohort 2) were retrospectively enrolled.

Result: In Cohort 1, with a cut-off value of median expression of the mRNA, patients with TOP2A with high mRNA level showed significantly worse 5-year breast cancer specific survival (BCSS) than those with low expression.(90.8% vs. 95.8%, $p = 0.004$). The role of TOP2A protein level of breast cancer were further investigated in Cohort 2, and high TOP2A protein expression of tumors was defined as ≥ 10% positive cancer cells by IHC. Patients with primary tumors exhibiting high TOP2A protein level had higher risks of all recurrence (HR: 1.823; $p = 0.039$) and distant recurrence (HR: 3.687; $p = 0.003$). In addition, in Cohort 2, 68.6% (661/963) patients received adjuvant chemotherapy and 33.2% (320/963) of them received anthracyclines-based regimen. We used propensity score matching (PSM) to balance baseline between anthracyclines-based and non-anthracyclines-based subgroups. Among the patients who developed both TOP2A protein and HER2 positive tumors and received chemotherapy, patients with anthracyclines based regimen had significantly better recurrence-free survival (RFS) than those with non-anthracyclines based regimen ($p = 0.046$).

Conclusions: Both high expression of TOP2A mRNA and protein predicts poor prognosis in T1N0 breast cancer patients. Patients with double positive for TOP2A protein and HER2 are more likely to benefit from anthracyclines-based regimen.

DUAL HORMONE RECEPTOR POSITIVE PATIENTS HAVE BETTER OUTCOMES THAN SINGLE-EXPRESSING IN HER 2- PATIENTS

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Background: Previous studies established that breast cancer patients with double hormone receptor (HR)-positivity have superior prognosis compared to those with discordant and double HR-negativity. In this study we aimed to investigate prognosis of our local, newly-diagnosed non-metastatic invasive breast cancer patients with discordant HR status.

Methods: A total of 6,134 females treated in our center from 2008-2014 were retrospectively analyzed. Clinico-histological features were evaluated, patients were stratified into ER+PR+ vs. ER+PR- vs. ER-PR+ vs. ER-PR- cohorts.

Result: Four thousands forty four patients (65.9%) expressed double HR+, 992 (16.2%) ER+PR-, 258 (4.2%) ER-PR+, and 840 (13.7%) double HR-. 5y-OS were 92.1%, 85.3%, 81.5%, 78% ($p < 0.01$). 5y-DFS were 90.8%, 84.6%, 84.7%, 78.1% ($p < 0.01$). Among 4601 HER2-negative patients, 5y-OS were 92.8%, 85.1%, 81.3%, 71% ($p < 0.01$), 5y-DFS were 91.2%, 85%, 85.1%, 74% ($p < 0.01$). However, no statistically significant difference was found in survival among HER2+ patients. In ER+PR- compared to ER-PR+ group, 90.2% vs. 90.7% received chemotherapy, 58.3% vs. 60% HER2+ patients received HER2-targeted therapy, and 73.6% vs. 78.7% received endocrine treatment. With multivariate analysis, ER+PR- patients had lower OS and DFS compared with double HR+ patients in OS (hazard ratio[HzR] 1.67, 95%CI:1.39-2.02 and 1.84 95%CI:1.38-2.47) and DFS (HzR 1.59, 95%CI: 1.29-1.96; and 1.59 95%CI: 1.13-2.25).

Conclusions: Patients survival with discordant HR status lied between patients with double HR+ and double HR- tumors. In general and among HER2- patients, single ER+ cohort had better OS than single PR+ patients, despite similar proportion among both cohorts receiving adjuvant treatments. However, our patients expressing discordant HR status HER2- showed better survival than those with triple-negative.

THE STUDY ON THE EXPRESSION OF 16 GENES AND THE SUB-TYPES IN ER POSITIVE BREAST CANCER

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Background: To explore the expression of 16 genes in ER positive breast cancer patients.

Methods: A total of 10 patients hospitalized in the First Affiliated Hospital of Shenzhen University (ShenZhen Second Peoples Hospital) from June 2008 to August 2011 were collected. They were confirmed ER positive breast cancer by immunohistochemistry(IHC) and histopathology after operation (regard ER expression ≥ 1% by IHC as positive). Their paraffin samples were well stored, and the clinicopathological details of them were completed. RNA was extracted from the paraffin samples for the genetic sequencing to analyze the expression of the 16 genes (12 mitotic kinases genes, including AURKA, AURKB, BUB1, BUB1B, CDK1, CHECK1, MELK, NEK2, PBK, PLK1, PLK4, and TTK;4 estrogen-related genes, including ESR1, PGR, BCL2, and SCUBE2).Then the correlation analysis between the expression of 16 genes and clinicopathological details was also studied, so as to explore whether the expression state could determine the criterion for sub-types of ER positive breast cancer.

Result: Among the ten patients, five were high expression of ER (by IHC), and five were in low expression. In the high expression team, the expression of ER-related genes were higher than the ER low expression team. The cluster-analysis also showed that ER high-expression patients were different from ER low-expression patients in genetic level.

Conclusions: There are different sub-types beneath the ER positive breast cancer based on the expression of 16 genes. This study shows a future about making criterion for sub-types of ER positive breast cancer. Hopefully it can help the clinicians do better in risk stratification and prognosis indication of ER positive breast cancer patients, and then can achieve the individualized treatment.

CLINICAL CHARACTERISTICS AND RESPONSES TO ENDOCRINE THERAPY OF INVASIVE LOBULAR CARCINOMA OF BREAST: A RETROSPECTIVE ANALYSIS

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Background: Invasive lobular carcinoma (ILC) is the second most common histologic form of breast cancer after invasive ductal carcinoma. However, the responses to endocrine therapies of ILC are not well understood. In this study, we retrospectively evaluated the clinical characteristics of ILC patients and responses to endocrine therapy.

Methods: Between January 2000 to September 2018, 3,932 patients diagnosed as breast cancer were retrospectively analyzed. Patients who were histologically confirmed as invasive lobular carcinoma were evaluated for their age, staging and ER, PR, HER2 expression at the primary site. Then we selected patients diagnosed as recurrent or metastatic disease, and evaluated the efficacy of endocrine therapy.

Result: In total, 3,932 patients were analyzed, including 3,641 with IDC (92.5%) and 182 with ILC (4.6%). In ILC patients, mean age was 52.7 years, and 80 patients (44%) were under 50 years of age. 135 (74.2%) patients were Luminal A, 35 (19.2%) patients were Luminal B HER2-, and 4 (2.2%) patients were Luminal B HER2+. Of the 174 patients, 14 (8.0%) patients had recurrence, and mean disease free survival (DFS) was 9.0 ± 2.5 years. 14 of 22 patients with initially metastatic and recurrent disease received palliative endocrine therapy. The response rate was 14.3% (CR = 1, PR = 1), progression free survival (PFS) was 1.2 ± 0.9 years, and median overall survival was 7.5 ± 3.1 years.

Conclusions: Although patients were diagnosed as hormone receptor positive ILC, most patients showed endocrine resistance from initial treatment. The mechanism of endocrine resistance in ILC needs to be further evaluated.

CLINICAL SIGNIFICANCE OF NEUTROPHIL TO LYMPHOCYTE RATIO IN PRIMARY AND RECURRENT BREAST CANCER

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Background: Our previous study has shown that TILs in recurrent tumors are significantly associated with survival after recurrence. The purpose of this study is to investigate clinical significance of NLR at primary surgery and at recurrence and to examine the association between lymphocyte ratio (NLR) and TILs.

Methods: The patients were eligible if they had primary surgery for breast cancer at our institute and their breast cancer recurred, and specimens of recurrent disease were available. NLR was defined as the absolute neutrophil count divided by the absolute lymphocyte count and he cutoff value was set at 3. For patients with TILs evaluable, the association between NLR and TILs was examined. High TILs were defined as ≥ 10%.

Result: Among 244 patients, 45 patients (19.4%) and 67 patients (29.1%) had high NLR at primary surgery and at recurrence, respectively. Neither NLR at primary surgery nor at recurrence was associated with ER, PgR, and HER2 expression, or breast cancer subtype. In addition, there was no significant correlation between NLR and TILs at primary surgery or at recurrence. NLR at primary surgery was not associated with disease-free survival (DFS), overall survival (OS) from primary surgery, or survival following recurrence (SFR). On the other hand, NLR at recurrence was significantly correlated with OS and SFR. In HER2-enriched (HR-/HER2+) and triple negative (HR-/HER2-) subtypes, low NLR at recurrence was a positive prognostic factor for SFR.

Conclusions: NLR at recurrence was a prognostic factor for OS and SFR. NLR may affect prognosis especially in HER2-enriched and triple-negative subtypes.

THE EFFICACY OF SCALP-COOLING SYSTEM FOR THE PREVENTION OF CHEMOTHERAPY-INDUCED HAIR LOSS IN 17 METASTATIC BREAST CANCER

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Background: I had the opportunity to exploit the computer-controlled chilled helmet-like silicon cap system (RV-01) and to apply it to more than 300 breast cancer patients in my breast clinic. Recently the effectiveness of scalp-cooling system has been announced in cases of adjuvant chemotherapy. This report may be the first with results about the efficacy of this device for the prevention of CIA for metastatic breast cancer patients treated with eribulin.

Methods: Twenty one patients with metastatic breast cancer were recruited and evaluated for CIA with or without scalp cooling. Their CIA were classified by Dean's grade scale and NCI-CTS grade sale. 17 patients were treated using RV-01 and 4 patients without. Mean age of using RV-01 and without 53 years and 64.3 years old, respectively.

Result: None of the 17 patients using RV-01 treated with regimens including eribulin ever used a wig. Hair loss in these patients ranged from G-0 to G-1 by NCI-CTC scale and G-0 to G-3 by Dean's scale. Discomfort such as headache and scalp pain was very well tolerated.

Conclusions: Scalp hypothermia is one approach that can be used to prevent hair loss for metastatic breast cancer patients treated with eribulin. Not only does RV-01 system promote QOL of patients as a safe tool for hair loss prevention, but it may contribute to better treatment as well.

DISCREPANCY IN UNMET NEEDS BETWEEN KOREAN BREAST CANCER SURVIVORS AND PHYSICIANS: A MULTICENTER, CROSS-SECTIONAL STUDY

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Background: Identification of supportive care needs in patients with cancer is essential for planning appropriate interventions. We aimed to determine patient-physician concordance in perceived supportive care needs in cancer care and to explore the predictors and potential consequences of patient-physician concordance.

Methods: A multicenter, cross-sectional, interview survey was performed to 332 Korean breast cancer survivors and 102 physicians. The Comprehensive Needs Assessment Tool for Cancer Patients was administered to survivors and their physicians. Data were analyzed using t-test, ANOVA and multiple regression analysis.

Result: The highest domain of unmet need was information and education (mean ± SD; 1.70 ± 1.14) and an item were Needed help in coping with the fear of recurrence (2.04 ± 1.09) in survivors. In contrast to survivors, the highest domain of unmet need was health care staff (mean ± SD; 1.970 ± 1.22) and an item was Wished my doctor to be easy, specific, and honest in his/her explanation (244 ± 0.93) in physicians.

Conclusions: Most prevalent unmet need in Korean breast cancer survivors was the information and education domain. In contrast to survivors, physicians thought 'health care staff' was the most prevalent unmet needs in breast cancer survivors.

A SCOPING REVIEW PROTOCOL OF RETURN-TO-WORK OF BREAST CANCER SURVIVORS IN KOREA

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Background: Individuals are often diagnosed with breast cancer at younger ages in South Korea, which means that a diagnosis coincides with prime work and child-bearing stages. Return to work (RTW) is an important component of cancer survivorship for both individual rehabilitation and economic development. Research has previously examined RTW of cancer survivors, but the focus is generally on Western populations. A gap exists in understanding the challenges that Korean breast cancer survivors face within a different cultural model and healthcare system. This review will examine the current research on RTW decisions and experiences in Korean breast cancer survivors.

Methods: In a scoping review, twelve databases were searched to identify articles published in English or Korean from January 2000 to February 2019. Eight articles were found to meet the inclusion criteria. Quality of these articles was determined using CASP appraisal checklists. Trends in RTW decisions/ experiences and significant correlations were identified and analyzed.

Result: Workers struggle most with fatigue and exhaustion, followed by difficulties with balancing work and treatment schedules, body image, financial burden, and identity. Comparatively, more education and consistent exercise are positively associated with RTW decisions. There is a gap in the research regarding different socioeconomic statuses, types of occupations, and inclusion of housekeeping tasks. Guidelines for legal measures, improved social support, and rehabilitation interventions are suggested in order to improve the experiences of working breast cancer survivors.

Conclusions: Findings can help guide future studies, along with the design of effective supportive interventions specifically targeted towards successful RTW and overall positive survivorship experiences.

PROPOSAL FOR CORRECTION OF A POOR AESTHETIC RESULT AFTER GYNECOMASTIA SURGERY

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Background: Gynecomastia develop as 30-70% in men after adolescent. There are several surgical methods of gynecomastia: liposuction alone, surgical excision of mammary tissue and liposuction, microshaver or Vaccum Assited Breast Biopsy and liposuction. In some cases, poor aesthetic result leads to reoperation. In this study, we tried to analyze the characteristics of the patients who were re-operated because of an unsatisfactory aesthetic result and to find out how to prevent re-operation from initial operation.

Methods: We conducted a retrospective study on 1,673 patients with gynecomastia who underwent subcutaneous mastectomy with liposuction at Damsoyu hospital between January 2014 and October 2018. Among these patients, patients who underwent gynecomastia surgery but were not satisfied with the aesthetic result were included in the study. All operations were performed with complete excision of mammary gland and liposuction.

Result: Forty-four patients visited our hospital for reoperation. The mean age of the patients was 26.5 (17-53) years. The median body mass index (BMI) was 24.3 (20.1-31.2) kg/m^2. The median duration from initial surgery to reoperation was 48 (6-240) months. The median follow-up period was 35.5 (3-63) months. All patients had remnant mammary tissue. There was no recurrence during follow up periods.

Conclusions: In the initial operation, complete removal of the mammary gland was not performed, which led to reoperation. Therefore, sufficient excision of the mammary tissue should be performed upon initial operation.

A MULTI-CENTER, OPEN-LABEL, PARALLEL, PHASE 2 CLINICAL TRIAL TO EVALUATE THE EFFICACY AND SAFETY OF LUMINOMARKTM (INDOCYANINE GREEN 0.01MG +HYALURONIC ACID SODIUM 4MG/2ML) FOR LOCALIZATION IN PATIENTS

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Background: With increasing screening for breast cancer, non-palpable breast lesions are detected more frequently. For surgery of non-palpable lesion, localization was needed and tattooing with charcoal and wire insertion were used so far. However, these methods could cause pigmentation or pain. The purpose of this study was to evaluate the efficacy and safety of LuminoMarkTM injection, novel material for localization.

Methods: Among patients scheduled for excision of non-palpable breast benign lesion, agreed patients were randomized into test group 1 (LuminoMarkTM 0.1 mL), test group 2 (LuminoMark™ 0.2 mL) and control group (Charcotrace 0.3-1 mL) during January and December 2018 in Samsung Medical Center and Myong-Ji Hospital. Localized lesions with LuminoMark™ were identified through Near-infrared fluorescence imaging. Forty four patients were included for analysis. Primary end point was the completeness of resection. Technical success rate, pigmentation and adverse events were also evaluated.

Result: Baseline characteristics were not different between test group 1 (15 patients), test group 2 (15 patients) and control group (14 patients). The completeness of resection was the ratio of major axis (cm) of resected mass to major axis (cm) on ultra-sound image. The mean value was 2.17 (± 0.50), 2.09 (± 0.52) and 3.67 (± 1.50) in test group1, 2 and control group, respectively (p value = 0.131). Technical fail were 2 cases in test 1 and control groups. Nine patients in control group had pigmentation. There was no adverse event in all group.

Conclusions: LuminoMarkTM injection was not inferior to Charcotrace for localization in patients with non-palpable breast lesions and it could be better method for cosmesis in that it did not make pigmentation.

CLINICAL OUTCOMES AFTER LETROZOLE TREATMENT ACCORDING TO THE ESTROGEN RECEPTOR EXPRESSION IN POSTMENOPAUSAL WOMEN: LETTER TRIAL (KBCSG-006)

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Background: The LETTER trial investigated adjuvant letrozole for hormone receptor (HR)-positive breast cancer in terms of efficacy and safety. We report a final analysis aiming to show clinical outcome with adjuvant letrozole for postmenopausal women with HR-positive breast cancer according to estrogen receptor (ER) expression.

Methods: In this multi-institutional, open-label, prospective phase 4 LETTER trial, postmenopausal patients with HR-positive breast cancer received adjuvant letrozole (2.5 mg/daily) until disease progression, unacceptable toxicity, or withdrawal of consent. The patients were stratified into three groups by ER expression following modified Allred score (AS); low (AS 3-4), intermediate (AS 5-6), and high (AS 7-8). ER expression was centrally reviewed. The primary objective was 5-year disease-free survival (DFS) rate. This trial is registered with ClinicalTrials.gov, number NCT01069211.

Result: Between April 25, 2010, and February 5, 2014, 452 patients were enrolled. At a median follow up of 62.0 months, there were 4 mortalities, 37 events of invasive disease, 27 recurrences, and 17 metastases. In overall patients, the 5-year DFS rate was 91.0% (95% CI 89.5-92.5). The 5 year DFS and recurrence-free survival (RFS) rates did not differ according to ER expression (5-year DFS, $p = 0.367$; 87.9% in low, 95.9% in intermediate, and 90.8% in high; 5-year RFS, $p = 0.496$; 90.4% in low, 95.9% in intermediate, and 93.7% in high, respectively). There were 25 drop-out patients due to adverse event (AE) of letrozole.

Conclusions: Adjuvant letrozole brings a favorable treatment outcome for postmenopausal with HR-positive breast cancer, offering good tolerability.

DO WE HAVE TO SAVE IPSILATERAL ARM IN SENTINEL LYMPH NODE BIOPSY ONLY GROUP? :PROSPECTIVELY PILOT STUDY

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Background: This study was aimed to investigate the negative effect of blood sampling and blood pressure measurement on lymphedema in patients with stage 0, I, or II breast cancer who underwent only sentinel lymph node biopsy.

Methods: From October 2016 to April 2017, total 46 patients, who underwent breast cancer surgery including three or less sentinel lymph node biopsy and had difficulty in blood sampling and blood pressure measurement from the contralateral arm, were enrolled. Blood sampling and blood pressure measurement were performed in the ipsilateral arm after surgery, and the arm volume, circumference in perometer and subjective symptoms of lymphedema were examined 3 months later. We defined lymphedema that is a difference of more than 2 cm in circumference or 200 mL in volume between both arms.

Result: The difference of arm volume after of blood sampling and BP measurement between both arms was 32.7 mL (range 5-194) and arm circumference was 0.02 cm (range 0-1.5). The lymphedema did not occur and no change in arm circumference of the ipsilateral arm after measurement of blood pressure and blood sampling. In addition, the subjective symptoms (pain, numbness, limitation of movement, swelling and discomfort, etc.) were few. (0 or 1: >93.5%).

Conclusions: In breast cancer patients with only sentinel lymph node biopsy, there is no significant difference between the incidence of lymphedema and the patient's discomfort after blood sampling and pressure measurement. Because this study was prospectively pilot study with a small population, we plan to examine a large-scale multicenter study in the future.

DISSEMINATED NECROTIZING LEUKOENCEPHALOPATHY FOLLOWING INTRATHECAL METHOTREXATE AND WHOLE-BRAIN RADIOTHERAPY FOR BRCA2-MUTATED BREAST CANCER WITH LEPTOMENINGEAL METASTASIS: A CASE REPORT

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Background: Disseminated necrotizing leukoencephalopathy (DNL) is a rare fatal complication seen most often in patients who received intrathecal methotrexate (IT-MTX) combined with radiotherapy for hematologic malignancy. No case of DNL has been reported in the solid tumor previously.

Methods: Case report.

Result: A 41-year-old female with locally advanced breast cancer underwent left mastectomy and axillary lymph node dissection (pT2N3M0 Stage IIIC, invasive lobular carcinoma, ER/PR positive, and HER2 negative). A germline BRCA2 mutation was found by genetic testing. The disease recurred with a solitary brain metastasis combined with leptomeningeal metastasis (LM) three years after surgery. LM was confirmed by the presence of malignant cells in cerebrospinal fluid. She received whole brain radiotherapy (WBRT) (30 Gy/10 fractions) and showed a clinical response. One month after the completion of WBRT, IT-MTX (15 mg once weekly) was started. After 14 cycles of IT-MTX, she was admitted due to cognitive impairment and seizure. MRI showed diffuse hyperintensities in white matter on T2-weighted image and multiple enhanced lesions in the bilateral frontal lobes on contrast-enhanced T1-weighted image. Her mental status progressively deteriorated over several weeks; she had finally become a state of akinetic mutism. She died six months after the diagnosis of DNL. Autopsy findings revealed a coagulative necrosis with demyelination and macrophage infiltration in white matter. Tumor cells infiltrated in subarachnoid space around cerebellum and brain stem. However, there was no tumor cell infiltration in necrotic area.

Conclusions: DNL is a rapidly progressive and irreversible complication from WBRT and IT-MTX therapy, and may occur in solid tumor.

A RARE CASE OF MIXED TYPE LIPOSARCOMA OF BREAST ARISING IN MALIGNANT PHYLLODES TUMOR

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Background: Breast cancer is the most common malignancy in females worldwide. Among them, liposarcoma of the breast is a very rare disease, and only 5% of liposarcomas are reported as mixed-type.

Methods: Here, we present a case of a 52-year-old woman with an extremely large mass on her entire left breast. The patient developed sepsis due to tumor necrosis, requiring emergency surgery. She underwent a left total mastectomy.

Result: Pathological analysis revealed the presence of liposarcoma in part of the tumor on the background of a malignant phyllodes tumor. In higher magnification, there were pleomorphic round cells with severe nuclear atypia and numerous mitoses and final diagnosis was mixed liposarcoma of myxoid and pleomorphic types arising in malignant phyllodes tumor.

Conclusions: Even though liposarcoma of the breast is a rare disease, rapidly-growing and large breast tumors diagnosed as malignant phyllodes tumor are encountered, and the possibility of this disease should be considered in the differential diagnosis. Meticulous inspection is needed because sarcomatous content might be present in only a small part of the tumor, like in the present case. Margin-free resection is essential for this disease and axillary nodal assessment is not necessary, except in the presence of clinical evidence of metastasis. The role of adjuvant radiotherapy and chemotherapy are still unclear and further studies are needed to verify the benefit of these treatments.

COMPLICATION OF AQUALLING GEL INJECTION FOR BREAST AUGMENTATION: CASE REPORT AND LITERATURE REVIEW

Seung Yeon Ko, Hansung Kim, Lee Su Kim

Hallym Univ. Sacred Heart Hospital, Korea

Background: AQUAfilling gel (Biomedica. spol, s,r,o, Czech Republic) was widely used for injection augmentation mammoplasty in Korea. AQUAfilling gel is a hydrophilic gel composed of 98% sodium chloride solution (0.9%) and 2% cation copolyamide. However, the safety of this procedure remained controversial.

Methods: Herein, we report a 30-year-old woman with a history of augmentation mammoplasty by AQUAfilling gel injection developed breast pain and engorgement. She gave birth three months before the symptoms. So we initially suspected puerperal mastitis. But it was not a typical aspect. Magnetic resonance imaging showed septated fluid containing lesions and increased vascularity on breast parenchyma in bilateral breasts. AQUAfilling gel was also observed inside the pectoralis muscle of both breasts.

Result: She was treated via surgical intervention for removal of necrotic infected tissue and filler, as well as massive irrigation. After the partial mastectomy, there were no complications. This case showed that the AQUAfilling gel can cause inflammation and had infiltrated the pectoralis muscle fibers.

Conclusions: Augmentation mammoplasty is one of the most popular esthetic operations in the world. AQUAfilling gel is easy to inject and is natural looking. But once a complication occurs, treatment is difficult. Also, AQUAfilling gel itself has not yet been proven to be safe, such as long-term toxicity of the gel material and its effect on surrounding tissues. So more research on this subject should be done. Hence, sufficient evidences of long-term safety must be accumulated and proved, until which time the aesthetic use of the unapproved filler must be restricted.

CLINICAL OUTCOME OF 15 CASES WITH ADENOMYOEPITHELIAL CARCINOMA AT SINGLE INSTITUTE

Heba Alqudaihi, Byung Ho Son, Sei Hyun Ahn, Jong Won Lee, Beomseok Ko, Il Yong Chung, Sae Byul Lee, Jisun Kim, Hee Jeong Kim, Gyungyub Gong

ASAN Medical Center, Univ. of Ulsan College of Medicine, Korea

Background: Adenomyoepithelial carcinoma of the breast is a rare tumor. Most of the literature consists of individual case reports or studies of fewer than five cases.

Methods: A retrospective medical record review was performed for 15 subjects confirmed with adenomyoepithelial carcinoma on the postoperative pathological diagnosis at Asan Medical Center from 2008 to 2018. Information regarding age at diagnosis, preoperative biopsy results, operation methods, the status of hormone receptor and HER2, and clinical outcome were collected.

Result: All cases were female diagnosed at median age of 50 years. In terms of preoperative biopsy results, surprisingly, 40% of the cases (6 out of 15) were benign in discordance with the final malignant pathology. During median follow-up 81 months (6-168), one case showed local recurrence after 3 years from treatment, she developed lung metastasis after a year from that. Another case developed lung metastasis after two years from management. Five of 10 patients who had hormone receptor and HER2 results were triple negative, and the remaining five were hormone receptor positive and HER2 negative.

Conclusions: Adenomyoepithelial carcinoma is an uncommon tumor that should be included in the differential diagnosis of breast tumors with suspicious or malignant features on preoperative CNB results. Adenomyoepithelial carcinoma has greater potential to recur locally and has significant metastatic potential. Surgical resection with safe margins is recommended, ALND is not indicated unless there is clinically detected lymph nodes. There is a little objective evidence to support a role for radiotherapy or chemotherapy in the management.

RAPID PROGRESSED PRIMARY BREAST LEIOMYOSARCOMA WITH AXILLARY LYMPH NODE METASTASIS

Eun Ji Lee, Byung Kyun Ko, Jin Sung Kim

Ulsan Univ. Hospital, Korea

Background: Primary leiomyosarcoma of the breast is a rare type of malignant connective tissue disease. Primary breast leiomyosarcoma is known to have low incidence of lymphatic spread. There are only few case reports with primary breast leiomyosarcoma. To the best our knowledge, Primary breast leiomyosarcoma with axillary lymph node metastasis has never been reported.

Methods: We report the case of a middle age women diagnosed primary breast leiomyosarcoma with axillary lymph node metastasis.

Result: A 52-year-old woman was diagnosed with primary left breast leiomyosarcoma and she had axillary metastasis. The patient has no family history of breast cancer or sarcomas. The patient first noticed palpable left breast mass 2 years ago. At that time, gun biopsy was done, which reported probably myofibroblastoma. After 2 years, the patient presented with growing breast mass. And mass wide excision was done within a week. The patient was diagnosed with malignant leiomyosarcoma of the left breast on pathology. Following CT scan and PET-CT revealed that she had enhancing small lymphadenopathy in left axillary space proven leiomyosarcoma on needle biopsy. We performed axillary lymph node dissection and received sequential adjuvant radiation therapy. Nevertheless, the progression of multiple leiomyosarcoma such as liver and ribs progressed rapidly within 4 months.

Conclusions: We presented a rare case of primary breast leiomyosarcoma with axillary lymph node metastasis. Primary breast leiomyosarcoma is known to have a relatively good prognosis. However, with axillary lymph node metastasis, it is predicted to have a rapid progression and a bad prognosis.

A FOOTBALL-SIZED RARE BREAST CANCER WITH POOR DIFFERENTIATION-A DILEMMA TO DIAGNOSIS

Lorraine Ma, Polly Cheung

Breast & Endocrine Surgery Centre, Ruttonjee Hospital, Hong Kong

Background: Rare breast cancers had always been a challenge to diagnosis and were difficult to manage.

Methods: We discussed on a lady with a huge breast tumour initially treated with chemotherapy for metaplastic carcinoma. She had disease progression and received palliative mastectomy.

Result: Final pathology revealed high grade sarcoma and target therapy (Pazopanib) was given with some response.

Conclusions: Both metaplastic carcinoma and sarcoma of the breast are rare and aggressive. They may present similarly but they behave differently. Management strategies are also distinct from one another. Re-biopsy of the tumour shall be considered if there is failure of response to treatment. This strongly embarks on a constant communication through a multidisciplinary team approach for timely management of such aggressive tumours.

CONCURRENT BILATERAL NEUROENDOCRINE CARCINOMA AND INVASIVE LOBULAR CARCINOMA OF BREAST: A UNIQUE CASE REPORT

Yeji Lee, Seong Uk Kwon, Dae Sung Yoon, Won Jun Choi, In Seok Choi, Sang Eok Lee, Ju Ik Moon, Si Min Park, In Eui Bae, Nak Song Sung

Konyang Univ. Hospital, Korea

Background: Bilateral breast cancer is not an uncommon entity and accounts for 4-20% of patients with primary operable breast cancer. Most bilateral breast cancers represent the same histological type and similar biological features. However, the occurrence of primary synchronous bilateral breast cancer with a different histologic type is extremely rare.

Methods: Neuroendocrine carcinoma of breast includes a heterogeneous group of tumors which is derived from neuroendocrine cells. Primary neuroendocrine carcinoma in the breast is very rare. They contribute less than 1% of all breast cancer, while invasive lobular carcinoma, which is the second most common histological subtype after invasive ductal carcinoma, accounts for 5-15% of breast cancer.

Result: Neuroendocrine carcinoma of breast (NECB) is very rare and is known to be less than 1% of all breast cancers. According to the World health organization (WHO), there are three categories of histologic types; solid carcinoid-like, large cell-type, and small cell-type. Except for small cell-type, NECB is known to progress slowly and prognosis better than invasive ductal carcinoma of breast. However, due to its rarity, there is no enough data on the optimal treatment of NECB, which is established in prospective clinical trials.

Conclusions: We report a rare case of concurrent bilateral breast cancer with two different histologic types, neuroendocrine carcinoma and invasive lobular carcinoma, in a 47-year-old premenopausal woman who presented with left breast lump accompanying intermittent pain.

THE ROBOT-ASSISTED NIPPLE-SPARING MASTECTOMY USING THE DA VINCI SP SYSTEM: THE FIRST EXPERIENCE

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Department of Surgery, Yonsei Univ. College of Medicine, Korea

Background: Recently the updated robotic platform, the da Vinci SP system (Intuitive Surgical, Sunnyvale, USA), has been introduced. The updated platform provides a single port robotic system with the new flexible 3D-camera and arms with wider range of motion compared to previous version of multi-ports robotic systems. Here, we report robot-assisted nipple-sparing mastectomy (RANSM) with immediate reconstruction using the updated platform.

Methods: A 37-year-old woman underwent bilateral RANSM with immediate reconstruction in December 2018 because the patient wanted contralateral prophylactic mastectomy. Primary lesion was ductal carcinoma in situ of the right that was detected by screening imaging studies.

Result: In brief, a single incision was made in the mid-axillary line. The initial incision size was 2.7 cm for the left, and 3 cm for the right. The operation times were 170 min for the left and 180 min for the right. The console times were 93 min for the left and 109 min for the right. The total operation time including reconstruction was 619 min. Breast volumes were 194 g for the left and 192 g for the right. Sentinel lymph node biopsy was only performed in the right side. Breast reconstruction was performed using implants. Post-operative pathology revealed that ductal carcinoma in situ in both breasts. There was no major complication except a minor skin burn on the right breast.

Conclusions: We documented the first clinical experience of RANSM using the da Vinci SP system. The initial operation using the updated platform was safely performed for bilateral breast of the patient with early breast cancer.

BIG-DATA BASED GUIDELINE FOR WORK-UP AND INTERVAL AFTER SURGERY IN BREAST CANCER SURVIVORS (BIG-WISE STUDY): A NATIONAL COHORT STUDY

So-Youn Jung, Young Ae Kim, Dong-Eun Lee, Jungnam Joo, Sun-Young Kong, Eun Sook Lee

National Cancer Center, Korea

Background: This study aimed to assess the trends of follow-up imaging modalities and clinical implication of them on mortality in Korean breast cancer patients.

Methods: This study included 96,575 Korean breast cancer women, who were diagnosed during 2002-2009 and registered in the merged data of the Korea Central Cancer Registry (KCCR), Statistics Korea, and Korean National Health Insurance Service (NHIS). We evaluated the number of breast imaging modalities (mammography), systemic scans for evaluating the presence of distant metastasis (chest X-ray, chest CT, bone scan, and PET-CT), and compared the prognostic effect on mortality.

Result: The median follow-up period was 72.9 months (range 12.0-133.3 months) and 7.5% of total patients died. During 3 years after diagnosis of breast cancer, mammography was examined in 89.6% and 3 or more mammography were in 54.7%, chest X-ray in 88.6% and 66.5%, chest CT in 40.3% and 16.2%, bone scan in 78.7% and 45.6%, and PET-CT in 40.3% and 8.5%. When we compared overall survival in the patients with recurrence after 3 years by the regularity of imaging modalities (<3 vs. ≥ 3), only mammography and chest X-ray improved the survival (HR 0.72, 95% CI 0.61-0.84; $p<0.001$ in mammography, HR 0.83, 95% CI 0.70-0.99; $p=0.03$ in chest X-ray).

Conclusions: This study showed the current trends and clinical implication of follow-up imaging modalities in Korean breast cancer patients. Because we could not consider the subtypes of breast cancer and patients' symptoms, we need to conduct prospective study in future.

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[성분 • 함량] 1실린지중 : 주성분 : 초산고세셀린 (별규) 3.78mg (고세셀린으로서 3.6mg) 부형제 : 락타이드/글리콜라이드 공중합체 (별규) 18.0mg [성상] 1회용 실린지 어프리케이터속에 살균된 백색–크림색의 원주형 데포가 들어있으며 이 속에 초산고세셀린(고세셀린으로서 3.6mg)이 생체내에서 분해되는 매트릭스에 분산되어 있다. [효능 • 효과] • 호르몬요법이 적합한 전립선암 • 호르몬요법이 적합한 폐경기전 및 주폐경기 여성의 진행성 유방암 • 조기유방암의 보조요법 : 에스트로겐 수용체(ER) 양성인 폐경기전 및 주폐경기 여성의 조기 유방암에 대한 표준 화학 요법의 대체요법 • 자궁내막증 • 자궁내막조직의 퇴축: 자궁내막 제거나 절제전에 자궁내막을 얇게 함을 목적으로 투여함 • 자궁근종: 자궁근종을 가진 빈혈환자에서 수술전 철분요법과 병행하여 환자의 혈액상태를 개선함을 목적으로 투여함 • 보조생식술: 배란촉진 과정시 뇌하수체 억제 목적 [용법 • 용량] 성인: 고세셀린으로서 3.6mg을 28일 간격으로 전방복벽에 피하주사한다. 신장애, 간장애 환자나 고령자의 경우에도 용량을 조절할 필요는 없다. 1. 전립선암, 유방암: 호르몬요법이 적합한 전립선암 또는 유방암의 관리에 고세셀린으로서 3.6mg 1데포를 28일마다 전방복벽에 피하주사한다. 국소진행 전립선암에 있어서 방사선요법과 병용하는 보조 호르몬요법의 경우 36개월로사용이 제한된다. 2. 자궁내막증: 자궁내막증을 이 약으로서 6개월 이상 치료한 임상자료가 없으므로 치료기간은 6개월 이하가 되도록 한다. 뼈 무기질 밀도의 감소 우려가 있으므로 반복적인 치료는 하지 않도록 한다. 이 약 투여시 호르몬 대체요법(에스트로젠 및 프로게스테론제제)을 병행하면 뼈 무기질 밀도 감소 및 혈관운동성 증상이 감소된다. 3. 자궁내막조직의 퇴축: 자궁내막의 퇴축을 목적으로 투여할때는 4주 혹은 8주간 치료한다. 자궁의 크기가 큰 환자에게 투여 시 또는 적당한 수술 일정을 결정하기 위해서 2번째 데포를 투여할 수 있다. 4. 자궁근종: 자궁근종에 의한 빈혈이 있는 여성에게는 고세렐린을서 3.6mg에 철분을 보충하여 수술 전 3개월까지 투여할 수 있다. 5. 보조생식술: 에스트로라디올 농도가 초기 황체기 수준이(약 150pmol / ℓ) 되도록 뇌하수체를 억제하기 위해 고세셀린으로서 3.6mg 1데포를 투여한다. 이는 7~21일 사이에 일어난다. 뇌하수체가 억제되면 생식샘자극호르몬(gonadotrophin)으로 배란을 촉진시킨다. 이 약에 의한 뇌하수체 억제는 일정하여 일부 경우, 성선자극호르몬 요구량이 증가될 수 있다. 적당한 시기의 황체기에 성선자극호르몬을 중지하고 사람융모성생식자극호르몬(hCG)을 투여하여 배란시킨다. 치료관찰, 난자 회수 및 임신기법은 각 병원의 일반적 방법에 따른다. [사용상의 주의사항] 1.경고 전이성 척추 손상(metastatic vertebral lesion)이나 요로폐쇄증을 수반한 환자는 치료 초기 몇 주 동안 세심하게 관찰하여야 한다. 2. 다음환자에게 투여하지 말 것. 1) 이 약 및 다른 LHRH 동족체에 대하여 과민증 환자 2)임부 및 수유부 3)호르몬 비의존성 전립선암 환자 4) 양쪽 고환 절제술을 받은 후, 이 약에 의해 더 이상 테스토스테론의 감소를 기대할 수 없는 환자 5) 원인 불명의 질 출혈 환자 6) 소아 7) 진단된 뇌하수체 샘종 환자 3. 다음 환자에는 신중히 투여할 것. 보조생식술의 경우: 다낭포성 난소 환자 [저장방법] 25℃ 이하 실온보관, 밀봉용기 [포장단위] 1데포 ※ 만약 구입시 사용기한이 경과되었거나 변질, 변패 또는 오손된 제품인 경우에는 구입처를 통하여 교환하여 드리며, 재정경제부 고시 "소비자 피해보상규정" 에 의거 소비자의 정당한 피해는 보상하여 드립니다. ※ 보다 자세한 제품정보는 알보젠코리아㈜으로 문의하시기 바랍니다. www.alvogenkorea.com 080–729–5800(수신자부담 문의전화) aZOL20140421

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