Global Breast Cancer Conference 2015 &
4th International Breast Cancer Symposium

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IBCS&GBCC Abstract Book

GBCC 2015 & 4th IBCS Abstract Book

한국유방암학회
Korean Breast Cancer Society

This work was supported by the Korean Federation of Science and Technology Societies(KOFST) grant funded by the Korean Government.

CONFERENCE OVERVIEW

Conference Overview

Title	Global Breast Cancer Conference 2015 & 4th International Breast Cancer Symposium (GBCC 2015 & 4th IBCS)
Date	April 23 (Thu.) - 25 (Sat.), 2015
Venue	The Shilla Jeju Hotel, Jeju Island, Korea
Hosted by	Organizing Committee of KBCS – GBCC & IBCS
Supported by	Korea Breast Cancer Foundation
Language	English & Korean (Simultaneous Interpretation to be provided) *Korean-Chinese interpretation will also be offered during some sessions.
Secretariat	**Secretariat for GBCC 2015 & 4th IBCS** INTERCOM Convention Services, Inc. 9th Fl. Samick Lavied'or Bldg., 234, Teheran-ro Gangnam-gu, Seoul 135-920, Korea Tel: +82-2-3452-7291 / Fax: +82-2-6254-8049 E-mail: gbcc@intercom.co.kr / Website: www.gbcc.kr

Venue Information

The Shilla Jeju Hotel

- Address: 75 Jungmungwangwang-ro 72 beon-gil, Seogwipo-si, Jeju-do, Korea (697-808)
- Tel: +82-64-735-5114
- E-mail: Jejushilla@samsung.com
- Website: www.shilla.net/jeju

CONFERENCE THEME

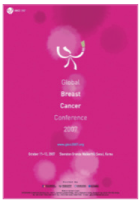
Since 2011, GBCC has held the "Theme Naming Contest" in search of brilliant and creative ideas. After the careful judging process by the Organizing Committee of KBCS – GBCC & IBCS, the theme for GBCC 2015 & 4th IBCS is selected as below:

Cutting edge with integrative collaboration!

Now that both the Global Breast Cancer Conference (GBCC) and the International Breast Cancer Symposium (IBCS) have emerged as world-renowned gatherings for breast cancer professionals across the globe, it is time to seek integrative collaboration and close cooperation among those experts to chart out the cutting edge guide on how to prevent, diagnose and treat breast cancer.

The Organizing Committee of KBCS – GBCC & IBCS is planning to play a central role in making Korea a breast cancer research hub of Asia by providing advanced information for Asian scholars at these breast conferences biennially held on Jeju Island, where globally renowned researchers also attend.

Previous Meetings


GBCC 2007

GBCC 2009

GBCC 2011

1st IBCS, 2012

2nd IBCS, 2013

GBCC 2013

3rd IBCS, 2014

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Exhibition Committee	Seung-Il Kim	*Severance Hospital*
Conference Operating Committee	Sung Hoo Jung	*Chonbuk National Univ. Hospital*
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Public Relations Committee	Sung-Won Kim	*Daerim St. Mary's Hospital*
Registration Committee	Doo Ho Choi	*Samsung Medical Center*
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International Cooperation Committee	Woo-Hee Jung	*Severance Hospital*
Social Program Committee	Jung Ho Kim	*Korea Breast Cancer Foundation*
Protocol Committee	Kweon Cheon Kim	*Chosun Univ. Hospital*
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General Practitioner Committee	Heeboong Park	*M.D. Park Medical Center*
Nursing Care Committee	Mi Young Kang	*Cheil General Hospital*

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Jung Sil Ro	National Cancer Center
Jung-Hyun Yang	Konkuk Univ. Medical Center
Keun-Young Yoo	Seoul National Univ. Hospital
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Min-Hyuk Lee	Soonchunhyang Univ. Seoul Hospital
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Young-Hyuck Im	Samsung Medical Center

ORGANIZING COMMITTEE OF KBCS – GBCC & IBCS

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Janice Tsang	Queen Mary Hospital, Univ. of Hong Kong	*Hong Kong*
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Toru Watanabe	Hamamatsu Oncology Center	*Japan*
Yong-Sheng Wang	Shandong Cancer Hospital & Institute	*China*
Yoon Sim Yap	National Cancer Centre Singapore	*Singapore*

GENERAL INFORMATION

Registration

The Registration Desk will be located in front of Mara Room (The Secretariat) during the conference and operate according to the schedule below:

Location: In front of Mara Room (6th Fl.)	
Operating Time:	
April 23 (Thu.)	09:00-18:00
April 24 (Fri.)	07:00-18:00
April 25 (Sat.)	07:00-12:00

Registrants will be allowed entry into all scientific sessions, the Breakfast, Luncheon and Dinner Symposium and the Poster & Sponsor Exhibition.

Meals will be served on a first-come, first-served basis during some sessions: Breakfast Symposium 1 & 2, Luncheon Symposium 1 & 2 and Dinner Symposium.

Speaker's Lounge & Preview Room

Invited speakers and moderators can pick up their name badge and registration packet at the Speaker's Lounge. Free paper session presenters also need to visit the Speaker's Lounge at least 30 minutes prior to the start of their session in order to preview and submit their presentation files.

Location: Ara Room (6th Fl.)	
Operating Time:	
April 22 (Wed.)	15:00-19:00
April 23 (Thu.)	07:00-19:00
April 24 (Fri.)	07:00-19:00
April 25 (Sat.)	07:00-13:00

Onsite Secretariat

Please feel free to visit the onsite office of the Secretariat during the conference if you have any questions or comments.

Location: Mara Room (6th Fl.)	
Operating Time:	
April 23 (Thu.)	07:00-19:00
April 24 (Fri.)	07:00-19:00
April 25 (Sat.)	07:00-13:00

Tel: +82-2- 3452-7291
E-mail: gbcc@intercom.co.kr

PROGRAM INFORMATION

Opening Ceremony

Date & Time: April 23 (Thu.), 11:00-11:10
Location: Halla Hall
* A conference opening address will be delivered by president and the Opening Ceremony will be followed by Plenary Lecture.

Welcome Reception

Date & Time: April 23 (Thu.), 18:30-20:00
Location: Halla Hall
Hosted by: Korea Breast Cancer Foundation
* Dress Code: Semi-formal Attire
* NOT included in the registration fee
* Pre-registrants are kindly required to bring a Welcome Reception invitation card included in a registration kit, and to wear their name badge to attend the Reception.
* A ticket to gain entry to the Welcome Reception will be available for USD 30 at the Registration Desk on a first-come, first-served basis.

Closing Ceremony

Date & Time: April 25 (Sat.), 12:00-12:20
Location: Halla Hall

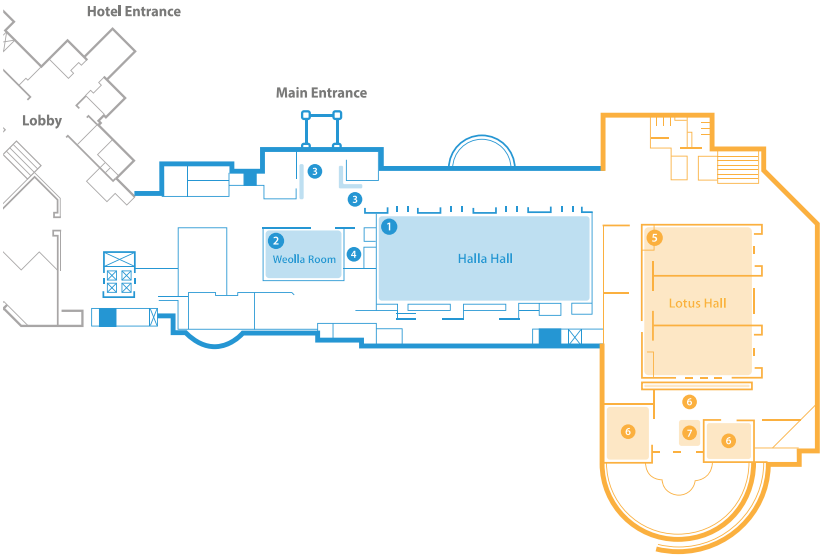
FLOOR INFORMATION

6th Fl. (Lobby Level)

1. Meeting Room 1: Halla Hall
2. Meeting Room 3: Weolla Room
3. Registration: Mara & Ora Room Lobby
4. Speaker's Lounge & Preview Room: Ara Room
- Exhibition: Halla Hall Lobby

3rd Fl.

5. Meeting Room 2: Lotus Hall
6. Poster Exhibition: Lilly & Rose Room
7. Cafeteria: Rose Room Lobby
- Exhibition: Lotus Hall Lobby



POSTER EXHIBITION

Poster Exhibition

In an effort to display as many posters as possible during the conference, different posters will be exhibited on Day 1 and Day 2 as follows:

Location: Lobby, Rose & Lilly Room (3rd Fl.)	
Operating Time:	
Day1: April 23 (Thu.) 12:00 - 24 (Fri.) 11:00	
Day2: April 24 (Fri.) 12:00 - 25 (Sat.) 11:00	

Poster Check-in

All poster presenters are required to check in at the poster check-in desk before putting up their posters.
- Check-in Desk: Lilly Room Lobby (3rd Fl.)
- Date & Time:
* Day1: April 23 (Thu.), 11:00
* Day2: April 24 (Fri.), 11:00

Assembly Supplies

Presenters will be provided with push pin to attach their posters onto the boards.

Affixing, Displaying, and Removal Schedule

Affixing Time:	Day1: April 23 (Thu.) 11:00 - 12:00 Day2: April 24 (Fri.) 11:00 - 12:00
Displaying Time:	Day1: April 23 (Thu.) 12:00 - 24 (Fri.) 11:00 Day2: April 24 (Fri.) 12:00 - 25 (Sat.) 11:00
Poster Take-down Time:	Day1: April 24 (Fri.) 11:00 - 12:00 Day2: April 25 (Sat.) 11:00 - 12:00

* Please note that any posters remaining after the removal time can be discarded.

Responsibility for Poster

Neither the GBCC 2015 & 4th IBCS Organizing Committee nor the conference venue is responsible for loss or damage of your poster or can be held liable for injuries to persons or damage to property owned by the poster presenter(s).

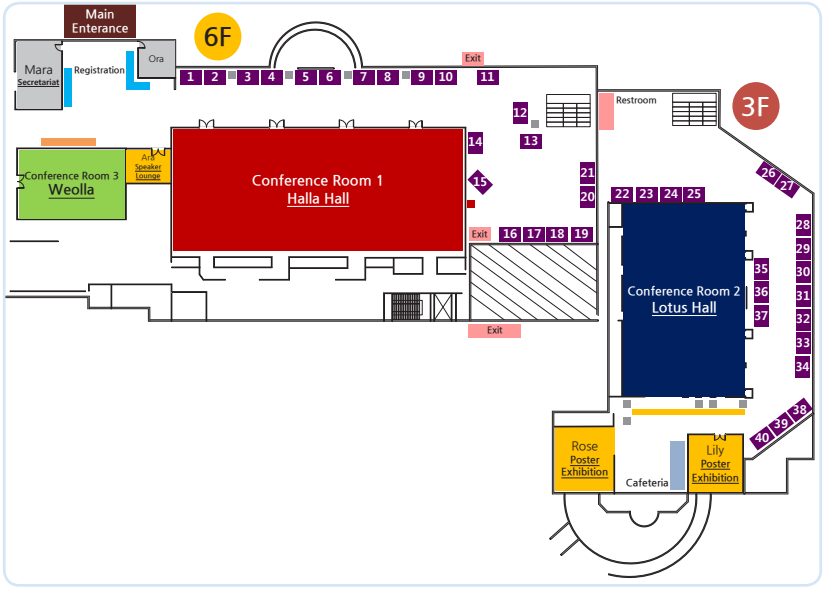
SPONSOR EXHIBITION

Sponsor Exhibition

The GBCC 2015 & 4th IBCS Exhibition will provide a market place for vendors from around the world and a chance for participants to keep abreast of the latest international developments in breast cancer.

Location: Lotus & Halla Hall Lobby (3rd Fl. & 6th Fl.)
Operating Time:

April 23 (Thu.)	10:00 - 18:00
April 24 (Fri.)	08:30 - 18:00
April 25 (Sat.)	08:30 - 12:30



SPONSOR EXHIBITION

Sponsor List

No.	Exhibitor	Booth No.
1	Roche Korea Co., Ltd.	1-4
2	AstraZeneca	5-6
3	Sanofi Korea	7-8
4	Novartis Korea	9-11
5	Korean Breast Cancer Society	12
6	National Biobank of Korea	13
7	Kyowa Hakko Kirin Korea Co., Ltd.	14
8	Dalim Corporation	15
9	Bio-Medical Science Co., Ltd.	16
10	Kwang Dong Pharmaceutical Co., Ltd.	17
11	Boryung Pharm	18-19
12	Eisai Korea Inc.	20-21
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14	Abnoba Korea	23
15	Johnson & Johnson Medical Ltd.	24
16	Devicor Medical Korea Inc.	25
17	Bukwang Pharm. Co., Ltd.	26
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30	Koonja Publishing Inc.	40

GBCC 2015 & 4th IBCS Abstract Book

- **IBCS&GBCC Abstract Book**
- **GBCC 2015 & 4th IBCS Publication Committee**
  Editor-in-chief: Yongsik Jung
  Members: Ji Young Kim, Min Hee Hur, So-Youn Jung
- **Vol. 01**
- **Editorial Office**
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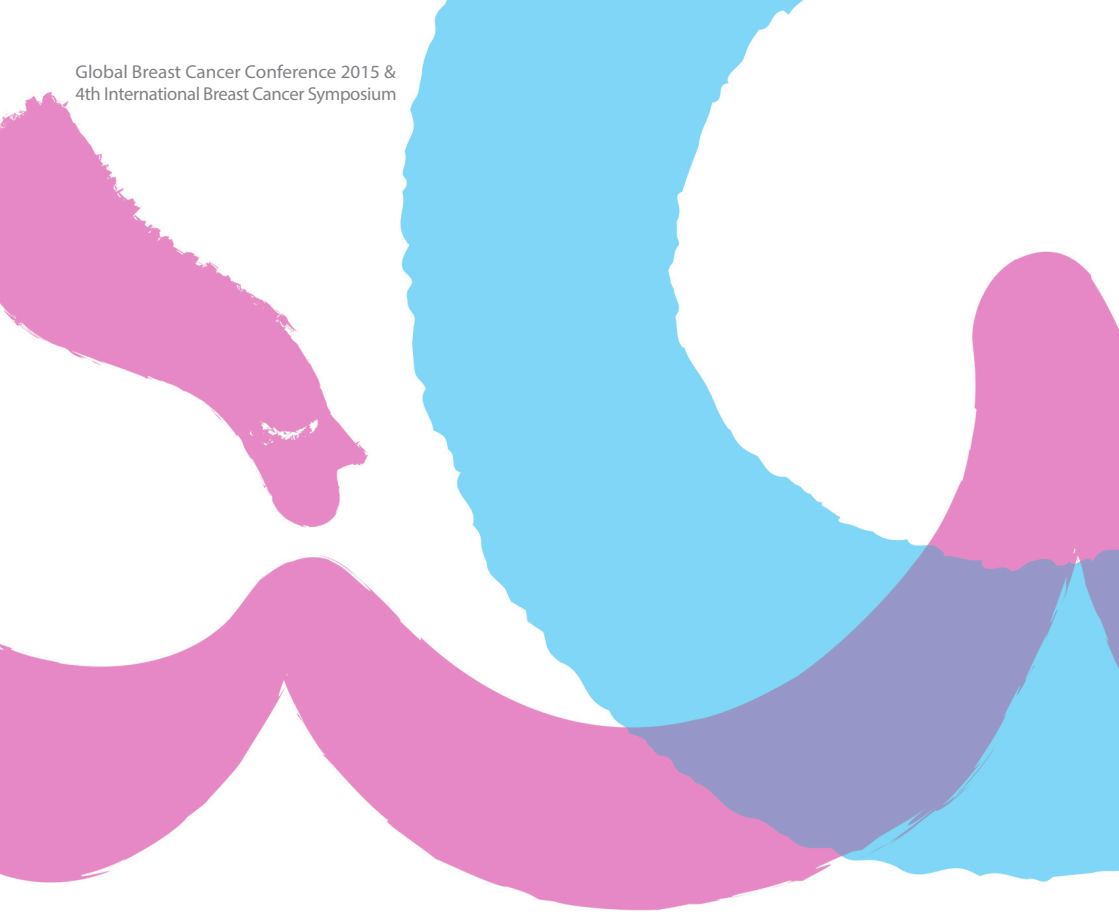
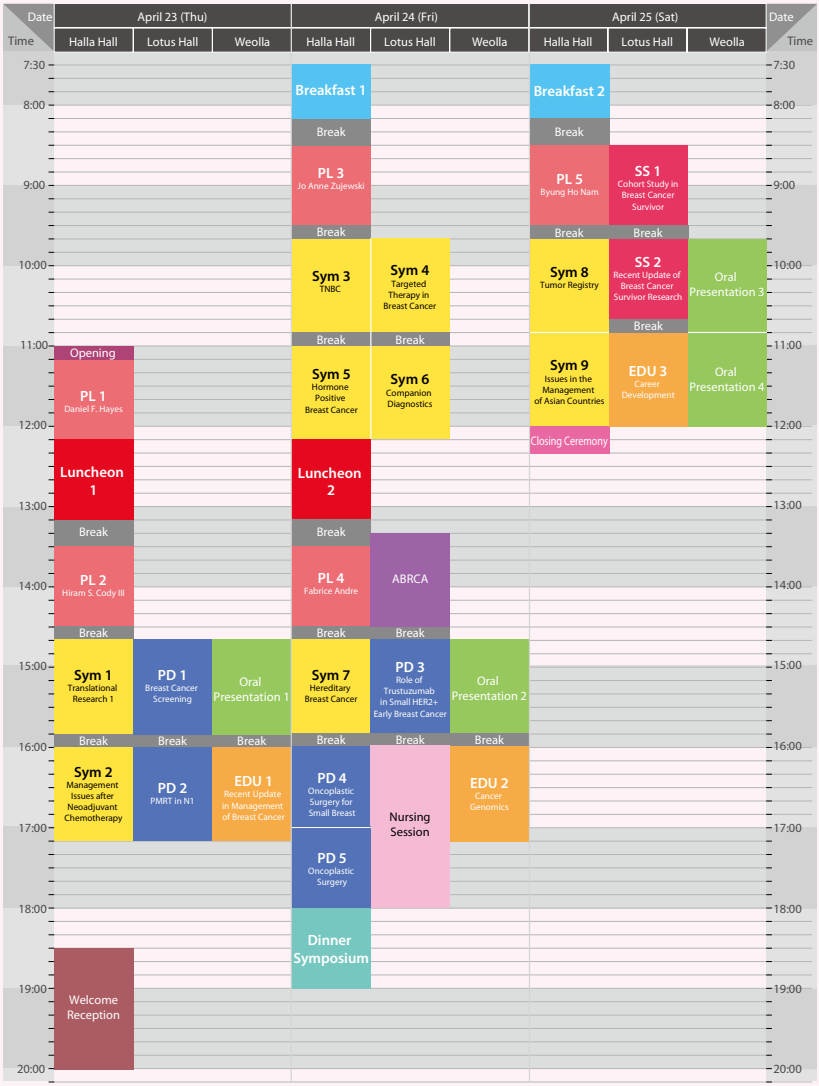


FUTURE CONFERENCES

5th IBCS
April 21 (Thu) – 23 (Sat), 2016

GBCC 2017 & 6th IBCS
April 20 (Thu) – 22 (Sat), 2017

PROGRAM AT A GLANCE



Reference

- PL: Plenary Lecture
- Sym: Symposium
- PD: Panel Discussion
- EDU: Education Session
- SS: Survivorship Session

Poster Exhibition

Location: Rose & Lilly Room

Operating Time:

Day1: April 23 (Thu) 12:00 - 24 (Fri) 11:00

Day2: April 24 (Fri) 12:00 - 25 (Sat) 12:00

PROGRAM DETAILS

DAY 1

April 23 (Thu.), 2015

11:00-11:10 Opening Ceremony — **Halla Hall**

11:10-12:10 Plenary Lecture 1 — **Halla Hall**

Moderator Dong-Young Noh
Department of Surgery, Breast Care Center, Seoul National University Hospital, Korea

PL01 Genetic Signature in Selecting Adjuvant Treatment *2*
Daniel F. Hayes
Internal Medicine, Hematology Oncology, University of Michigan Comprehensive Cancer Center, U.S.A.

12:10-13:10 Luncheon Symposium 1 (Sponsored by AstraZeneca) — **Halla Hall**

Moderator Paul Mainwaring
Mater Medical Center, Queensland University, Australia

LS01 Endocrine Therapy in Advanced Breast Cancer *100*
Young-Hyuck Im
Department of Hematology-Oncology, Samsung Medical Center, Korea

13:10-13:30 Coffee Break

13:30-14:30 Plenary Lecture 2 — **Halla Hall**

Moderator Min Hyuk Lee
General Surgery, Soonchunhyang University Hospital, Korea

PL02 Recent Consensus of Sentinel Lymph Node Biopsy *4*
Hiram S. Cody III
Breast Service, Department of Surgery, Memorial Sloan Kettering Cancer Center, U.S.A.

14:30-14:40 Coffee Break

14:40-15:50 Symposium 1: Translational Research 1 — **Halla Hall**

Moderator Min Yu
Stem Cell Biology and Regenerative Medicine, University of Southern California, U.S.A.
Seung Il Kim
Department of Surgery, Yonsei University Severance Hospital, Korea

SP01-1 Tumor Microenvironment on Metastasis Research *27*
Zena Werb
Department of Anatomy, University of California, San Francisco, U.S.A.

SP01-2 Circulating Tumor Cell *28*
Min Yu
Stem Cell Biology and Regenerative Medicine, University of Southern California, U.S.A.

SP01-3 PDX *30*
Hyeong-Gon Moon
Department of Surgery, Seoul National University Hospital, Korea

14:40-15:50 Panel Discussion 1: Breast Cancer Screening — Lotus Hall

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

PN01-1 Pros — *12*
Haydee Ojeda-Fournier
Department of Radiology, UC San Diego Health System, Moores Cancer Center, U.S.A.

PN01-2 Cons — *14*
Jae Kwan Jun
National Cancer Control Institute, National Cancer Center, Korea

14:40-15:50 Oral Presentation 1 — Weolla Room

Moderator Vani Parmar
Department of Surgical Oncology, Tata Memorial Hospital, India
Byung Ho Son
Department of General Surgery, ASAN Medical Center, Korea

OP01-1 Alisher Kakhkharov — *112*
Tashkent medical academy, Uzbekistan

OP01-2 Kyung Hwan Kim — *113*
Yonsei Cancer Center, Yonsei University College of Medicine, Korea

OP01-3 Kun Wang — *114*
Guangdong General Hospital

OP01-4 Guiyun Sohn — *115*
ASAN Medical Center, Korea

OP01-5 Joanne Wing Yan Chiu — *116*
Queen Mary Hospital, University of Hong Kong

OP01-6 Kai Chen — *118*
Sun Yat-sen Memorial Hospital, Sun Yat-sen University

OP01-7 Lu Cao — *119*
Fudan University Shanghai Cancer Center

OP01-8 Ji Hyun Park — *120*
ASAN Medical Center

15:50-16:00 Coffee Break

16:00-17:10 Symposium 2: Management Issues after Neoadjuvant Chemotherapy — Halla Hall

Moderator Seigo Nakamura
Department of Surgery, Division of Breast Surgical Oncology, Showa University, Japan
Kyung-Hwan Shin
Proton Therapy Center/Radiation Oncology, National Cancer Center, Korea

SP02-1 Radiation Therapy after NAC (Neoadjuvant Chemotherapy) — *31*
Julia White
Department of Radiation Oncology, The Ohio State University, U.S.A.

SP02-2 Surgical Issues *33*
Hiram S. Cody III
Breast Service, Department of Surgery, Memorial Sloan Kettering Cancer Center, U.S.A.

SP02-3 Response Evaluation *35*
Haydee Ojeda-Fournier
Department of Radiology, UC San Diego Health System, Moores Cancer Center, U.S.A.

16:00-17:10 Panel Discussion 2: PMRT in N1 Lotus Hall

Moderator Chang-Ok Suh
Department of Radiation Oncology, Yonsei University, Korea

PN02-1 Pros *15*
Jin Hee Kim
Department of Radiation Oncology, Keimyung University Dongsan Medical Center, Korea

PN02-2 Cons *17*
Won Park
Department of Radiation Oncology, Samsung Medical Center, Korea

16:00-17:10 Education Session 1: Recent Update in Management of Breast Cancer Weolla Room

Moderator Nam Sun Paik
Division of Breast Surgery, Ewha Womans University Cancer Center for Women, Korea

ED01-1 Medical Oncology *86*
Jin-Hee Ahn
Department of Oncology, ASAN Medical Center, Korea

ED01-2 Surgical Oncology *88*
Kazuhiko Sato
Department of Breast Oncology, Tokyo West Tokushukai, Japan

ED01-3 Radiation Oncology *90*
Yong Bae Kim
Department of Radiation Oncology, Yonsei University Medical Center, Korea

18:30:20:00 Welcome Reception Halla Hall

April 24 (Fri.), 2015

07:30-08:10 Breakfast Symposium 1 (Sponsored by Sanofi-Aventis) Halla Hall

Moderator Kyung Hae Jung
Department of Oncology, ASAN Medical Center, Korea

BS01 Adjuvant Non-Anthracycline Regimen in Operable Breast Cancer - Changing the Standard of Care *102*
Yeesoo Chae
Department of Oncology, Kyungpook National University Medical Center, Korea

08:10-08:30 Coffee Break

08:30-09:30 Plenary Lecture 3 Halla Hall

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

PL03 Precision Medicine - Implications for Breast Cancer Clinical Trial Design *7*
Jo Anne Zujewski
Clinical Investigations Branch, Cancer Therapy Evaluation Program, NIH Clinical Center, U.S.A.

09:30-09:40 Coffee Break

09:40-10:50 Symposium 3: TNBC (Triple Negative Breast Cancer) Halla Hall

Moderator Chiun-Sheng Huang
Department of Surgery, National Taiwan University Hospital, Taiwan
Jee Hyun Kim
Department of Internal Medicine, Seoul National University Bundang Hospital, Korea

SP03-1 Current Management of TNBC *37*
Joohyuk Sohn
Department of Internal Medicine, Yonsei University Medical Center, Korea

SP03-2 Heterogeneity of TNBC *38*
Rebecca Dent
Division of Medical Oncology, National Cancer Centre Singapore, Singapore

SP03-3 Subtype-Directed Therapy of TNBC *39*
Ruth M. O'Regan
Division of Hematology/Oncology, University of Wisconsin, U.S.A.

09:40-10:50 Symposium 4: Targeted Therapy in Breast Cancer Lotus Hall

Moderator Janice Tsang
Department of Clinical Oncology, Queen Mary Hospital / Hong Kong Breast Oncology Group, Hong Kong
Kyung Hae Jung
Department of Oncology, ASAN Medical Center, Korea

SP04-1 PD1/PDL1 Targeted Immunotherapy in Breast Cancer 41
David Page
Department of Medicine, Memorial Sloan-Kettering Cancer Center

SP04-2 PI3K/AKT/mTOR Pathway Inhibitors in Breast Cancer 42
Yoon Sim Yap
Department of Medical Oncology, National Cancer Centre Singapore, Singapore

SP04-3 CDK 4/6 Inhibitors 43
Sudeep Gupta
Department of Medical Oncology, Tata Memorial Centre/Hospital, India

10:50-11:00 Coffee Break

11:00-12:10 Symposium 5: Hormone Positive Breast Cancer — Halla Hall

Moderator
Chikako Shimizu
Department of Breast and Medical Oncology, National Cancer Center, Japan
Sei-Hyun Ahn
Department of Surgery, ASAN Medical Center, Korea

SP05-1 Adjuvant Endocrine Therapy in Postmenopausal Women 44
Seigo Nakamura
Department of Surgery, Division of Breast Surgical Oncology, Showa University, Japan

SP05-2 Adjuvant Endocrine Therapy in Premenopausal Women in 2015 45
Woo Chul Noh
Department of Surgery, Korea Cancer Center Hospital, Korea

SP05-3 Luminal B Breast Cancer 47
Giuseppe Viale
Department of Pathology, IEO Istituto Europeo di Oncologia, Italy

11:00-12:10 Symposium 6: Companion Diagnostics — Lotus Hall

Moderator
Ju-Seog Lee
Systems Biology, MD Anderson Cancer Center, U.S.A.
Woo-Hee Jung
Department of Pathology, Gangnam Severance Hospital, Korea

SP06-1 Ki-67 Labeling Index in Breast Cancer 48
Gyungyub Gong
Department of Pathology, ASAN Medical Center, Korea

SP06-2 ER, PR and HER2 Testing in Breast Cancer 50
Young Kyung Bae
Department of Pathology, Yeungnam University Medical Center, Korea

SP06-3 NGS-Based Diagnostics 51
Woong-Yang Park
Samsung Genome Institute, Samsung Medical Center, Korea

DAY 2

12:10-13:10 Luncheon Symposium 2 (Sponsored by Roche) — Halla Hall

Moderator Toru Watanabe
Department of Medicine, Hamamatsu Oncology Center, Japan

LS02 Current and Future Perspectives in Treatment of Metastatic TNBC *105*
Yeon Hee Park
Department of Hematology-Oncology, Samsung Medical Center, Korea

13:10-13:30 Coffee Break

13:30-14:30 Plenary Lecture 4 — Halla Hall

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

PL04 Steps towards Precision Treatment in Breast Cancer: Lessons from Safir01 Trial *8*
Fabrice Andre
Breast Cancer Unit, Isnstitut Gustave Roussy, France

13:20-14:30 ABRCA — Lotus Hall

Moderator Soo Hwang Teo
Breast Cancer Research Group / Faculty of Medicine, Cancer Research Initiatives Foundation, Malaysia
Sung-Won Kim
The Breast & Endocrine Service, Department of Surgery, Daerim St. Mary's Hospital, Korea

AB01-1 Cancer Genetic Risk Assessment in Breast Cancer *73*
Soo Hwang Teo
Breast Cancer Research Group / Faculty of Medicine, Cancer Research Initiatives Foundation, Malaysia

AB01-2 Clinical Significance of Variants of Unknown Significance (VUS) in BRCA1/2 Genes *74*
Ava Kwong
Department of Surgery, Queen Mary Hospital, Hong Kong

AB01-3 Risk-Reduction Surgery in BRCA Mutation Carriers *75*
Sung-Won Kim
The Breast & Endocrine Service, Department of Surgery, Daerim St. Mary's Hospital, Korea

AB01-4 Genetic Counseling in Asia *77*
Seigo Nakamura
Department of Surgery, Division of Breast Surgical Oncolog, Showa University, Japan

14:30-14:40 Coffee Break

14:40-15:50 Symposium 7: Hereditary Breast Cancer — Halla Hall

Moderator Ava Kwong
Department of Surgery, Queen Mary Hospital, Hong Kong
Sung-Won Kim
The Breast & Endocrine Service, Department of Surgery, Daerim St. Mary's Hospital, Korea

SP07-1 Management of BRCA1/2 Mutation Carriers *52*
Steven Narod
Familial Breast Cancer Research Unit, Women's College Research Institute, Canada

SP07-2 Characterising Cancer Risks for Carriers of Mutations in BRCA1, BRCA2, PALB2 and RAD51C Genes *53*
Antonis Antoniou
Public Health and Primary Care, University of Cambridge, U.K.

SP07-3 Absolute Risks and Hormonal/Lifestyle Risk Modifiers among BRCA Mutation Carriers, the IBCCS Experience *54*
Matti Rookus
Department of Epidemiology, Netherlands Cancer Institute, Netherland

14:40-15:50 Panel Discussion 3: Role of Trustuzumab in Small HER2+ Early Breast Cancer Lotus Hall

Moderator Yen-Shen Lu
Department of Oncology, National Taiwan University Hospital, Taiwan

PN03-1 Pros *19*
Seock-Ah Im
Department of Internal Medicine, Seoul National University Hospital, Korea

PN03-2 Cons *20*
Janice Tsang
Department of Clinical Oncology, Queen Mary Hospital, Hong Kong

14:40-15:50 Oral Presentation 2 Weolla Room

Moderator Visnu Lohsiriwat
Department of Surgery, Faculty of Medicine Siriraj Hospital, Thailand
Renbin Liu
The Breast Cancer Center, The Third Affiliated Hospital, China

OP02-1 Annie Tsz-Wai Chu *122*
The University of Hong Kong

OP02-2 Zhengkui Sun *124*
Jiangxi Cancer Hospital

OP02-3 Kevin Nguyen *125*
The University of Melbourne

OP02-4 John Hopper *127*
The Unversity of Melbourne

OP02-5 Hee Jeong Kim *129*
ASAN Medical Center

OP02-6 Tae In Yoon *131*
ASAN Medical Center

OP02-7 Marek Svoboda *132*
Masaryk Memorial Cancer Institute

OP02-8 Jun Ho Lee *134*
Samsung Medical Center, Sungkyunkwan University School of Medicine

15:50-:16:00 Coffee Break

DAY 2

16:00-17:10 Panel Discussion 4: Oncoplastic Surgery for Small Breast — Halla Hall

Moderator Ho Yong Park
Department of Surgery, Kyungpook National University Hospital, Korea

PN04-1 Pros 21
Barbara Lynn Smith
Division of Surgical Oncology, Massachusetts General Hospital, U.S.A.

PN04-2 Cons 23
Ava Kwong
Department of Surgery, Queen Mary Hospital, Hong Kong

16:00-18:00 Nursing Session: Women's Health Care in Breast Cancer — Lotus Hall

Moderator Mi Young Kang
Department of Oncology, Cheil General Hospital, Korea

NS01-1 Women's Health Care in Breast Cancer 78
So Young Park
Department of Internal Medicine, Cheil General Hospital, Korea

NS01-2 Managing Menopausal Symptoms among Breast Cancer Survivors 79
Hye Jin Joh
Seoul St. Mary's Hospital, Korea

NS01-3 Adopting Self-Awareness after Breast Treatment 81
Young Ran Yoon
Nursing Department of Woman Cancer Center, EWHA Womans University Mokdong Hospital, Korea

NS01-4 Pregnancy in Young Women with Breast Cancer 82
Eunkyung Hwang
Breast Care Center, Seoul National University Hospital, Korea

NS01-5 The Role of Oncology Nurse in Sexual Management 83
Eun-Young Jun
Nursing, Daejeon University, Korea

16:00-17:10 Education Session 2: Cancer Genomics — Weolla Room

Moderator Lee Su Kim
Division of Breast and Endocrine Surgery, Hallym University Sacred Heart Hospital, Korea

ED02-1 Understanding of Genomics Technology 92
Ju-Seog Lee
Systems Biology, MD Anderson Cancer Center, U.S.A.

ED02-2 Overview of Breast Cancer Genomics 93
Joon Jeong
Department of Surgery, Division of Breast and Endocrine Surgery, Gangnam Severance Hospital, Korea

17:00-18:00 Panel Discussion 5: Oncoplastic Surgery — Halla Hall
: Reconstruction Using Autologous Tissue vs. Artificial Implant

Moderator Barbara Lynn Smith
Division of Surgical Oncology, Massachusetts General Hospital / Harvard Medical School, U.S.A.

PN05-1 Autologous Tissue *24*
Kyung Won Minn
Department of Plastic and Reconstructive Surgery, Seoul National University Hospital, Korea

PN05-2 Artificial Implant *25*
Yoshiko Iwahira
Breast Surgery Clinic, Japan

18:00-19:00 Dinner Symposium (Sponsored by Kyowa Kirin) — Halla Hall

Moderator Jung Han Yoon
Division of Breast-Endocrine Surgery, Chonnam National University Hwasun Hospital, Korea

DS01 Clinical Impacts of Primary Prophylaxis for FN(Febrile Neutropenia) in Breast Cancer Patients *108*
Young Jin Suh
Breast Surgical Oncology/Surgery, St. Vincent's Hospital, Korea

DAY 3

April 25 (Sat.), 2015

07:30-08:10 Breakfast Symposium 2 (Sponsored by Novartis) — Halla Hall

Moderator — Benita Tan
Singhealth Duke-NUS Breast Centre, Singapore General Hospital & National Cancer Center, Singapore

BS02 — The Role of The Everolimus in The Treatment Landscape for ER+ Advanced Breast Cancer Patients — *110*
Fabrice Andre
Breast Cancer Unit, Institut Gustave Roussy, France

08:10-08:30 Coffee Break

08:30-09:30 Plenary Lecture 5 — Halla Hall

Moderator — Jungsil Ro
Center for Breast Cancer, National Cancer Center, Korea

PL05 — Development of Multinational Breast Cancer Data Base: Strategy and Challenge — *9*
Byung Ho Nam
Center for Clinical Trials, National Cancer Center, Korea

08:30-09:30 Survivorship Session 1: Cohort Study in Breast Cancer Survivor — Lotus Hall

Moderator — Wei Zheng
Division of Epidemiology, Vanderbilt Uni. School of Medicine, U.S.A.
Eun Sook Lee
Research Institute / Center for Breast Cancer, National Cancer Center, Korea

SS01-1 — Breast Cancer Survivor Study from the Shanghai Women's Health Study — *63*
Wei Zheng
Division of Epidemiology, Vanderbilt Uni. School of Medicine, U.S.A.

SS01-2 — The Pathways Study: a Prospective Study of Breast Cancer Survivorship — *64*
Janise M. Kim Roh
Division of Research, Kaiser Permanente Northern California, U.S.A.

SS01-3 — Breast Cancer Survivors in Korea: Today and Tomorrow — *66*
So-Youn Jung
Department of Surgery, Center of Breast Cancer, National Cancer Center, Korea

09:30-09:40 Coffee Break

DAY 3

09:40-10:50 Symposium 8: Tumor Registry — Halla Hall

Moderator Young Jin Suh
Breast Surgical Oncology/Surgery, St. Vincent's Hospital, Korea

SP08-1 Breast Cancer in the Gulf: Building an Integrated Registry *55*
Shaheenah Dawood
Dubai Hospital, U.A.E.

SP08-2 National Clinical Database - Breast Cancer Registry in Japan *56*
Reiko Yoshida
Breast Center, Showa University, Japan

SP08-3 From institutional to Territory-Wide Breast Cancer Registry – The Hong Kong Experience *57*
Roger Kai Cheong Ngan
Department of Clinical Oncology, Queen Elizabeth Hospital, Hong Kong

09:40-10:40 Survivorship Session 2: Recent Update of Breast Cancer Survivor Research — Lotus Hall

Moderator Kazuhiko Sato
Department of Breast Oncology, Tokyo West Tokushukai, Japan
Ku Sang Kim
Breast-Thyroid Center, Ulsan City Hospital, Korea

SS02-1 Nutrition for Breast Cancer Survivors *67*
Jung Eun Lee
Department of Food & Nutrition, Sookmyung Women's University, Korea

SS02-2 Breast Cancer Survivorship: Cultural and Socio-Ecologic Considerations *68*
Kimlin Tam Ashing
Department of Population Sciences, City of Hope Comprehensive Cancer Center, U.S.A.

SS02-3 Targeting Distress During the Treatment of Breast Cancer Survivors *71*
Jong Won Lee
Department of Surgery, Division of Breast and Endocrine Surgery, ASAN Medical Center, Korea

DAY 3

09:40-10:50 Oral Presentation 3 — Weolla Room

Moderator
Thinh Dang Huy Quoc
Department of Radiation Oncology, Ho Chi Minh City Oncology Hospital, Vietnam
Jae Hong Seo
Department of Medical Oncology, Korea University Guro Hospital, Korea

10:50-12:00 Symposium 9: Issues in the Management of Asian Countries — Halla Hall

Moderator
Yong-Sheng Wang
Breast Cancer Center, Shandong Cancer Hospital & Institute, China
Chanheun Park
Breast-Thyroid Cancer Center, Kangbuk Samsung Hospital, Korea

DAY 3

10:50-12:00 Education Session 3: Career Development — Lotus Hall

Moderator Daniel F. Hayes
Internal Medicine, Hematology Oncology, University of Michigan Comprehensive Cancer Center, U.S.A.
Young-Jin Suh
Breast Surgical Oncology/Surgery, St. Vincent's Hospital ,Korea

ED03-1 How to Write a Good Research Grant Proposal *94*
Fabrice Andre
Breast Cancer Unit, Institut Gustave Roussy, France

ED03-2 Career Development as a Junior Researcher *95*
Daniel F. Hayes
Internal Medicine, Hematology Oncology, University of Michigan Comprehensive Cancer Center, U.S.A.

ED03-3 How to Succeed as a Private Breast Practitioner in Korea *96*
Heeboong Park
Breast Clinic, Park Surgical Clinic, Korea

ED03-4 How to Build and Maintain the Multinational Network *97*
Vani Parmar
Department of Surgical Oncology, Tata Memorial Hospital, India

10:50-12:00 Oral Presentation 4 — Weolla Room

Moderator Teresa T Sy Ortin
Benavides Cancer Institute, University of Santo Tomas Hospital, Philippines
Keun Seok Lee
Center for Breast Cancer, National Cancer Center, Korea

OP04-1 Tsun Leung Chan *147*
Hong Kong Sanatorium and Hospital

OP04-2 Seokwon Lee *148*
Biomedical Research Institute, Pusan National University Hospital

OP04-3 David Teguh *149*
Academic Medical Center (AMC), University of Amsterdam (UVA)

OP04-4 Min Hee Hur *150*
Cheil General Hospital and Women's Healthcare Center, Kwandong University College of Medicine

OP04-5 Danbee Kang *152*
SAHIST, Sungkyunkwan University

OP04-6 Yongsheng Wang *154*
Shandong Cancer Hospital and Institute

OP04-7 Beom Seok Ko *156*
University of Ulsan, College of Medicine, ASAN Medical Center

OP04-8 Ha Woo Yi *158*
Samsung Medical Center, Sungkyunkwan University School of Medicine

12:00-12:10 Closing Ceremony — Halla Hall

POSTER EXHIBITION

Plenary Lecture

GBCC 2015 & 4th IBCS
Abstract Book

Genetic Signature in Selecting Adjuvant Treatment: Early vs. Late Recurrence (Genetic Signatures in Selecting Adjuvant Treatment)

Daniel F. Hayes

Division of Hematology/Oncology, Department of Internal Medicine, University of Michigan Comprehensive Cancer Center, U.S.A.

Adjuvant systemic therapy for early stage breast cancer clearly reduces the odds of recurrence and mortality. Estrogen receptor (ER) and HER2 are used to select patients who should or should not receive adjuvant endocrine therapy (ET) or anti-HER2 therapy (such as trastuzumab), respectively. However, currently, there are no reliable and validated biomarkers that identify patients for whom adjuvant chemotherapy is unlikely to be active. Therefore, the decision to give or withhold adjuvant chemotherapy is based on prognosis. Clinical and pathologic prognostic factors (TNM) are important considerations, but more recently tumor biology has also entered the decision-making arena. For patients with node negative, ER positive, HER2 negative tumors, multi-gene assays, such as the 21-gene recurrence score (RS) (OncotypeDx™) have been found to be reliable indicators of subsequent relapse. Patients with node negative, ER positive, HER2 negative tumors that have a low RS, and who reliably take adjuvant endocrine therapy for at least 5 years or more, have a < 10% chance of developing metastases over the subsequent 10 years. If we assume that adjuvant chemotherapy reduces the odds of recurrence by approximately one-third, then no more than 2-3%, at most, patients can benefit from it, and this absolute benefit does not outweigh the 1-3% risk of life-threatening or long-term life altering toxicities, such as infection, bleeding, heart failure, secondary leukemia, or peripheral neuropathy. Thus, the American Society of Clinical Oncology Breast Cancer Tumor Marker Guidelines Panel recommends use of the 21-gene RS to determine if such patients should not have adjuvant chemotherapy. More recently, other assays, such as the PAM50, Endopredict, and the Breast Cancer Index (BCI) have been reported to be similarly useful in this setting.

A second issue is whether chemotherapy may not work in patients with low RS, or "luminal A" cancers. In other words, regardless of prognosis, if the chemotherapy does not work, it should not be given, in a manner similar to not recommending ET or anti-HER2 therapies to patients with negative ER or HER2 cancers. Several historical studies have suggested that ER positive cancers are less likely to respond to chemotherapy

than ER negative ones. More recently, two studies have suggested that cancers with low RS/luminal A phenotypes are resistant to chemotherapy, in the node negative and node positive settings. However, the Early Breast Cancer Trialists Cooperative Group did not identify a subset of patients for whom chemotherapy appeared to be inactive. Therefore, SWOG is conducting a prospective randomized clinical trial testing whether chemotherapy does or does not work in node positive, ER positive breast cancer with low RS (S1007, the RxPonder trial). In the meantime, the 21-gene RS or equivalent assays can be used to elect not to treat node negative, ER positive, HER2 negative patients with adjuvant chemotherapy, but outside of a research trial, adjuvant chemotherapy is recommended for those with node positive disease.

Management of the Axilla Post z0011: Where Do We Go from Here?

Hiram S. Cody III

Breast Service, Department of Surgery, Memorial Sloan Kettering Cancer Center, U.S.A.

The widespread adoption of sentinel lymph node (SLN) biopsy as standard care for axillary staging in cN0 breast cancer is supported by the results of at least 69 observational studies, 7 randomized trials, 3 meta-analyses, an ASCO Guideline, and an extensive literature covering all aspects of the procedure. These studies establish that patients with *negative SLN* do not require axillary dissection (ALND), that axillary local recurrence (LR) after a negative SLN biopsy is rare (0.3%), that disease-free (DFS) and overall survival (OS) are unaffected by the addition of ALND to SLN biopsy, and that the morbidity of SLN biopsy is less than that of ALND. The logical next question in the evolution of axillary staging is to ask whether there are SLN-positive patients who can avoid ALND, and it is clear that there are: 50% or more of *SLN-positive* patients have disease limited to the SLN.

Do all patients with positive SLN require ALND? Large retrospective studies from the National Cancer Data Base (1998-2006, n = 97,314) and from the SEER database (1998-2004, n = 26,986) observed declining rates of ALND for SLN positive patients; 11-23% with SLN macrometastases and 33-36% with SLN micrometastases did not have ALND, with no effects on axillary LR or on survival. More definitive answers come from two randomized trials, IBCSG 23-01 and ACOSOG Z0011. In IBCSG 23-01, 931 patients with SLN micrometastases were randomized to ALND vs no ALND; additional positive nodes were found in 13% of the ALND arm, but at 5 years there were no differences in local, regional or distant relapse, or in death from disease. In ACOSOG Z0011 813 patients cT1-2N0 breast cancer and 1-2 positive SLN were randomized to ALND vs no further surgery. All were SLN-positive by *routine H&E staining* and all had breast conservation including whole-breast RT; patients with 3 or more positive SLN (or with matted nodes) were excluded and axillary-specific RT was not allowed. Additional positive nodes were found in 27% of ALND arm, but at 6 years there were no differences between the ALND and no-ALND arms in local (3.6% vs 1.9%), regional (0.5% vs 0.9%), or overall locoregional recurrence (4.1% vs 2.8%), nor were there any differences in disease-free or overall survival.

The principal implications of Z0011 are surgical, and over the last 2 years many in-

stitutions and surgeons in the US have found the results to be persuasive and practice-changing, incorporating into their treatment guidelines a policy of "no-ALND" for SLN-positive patients who meet the Z0011 selection criteria. At our institution we have done so since 2010; for "Z0011-like" patients we have largely abandoned preoperative axillary ultrasound, axillary FNA-core biopsy, and intraoperative frozen section of SLN, with a substantial decline in the rate of completion ALND for SLN-positive patients. The response to Z0011 worldwide, and especially in Europe, has been mixed; the 2011 St Gallen Consensus acknowledged the results of Z0011 without making a straightforward recommendation, but a substantial majority of panelists in the most recent 2015 St Gallen Consensus supported Z0011 (Monica Morrow, personal communication).

What are the implications of Z0011 for the medical oncologist? Two large trials which randomized SLN-positive patients to ALND vs no-ALND (ACOSOG Z0011) and ALND vs axillary RT (EORTC AMAROS) found no differences in the usage of chemotherapy, hormonal therapy, or RT based on the performance of ALND.

What are the implications of Z0011 for the radiation oncologist? Positive axillary nodes were left behind in a presumed 27% of the Z0011 patients in the no-ALND arm, but only 0.9% developed axillary LR. Although the Z0011 protocol did not allow the use of supraclavicular or axillary RT, a recent audit found that more than 50% of the evaluable Z0011 patients received "high tangents" and about 20% of patients had received RT to axillary and/or supraclavicular nodes. Although these protocol violations were equally distributed between the two study arms, they may in part account for the low rates of axillary LR.

Looking ahead, can we extend the success of Z0011 to Z0011-ineligible patients, specifically those treated a) by mastectomy *without* RT, b) by *partial* breast RT (PBI), and c) by neoadjuvant chemotherapy (NAC)?

Regarding mastectomy, we have recently reported on 535 SLN-positive patients from the pre-Z0011 era who had either mastectomy or breast conservation *without other axillary-specific treatment*: among 234 with N1mi or N1 disease, there were no differences at 4 years in regional node recurrence between mastectomy (97 patients, 2.5%) and breast conservation (134 patients, 1.5%). These results are encouraging but are subject to selection bias, require confirmation on a wider basis, and are not sufficient to change practice.

Regarding PBI, the MammoSite Registry Trial (in which PBI was delivered through an intracavitary balloon) has reported 5-year axillary LR of 0.8% in SLN-negative patients, a result quite similar to that of negative SLN biopsy in general (0.3%). TARGIT, an international multicenter randomization of PBI given as a single intraoperative dose

to the tumor site (in 1,113 patients) vs conventional whole-breast RT (in 1,119 patients); 4 year LR was 1.20% and 0.95%, respectively ($p = 0.41$). Since most of the above patients were SLN negative, the data to support a policy of "no-ALND" for SLN-positive patients treated with PBI are insufficient.

Regarding neoadjuvant chemotherapy (NAC), the false-negative rate of SLN biopsy *after NAC* (in 27 studies comprising 2148 patients) is roughly comparable to that of SLN biopsy in general, 10.5%. Two important trials have addressed this question prospectively, ACOSOG 1071 (Alliance) and SENTINA. ACOSOG 1071 is a prospective observational validation study in which 708 patients with biopsy proven cN1-2 nodal metastasis received NAC followed by SLN biopsy and a "backup" ALND. The success rate of SLN biopsy was 92.5%, 40% of patients were ypN0, and with the removal of at least 2 SLN the FNR was 12.6%. In SENTINA, 1737 patients were stratified by clinical node status. Among those who were cN1-2 *prior to NAC* and became cN0 or were SLN-positive *after NAC*, SLN were identified in 80% and the FNR was 14%. Both studies emphasize the importance of technique for SLN biopsy post-NAC; FNR were higher in patients mapped with a single agent (16-20%) or only one SLN was removed (24-31%). With dual agent mapping and the removal of 3 or more SLN, the FNR in both studies were an acceptable 5-9%).

The historic rationale for axillary surgery in breast cancer is threefold: prognostication, local control, and the possibility of a survival benefit. Prognostication and the prediction of response to therapy are increasingly based on primary tumor characteristics and gene expression profiling rather than axillary node status. Local control and survival in SLN-positive patients are comparable for ALND vs axillary RT. Improvement in systemic therapies increases survival but enhances local control as well. It seems clear that the next generation of clinical trials for cN0 patients will compare SLN biopsy to no axillary staging at all, and for cN1-2 disease will use new combinations of NAC and RT to minimize the extent of axillary surgery. The "SLN biopsy of the future" may be no SLN biopsy at all and that the "ALND of the future" will increasingly be limited to the salvage of locally persistent or recurrent disease.

Precision Medicine - Implications for Breast Cancer Trial Design

Jo Anne Zujewski

Clinical Investigations Branch, Cancer Therapy Evaluation Program, National Cancer Institute, U.S.A.

Breast cancer is the leading cause of cancer in women world-wide. In 2015, Precision medicine is an emerging approach for disease treatment and prevention that takes into account individual variability in genes, environment, and lifestyle for each person. While significant advances in precision medicine have been made for select cancers, the practice is not currently in use for most diseases. Efforts are underway to help make precision medicine the norm rather than the exception. In 2000, it was recommended that most women diagnosed with early stage breast cancer should receive combination chemotherapy. Those who had tumors that were hormone receptor positive should also receive hormonal therapy. Since that time, it has been recognized that breast cancer can be characterized into at least 5 different molecular subtypes based upon the gene expression profile in the tumor (luminal A, Luminal B, HER2 enriched, basaloid, and normal). Each subtype also exhibits marked heterogeneity. Initiatives such as the Cancer Genome Atlas have characterized the genomic landscapes for breast cancer has been characterized and valuable new insights into 'driver' mechanisms responsible for the origin and progression of breast cancer. Although not all targets are 'druggable' at this time, the cancer genome reporting has led to a number of hypothesis-driven drug discovery efforts. In addition, large-scale screens with carefully genomically annotated tumor cell lines also result in the identification of genetic, lineage and gene-expression-based predictors of drug sensitivity Molecular diagnostic tools need to be developed to identify which subgroups of patients will benefit from particular therapeutics. Scientific evidence needed to move the concept of precision medicine into every day clinical practice. Ongoing research is focused on developing agents targeted towards aberrant pathways as well as understanding the mechanisms of drug response and drug resistance. A new paradigm for clinical trial design is clearly needed. Using molecular markers to stratify patients into appropriate clinical trials can improve success rates of trials. There have been efforts developing the most efficient way of testing multiple drugs in a trial with patients of multiple types of cancer as well as multiple subtypes of the same cancer.

PL04

Steps towards Precision Treatment in Breast Cancer: Lessons from Safir01 Trial

Fabrice Andre

Breast Cancer Unit, Institut Gustave Roussy, France

Development of Multinational Breast Cancer Data Base: Strategy and Challenge

Byung Ho Nam

Center for Clinical Trials, National Cancer Center, Korea

According to WHO's report, 1.7 million women were diagnosed with breast cancer in 2012 and there were 6.3 million women alive who had been diagnosed with breast cancer in the previous five years. Since the 2008 estimates, breast cancer incidence has increased by more than 20%, while mortality has increased by 14%. Breast cancer is also the most common cause of cancer death among women (522,000 deaths in 2012) and the most frequently diagnosed cancer among women in 140 of 184 countries worldwide. It now represents one in four of all cancers in women.

Incidence has been increasing in most regions of the world, but there are huge inequalities between rich and poor countries. Incidence rates remain highest in more developed regions, but mortality is relatively much higher in less developed countries due to a lack of early detection and access to treatment facilities. For example, in western Europe, breast cancer incidence has reached more than 90 new cases per 100,000 women annually, compared with 30 per 100,000 in eastern Africa. In contrast, breast cancer mortality rates in these two regions are almost identical, at about 15 per 100,000, which clearly points to a later diagnosis and much poorer survival in eastern Africa.

"An urgent need in cancer control today is to develop effective and affordable approaches to the early detection, diagnosis, and treatment of breast cancer among women living in less developed countries," explains Dr Christopher Wild, Director of IARC. "It is critical to bring morbidity and mortality in line with progress made in recent years in more developed parts of the world."

International collaboration is needed to examine and evaluate current worldwide status of incidents, prevention, screening, treatment, survival, quality of lives, etc. of breast cancer patients. To develop a comprehensive platform for database structure and incorporate all these information from all over the world, and facilitate those data base would be a huge challenge. A detail, and thoroughly planned strategy should be developed. Each country has different system for cancer registry, government regulation, health care and insurance, treatment, etc. Depending on the objectives of developing multinational database, different approaches should be employed. Examining each country's cancer registry system would be a good start. Possibly a pilot study can be

performed to investigate feasibility of constructing an international breast cancer patient cohort by selecting several countries. Through this pilot study, we can develop a practical logistic procedure for developing and operating multinational breast cancer database. It would require each country's sincere commitment and serious effort with financial support. Even though it is not an easy task, but will be definitely rewarding for all of us.

Panel Discussion

GBCC 2015 & 4th IBCS
Abstract Book

PN01-1

Breast Cancer Screening: Pros

Haydee Ojeda-Fournier

Department of Radiology, UC San Diego Health System, Moores Cancer Center, U.S.A.

Breast cancer remains the most common cancer in American women and accounts for 29% of all female cancer in the United States. The lifetime risk of an American woman being diagnosed with breast cancer is 1 in 8. The American Cancer Society estimates that in 2015 there will be 231,840 cases or invasive breast carcinoma and an additional 60,290 cases of in situ disease. In addition, 40,290 deaths are estimated to occur in 2015. Breast cancer screening has become highly politicized in the United States. Heated debates regarding the efficacy of mammographic screening, limitations caused by breast density, age to start screening, and supplemental imaging for breast cancer diagnosis has become a frequent lay media occurrence.

The basic principles for screening populations include: 1) Disease has to be common, 2) There is an asymptomatic period, 3) There is effective treatment during the asymptomatic period, 4) The screening test is highly sensitive and specific, and 5) The test is affordable with low risk to the patient. Breast cancer screening with mammography meets most of the requirements for screening since the breast cancer is common and important, there is an asymptomatic period during which the detection of the disease can be of benefit because of effective treatment, and the test used for screening, that is mammography, is inexpensive and readily available. Screening mammography has moderate sensitivity, however it lacks specificity.

There is enough evidence to suggest that women should not be routinely taught self-breast exam as there is no clear benefit and there is a documented potential harm from unnecessary biopsies driving higher costs. Likewise, the efficacy of the clinical breast exam (CBE) has been called into question although it is routinely used as an adjunct to mammography, and in some countries, as the main approach to breast cancer screening.

Mammography continues to be the gold standard in screening for breast cancer and is the only imaging modality to have been studies in large population based randomized clinical trials. More that 93% of the studies in the United States are performed with digital technology on dedicated mammography units, with specialty trained radiologists and technologist, and medical physicist closely overseeing the quality assurance and quality control of the operational mammographic units.

The standard bilateral screening mammogram consists of four views: bilateral cra-

niocaudal and bilateral mediolateral oblique views. "Craniocaudal" and "mediolateral oblique" indicate the direction of the x-ray beam. The sensitivity and specificity of mammography from data from seven randomized controlled trials ranged from 68-88% and 82-98% respectively. The negative and positive predictive value and accuracy of mammography has also been reported as 99.8%, 35.8% and 98.6% in one study. Digital breast tomosynthesis (DBT) is essentially a modification of digital mammography that allows for the acquisition of three-dimensional (3D) thin section data of the breast. DBT is emerging as a better mammogram.

Dynamic contrast enhanced breast magnetic resonance imaging (DCE-MR) is the most sensitive study to evaluate the breast regardless of breast density. DCE-MR does not meet criteria for a screening study since it is not widely available, it is expensive, and is not consider acceptable by some since it requires placement of an IV and takes close to one hour to acquire images. There is strong evidence in the literature to support annual DCE-MR screening for women with a known BRCA mutation or untested first-degree relative of a BRCA mutation carrier. Also, the evidence supported annual DCE-MR for patients with a 20-25% lifetime risk of developing breast cancer.

Handheld screening ultrasound has been demonstrated to increase the cancer detection rate compared to mammography however, the American College of Radiology Imaging Network (ACRIN) 6666 trial demonstrated that it is associated with a 5% biopsy rate with a positive predictive value of only 11%. DCE-MR in combination with digital mammography is the best combination to screen patients, especially those at high risk.

Knowledge of the limitations of mammographic screening continues to drive development and investigations of new technologies. Some recent developments such as digital breast tomosynthesis (DBT), are quickly becoming mainstream. Preliminary data suggests that DBT will address some of the limitations of traditional mammography such as imaging the women with dense breast tissue and decreasing recall rates which are mostly due to overlap of tissue on mammography. As new technologies become available, physicians will continue to collect data and make screening recommendations hopefully not based on public opinion but on data.

PN01-2

Breast Cancer Screening: Cons (Why Do We Need to Balance the Benefits and Harms of Breast Cancer Screening in Korea?)

Jae Kwan Jun

National Cancer Control Institute/Graduate School of Cancer Science & Policy, National Cancer Center, Korea

In 1999, the Korean Government embarked on the National Cancer Screening Program (NCSP). The NCSP for breast cancer is recommended to Korean women aged 40 and over, biennially. The total number of examinees in 2012 amounted to 3,351,639 and participation rate was 51.9%. Unfortunately, to date, there is no evidence that the NCSP for breast cancer is effective. Findings from recent largest studies of mammography showed that breast cancer death rate may be unaffected by routine mammographic screening. Despite of them, mammography must be the only proven method for breast screening. However, these latest findings fanned a growing controversy, as experts debate about how to balance mammography's benefits and harms. Much of them have focus on the negative aspects of screening, such as false-positive and negative screens, overdiagnosis and anxiety. Both individuals and the public should be fully and fairly informed about the pros and cons of mammography. Also, the cost-effectiveness should at least be considered during the decision-making process. These issues raise substantial challenges for the informed decision making and the shared decision making for breast cancer screening in Korea.

PN02-1

PMRT in N1: Pros (Post-mastectomy Radiotherapy in N1: Pros)

Jin Hee Kim

Department of Radiation Oncology, Dongsan Medical Center, Korea

Post-mastectomy radiation therapy (PMRT) has been used after mastectomy for many decades. For many women with early-stage breast cancer, mastectomy can remove any detectable macroscopic disease, but some tumor foci might remain in loco-regional tissue (ie, chest wall or regional lymph nodes (LNs)) that could, if untreated, lead to recurrence of the disease and death from breast cancer. Radiotherapy has the potential to eliminate such tumor foci, and guidelines now recommend that PMRT be given for women with four or more positive axillary LNs, but not given for most women with node-negative disease. Patients with stage III breast cancer (four or more positive LNs or T3/T4 primary tumors) have benefit from adjuvant radiation. Most of these guidelines conclude, however, that there is insufficient evidence to make firm recommendations for women with one to three positive LNs. Recently, The EBCTCG presented results for PMRT in The Lancet(1). The results of this EBCTCG meta-analysis clearly confirm that PMRT should be considered equally for patients with one to three involved axillary LNs as it should be for patients with four or more affected axillary LNs.

In these trials of the EBCTCG meta-analysis, 90% of women with one to three positive nodes and 95% of women with four or more positive nodes received some form of systemic treatment for their breast cancer. The most common chemotherapy was CMF (cyclophosphamide, methotrexate, and fluorouracil) and the most common endocrine therapy was tamoxifen. There have been substantial changes in practice since these women were treated. For example, breast screening has improved and local therapies are more targeted. Also, the accuracy of lymph-node analysis has increased, with more frequent use of serial sectioning and more frequent recognition of micro-metastases. Hence, some of the women who were classified as having node-negative disease in these trials might have been found to be node positive if they had been assessed today. Furthermore, many women now receive better systemic therapy that is more effective at treating both local and distant disease. Therefore the absolute risk of a recurrence is likely to be lower for women being considered for PMRT today than for the women in these trials and the absolute risk reductions achieved with radiotherapy are also likely to be smaller. The proportional gains from radiotherapy might, however, be greater for

women irradiated today than suggested by this example, because radiotherapy planning has changed substantially and women today receive better coverage of target areas(2). Furthermore, doses to normal tissues are lower today, so the risks of radiotherapy are also likely to be lower. This meta-analysis also shows the importance of the extent of axillary surgery, with a greater benefit of PMRT for patients who had axillary sampling as compared with a complete axillary dissection, even in node-negative patients. However, it should be noted that the sentinel lymph-node procedure was not yet used in these trials, so care should be taken not to extrapolate the results to this now common procedure. Notwithstanding this limitation, the findings warn against the current trend of omission of further regional treatment after a positive sentinel LN on the basis of data for regional recurrences and short-term follow-up.

In summary, several meta-analyses conclusively demonstrated that radiation has important role in the management of locally advanced breast cancer. By reducing the risk of recurrence after mastectomy, radiation offers an incremental improvement in overall survival. After mastectomy and axillary dissection, PMRT reduced both recurrence and breast cancer mortality in the women with one to three positive lymph nodes in several trials even when systemic therapy was given. Radiation seems offer the greatest benefit when given using modern treatment technique that minimize the risk of normal tissue injury and maximize the probability of tumor control and when given to patients who also receive systemic treatment.

PMRT in N1: Cons

Won Park

Department of Radiation Oncology, Samsung Medical Center, Korea

While the effect of post-mastectomy radiotherapy (PMRT) in pathologic N1 (pN1) breast cancer after mastectomy has been beneficial in recent meta-analysis, the necessity of PMRT in all cases of pN1 is still controversial. Further practice guidelines for PMRT have not been consistent. The NCCN guideline changed its guideline from 'consider' to 'strongly consider' PMRT in pN1 patients. However, the consensus from the St. Gallen breast cancer meeting in 2013 reported that the majority would not advise PMRT for those with pN1, except in the presence of adverse tumor pathology.

A meta-analysis done by EBCTCG included 8,135 women randomly assigned to treatment group during 1964-86 in 22 trials. In the women with pN1, radiotherapy reduced both recurrence and breast cancer mortality after mastectomy. Locoregional recurrence rate at 10 years and breast cancer mortality rate at 15 years reduced from 20.3 % and 50.2% without radiotherapy to 3.8% and 42.3% with radiotherapy, respectively. These results might encourage proponents of PMRT for all women with node positive breast cancer.

However, the risk associated locoregional recurrence without radiotherapy under present systemic and targeted therapy has decreased. In studies by NSABP and ECOG, 13% locoregional recurrence rate without radiation in pN1 breast cancer was reported. Result from 21-gene analysis of NSABP B-28, 10 year cumulative locoregional recurrence rate in pN1 breast cancer patients treated with lumpectomy with radiotherapy or mastectomy without PMRT was only 6%. We analyzed pN1 breast cancer patients treated with mastectomy without radiotherapy or breast conserving surgery. The locoregional recurrence rate was 14%. If the locoregional recurrence rate in pN1 women without radiotherapy was decreased under modern systemic treatment after surgery, the benefit of overall survival with additional radiotherapy might be reduced. Also, because PMRT is associated with long-term side effects that may ultimately negatively impact on patient's quality of life, it is important to identify beneficial patients with PMRT.

Studies attempting to identify clinical-pathologic characteristics and risk of LRR have been conflicting. There are a multitude of risk factors for locoregional recurrence and for predicting the beneficial groups for PMRT in pN1 breast cancer such as tumor

size, pathologic grade, total number of dissected nodes, number of involved lymph nodes, lymph node ratio, lymph node extracapsular extension, involved axillary lymph node level, lymphvascular space invasion, location of the primary tumor and the receptor status for ER, PR, and HER2. More recent analyses of molecular and genetic markers are also under investigation to predict locoregional recurrence.

The ongoing randomized controlled MRC SUPREMO trial (BIG 2-04) is designed to evaluate the results of PMRT in the management of the 3700 patients who underwent mastectomy with pN1 disease or pT2N0 with grade III and/lymphovascular invasion. The recruitment has closed at April 2013. It may provide us better information regarding the role of PMRT in pN1 breast cancer patients.

Role of Trustuzumab in Small HER2+ Early Breast Cancer: Pros

Seock-Ah Im

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Addition of trastuzumab to adjuvant chemotherapy has dramatically reduced the risk of recurrence and has become the standard of care for human epidermal growth factor receptor 2 (HER2)-positive (+) early breast cancer (eBC). No single standard treatment exists for patients with small, node-negative, and HER2+ eBC, because limited number of small node-negative patients were eligible for the pivotal trials of adjuvant trastuzumab. Especially, the pivotal trastuzumab adjuvant trials exclude the patients with tumors less than 1cm.

Retrospective analysis of 965 patients with T1a/b node-negative tumors who did not receive adjuvant systemic therapy revealed lower recurrence-free survival rates in patients with HER2+ eBC than those with HER2 ? eBC (1). Furthermore, patients with small tumors and HER2+ disease have the lowest rates of recurrence-free survival when compared with those with HR-positive or triple-negative disease among 1112 T1a/b eBC (2). Recently, the meta-analysis of five trials: HERA, NCCTG N9831, NSABP B31, PACS 04 and FinHER showed that patients with small tumors ≤ 2 cm benefit substantially from adjuvant trastuzumab therapy in terms of both DFS and OS, regardless of HR status (3).

Now, an uncontrolled trial in this setting has demonstrated that weekly adjuvant treatment with trastuzumab and paclitaxel for 12 weeks, followed by trastuzumab monotherapy for 9 months, was associated with better outcomes than those expected based on historical data: after a median of 4 years follow up, 12 relapses were seen among 406 patients, equating to a 98.7% 3-year invasive-disease-free survival rate. However, grade 3 neuropathy and clinically relevant asymptomatic declines in ejection fraction were each reported for 13 patients, and two patients had symptomatic congestive heart failure. Although promising, these results do not confirm trastuzumab therapy as the standard for all patients with small, HER2+ eBC, and particularly those with $\leq$ 0.5 cm (T1a) tumors or ER+ $\leq$ 1 cm (T1a/b) tumors. Paclitaxel and trastuzumab can be considered a reasonable and appealing approach for the majority of patients with stage I HER2+ eBC and standard regimens from the pivotal trials can be considered for patients with particularly high risk features.

PN03-2

Role of Trustuzumab in Small HER2+ Early Breast Cancer: Cons

Janice Tsang

Department of Clinical Oncology, Queen Mary Hospital/Hong Kong Breast Oncology Group, Hong Kong

PN04-1

Oncoplastic Surgery for Small Breast: Pros (Oncoplastic Surgery in Women with Small Breasts: Why It Makes Sense)

Barbara Lynn Smith

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Treatments for breast cancer have improved and survival after treatment also continues to improve. With longer survival, quality of life issues have become more important to patients and their physicians. In breast cancer, these improvements require increased attention to cosmetic outcomes after treatment. Use of oncoplastic techniques during lumpectomy surgery and use of immediate reconstruction with mastectomy surgery provide improved cosmetic results and improve quality of life for breast cancer patients.

Lumpectomy with radiation provides the same survival as mastectomy for most patients with early stage breast cancer. Successful lumpectomy surgery requires that microscopically clear margins are obtained, with no tumor extending to the margin of the lumpectomy specimen. Achieving clear margins may require excision of a large volume of breast tissue and simple closure of the incision may result in a poor cosmetic result, particularly in women with small breasts. Use of oncoplastic techniques and other surgical approaches can improve cosmetic result. Each patient and her surgeon must decide whether lumpectomy with oncoplastic surgery or mastectomy with reconstruction will give her the best overall result.

Factors arguing for lumpectomy with oncoplastic surgery rather than mastectomy in women with small breasts:

- Access to radiation therapy ? if no access, mastectomy required for patients under age 70
- No contraindications to radiation therapy
- Lateral or upper breast lesions (poorer cosmetic results for medial and lower inner quadrant lesions)
- No access to immediate reconstruction

Options for improving lumpectomy outcomes in women with small breasts will be reviewed including:

- Use of multiple localizing wires allow more precise excision of non-palpable lesions

with a smaller overall volume of tissue
- Careful incision placement to improve lumpectomy cosmetic result and allow skin and nipple sparing mastectomy if clean margins are not obtained
- Careful specimen margin orientation to allow targeted and limited re-excision of positive margins rather than global re-excision
- Oncoplastic local advancement flap closure of lumpectomy defects

For patients who require or prefer mastectomy, immediate reconstruction is available to women with small breasts. Nipple sparing mastectomy with single stage implant reconstruction or expander reconstruction is available to women with small breasts.

PN04-2

Oncoplastic Surgery for Small Breast: Cons

Ava Kwong

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Oncoplastic breast conservation surgery has given a new light to the options of performing breast conserving surgery by combining oncological principles of breast cancer surgery with plastic surgery techniques. The ultimate oncoplastic achievement would be the conversion of what normally would be considered as an oncologic and/or cosmetic failure when using standard techniques of breast conserving surgery into both oncological and cosmetic success and to avoid mastectomy where possible.

For larger breasts, the technique is more forgiving. However for smaller breast, there is still a limitation of the cosmetic outcome when a high percentage of breast volume has been excised no matter how good the technique or the surgeon is.

Hence despite the uprise of interest and practice of oncoplastic surgery, oncoplastic surgery is not for everyone.

This house believe that oncoplastic surgery should not be performed in patients with small breasts.

PN05-1

Oncoplastic Surgery: Reconstruction Using Autologous Tissue

Kyung Won Minn

Department of Plastic and Reconstructive Surgery, Seoul National University Hospital, Korea

Breast cancer has become the most common cancer among women. The improvement of breast cancer treatment has met the needs of patients for not only long-term safety, but also better esthetic outcome. Since its opening in 2004, we managed the breast reconstruction clinic in the breast cancer center of Seoul National University Hospital, and analyzed the cases of breast reconstruction with autologous tissue. In 2014, breast reconstruction was conducted by 19% of mastectomy, and reconstruction using autologous tissue was 47% of all reconstructions. Breast reconstruction is performed in an immediate or delayed manner after mastectomy, depending on the adjuvant radiation therapy, and comprised with various surgical options. In this talk, details on options for proper breast reconstruction will be presented and discussed.

PN05-2

Oncoplastic Surgery: Reconstruction Using Artificial Implant (Breast Reconstruction with Expander/Implant for Irradiated Patients)

Yoshiko Iwahira

Breast Surgery Clinic, Japan

Radiation therapy has a significant magnifying ill effect on breast reconstruction. It is very difficult to reconstruct an irradiated breast and very hard to expand. I will do presentation about the association between complication and the timing of the radiotherapy, before and after breast reconstruction.

164 tissue expander/implant reconstruction patients who underwent mastectomies and radiation therapy were evaluated.

I classified these patients with 4 groups. Type 1 is a delayed reconstruction patient group who had radiation done after mastectomy. Type 2 patients are performed partial mastectomy and radiotherapy before total mastectomy. Type 3 and 4 are immediate reconstruction patient group. These patients are inserted expander as soon as mastectomy was done. In type 3, radiotherapy was done during expansion. Type 4 patients had radiotherapy performed after implant exchange.

73.4% of the cases reconstruction was accomplished without any complication. Complications are seen not only during expansion but also after reconstruction. Typical complication during expansion is Inflammation, extrusion. Moreover, the other is an aesthetic fault such as capsular contracture after reconstruction. In 35.2% of the patients, capsular contracture was Baker grade I. The other 62.9% of the patients were more than Baker grade II. Especially, Baker III contracture was seen in Type1 and 3.

From these result, tissue deficiency and radiation during expansion made complication rates higher.

Symposium

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Abstract Book

SP01-1

Tumor Microenvironment on Metastasis Research (The Tumor Microenvironment in Breast Cancer Metastasis)

Zena Werb

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Most cancer deaths are due to metastasis ? the spread of cancer from its site of origin to distant, vital organs, and the physiological damage caused by tumor growth in those organs. While the broad outlines of the process of metastatic spread are known, much of the details of the process remain poorly understood. Both extrinsic and intrinsic mechanisms regulate the development of the aberrant tumor organ and regulate its progression. It is now well established that the local microenvironment, or niche, of cells plays an important role in the fundamental cellular behaviors and contributes to cancer progression. We will first consider one mechanism by which the tumor microenvironment fosters tumor development and metastasis. We will consider macromolecules that mediate the tumor regulation of microenvironment and metastasis. A significant factor is the molecular nature by which the tumors regulate the stromal microenvironment that fosters metastasis. Finally, prevailing theories hypothesize that metastases are seeded by rare tumor cells with unique properties, which may function like stem cells in their ability to initiate and propagate new tumors in metastatic sites. We have begun to elucidate the identity of metastasis-initiating cells in human breast cancer. These findings give new insights into metastasis initiation and progression, and open up new targets for the management of metastatic disease.

Circulating Tumor Cell (Ex vivo culture of circulating tumor cells isolated from breast cancer patients)

Min Yu

Stem Cell Biology and Regenerative Medicine, University of Southern California, U.S.A.

The leading cause of breast cancer mortality is metastasis? cancer cells spreading and growing in distant organs throughout the body. Circulating tumor cells (CTCs) are the population of tumor cells shed from primary or metastatic tumors into blood circulation. CTCs may contain potential metastatic cancer stem cells, identification of which has been difficult due to the scarcity of the material needed for downstream analyses. Additionally, functional analyses of CTCs from blood of patients with cancer may allow individualized testing for susceptibility to therapeutic regimens, provided with sufficient CTC quantity.

In order to address those questions, we established ex vivo cultures of CTCs after testing a range of culture conditions. We isolated CTCs using methods to deplete normal blood cell components from blood samples of patients with metastatic estrogen receptor (ER)-positive breast cancer. We performed next-generation sequencing to detect the pre-existing and acquired mutations in CTCs and tested the CTC lines for sensitivity to panels of single drug and drug combinations.

CTC cultures were established from 6 patients with metastatic luminal breast cancer. These CTC lines revealed pre-existing mutations including TP53 and PIK3CA, and newly acquired mutations (Yu, et al, Science 2014). We uncovered three point mutations at the ligand-binding domain of the ESR1 gene encoding estrogen receptor α, corroborating several recent publications demonstrating the presence of these mutations in 18-53% of metastatic biopsies. We tested the CTC lines for their sensitivity to panels of single drug and drug combinations. In several CTC lines, inoculation of 20,000 cells into immunodeficient mice was sufficient for tumorigenesis. Serially diluted number of CTC lines down to as low as 20 cells also give rise to tumor growth, suggesting tumor-initiating characteristics of these cells.

In summary, ex vivo expansion of CTCs may support precision cancer therapy by enabling noninvasive monitoring for acquired mutations combined with individualized testing for drug susceptibility. Furthermore, patient-derived CTC lines will allow detailed interrogation of cancer stem cell properties at single cell level and its derived

clonal populations, enabling the development of targeted therapies against the metastasis initiating cancer stem cells.

SP01-3

Translational Research 1: PDX (Patient-derived Xenograft Models for Breast Cancer Research)

Hyeong-Gon Moon

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Patient-derived xenograft model (PDX model) is a promising tool to study the characteristics of various solid tumors. There are general expectations that the PDX model can be used as a platform to study the individual patient's sensitivity to targeted agents as well as its ability to guide our understanding in tumor biology including the tumor's clonal evolution.

We have focused on the development of PDX model by using primary breast tumor tissue obtained during the surgery in Seoul National University Hospital. Since 2012, we have performed more than 100 xenotransplantation of primary breast tumors into the NSG mouse. Our experience of PDX model in breast cancer as well as its potential utility in developing effective biomarker in breast cancer will be discussed in my presentation. Briefly, we have focused on identifying a novel prognostic gene signature in triple negative breast cancer patients using the PDX model.

Furthermore, out preliminary experience with serial transplantation of tumors from a small number of breast cancer patient will be discussed in the context of genomic stability and evolution of xenograft tumors. The potential use of xenograft as the tool to understand the in vivo tumor evolution has been highlighted in several previous literature. Although limited in numbers of patients studied, my presentation will cover the genomic evolution of breast tumor in response to different microenvironment.

SP02-1

Radiation therapy after NAC (Neoadjuvant Chemotherapy) (The Implications of Neoadjuvant Chemotherapy on Local Regional Radiotherapy for Breast Cancer)

Julia White

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The increase use of neoadjuvant chemotherapy for breast cancer management can have significant implications for local regional radiotherapy that is used post lumpectomy for breast conservation and its use post mastectomy in axillary node positive breast cancer.

Neoadjuvant chemotherapy can expand the role for radiotherapy by enabling women who present with disease that initially is suitable only for mastectomy but due to excellent response are able to undergo breast conservation with lumpectomy and breast radiotherapy. There had been lingering reticence about breast conservation in this setting based on analysis from the NSABP B18 clinical trial that reported the in-breast recurrence rate was higher in patients who were initially mastectomy candidates but were converted to breast conservation by neoadjuvant therapy in comparison to those who were considered suitable candidates for breast- conserving surgery initially; 15.7 *vs.* 9.9%, respectively; $p = 0.04$. More recent studies have found that this difference in local recurrence is because women who are initial mastectomy candidates but who are down staged to be suitable for breast conservation tend to have breast cancer with more aggressive biologic features such as higher stage, and grade then the group of women who are breast conservation candidates at the outset. A growing body of literature now supports that when appropriately selected by down staging, lumpectomy and breast radiotherapy can yield comparable local regional cancer outcomes in comparison to mastectomy post neoadjuvant chemotherapy irrespective of age, subtype and, or whether mastectomy was initially intended . As newer neoadjuvant agents are utilized resulting in even higher rates of pathologic response in some breast cancers, women with more locally advanced breast cancer are even better poised to feasibly and safely achieve breast conservation when desired.

On the other hand, neoadjuvant chemotherapy response can complicate the role for postmastectomy radiotherapy. The benefit of postmastectomy radiotherapy to reduce

local regional recurrence, distant metastases and improve breast cancer survival has been established for axillary node positive breast cancer by numerous randomized clinical trials and met analyses based on pathologic staging from mastectomy as the first line of breast cancer therapy. In contrast, radiotherapy is not typically recommended after mastectomy when negative axillary nodes are found. When neoadjuvant chemotherapy is delivered as the first line of breast cancer treatment there are conflicting opinions regarding which factors are most important for determining post mastectomy radiotherapy benefit: the clinical stage pre neoadjuvant chemotherapy or the pathologic stage at surgery post neoadjuvant chemotherapy. This is especially applicable for women who present with positive axillary nodes whose disease is down staged to pathologically node negative (ypN0) following neoadjuvant chemotherapy. Numerous studies have reviewed and reported their institution's clinical experience with inconsistent findings. Therefore, it is unknown whether complete response in the lymph nodes from neoadjuvant chemotherapy means that postmastectomy radiotherapy is no longer of benefit. Prospective data is needed to ensure omission of postmastectomy radiotherapy is safe given the extensive data supporting its benefit in improving survival for the treatment of node positive breast cancer. There is an open phase III clinical trial, NSABP B51/RTOG 1304 (NCT01872975) that is designed to address this question of whether local regional radiotherapy improves outcome in patients with positive axillary nodes that convert to pathologically node negative after neo adjuvant chemotherapy.

Management Issues after Neoadjuvant Chemotherapy: Surgical issues (Neoadjuvant therapy and axillary surgery)

Hiram S. Cody III

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Neoadjuvant chemotherapy (NAC) for breast cancer is well-established, and in multiple randomized trials has been associated a modestly increased rate of breast conservation, variation in response by biologic subtype, and survival comparable to that of postoperative adjuvant chemotherapy. With current regimens of NAC, about 40% of axillary node-positive patients become node-negative.

Sentinel lymph node biopsy has become standard care for axillary staging in virtually all patients with cN0 operable breast cancer and has been logically extended to the neoadjuvant setting, where it can be done before or after NAC. The arguments in favor of "SLN upfront" are that:

1) axillary staging is more accurate,
2) SLN-negative patients require no further axillary surgery,
3) SLN-positive patients can proceed directly to ALND post-NAC.

The arguments in favor of "SLN post-NAC" are that:

1) upfront axillary staging is irrelevant (chemotherapy is given regardless),
2) every patient must have two operations,
3) 40% of node-positive patients achieve a pathologic CR and may not require ALND.

In the US, the emerging consensus favors SLN post-NAC, and 27 retrospective studies (in which SLN biopsy with a backup ALND was done after NAC) show that the success rate is slightly lower (91%) and the false-negative rate was roughly comparable (10.5%) to that of SLN biopsy in general.

These studies do not address the performance of SLN biopsy in patients with proven axillary node metastases but two recent prospective observational studies have. In ACOSOG 1071, 607 patients with cT0-4, pN1-2 breast cancers had SLN biopsy and

ALND after NAC, with success and false-negative rates of 92.5% and 12.6%, respectively. In SENTINA, among 592 comparable patients, the authors observed 80% success and 14% false-negatives. Taken together, these trials show that the technique of SLN biopsy matters: false-negatives were minimized by the removal of at least 2 SLN, by using dual agent mapping (dye plus isotope), and by the performance of SLN biopsy once, after NAC (rather than twice, before and after NAC).

On a cautionary note, Mamounas has recently reported on pattern of 10-year patterns of locoregional recurrence after NAC in NSABP B-18 and B-27; the highest rates of regional node recurrence were in clinically node-positive patients whose nodes remained positive after NAC. Two new randomized trials aim to clarify management of the axilla in node-positive patients after NAC. NSABP B-51/RTOG 1304 (www.nsabp.pitt.edu/) comprises patients whose SLN become negative after NAC, randomizing to axillary RT vs no RT, and Alliance 11202 (www.allianceforclinicaltrialsinoncology.org/) comprises those whose SLN remain positive, randomizing to ALND vs no further surgery. Each promises a more conservative approach to the axilla following NAC in patients with nodal metastases.

SP02-3

Management Issues after Neoadjuvant Chemotherapy: Response evaluation

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There is no difference in disease free or overall survival in patients who undergo adjuvant v. neoadjuvant chemotherapy. Thus, neoadjuvant chemotherapy is recommended in patients with locally advanced breast cancer who would like to consider breast conservation and is also the primary treatment in patients with inflammatory breast cancer. MR has emerged as the most sensitive imaging modality to assess the response of tumor to neoadjuvant chemotherapy.

Dynamic contrast enhanced breast MR imaging (DCE-MR) is now recognized as an important adjunct imaging modality in the evaluation of patients. neoadjuvant chemotherapy includes decreasing the size of tumor to render the patient a candidate for breast conservation, predicting long-term disease free survival, and primary treatment of inflammatory breast cancer.

Women who undergo routine mammographic screening represent less than 10% of patients with locally advanced breast cancer, however in many underserved populations and globally, where routine mammographic screening is not available or underutilized, locally advanced breast cancer can be seen in up to 60% of diagnosed breast cancers. On presentation locally advanced breast cancers are generally not amenable to breast conserving surgery. If the woman desires breast conservation, then neoadjuvant chemotherapy may be recommended.

Neoadjuvant chemotherapy refers to chemotherapy given before surgical therapy. It is also the initial therapy for inflammatory breast cancer. Adjuvant therapy is chemotherapy or hormonal therapy that is given after surgical therapy. National Surgical Adjuvant Breast and Bowel Project (NSABP) initiated the B-18 randomized clinical trial comparing preoperative and postoperative chemotherapy in patients with operable breast cancer. The study showed that there was no difference in survival, whether overall or disease free, between the two groups utilizing the same chemotherapy regimen. The study showed that patients that underwent preoperative chemotherapy were more likely to undergo lumpectomy after shrinkage of tumor than those having surgery before chemotherapy.

The Response Criteria in Solid Tumors (RECIST), established by the World Health Organization, is the accepted standard for measuring tumor response to treatment. only up to 30% of patients will shown pCR, there will be a significant number (70% or greater) of patients who will derive partial, or in some cases, no benefit from neoadjuvant chemotherapy. There has been considerable effort in studying the role of DCE-MR in predicting early response to neoadjuvant chemotherapy. Identifying early markers for response to neoadjuvant chemotherapy could potentially spare patients for whom chemotherapy is ineffective, unnecessary toxicity and would expedite the surgical therapy. The American College of Radiology Imaging Network (ACRIN) study 6657, the imaging component of the Investigation of Serial Studies to Predict Your Therapeutic Response with Imaging And moLecular Analysis (I-SPY TRIAL), is one such multicenter prospective randomized breast cancer trial.

Mammography, ultrasound and MRI are typically used in conjunction with one another although the accuracy of each modality varies in determining extent of disease. DCE-MR demonstrates excellent tissue contrast, but it is an expensive time consuming study that requires intravenous contrast administration. Mammography is limited by overlapping tissue and inability to distinguish benign tissue and malignant tissue. Sonography is limited by operator dependence and reproducibility issues, and by posterior acoustic shadowing limiting visualization. DCE-MR is unique in the evaluation for breast malignancy because unlike mammography and ultrasound, DCE-MR allows for the characterization of lesion morphology and its microvascular properties by assessing signal intensity changes over several minutes following contrast agent injection. This enhancement kinetic, correlate with the degree of angiogenesis measured by histopathology assessment of microvessel density and pathologic tumor grade.

Diffusion weighted MR (DW-MR) and apparent diffusion coefficients (ADC). DW-MR evaluates the movement of water molecules in tissue. Water diffusion is quantified from DW-MR images by calculating the apparent diffusion coefficient (ADC). An advantage of DW-MR is that contrast does not have to be administered. DW-MR and DCE-MR concluded that DW-MR has high sensitivity in predicting pathologic response to neoadjuvant chemotherapy whereas DCE-MR is specific to assessing such response. Tumor ADC could potentially be used as a biomarkers for tailoring chemotherapy regimens early in the treatment phase.

SP03-1

Current Management of Triple Negative Breast Cancer

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Triple negative breast cancer (TNBC) comprises 15% of breast cancers, and it has the poorest survival outcome among the subtypes of breast cancer. TNBC lacks of effective therapeutic targets such as estrogen receptor (ER) or human epidermal growth factor receptor 2 (HER2) compared with other breast cancer subtypes. TNBC has overlapped populations with the patients with Basal-like and BRCA mutant breast cancer. For example, 80% of BRCA mutant breast cancer is TNBC and/or Basal-like breast cancer. Also, about 80% of TNBC is classified as Basal-like breast cancer. It has not been a couple of decades since the clinical trial was conducted only for TNBC in breast cancer trials. Therefore, most of the mainstream practices are based upon the results of the trials for the entire breast cancer patients. Recently, there were several intriguing studies conducted only for the TNBC with the drugs that has therapeutic implications in TNBC. Several molecular targets including the epidermal growth factor receptor (EGFR), the poly ADP ribose polymerase (PARP), and angiogenesis ligands and receptors, are currently under clinical investigation for the treatment of this disease. Here, current management of TNBC will be reviewed in (neo) adjuvant and metastatic setting with the introduction of clinical trials targeting aforementioned molecules.

Heterogeneity of TNBC

Rebecca Dent

Division of Medical Oncology, National Cancer Centre Singapore, Singapore

Subtype-Directed Therapy of Triple Negative Breast Cancer

Ruth M. O'Regan

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Triple negative breast cancer (TNBC), characterized by the absence of hormone receptors and HER2, has a poor outcome with a high propensity to distant recurrence within a short interval from diagnosis. Systemic chemotherapy remains the mainstay for treating patients with TNBC but is often ineffective due to inherent chemo-resistance. Attempts to utilize targeted agents in patients with TNBC have to date produced strikingly unpromising results. One of the reasons for the lack of success of targeted agents to date is because of the now well-recognized heterogeneity of TNBC. A striking example of this was the negative results noted in a randomized trial in which iniparib, a purported PARP inhibitor was added to standard chemotherapy, in patients with metastatic unselected TNBC. This group of agents clearly has activity in cancers with defective DNA repair, such as those associated with BRCA mutations, but have not, to date, been shown to be effective in TNBC as an entity.

Intrinsic subtyping identifies TNBC broadly as being basal or non-basal like and recent evidence suggests the possibility of differential sensitivity to chemotherapeutics based on basal-like designation. Though the majority of TNBC is characterized as basal-like, not all TNBC is basal-like and there are basal-like cancers that are non-TNBC. Lehmann et al identified 6 distinct subtypes of TNBC and identified corresponding cell lines allowing an assessment of sensitivity to chemotherapy and other targeted therapeutics. Two of these subtypes fall under a basal-like phenotype designation, distinguished by basal-like 2 subtype having genes associated with growth factor signaling. Two subtypes are defined as mesenchymal in nature both being driven by genes associated with epithelial-to-mesenchymal transition, with the MSL subtype additionally having genes associated with growth factor signaling. There is an immuno-modulatory subtype, which is of significant interest given the wealth of new agents targeting immune processes. Lastly, the androgen receptor (AR) subtype has a luminal phenotype, similar to luminal cancers that are estrogen receptor-positive. Targeting AR in TNBC with an anti-androgen have shown modest activity to date but ongoing trials are evaluating newer anti-androgens and adding growth factor pathway inhibitors to stan-

dard anti-androgen therapy. Attempts to target the genes associated with these designated subtypes is in its infancy and will likely require global efforts.

The inherent chemo-resistance noted with TNBC has led to the evaluation of novel chemo-therapeutics in clinical trials. Additionally, there is significant research attempting to determining what the underlying cause of chemo-resistance is and to identify genes that drive chemo-resistant TNBC. The lack of significant benefit of chemotherapeutics in TNBC has led to the use of pre-operative chemotherapy, which allows real-time assessment of chemo-sensitivity, as an emerging standard approach in the treatment of early stage disease. Given that complete pathologic response is a robust predictor of prognosis in patients with TNBC, a case could be made for the evaluation of novel therapeutic approaches in this "post-neoadjuvant" setting, given the difficulty in their evaluation in rapidly progressing metastatic disease.

SP04-1

PD1/PDL1 Targeted Immunotherapy in Breast Cancer

David Page

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Immunotherapy with immune checkpoint antibodies has dramatically improved the treatment of metastatic melanoma and other cancers, however immunotherapy remains relatively unexplored in breast cancer. Immune checkpoint antibodies function by binding and blocking key regulatory proteins, cytotoxic T-lymphocyte antigen 4 (CTLA4), programmed death 1 (PD-1), or programmed death ligand 1 (PD-L1), thereby "releasing the brakes" on lymphocytes and permitting a robust immune response against the tumor. Recently, the first phase I data of these agents have been described in both early stage and metastatic breast cancer, with reports of objective response. These clinical data will be reviewed, as well as potential future directions for immunotherapy in breast cancer.

SP04-2

PI3K/AKT/mTOR Pathway Inhibitors in Breast Cancer

Yoon Sim Yap

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The phosphatidylinositol 3-kinase(PI3K)/protein kinase B (AKT)/ mammalian target of rapamycin (mTOR) pathway controls important hallmarks of cancer, and is frequently activated in breast cancer.

The rationale and preclinical data for targeting this pathway in different subtypes of breast cancer will be discussed. Currently, results from randomised clinical trials are limited to mainly mTORC1 inhibitors. Although there is evidence of some efficacy in hormone receptor positive and HER2 negative breast cancers as well as HER2-overexpressing breast cancers, toxicity may be an issue in some patients, affecting dose intensity.

There is a need to establish predictive biomarkers to identify patients who may benefit from PI3K/AKT/mTOR inhibitors. More effective strategies using new generation inhibitors and novel combinations with other drugs to overcome resistance to PI3K/AKT/mTOR inhbitors are being explored.

CDK 4/6 Inhibitors

Sudeep Gupta

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In vitro studies of in ER+ breast cancer cell lines suggest that antiestrogens act on sensitive cell populations in early to mid-G1 phase. G1/S transition is under the control of cyclin dependent kinases (CDKs) which are activated by specific regulatory cyclins. CDK4 and CDK6 are activated by binding to D-type cyclins and act early in G1 phase. The retinoblastoma protein (pRb), which mediates G1 arrest is the primary target of activated CDK 4/6. Phosphorylation of pRb by active CDK 4/6 ?cyclin D leads to transcription of genes requisite for entry into the S-phase.

Dysregulation of cell cycle checkpoints due to aberrations in cyclin/CDK/pRb pathway have been frequently observed in breast cancer, including amplification of cyclin D1 and CDK4 as well as loss of CDKN2A, all of which lead to upregulation of the pathway. Recent preclinical data also suggests that ERα retains genomic activity and drives a CDK4/E2F dependent transcriptional program despite estrogen deprivation. Patients with ER+ breast cancer whose tumors exhibit the gene expression signature of pRb loss have poorer outcome on adjuvant tamoxifen. Therefore, activation of the CDK/pRb/E2F axis promotes endocrine resistance and this axis, therefore, represents a valid target for therapeutic modulation.

In vitro data from human breast cancer cell lines demonstrated preferential sensitivity of ER+ cell lines to CDK 4/6 inhibition and preclinical endocrine sensitive and resistant mouse xenograft models also showed tumor growth inhibition by these agents. Several agents are currently in various phases of clinical development for ER positive breast cancer and will be the subject of this presentation.

SP05-1

Adjuvant Endocrine Therapy in Postmenopausal Women (Adjuvant Treatment for Postmenopausal Women with Hormone Receptor Positive Breast Cancer)

Seigo Nakamura

Division of Breast Surgical Oncology, Department of Surgery, Showa University School of Medicine, Japan

Adjuvant treatment for postmenopausal women with hormone receptor positive breast cancer has been (1) 5 years of an aromatase inhibitor or (2) tamoxifen followed by an aromatase inhibitor (in sequence) in ASCO guideline since 2010. The guideline updated last year recommends that pre- or perimenopausal women who have received 5 years of adjuvant tamoxifen should be offered 10 years total duration of tamoxifen. Because the two largest studies (ALTAS and ATTOM) with longest follow-up showed survival advantage ,lower risks of breast cancer recurrence and cintlalateral breast cancer with a 10-year duration of tamoxifen treatment. Therefore,postmenopausal women who have received 5 years of adjuvant tamoxifen should be offered the choice of continuing tamoxifen or switching to an aromatase inhibitor for 10 years total as adjuvant endocrine therapy.

There are insufficient data to recommend an aromatase inhibitor for a duration > 5 years. However, tamoxifen for a duration of 2 to 3 years with a switch to an aromatase inhibitor for up to 5 years, for a total duration of up to 7 to 8 years is also recommended.

Potential harms include risk of endometrial cancer in women continuing tamoxifen, hot flashes and other menopausal symptoms with either tamoxifen or aromatase inhibitors, deep-vein thrombosis or pulmonary embolism with tamoxifen, ischemic heart disease with aromatase inhibitor, osteopenia/osteoporosis with aromatase inhibitor and uterine cancer with tamoxifen.

However, these drugs have more advantage increased both distant disease-free survival and overall survival, moreover, reduced risk of contralateral breast cancer.

Adjuvant Endocrine Therapy in Premenopausal Women in 2015

Woo Chul Noh

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Almost 60% of newly diagnosed breast cancer patients are premenopausal in Korea. Among them, more than half have hormone receptor positive tumors. While there has been a rapid progress in endocrine treatment for postmenopausal women over the past decades, researches for premenopausal women are not yet sufficient.

We have several options available for endocrine therapy for premenopausal women, including (1) cytotoxic chemotherapy; (2) selective estrogen receptor modulator like tamoxifen; (3) estrogen deprivation strategies such as permanent ovarian ablation or reversible ovarian function suppression (OFS) using GnRH agonists. However, there is uncertainty about how best implement adjuvant endocrine therapy to individual patients using tamoxifen and OFS as well as how to integrate these approaches with chemotherapy.

Among various issues regarding hormonal therapy for premenopausal women, we will be focusing on the role of OFS either with tamoxifen or with aromatase inhibitors in this presentation.

AIs + OFS for premenopausal women in adjuvant setting

In ABCSG-12 trial, 1803 premenopausal women with early breast cancer patients were assigned to goserelin plus tamoxifen or anastrozole with or without zoledronic acid for 3 years. Updated results at 62 months showed no difference in DFS between patients in tamoxifen group and anastrozole group. Recently however, the result of the combined analysis of two international collaborative group trials, SOFT and TEXT were reported. The analysis revealed a significant improvement in DFS with 5 years of OFS and exemestane, as compared with 5 years of OFS and tamoxifen at a median F/U of 68months. Although this apparently opposing result has yet to be clearly explained, for premenopausal women with high-risk breast cancer requiring chemotherapy, OFS with exemestane for 5 years can be a new therapeutic option with the potential to reduce risk of distant metastasis in a subset of patients.

Tamoxifen + OFS for premenopausal women in adjuvant setting

The results of SOFT trial which compared 5 years of tamoxifen and 5 years of tamoxifen plus OFS were released in SABCS 2014.

Adding OFS to tamoxifen did not provide a significant benefit in the overall study population. Furthermore, among women who had received prior chemotherapy they actually failed to show the statistically significant 5 year DFS by adding OFS to tamoxifen (hazard ratio for recurrence, 0.78;95% CI, 0.60 to 1.02).

However, based on the strong tendency toward OFS+tamoxifen group, they concluded that in women who had a sufficient risk of recurrence to warrant adjuvant chemotherapy and who remain premenopausal, OFS in addition to tamoxifen reduced the risk of breast cancer recurrence.

ASTRRA trial

In Korean Breast Cancer Society, the prospective randomized clinical about the role of the addition of OFS to tamoxifen in young women with hormone-sensitive breast cancer who remain premenopausal or regain menstruation after chemotherapy (ASTRRA trial) was designed and conducted since April 2009.

In this study, premenopausal women with estrogen receptor-positive breast cancer treated with definitive surgery were enrolled after completion of neoadjuvant or adjuvant chemotherapy. Ovarian function was assessed at the time of enrollment and every 6 months for 2 years by follicular-stimulating hormone levels and bleeding history. If ovarian function was confirmed as premenopausal status, the patient was randomized to receive 2 years of goserelin plus 5 years of tamoxifen treatment or 5 years of tamoxifen alone. The primary end point will be the comparison of the 5-year DFS rates between the OFS+tamoxifen and tamoxifen alone groups.

Patient recruitment was finished on March 2013 with the inclusion of a total of 1,483 patients. The interim analysis will be performed at the time of the observation of the 187th event. This study will provide evidence of the benefit of OFS plus tamoxifen compared with tamoxifen only in premenopausal patients with estrogen receptor-positive breast cancer treated with chemotherapy.

Luminal B Breast Cancer

Giuseppe Viale

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The St Gallen International Expert Consensus on the Primary Therapy of Early Breast Cancer has re-emphasised the important role the biological characteristics of the tumours to inform the choice of the systemic treatment. Also, it has been confirmed that the immunohistochemical assessment of estrogen (ER) and progesterone receptor (PgR) status, of HER2 amplification or overexpression and of the Ki-67 labeling index may be a useful surrogate to distinguish luminal A?like breast cancer from luminal B?like disease, overcoming the need for molecular assays. Luminal B-like breast cancer may be distinguished from Luminal A-like tumours according to a higher Ki-67 labeling index and a low/absent expression of PgR (< 20% immunoreactive cells). With the aim of verifying the suitability of the new surrogate definitions of luminal subtypes in terms of distant disease control we have investigated 9,415 women with a median follow-up of 8.1 years who (1) had ER-positive, human epidermal growth factor receptor 2 (HER2)-negative early breast cancer and (2) had undergone surgery at the European Institute of Oncology between 1994 and 2006. We evaluated distant disease-free survival of patients with "low" (< 14%), "intermediate" (14% to 19%) or "high" (≥ 20%) Ki-67 labeling index stratified by PgR expression (negative or low versus high). We calculated the cumulative incidence of distant events, considered competing events and performed multivariable analysis adjusted for pathologic tumor stage, pathologic node stage, tumor grade, peritumoral vascular invasion and menopausal status.

In this large series of patient, lack of substantial PgR positivity was significantly associated with poorer outcomes only for patients with an intermediate Ki-67 labeling index ($p < 0.001$). The 4,890 (51.9%) patients with low Ki-67 labeling index (any PgR expression level) or with intermediate Ki-67 labeling index but substantial PgR positivity had comparably good outcomes and thus may represent a more accurate grouping of those with luminal A?like disease.

This newly-proposed pathological definition of intrinsic molecular subtypes using immunohistochemical surrogates will eventually enrich the population of patients with Luminal A-like tumours as compared with the previous (2011) definitions of the St. Gallen panelistsmay. The long-term prognosis of these patients is indeed quite favourable, and they could well be spared chemotherapy in the adjuvant setting.

SP06-1

Ki-67 Labeling Index in Breast Cancer

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Assess the uncontrolled proliferation in breast cancer, the most widely practiced measurement includes the immunohistochemical staining of Ki-67 antigen. Ki-67 is a protein expressed in all phases of the cell cycle (except for resting Go) used as a tumor proliferation marker. Ki-67 index is defined by the percentage of tumor cells with positive nuclear staining out of all tumor cells within a given histological field. Several studies have shown the prognostic and predictive role of Ki-67with a high Ki-67 index having higher risks of recurrence and metastasis. High Ki-67 is also associated with greater treatment response to epirubicin-based adjuvant chemotherapy in luminal types. Furthermore, a more recent study has shown that in the neoadjuvant endocrine therapy setting, Ki-67 indices before treatment and 2 weeks after treatment are strongly associated with time to relapse as well as response to endocrine treatment. The Ki-67 seems to be a promising one and is a candidate as prognostic and predictive biomarker next to hormone receptor and HER2. Although ASCO (American Society of Clinical Oncology) Tumor Marker Guideline Panel has never recommended the use of any proliferation marker, Ki-67 is suggested as a marker for differentiation of luminal A and luminal B (HER2 negative) in St. Gallen Panel 2011. The International Ki-67 in Breast Cancer Working Group agreed that Ki-67 measurement by immunohistochemistry was the current assay of choice for measurement and monitoring tumor proliferation in standard pathology specimen. However, they recognized the poor agreement on the use of Ki-67. In 2011, they proposed the guidelines for the analysis, reporting and use of Ki-67 that should reduce inter-laboratory variability and improve inter-study comparability of Ki-67 results in pre-analytical, analytical, interpretation and data handling settings. However after the release of recommendation from the International Ki-67 in Breast Cancer Working Group in assessment of Ki-67 in Breast cancer, there are many issues still to be resolved: 1) definition of cut-off points for Ki-67, 2) standardization of analysis methods for Ki-67, 3) concordance of core biopsies and related surgical specimens and 4) validation of automated analysis systems.

The Korean Breast Pathology Ki-67 Study group conducted a multicenter study to examine concordance in Ki-67 counting and to find the factors contributing to variability in its measurement. With this study, we could reach the following conclusions: 1)

inter-observer variabilityof Ki-67 index for direct counting and categorical estimation was relatively high, 2) tumors with hot spotsshowed greater inter-observer variability as opposed to those without, and 3) restricting the measurement area by constructing TMAs yielded lower inter-observer variability but counting from the hot spot area did not improve inter-observer concordance.

In this session, I would like to sum up the issues in relating to Ki-67 with the review of updated results from domestic and international studies.

SP06-2

ER, PR and HER2 Testing in Breast Cancer

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Estrogen receptor (ER) and progesterone receptor (PR) are prognostic markers of breast cancer and predictive markers of response to endocrine therapy. Assessment of the ER/PR status should be performed in all primary breast cancers and is therefore a routine part of pathology practice. Although immunohistochemistry (IHC) is the standard method for ER/PR measurement in clinical specimens, results can be influenced by variations in preanalytic (tissue handling, type of fixative, and duration of tissue fixation), analytic (antibody selection, use of positive and negative controls), and postanalytic (threshold for positivity and interpretation) variables. While clinicians often give little thought to how the laboratory measures ER/PR, it is worth noting that there are several potential pitfalls in these analyses, and oncologists should work closely with pathology laboratories to assure optimal testing practices.

HER2 is an oncogene protein that is a member of the epidermal growth factor receptor family and overexpressed in approximately 10-20% of breast cancers that have amplification of the corresponding gene. HER2 overexpression and/or gene amplification is associ ated with poor prognosis and a marker predictive of response to trastuzumab (Herceptin®), a humanized monoclonal antibody to the receptor protein. An accurate assessment of HER2 status is therefore important in the management of breast cancer patients, and HER2 status should be determined for all invasive breast cancers either at the time of diagnosis or at the time of recurrence. It is now recommended that HER2 testing be conducted using an algorithm that defines positive, equivocal, and negative values for both HER2 protein expression (IHC) and gene amplification (in situ hybridization). Accuracy of HER2 testing by IHC is dependent on the experience of the testing laboratory, as well as the reagents used for testing. Others issues should be discussed here are changes in updated ASCO/CAP guideline for HER2 testing and histopathologic features suggestive of HER2 test discordance.

SP06-3

NGS-Based Diagnostics

Woong-Yang Park

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SP07-1

Management of BRCA1/2 Mutation Carriers

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Approximately 5% of all breast cancers are diagnosed in women with a BRCA1 or BRCA2 mutation. The prevalence of mutations is higher than this in women who are diagnosed under age 40 or who have triple-negative breast cancer. Genetic testing is now done in several centers at the onset of diagnosis in order to aid in the management of the breast cancer. There are three principal ways in which a BRCA1 or BRCA2 carrier might be treated differently than a non-carrier. First, bilateral mastectomy has been shown to reduce the mortality from breast cancer at twenty years due to the elimination of second primary contralateral cancers. Second, oophorectomy after the diagnosis of breast cancer has been shown to result in a 62% reduction in mortality for BRCA1 carriers and a 43% reduction in mortality for BRCA2 carriers. The reduction in mortality from oophorectomy is present in women with ER-positive and ER-negative cancers. In Poland women with BRCA1 mutations are treated with neoadjuvant cis-platinum as a single agent drug. The rate of PCR is 68%. Among 48 Polish patients who were treated with cisplatinum and oophorectomy the five year survival rate is 100%. Further studies on the long term effects of cisplatinum on BRCA1 carriers are needed to change practice.

SP07-2

Characterising Cancer Risks for Carriers of Mutations in BRCA1, BRCA2, PALB2 and RAD51C Genes

Antonis Antoniou

Public Health and Primary Care, University of Cambridge, United Kingdom

The presentation will provide an overview of the latest developments and challenges in understanding the penetrance of mutations in the BRCA1, BRCA2, PALB2 and RAD51C genes. Genetic counselling currently relies on average cancer risk estimates obtained from retrospective penetrance studies involving large numbers of families segregating mutations in these genes. The talk will present penetrance estimates from ongoing prospective analyses, based on data from the International BRCA1/2 Carrier Cohort Study, the largest cohort of BRCA1/2 mutation carriers worldwide that includes > 10,000 mutation carriers at baseline with prospective follow-up information. Several common alleles and other risk factors have now been shown to modify breast cancer risk for BRCA1 and BRCA2 mutation carriers. The talk will review the latest efforts and results from the Consortium of Investigators of Modifiers of BRCA1/2 to identify genetic modifiers of risk and provide individualised cancer risks for BRCA1 and BRCA2 mutation carriers on the basis of polygenic risk scores. We will also present penetrance estimates based on analyses of combined data from families segregating mutations in PALB2 and RAD51C, the largest efforts of their kind. Finally the presentation will demonstrate how the effects of common and rare breast cancer susceptibility variants are incorporated into the BOADICEA model to provide comprehensive risks of developing breast cancer in the future.

SP07-3

Absolute Risks and Hormonal/Lifestyle Risk Modifiers among BRCA Mutation Carriers, the IBCCS Experience (Hormonal and Behavioral Risk Factors and Risk of Breast Cancer)

Matti Rookus

Department of Epidemiology, Netherlands Cancer Institute, Netherlands

The finding that breast cancer risk among BRCA1/2 mutation carriers varies according to birth cohorts illustrates ? apart from screening effects - the modifying effects of hormonal and behavioral risk factors on the risk of breast cancer in BRCA1/2 mutation carriers. Indeed, retrospective studies have shown that the risk factors as known in the general population (such as, age at menarche and menopause, reproductive risk factors, exogenous hormones, overweight and physical activity, alcohol consumption, diagnostic radiation) are also associated with the risk of breast cancer among BRCA1/2 mutation carriers. As the retrospective studies may not be free of some bias (e.g. recall bias, survival bias, oversampling of breast cancer cases) prospective data are needed to confirm the associations and their magnitudes. This is essential information for the decision on whether or not hormonal and behavioral risk factors should be included in risk breast cancer risk prediction models tailored to BRCA1/2 mutation carriers, such as the BOADICEA model. During the presentation an overview of the existing information on the hormonal and behavioral risk factors and risk of breast cancer BRCA1/2 mutation carriers will be given and the first preliminary results of the ongoing prospective analyses of the International BRCA1/2 Carrier Cohort Study (IBCCS) will be presented.

SP08-1

Breast Cancer in the Gulf: Building an Integrated Registry

Shaheenah Dawood

Dubai Hospital, U.A.E.

SP08-2

National Clinical Database-Breast Cancer Registry in Japan

Reiko Yoshida

Breast Center, Showa University, Japan

The National Clinical Database-Breast Cancer Registry (NCD-BCR) data in Japan was used to retrieve records on more than 300,000 cases from more than 800 hospitals from 2004. This Japanese BCR has been conducted by the Registration Committee of the Japanese Breast Cancer Society and supported by the Public Health Research Foundation until 2012. From 2012 this dataset move to The National Clinical Database (NCD) in Japan. The NCD is a nationwide project in cooperation with the certification board of the Japan Surgical Society. More than 50 items on the demographic and clinicopathological factors of newly- diagnosed primary breast cancer patients were voluntarily registered to the JBCS through the Web-based system from affiliated institutes. We introduce our registry system and recent trends in the management of breast cancer patients in Japan.

SP08-3

From Institutional to Territory-Wide Breast Cancer Registry-The Hong Kong Experience

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Breast cancer is the commonest female cancer in Hong Kong, with more than 3,500 new cases diagnosed in 2012. Over the past decade, there has been a 70% increase in the number of new breast cancer cases diagnosed annually in Hong Kong, due to an average annual percent change of 2.4% in the age-standardized incidence of breast cancer, as well as an ageing and growing population. Fortunately, the age standardized mortality of breast cancer has largely remained steady. The Hong Kong Cancer Registry is a population-based cancer registry, a voting member of the International Agency of Cancer Registry under the International Agency for Research on Cancer of the WHO, which registers all newly diagnosed cancer patients in the whole territory of Hong Kong. The Registry reports the incidence and mortality statistics of all cancers diagnosed in Hong Kong, analyzes the historical trends of incidence and mortality, as well as projects the future cancer burdens of the territory. However, due to resource prioritization, clinical outcomes such as the relative stage-specific survivals have been reported only for a few cancers over specific periods. Survivals of 18,300 breast cancer patients diagnosed from 1997-2006 have been analyzed and partially published.

Overall, around 90% of breast cancer patients in Hong Kong are being managed in the public health care system provided by the Hospital Authority (HA), which is a statutory body fully subsidized by the Hong Kong Government administering all the public hospitals and specialist clinics in the territory. The HA's Clinical Management System (CMS) is a computer system used by all health care professionals in the public sector in the daily patient management including ordering investigations, writing discharge summaries and clinical progress notes, and prescribing medications. Conceivably, it stores all pathology, laboratory and radiological reports, as well as all surgical records, outpatient and inpatient clinical notes and prescriptions. With respect to breast cancers, detailed data on patient demographics, tumor attributes, clinical staging, treatments of surgery, radiotherapy and chemotherapy, as well as clinical outcomes of recurrences, metastases and survival can be retrievable through diligent searches by trained personnel, although those data were not registered in pre-organized formats in the CMS. Being the largest oncology center in Hong Kong, the Department of Clinical Oncology of

Queen Elizabeth Hospital is managing around 1,000 new breast cancer patients every year. Since last year, the Department has initiated retrospective collection of such data through a web-based structured data collection system on more than 7,000 patients treated in the Department from 2005-2012, with a plan to prospectively register data of newly diagnosed patients in the Department almost real time.

With additional funding from the Government and building on the Department's system, the Hong Kong Cancer Registry, accessing through the CMS which links up all public hospitals, is embarking on a new initiative to retrieve the pertinent clinical data described above of all breast cancer patients treated in the public hospitals and clinics of Hong Kong from 2010 onwards. Such data will be helpful to elucidate the clinico-pathological patterns and stages of breast cancers at diagnosis, investigations, details of various modalities of treatment, and also outcomes including recurrences and metastases and survivals. The impact of new cancer therapies introduced such as anti-HER2 therapies on outcomes over time can also be estimated and benchmarked against the access to such treatments. Such local data can also be compared with those of other areas or ethnic groups, and they can also be pooled with other databases to form even larger regional or international databases to better assess clinical outcomes and identify unmet clinical needs.

SP09-1

Transformation of Breast Cancer in Taiwan

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Restricted Access to Medical Resources in Underdeveloped Countries (Restricted Access to Medical Resources in Low and Middle Income Countries (LMICs))

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The incidence of breast cancer is rising in low- and middle-income countries (LMICs). However, survival rates remain relatively low because of some barriers in early detection and access to treatment.

This article reviews the literature and give out available data on breast cancer care status including clinical stage, time intervals to care, and access barriers in different countries.

Actually there are very limited data on cancer in developing countries due to lack of functioning cancer registries.

Most available studies showed that more than 2/3 patients in LMICs are diagnosed at advanced stages due to lack of breast screening program and low awareness of public about breast cancer. In addition, there are long delays between symptom discovery and treatment start due to lack of cancer treatment facilities and capcity as well. As a result, the treatment outcomes of breast cancer in LMICs are still very poor. Though cancer survival data are not available and strong reliable in majority of developing countries, but the few data available are in line with the observed incidence/mortality differences. The 5-year survival rates for breast cancer are much worse in LMICs such as Gambia (12%), Algeria (38.8%), India (52%) and Brazil (58.4%) in comparison to high income countries (HICs) such as the United States of America (83.9%), Sweden (82.0%), Japan (81.6%) and Australia (80.7%).

So the challenges are indeed great. However, there is increasing international and national attention to this problem. A broad partnership among Asian institutions, international organisations, and national governments is needed to effectively prevent, detect and treat the rising number of breast cancers in the developing world.

SP09-3

Onco-Fertility (Fertility Issues in Young Women with Breast Cancer in Japan)

Chikako Shimizu

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Breast cancer incidence in all ages is higher in the Western than in Asian countries, but the estimated breast cancer incidence in young women under 40 years of age ubiquitously approximates 25 per 100,000 women either in Asian or Western countries.

Younger women with breast cancer are known to have worse prognoses than their older counterpart. Adjuvant chemotherapy is used frequently in younger women, because of longer life-expectancy, better tolerability to aggressive treatments and documented survival advantages compared to women not treated with adjuvant therapy. Superiority of longer duration of adjuvant tamoxifen has also been demonstrated. These treatments, which aims to improve survival outcome, however, affect patients' quality of life, especially in patients who wish to build a family in the future.

Highly specialized, multidisciplinary care is necessary to meet the fertility need of breast cancer patients. Although, numerous advances have been made in breast cancer treatment and reproductive technology, access to treatments are limited by access to information, local health-care resource, cost and cultural value. To overcome the information barrier, we have developed a clinical practice guideline to support fertility decision-making process of patients and healthcare providers. In this guideline, the scientific data related to pregnancy and fertility preservation in breast cancer patients are evaluated. This guideline is expected to enable both breast cancer specialists and reproductive specialists to share the latest medical information and ethical concerns on fertility issues in patients with breast cancer. Healthcare providers are required to open participatory dialogue with patients about disease, care options and potential risks and likely benefits for their particular circumstances.

Survivorship Session

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Abstract Book

SS01-1

Breast Cancer Survivor Study from the Shanghai Women's Health Study (Lifestyle and Genetic Determinants of Breast Cancer Survival: Results from Shanghai Studies)

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Breast cancer is the most commonly diagnosed malignancy among women in most parts of the world, including many Asian countries. Despite the generally favorable prognosis for most patients, breast cancer survival varies considerably between individuals even after adjustment for known prognostic factors. To identify lifestyle and genetic determinants as well as biomarkers for breast cancer survival, we have initiated multiple breast cancer studies in Shanghai over the past 20 years, including the Shanghai Breast Cancer Survival Study, a population-based cohort study including 5,042 breast cancer patients, aged 20-75, who were recruited approximately 6 months after cancer diagnosis. An in-person interview was conducted at the baseline survey to obtain detailed information regarding lifestyle factors, medical history, and quality of life. Medical charts were reviewed to obtain data on cancer diagnosis and treatment. Genomic DNA and tumor tissues were collected from the large majority of patients for studying genetic and other biomarkers. These patients have been followed, through multiple in-person surveys conducted at 6, 18, 36, and 60 months and 10 years after cancer diagnosis, for breast cancer outcomes, including cancer recurrence, survival, and quality of life. Additional data on lifestyle exposures, cognition and bone density were obtained during these follow-up surveys. Over the years, data and biological samples collected in the Shanghai Breast Cancer Survival Study have been used to investigate a wide range of important issues related to genetic and lifestyle determinants for the outcomes, including quality of life, among breast cancer survivors, resulting in more than 60 papers published in peer reviewed life science journals. Recently, we have expanded our research to investigate tumor markers for the prediction of breast cancer outcomes. We have also established a consortium including 18,300 breast cancer survivors from multiple studies conducted in China and the United States. In this talk, I will present some recent results from the Shanghai Breast Cancer Survival Study to illustrate the importance of conducting research to understand the influence of genetic and modifiable lifestyle factors on breast cancer recurrence, mortality, and quality of life.

The Pathways Study: a Prospective Study of Breast Cancer Survivorship

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With over 3 million breast cancer survivors in the United States today, relatively little is known regarding whether factors other than those that are diagnostic and medical care-related may influence prognosis. The Pathways Study was designed to examine the effects of lifestyle (e.g., diet, physical activity, complementary and alternative medicine [CAM]), psychosocial (e.g., quality of life), molecular and genetic, medical care, and neighborhood contextual (e.g., social and built environment characteristics) factors on breast cancer prognosis.

Women newly-diagnosed with invasive breast cancer were identified daily from electronic pathology records from January 2006 to April 2013 at Kaiser Permanente Northern California (KPNC), a large, integrated health care organization. Eligibility included age at diagnosis of at least 21 years, no previous history of invasive cancer, and English, Spanish or Chinese-speaking. Women were enrolled during an in-person baseline interview that took place on average two months post-diagnosis, with collection of blood and saliva specimens. Active follow-up to update lifestyle and other factors and ascertain outcomes occurs periodically via mailed questionnaires and telephone interviews. Our primary outcomes include breast cancer recurrence, death including deaths due to breast cancer, and second primary cancers including breast cancer. Outcomes are identified via self-report, report from relatives, and through periodic search of KPNC electronic databases and are confirmed via medical record review.

The final study cohort consists of 4,505 women, with blood and saliva collected from 90% and 95% of participants, respectively. The majority of specimens were obtained before treatment. The cohort has substantial racial/ethnic diversity: 64.2% White, 12.4% Hispanic, 12.8% Asian, 7.9% African American, 2.7% other. The mean age at diagnosis was 59.6 years (range: 23.6-94.8 years). Educational attainment is high, with 84.1% of the cohort having at least some college education. Most women were diagnosed with AJCC Stage I or II (89%) cancers, with the majority being ER+ (83%), PR+ (63%), and HER2- (83%), and 11.6% with triple negative tumors. As of February 2015, 366 recurrences, 252 second primary cancers, and 437 deaths have been confirmed, with almost half (46%) of the deaths due to breast cancer.

The Pathways Study is a rich, unique resource collecting data on multiple factors that may influence breast cancer prognosis, including lifestyle, molecular, medical, and neighborhood contextual factors. To date, 30 papers have been published on topics ranging from CAM use, quality of life, and physical activity during treatment, to tumor DNA methylation profiles and correlates of breast cancer molecular subtypes. The Pathways Study promises to be a rich resource in the coming years to provide findings on factors influencing prognosis to ultimately help guide breast cancer care.

The Pathways Study is supported by National Cancer Institute grant R01 CA105274.

Breast Cancer Survivors in Korea: Today and Tomorrow

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Breast cancer is the second most frequent malignancy in Korean women, with a continuously increasing incidence. Five-year survival rate of breast cancer during 2006-2010 greater than 91% and the number of breast cancer survivors was more than 110,000 in 2011. Korean health insurance has supported the greatest expense for breast cancer patients. However, it is questionable whether the clinicians and government take care of breast cancer survivors with adequate evidence, well-designed cohorts, and enough funds.

Well-established cohorts are necessary to comprehensively assess the long-term health and care needs of breast cancer survivors. There are several cohorts for breast cancer survivors such as Shanghai women's health study, pathways study, and Nurses' Health Study I & II in USA and Korean central cancer registry, Korean Genome and Epidemiology Study (KoGES), Seoul breast cancer study and Korean Hereditary Breast Cancer Study (KOHBRA) in Korea. Today, we will review previous studies for breast cancer survivors in Korea, the recent cohorts for them, and seek to the way to establish ideal cohorts in Korea.

Nutrition for Breast Cancer Survivors

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Breast cancer survivors tend to be particularly careful about their diets and use of supplements; however, little is known about the association between dietary factors and breast cancer prognosis among breast cancer patients. Although breast cancer prevention and etiology studies have long provided information on dietary modification strategies for cancer prevention, research on diet for breast cancer survivors is relatively limited. At this time, we do not have specific dietary guidelines for breast cancer survivors yet. Breast cancer survivors are recommended to follow the healthy diet for overall cancer prevention. Several guidelines including National Cancer Institute guidelines for cancer prevention, American Cancer Society Guidelines on Nutrition and Physical Activity, and American Institute for Cancer Research recommendations for cancer prevention are often used to decrease the chance of a breast cancer recurrence or deaths.

Over the last few years, the role of diet on breast cancer prognosis has been actively explored. A few large intervention trials and prospective studies analyzed the effect of diet on breast cancer prognosis, and the evidence from studies on diet and food choices for breast cancer patients is increasing, but is not yet conclusive.

We conducted a pilot study to evaluate dietary intake among Korean female breast cancer survivors. Our study results suggested that intakes of nutrients and foods varied by time since surgery and cancer stage among breast cancer survivors and dietary intakes among breast cancer survivors differed from that in the general population. Further prospective studies are warranted to explore the associations of dietary components, food intake, and dietary pattern with breast cancer prognosis among Korean breast cancer survivors.

Breast Cancer Survivorship: Cultural and Socio-ecologic Considerations

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Breast cancer is the most frequently diagnosed cancer in Asian-American women [Breast Cancer Facts and Figures, ACS, 2015]. The current 5-year survival rate is 91.4% for aggregated subgroups of Asian-American breast cancer survivors (BCS). Despite the increasing Asian-American representation among BCS, the disease impact on Asian-American health-related quality of life (HRQOL) remains understudied. Limitations in the small but growing literature on survivorship outcomes among Asian-Americans include subject recruitment and measurement challenges [Ashing-Giwa, 2004; Kagawa-Singer, 2010], small Asian-American samples, few studies on long-term survivors, and often non-inclusion of Asian-American cases in population-based studies.

HRQOL is a multifarious construct measuring physical, social, emotional, and functional well-being [Cella, 2006]. HRQOL data are relevant to assessing cancer outcomes including treatment side effects and distress [Kagawa-Singer, 2010; Lim, 2009; Wong, 2007; Lam, 2011]. Although these HRQOL dimensions are documented to have cross-cultural relevance, no prospective study with Asian-American BCS was found. Survivorship research suffers from a lack of ethnic minority representation that this increasingly diverse survivor population is composed of.

This study examined the predictors of change in health-related quality of life (?HRQOL) among Asian-American breast cancer survivors (BCS).

Breast Cancer in Asian-Americans

Differences in the breast cancer epidemiology and outcomes have been documented among Asian-American subgroups. Japanese American has the highest incidence, and Filipina-Americans had some of highest incidence and mortality rates among all Asian-American subgroups in California [Gomez, 2014). Korean-Americans may have a greater likelihood of being diagnosed with HER2-postive breast cancer [Telli, 2011]. Since 1990, the average annual percent increase of breast cancer incidence rates of Chinese-, Korean- and Filipina-American were 1.8%, 5.4% and 2.2%, respectively [Liu, 2011].

Chinese-American BCS studies suggested that a BC diagnosis may be more detri-

mental to Chinese immigrants' well-being compared to those born in the U.S. Language barriers, inadequate medical communication, and culturally dissonant in-patient services are also other major concerns for the Asian-American community [Ashing-Giwa, 2003; Lu et al, 2013].

Filipina-American BCS note the burden of multiple roles such as patient, caregiver, and financial provider in their families. They reported worse functional strain and expressed a greater reliance on social support networks compared to other Asian-American BCS [Ashing-Giwa, 2003; Burke, 2011;].

Among Korean-American BCS, women reported unmet social support needs and psychological distress [Lim, 2012]. Korean-American BCS have shown greater distress and poorer HRQOL compared to Filipina-, Chinese- and Japanese-American BCS [Ashing-Giwa, 2003]. Korean-American BCS' lower quality of life may be due to socio-cultural barriers (i.e., lower socio-economic status, relatively recent immigration), access and quality of care (i.e., health care coverage and cost, language issues), and their personal and social environment (i.e., work, life and family demands, and functional strain) [Ashing-Giwa, 2007; Lim, 2012]. However, research also showed the mediating effects of family support, religiosity and spirituality on quality of life [Ashing-Giwa, 2003; Lim, 2012]. The emerging data documenting health disparities and differential outcomes within Asian-American subgroups warrants studies disaggregating Asian-American subgroups.

We employed a prospective cohort design with BCS recruited from hospitals and community organizations. BCS completed a self-report questionnaire at baseline and 12 months with measures consisting of the demographic and medical characteristics, FACT-B, Brief Symptom Inventory (BSI), quality of care, family communication and daily stress.

Participants included 116 BCS: 73 (63%) Chinese-, 25 (21%) Korean-, and 18 (16%) Filipina-Americans who were 1-3 years post diagnosis. Significant Asian-American subgroup differences were observed for several measures at baseline and follow-up ($p < 0.05$). Korean-Americans had the lowest scores on social support, family communication, general health perception, and quality of care; as well as experienced the highest distress (BSI-18) ($p < 0.05$ to $p < 0.001$) . Similar ethnic patterns in survivorship outcomes were documented for the 1-year follow-up assessment. However, at follow-up Chinese-Americans reported the lowest scores on general health perception ($p = 0.002$). Filipina-Americans had significantly better outcomes in all domains and across all the HRQOL measures at baseline and follow-up ($p < 0.05$).

The regression model explained 64% of variance in 1-yearchange in HRQOL. Income, native-language, headache, distress level, Co-Morbidity, Distress, and General

Health Perception were significant HRQOL determinants. Our preliminary results showed no notable change in HRQOL over 1-year.

Conclusions: Asian-American subgroup differences in predicting HRQOL were noted. Filipina-Americans reported the most favorable HRQOL, while Chinese-Americans endorsed moderated HRQOL and Koreans expressed poor HRQOL ($p < 0.001$). Regression analyses demonstrated that change in socio-ecological factors in conjunction with medical-characteristics dictates change in HRQOL outcomes. Further, the influences of culture, immigration and social-ecology are complex; hence research with larger samples is necessary to understand the survivorship experience of our diverse Asian-American population.

Targeting Distress During the Treatment of Breast Cancer Survivors

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Special Session

GBCC 2015 & 4th IBCS
Abstract Book

AB01-1

Cancer Genetic Risk Assessment in Breast Cancer (Challenges of Providing Access to Genetic Counseling and Genetic Testing to Individuals with Genetic Predisposition to Breast Cancer in Asia)

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Asia is witnessing an explosion of breast cancer similar to that experienced in Western countries last century with incidence increasing 3% per year primarily due to women having fewer children and at later ages, and mortality rapidly rising spurred on by late presentation. The World Health Organisation estimates that at least 500,000 breast cancers are diagnosed in Asia each year, and the majority will be young (< 50). Therefore, every year 14-30,000 cases are caused by mutations in BRCA1 or BRCA2. Yet over the nearly 20 years since the discovery of BRCA1 fewer than 1,000 Asian BRCA1 and BRCA2 families have had the benefit of genetic testing. In my talk, I will describe what we currently know about prevalence of high penetrance genes in individuals selected by age and family history of breast cancer, and outline the challenges of cancer genetic risk assessment in Asian populations where the population risk to breast cancer is lower and where cancer history is not known or poorly reported. In addition, I will review the opportunities for targeted genetic screening in the most cost-effective way.

Clinical Significance of Variants of Unknown Significance (VUS) in BRCA1/2 Genes

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Germline mutations in the human breast cancer susceptibility genes BRCA1 and BRCA2 are responsible for 30-70% of hereditary breast and ovarian cancer and 5-10% of all breast and ovarian cancers in heterogeneous Caucasian populations. BRCA1 and BRCA2 mutations confer greatly increased risk of breast and ovarian cancer. BRCA 1 and BRCA 2 genes are large genes with 5,592 and 10,254 bp (coding sequence length), and hence there are multiple sites where mutations can occur and recurrent mutations may not be as common A large number of distinct mutations in the BRCA1 and BRCA2 genes have been reported worldwide, but population-specific variation in the distribution of BRCA1 and BRCA2 mutations is well recognized.

Most reported disease ?associated alleles of BRCA1 and BRCA2 have been attributed to frame-shift, nonsense, insertions, deletions or splice site alterations that lead to truncation of BRCA1 or BRAC2 proteins. Besides clear pathogenic mutations, many variants (variant of unknown significance, VUS) are also found. Worldwide, VUS account for approximately half of all unique variants detected. However identifications of VUS are being increasingly reported as more studies on different ethnic populations particularly in ethnicities which are still comparatively less tested. Moreover with the use of NGS (Next Generation Sequencing), the detection rate of VUS has been increased in hereditary breast cancers. Whole-genome, whole-exome sequencing and multi-gene panels are gaining popularity in genetic testing, nevertheless, the discovery of VUS with unknown cancer risk remains the main challenge in terms of clinical interpretation and management.

With the increasing VUS being found, it is important to define which VUS are likely to be pathogenic. Various techniques use to characterize these VUS are discussed. Experience in Asian Countries will be shared.

Risk-Reduction Surgery in BRCA Mutation Carriers

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Options for risk reduction should be discussed in a shared decision-making environment. For breast cancer risk reduction, primary goals are prevention and early detection of cancer development. To this end, 4 strategies have been implemented: healthy life style, surveillance, chemoprevention, and risk-reducing surgery.

For healthy lifestyle, one should consider breast cancer risks associated with hormone therapy, limited alcohol consumption, exercise, and weight control.

Training breast self-examination with regular monthly practice should begin at 18 years of age, and semiannual clinical breast examinations should begin by age 25 for women that are carriers of BRCA1/2 mutations. In addition, women should begin annual breast MRI screening at age 25 or on an individualized timetable based on the earliest age of cancer onset in family members. Women should also begin annual mammographic screening at age 30. For the purpose of early detection of ovarian cancer (OC), women not opting for risk-reducing oophorectomy should consider concurrent transvaginal ultrasonography and CA125 determination every 6 months, starting at age 30, or 5-10 years before the earliest age of first diagnosis of OC in the family.

Carriers of BRCA mutations should also consider chemoprevention options for breast cancer (BC) and OC, including discussing risks and benefits. Half of BC cases can be prevented by 5 years of tamoxifen use in BRCA2 mutation carriers. Although tamoxifen use has not been associated with reduction in BC risk in those with BRCA1 mutation, it is important to note that this analysis was conducted on a very small number of individuals with BRCA1/2 mutations. Oral contraceptive use significantly reduced the risk of OC by approximately 50% for both BRCA1 and BRCA2 mutation carriers. However, studies on the effects of oral contraceptive use on BC risk among BRCA mutation carriers have reported conflicting data.

The NCCN Guidelines also support discussion of the option of risk-reducing mastectomy (RRM) for women on a case-by-case basis. Counseling regarding the degree of protection offered by such surgery and the degree of cancer risk should be provided. Contralateral RRM (CRRM) can be performed to reduce the risk of contralateral BC but absolute 20-year survival benefit from CRRM is less than 1%. The panel recommends bilateral risk-reduction salpingo-oophorectomy (RRSO) for women with a

known BRCA mutation, ideally between the ages 35 and 40 years, upon completion of child bearing, or at an individualized age based on the earliest age of OC diagnosed in the family. Ninety percent of BC can be prevented by RRM, and 97% of OC can be prevented by RRSO. RRSO is also reported to reduce the risk of BC in carriers of BRCA mutations by approximately 50%. According to a prospective, multicenter cohort study, RRSO is associated with a lower risk of OC, first diagnosis of BC, all-cause mortality, BC-specific mortality, and OC-specific mortality.

Risk-reducing surgery is not commonly performed in Korea; the first reports of contralateral RRM and bilateral RRM were in 2008 and 2010, respectively. According to nationwide survey in 2013 from 26 institutions, chemoprevention by tamoxifen and oral pill were recommended for BRCA1/2 mutation carriers in 9 and 3 of 26 centers, respectively. Only 9 unaffected carriers were actually managed by tamoxifen. RRM, CRRM, and RRSO were performed in 2, 17 and 117 carriers, respectively. Korean hereditary breast cancer management guideline was launched on May 2013 and we can refer to this guideline while we are managing the high-risk patients.

Genetic Counseling in Asia

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NS01-1

Women's Health Care in Breast Cancer

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Breast cancer is the second most common cancer diagnosis in Korean women, and 91% of women with breast cancer survive for at least five years in 2007-2011 Korean data.

Breast cancer survival has been attributed to advances in screening mammography and combination treatment with surgical techniques, focused radiation and more effective adjuvant therapy.

The overall quality of life of a woman with breast cancer is affected by cancer treatment itself as well as hormone-related problems. Thus, the health care provider should notice issues of fertility and pregnancy after breast cancer treatment, management of vasomotor symptoms (VMS) and other sexual health issues, and prevention and treatment of bone loss.

In addition to surveillance to monitor for recurrence, it is important to manage treatment-related adverse effects and enhance women's identities in patients with breast cancer.

Appropriate counseling and evidence-supported surveillance strategy will impact patients' satisfaction for cancer-related treatment and overall care.

Managing Menopausal Symptoms among Breast Cancer Survivors

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Breast cancer treatments can cause the early onset of menopausal symptoms for pre-menopausal women, or the return or aggravation of symptoms for peri-menopausal or post-menopausal women. The most commonly reported menopausal symptoms in breast cancer survivors are vasomotor symptoms and impaired sexual functioning. The former include hot flushes, night sweats and sleep disturbances; the latter includes vaginal dryness, painful inter-course and loss of sexual interest. Vasomotor symptoms and vaginal dryness are the most common complaints for which breast cancer survivors seek advice. Though for some women these symptoms are bearable, for others these have a large impact on their quality of life. In a recent study of disease-free breast cancer survivors, psychological effects of cancer diagnosis and treatment were reported by about 70% and sexual dysfunction resulting in impaired quality of life by 35%. Despite this high impact, physicians consider such side-effects an unavoidable consequence of a valuable oncological treatment, and may therefore incline towards under-treatment.

However, few patients appear to be provided with the opportunity to discuss such symptoms with a health professional as part of their treatment. Therefore, we should continue to pay attention to menopausal symptoms for several years after primary therapy for the breast cancer. And then, we need to provide education to each patient so that they can manage menopausal symptoms. Education options for menopausal symptoms in breast cancer survivors include:

- The use of hormone replacement therapy for menopausal symptoms in breast cancer survivors should be avoided.
- Vasomotor symptoms:
- Non-hormonal treatment of hot flushes is effective in about half of patients and can consist of lifestyle adaptation, acupuncture, venlafaxine, gabapentin or clonidine.
- Impaired sexual functioning:
- Non-hormonal vaginal lubricants like vaginal gel or moisturizer can be helpful.
- Vaginal estriol is effective in treating severe vaginal atrophy and when given locally for a short period (a maximum of 6 weeks) is most probably safe (although this is not

proven).
- Psycho-education. Psychosexual couple therapy can be effective, as can behavioral therapy. There is moderate support for the effectiveness of both.

Managing menopausal symptoms may improve quality of life and cancer therapy adherence and decrease the risk of tumour recurrence. So it is important for nurses not only to understand the patient needs of the menopausal woman, but also to be able to differentiate between quality of life issues related to menopause and to cancer treatment in order to provide holistic nursing care.

In addition, health professionals should consider discussing such symptoms when patients start treatment and assess these symptoms at follow-up appointments to identify potential interventions. Therefore as health professionals, we should be to prepare all patients for possible menopausal symptoms early on in their treatment and to offer on-going support.

NS01-3

Adopting Self-Awareness after Treatment for Breast Cancer

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Breast cancer is the most frequently occuring cancer in women, but greatly improved the survival rate of patient with breast cancer brought to the development of current medical technology has shown a high survival rate of up to 91% in Korea. However, they may be breast cancer recurrence and metastasis after 10years because of the slow growth of cancer cell in many case been reported of up to 20-30% of breast cancer patient were found to experience a very high degree of instability, even after completion of the treatment.

The psychological and social problems in breast cancer survivor in the country studies have been reported to be more serious than the physical symptoms showed that extent of the completed de-stress similar to the patient being treated breast cancer survivors.

Furthermore, the interest in the patient with cancer in physical therapy from the cacner of social and psychological well being been expanded into the realm of overcoming the disease effectively, as well as focused happy to live a life after treatment.

Therefore,it is necessary to develop the medical service after treatment end that allows you to proactively manage their health and live of breast cancer survivor. The need comprehensive intervention for improve the quality of life.

This lecture consists of a review of the literature. The research that contributes to the holistic care of breast cancer survivors and expect to be made subject to realization of such high quality patient centered cancer care medical service.

NS01-4

Pregnancy in Young Women with Breast Cancer

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In Korea, about 15% of the breast cancer women are diagnosed at the age of no more than 40's. As for young women with breast cancer, there are unique things to be considered such as development task, reproductive health, pregnancy and prevention of conception, pregnancy associated breast cancer and sudden menopause symptoms.
Absolutely, the pregnancy related issue is one of the most concerning one regarding the young breast cancer women especially when taking their family developmental stage into account.

Since chemotherapy and hormonal therapy can affect their reproductive health, their plan to have babies must be checked. Then delicate counseling about their family developmental task and information about proper method to preserve ovarian function or to prevent conception must be provided. Also, those women must be referred to gynecology timely to ensure gynecologic health including checking endometrium thickness when taking tamoxifen.

For pregnancy associated breast cancer women, both fetal and maternal safety must be considered from the stage of diagnosis through the whole process of therapies.
Throughout the entire process, oncology nurses should play a key role to make these courses smoothly and the patients understand by educating them and coordinating with them.

In addition, oncology nurses should understand that many of the young breast cancer women undergo sudden and unexpected menopause symptoms caused by systemic therapies. Therefore proper strategies that they can practice to overcome these symptoms should be introduced to the patients.

In any case, there may be many things that we don't know about them. Therefore oncology nurses must listen to them carefully and concentrate on their needs. And we need to keep going on studying to develop education and interventions. Then we can provide considerate counseling and education.

The Role of Oncology Nurse in Sexual Management

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Sexuality is integral to every person and is an essential component for general well-being, quality of life, and overall health. Many cancer patients whose treatments have permanently altered the way that they are able to express their sexuality might say that there is no such thing as sexuality after cancer.

Nurses spend the most time with patients and, as part of holistic nursing practice, they are expected to possess the sensitively address issues of sexuality with their patients. However, nurses are unprepared and uncomfortable when initiating discussion about sexuality with their patients. Nurses have multiple barriers to addressing sexuality issues with their patients, including lack of necessary knowledge, confidence, and comfort initiating the discussion. Even though nurses understood the need to address sexual problems their patients assessments but were afraid they wouldn't have the answers to patients' questions.

Nursing standard of care promote the notion of holistic care, and that includes ensuring that our patients have the knowledge they need about the side effects of cancer treatments on their sexuality. Unless nurses signal their willingness to discuss such topics, most patients will hesitate to bring them up and will continue to wonder, and perhaps worry about the effects their illnesses and treatments will have on their own sexuality and their relationships with their significant others.

To provide an effective sexual assessment and to plan for and initiate an appropriate intervention, it is beneficial to use a combination of methods to assess the breadth and depth of changes to the patient's sexuality and sexual functioning. Topics that may be discussed include current relationships, normal patterns of sexual activity, level of intimacy, satisfaction with current activities, communication patterns, disease and treatment issues, and coping skills. When conducting either type of assessment, the initial steps are to legitimize and normalize the sexuality discussion by making the conversation a routine part of the nursing assessment while emphasizing the importance of accurately assessing beliefs and concerns about sexual function and sexuality. If you ask questions, should be short and to the point. A combination of direct and open-ended questions is the best approach for a more intensive assessment. Questions should be appropriate to the patient's age, gender, sexual orientation, and cultural beliefs; however,

nurse bias and personal beliefs should not be allowed to interfere with comprehensive assessment.

To help support nurses in addressing sexual issues with patients, sexual assessment and intervention are described by PLISSIT Model. PLISSIT Model is a four-step model that was first conceptualized by Annon(1976). It provides a systematic approach to learning about a patient's sexual concerns and discussing supportive interventions based on four sequential intervention levels requiring increasing knowledge and expertise. By assessing patients' sexuality, nurses give patients permission to voice their concerns. Nurses can provide limited information by educating patients about medication and treatment effects on sexuality. Also, nurses can offer specific suggestions such as positions for intercourse that may reduce dyspareunia, whereas intensive therapy is indicated for those with serous sexual problems and is conducted by certified sexual therapists.

Strategies to enhance nurse-patient interactions include an understanding of the nurse's communication style, socio-cultural and socio-sexual beliefs and values, and the importance of content and timing; while strategies that will decrease barriers to conducting an assessment initially focus on the nurse's knowledge and skill, and the nurse's level of comport and confidence. Nurses should educate cancer patients, so that they become comfortable discussing sexuality and are aware of available resources. Every interaction between nurses and patients offers an opportunity to discuss the patients sexuality and any changes they may be experiencing. Oncology nurses are the ideal healthcare professionals to assess the sexual health status of their patients and to intervene to sensitively address sexual problem. Therefore, oncology nurses can provide patients with chance to talk about their sexuality while indicating their willingness to provide assistance and additional resources.

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Recent Update in Management of Breast Cancer: Medical Oncology

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The current guidelines concerning adjuvant hormonal therapy for premenopausal women with ER?positive breast cancer recommend continuing tamoxifen for up to a total of 10 years (1). A meta-analysis of these trials showed a reduction in the risk of death and relapse of about 10% and 30% in patients with ER+ breast cancer, respectively (2). A joint analysis of the TEXT (Tamoxifen and Exemestane Trial) and SOFT (Suppression of Ovarian Function Trial) was recently published (3). The results of the long-awaited SOFT and TEXT trials established adjuvant endocrine therapy with exemestane plus ovarian suppression or ablation as a new treatment option for premenopausal women with ER-positive early stage breast cancer with a 4% absolute improvement in 5-year freedom from the disease, without any significant difference in overall survival and at the expense of higher toxicity and more frequent early cessation of endocrine therapy. Particularly, for some patients with a breast cancer that may place them at a higher than average risk of recurrence (including those who are 35 years or younger or who underwent chemotherapy), ovarian suppression plus the aromatase inhibitor, exemestane, may be recommended. Recent results of the PALOMA-1/TRIO-19 trial suggest that cyclin-dependent kinase (CDK) 4/6 inhibition could be one of the good answer for overcoming endocrine resistance (4). In this trial, median progression free survival was 10.2 months for patients given letrozole alone, compared with 20.2 months for those given palbociclib plus letrozole (HR 0.4888, 95% CI 0.319-0.748; one-sided $p = 0.0004$). Several adverse events were seen in more than 0% of patients, with increases noted in the palbociclib group, but most were mild or manageable.

Pertuzumab is the first neoadjuvant drug to receive accelerated approval by the FDA based on pathological complete response as the primary end point (5). In the CLEOPATRA study, first-line treatment with pertuzumab/trastuzumab/docetaxel significantly improved overall survival for patients with HER-2-positive metastatic breast cancer, providing a 15.7 month increase in the median values. The median overall survival of 56.5 months is unprecedented in first-line and this substantial improvement confirms the pertuzumab containing regimen as standard of care in this setting (6). This finding suggests that a study of pertuzumab and trastuzumab in earlier stages of

the disease is warranted. A study of adjuvant therapy in patients with newly diagnosed HER2-positive breast cancer has been initiated [APHINITY, NCT01358877].

The field of breast cancer, particularly HER2-positive breast cancer, is now expanding with the addition of multiple active targeted therapies. In the future, we anticipate the routine use of genomics to identify biomarkers and accordingly select patients who will optimally benefit from particular anti-HER-2 agents or combinations.

Surgical Oncology
(Recent Updates in Surgical Management of Breast Cancer)

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Recent advances in systemic treatments such as chemotherapy, hormonal therapy, and targeted therapies contribute not only to reducing the risk of distant metastases but also local recurrences after surgery. Excellent disease management leads to changes in local treatments for breast cancer patients in order to pursue less invasive surgical plans. This discussion of recent updates in the management of breast cancer will focus on three topics that are especially important from an Asian patient's perspective: 1) the achievement of better cosmetic outcomes after surgery. After the introduction of mammography screening for breast cancer, the ratio of patients who underwent breast-conserving surgery (BCS) had increased. In order to minimize the risk of ipsilateral local breast tumor recurrence (IBTR) and avoid re-excision, wider margins of cancer-free tissue had to be achieved. There is a trade-off between wider margins and cosmetic effects. It can be difficult to achieve wider margins in Asian women because they have the smallest breast sizes of all the races. ASTRO and SSO established the consensus guideline on margins for BCS, which stated that wider margins did not lower the risk of IBTR. Introduction of neoadjuvant treatment and oncoplastic surgery is extending the indications for BCS in patients who are unsuitable for conventional conservation techniques. 2) The preservation of axillary nodes. For women with clinically node-negative disease, sentinel node (SN) biopsy has become the standard of care to determine the presence of cancer in the axillary nodes, which can be safely preserved only in patients without SN involvements. However, recent data argued against axillary node dissection for SN positive patients who met the criteria. Even for women with clinically node-positive disease, SNB might still be taken into consideration after the completion of neoadjuvant chemotherapy. 3) More convenient adjuvant radiotherapy. About 20% of patients who underwent BCS in Japan did not receive long-term adjuvant radiotherapy. Trials in the UK suggested that lower total doses of radiotherapy delivered in fewer, larger doses (40 Gy in 15 fractions) are at least as safe and effective as the standard regimen (50 Gy in 25 fractions) for women requiring adjuvant radiotherapy for early breast cancer. On the other hand, the efficacy and safety of partial-breast irradiation (PBI) using vari-

ous techniques have been investigated since the late 1990s. Without data, the ASTRO has recommended against treating young women with PBI, because young age itself is a risk factor for local recurrence after BCS. In Asian countries, the peak incidence tends to be for women between 45 and 50 years, while in US and European countries the peak incidence tends to be between 55 and 60 years of age. A substantial proportion of potential candidate patients in Japan are interested in the convenience of PBI as an alternative to whole-breast irradiation (WBI), especially for young breast cancer patients who are likely to be much busier with daily work, children, and household duties. We initiated a prospective observational study on PBI with multicatheter brachytherapy as an alternative to WBI after BCS; multicatheter brachytherapy has already been performed in more than 260 breast cancer patients. Data regarding the long-term efficacy of our technique in Japanese breast cancer patients indicated a few instances of local recurrence and a low rate of adverse events. We introduced personalized radiation therapy after BCS in order to perform radiation therapy in most patients for reducing the incidence of local breast cancer relapse. Even for patients with localized ipsilateral breast tumor recurrences after BCS followed by WBI, mastectomy is generally preferred over BCS. One option for local management is to treat these patients with PBI after resection of the recurrent tumor. This approach is based on the hypothesis that re-irradiation to a limited area will be effective and result in an acceptable frequency of side effects.

The entire human genome has been already sequenced and could be used to examine genetic profiling of breast cancer to evaluate individual risk of recurrence after surgery. These efforts might impact optimal surgical management of breast cancer.

Radiation Oncology (Should Radiotherapy be Omitted in Some Early Breast Cancer Patients?)

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Invasive breast cancer

According to two meta-analysis of Early Breast Cancer Trialists' Collaborative Group (EBCTCG) in 2005 and 2011, about one breast cancer death was avoided by year 15 for every four recurrences avoided by year 10 (1, 2). Radiotherapy (RT) reduced the local recurrence risk in all subgroups of patients, but the absolute value of reduction risks was different among subgroups. In 2005 reports, the absolute reduction of recurrence risk by RT was dependent most on the risk of local recurrence without RT. Particularly, when patients were divided into 3 categories (< 10%, 10-20%, and > 20%) according to absolute reduction of 5-year local recurrence risk after lumpectomy or mastectomy, there was no improvement of 15-year breast cancer mortality in group of absolute reduction of risk < 10%. The patients with low local recurrence risks would be confined as those with tumor size less than 2 cm, negative lymph node metastasis, low grade tumor, old age, and the use of tamoxifen.

CALGB 9343 demonstrated the role of RT in these low risk patients (3, 4). With 10-year follow-up, locoregional recurrences were observed in 10% of patients receiving Tamoxifen alone and only 2% of those receiving Tamoxifen and RT. However, this absolute difference of locoregional recurrence could not result survival benefit. On the basis of this result, Hepel et al. suggested treatment algorithm for management of women older than age 70 years with T1N0 and ER-positive invasive breast cancer through considering life expectancy and comorbidity conditions (5). Patients with life expectancy < 5 years and severe comorbidity may be considered to be only observed and those with life expectancy > 5 years should be treated endocrine therapy and/or RT depending on the risk of local and systemic recurrence.

Recently, the result of PRIME II trial was reported (6). In 1,326 women ≥ 65 years with low risk early breast cancer managed by breast conservation, ipsilateral breast tumor recurrence at 5 years was reduced to one-fourth. However, the absolute value of reduction was very small (2.8%) and there were no significant differences in regional recurrence, contralateral breast cancer, distant metastasis, nor survival.

Methods increasing convenience of breast radiotherapy

We can guess some reasons to avoid RT for patients with early breast cancer. The first is the issue of convenience. Because conventional RT consists of 28 fractions to whole breast followed by 5 fractions to tumor bed, patients should visit the outpatient clinic daily during 6-7 weeks. There were some reports that long distance to RT facility increase the use of mastectomy (7). Of the proposed alternatives to increase convenience, hypofractionated RT has successfully been performed (8). Hypofractionated whole breast irradiation has shown similar efficacy and toxicity compared with conventional fractionation in phase III randomized trials and has been used as standard treatment (9, 10). In addition to, partial breast irradiation using external beam radiotherapy, brachytherapy, intraoperative radiotherapy has been actively studied. These treatments reduce treatment fractions dramatically and are intended to improve patients' convenience. These are still in the research stage, but years later, will be used in earnest after the report of results.

The second is the matter of complication and cardiac toxicity is representative. A population-based study showed that incidental exposure of the heart to RT for left breast cancer increase the rate of major coronary events by 7.4% per gray (11). To reduce cardiac toxicity, there are several methods have been introduced and deep inspiration breathing hold technique has been widely used (12). This method can reduce the irradiated cardiac volume, because the heart is moving downwards during breath hold. Intensity-modulated radiotherapy or proton therapy is also studied to reduce cardiac dose.

The third problem is the occurrence of secondary malignancy caused by RT. In patients treated with breast RT, contralateral breast cancer, lung cancer, esophageal cancer, or soft tissue sarcoma of chest wall could be occurred as a secondary malignancy (1). However, analysis of Surveillance, Epidemiology and End Results (SEER) cancer registries showed an only 5% of second cancers after radiotherapy in patients with breast cancer were related to RT (13). In addition, latency between radiation exposure and solid cancer induction was known at least 5 years depending age at exposure or radiation dose. Considering the clinical benefit of RT, radiation induced secondary malignancy does not give the rationale to omit RT.

ED02-1

Understanding of Genomics Technology

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All cancers arise as a result of accumulated genetic and epigenetic alterations. Therefore, analyses of cancer genome sequences and structures provide insights for understanding cancer biology, diagnosis and therapy. The application of microarray or second-generation sequencing technologies is allowing substantial advances in cancer genomics. Thus, our understanding of the complexity of cancer has significantly increased through large-scale genomic studies from large collaborations such as the International Cancer Genome Consortium (ICGC http://www.icgc.org/) and The Cancer Genome Atlas (TCGA http://cancergenome.nih.gov/). However, the translation of these data sets into clinically actionable information is still in its infancy; nevertheless, insights from sequencing studies have led to the discovery of a variety of novel diagnostic and prognostic biomarkers and potentially actionable therapeutic targets. Here, I will review recent advances in cancer genomics and discuss what the new findings have taught us about cancer biology and, more importantly, how these new findings guide more effective diagnostic and treatment strategies.

Overview of Breast Cancer Genomics

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The rapid advancement of genomics has brought numerous molecular profiling studies of breast cancers. Nowadays, molecular approach based on genomics plays a central role in understanding tumor heterogeneity and discovering novel actionable targets in breast cancer. In 2000, first study on genomic classification was reported by Perou et al. from Stanford Universtiy. They analyzed variation in gene expression patterns in normal and malignant human breast tissues from 42 individuals. Hierarchical clustering analysis, which organizes tumor samples based on their overall similarity in there gene expression patterns, showed that most tumor specimen pairs clustered together. These molecular portraits revealed by the patterns of gene expression not only uncovered similarities and differences between the tumor samples but identified specific features of physiologic variation. Sorlie et al. from the same Stanford group, refined this classification by analyzing a larger number of breast cancer using a similar microarray cDNA platform. They were able to identify three subgroups characterized by low or absent ER gene expression: the basal-like subgroup; the erbB2-positive subgroup; and the normal breast-like group. The novel finding in that study was the recognition within the luminal/ER-positive tumors of at least two different subgroups with distinct molecular signature: the luminal subgroup A and the luminal subgroup B or C. Thereafter, similar studies based on gene expression profiling has been carried out by other investigators and showed that distinction molecular subtypes can be used in discriminating a prognosis and in identifying therapeutic targets for personalized medicine.

The advent of genomics technology has enabled in developing molecular predictors. Part of gene expressions-based assays has been validated and used in daily practice. The 21-gene Recurrence Score assay (RS) was developed using a RT-PCR-based approach and represents one of the most validated gene expression assays yet developed. This assay classifies the patients as low, intermediate and high risk groups, and provides significant prognostic information. Furthermore, this assay is utilized as a clinical decision-making tool for the addition of chemotherapy in patients with hormone receptor-positive, node-negative breast cancer.6 Finally, the main reclassification effect of the RS when compared with classic biomarkers is the reduction of the patients with high risk. As a result, the adoption of RS in daily practice has brought the change from planned chemo-endocrine therapy to endocrine therapy alone. Recent research with genomics has given new clues in searching treatment strategies for triple-negative breast cancer (TNBC). Cluster analysis conducted by Lehmann et al. identified 6 TNBC subtypes displaying unique GE and ontologies, including 2 basal-like (BL1 and BL2), an immunomodulatory (IM), a mesenchymal (M), a mesenchymal stem-like (MSL), and a luminal androgen receptor (LAR) subtype. Their study can be useful in biomarker selection, drug discovery, and clinical trial design that will enable alignment of TNBC patients to appropriate targeted therapies. Lastly, with the advent of Massively Parallel Sequencing, it is likely that mainstream of genomic studies is moving from microarray-based to sequencing-based.8 For instance, gene expression profiling can be accomplished using the sequencing and counting of mRNA molecules, which is called mRNA-seq; this approach is more quantitative, more sensitive, and also provides sequence information that alternative splicing and single nucleotide variants can be simultaneously detected. The promise of gene expression patterns, when possibly couple with somatic mutational profiles, is the near future when we will be able to use the detailed tumor-specific, and patient-specific, information as a means to personalize therapy for breast cancer patients.

How to Write a Good Research Grant Proposal

Fabrice Andre

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Career Development as a Junior Researcher

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How to Succeed as a Private Breast Practitioner in Korea

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Breast Clinic, Park Surgical Clinic, Korea

ED03-4

How to Build and Maintain the Multinational Network

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Cancer is a global concern with rising incidences as a result of screening, increasing awareness, and changing lifestyles in both developed and developing countries across the world. The International Agency for Research of Cancer GLOBOCAN project estimated that burden of cancer in India is almost likely to double from 1 million cases in 2012 to 1.7 million in 2035. This is not due to widespread screening but more due to increased awareness and changing lifestyles. A multinational network not only helps to realize and understand this rising concern on a global perspective, but also brings to fore the varieties of lacunae in health care across the globe, variations in social issues specific to a segment of population, and eventually help to bridge the gap between the various segments of population with sharing of resources and intellectual exchange. The National Cancer Grid in India was developed in 2012 to make cancer care in India standardized, uniform and accessible to all with intellectual exchange between centres within the country. It addresses issues in the areas of patient care, education and training of personnel, collaborative research, and cancer policy in the country. Based on a similar model, a multinational breast cancer network can be evolved and will be presented at the Global Breast Cancer Conference.

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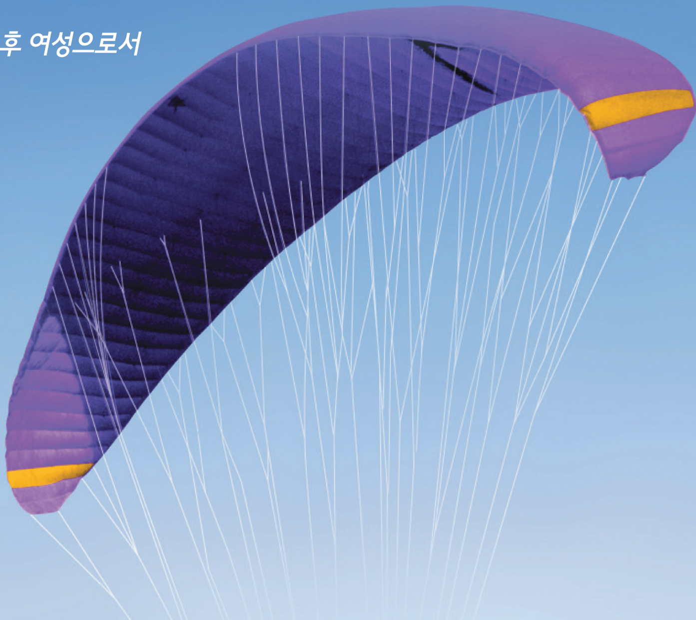

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원료약품의 분량 1mL중 주성분 풀베스트란트 (별규) 50mg **성상** 무색에서 노란색의 맑은 점성 액이 들어있는 프리필드시린지 **적응증 (효능 · 효과)** 에스트로겐 수용체 양성의 폐경기 이후 여성으로서 항에스트로겐 투여 후 질병이 재발된 국소 진행성 또는 전이성 유방암 **용법 · 용량** 성인 여성(노인 환자 포함): 한달 간격으로 500mg을 투여한다. 첫 투여 2주 후 500mg을 추가적으로 투여한다. 이 약은 각 둔부에 한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

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Breast cancer is a heterogeneous disease. About two thirds of the patients with breast cancer are estrogen receptor (ER) positive. Although most patients with early-stage breast cancer are treated with curative intent, 20-30% of those patients will eventually experience recurrence with metastatic disease. Endocrine therapy is the mainstay of first-line treatment for patients with ER+ advanced or metastatic breast cancer unless their tumors are rapidly progressive in nature or symptomatic disease. The aim of endocrine therapy is to modulate and disrupt the process by blocking pituitary production of LH/FSH (GnRH analogues), antagonizing the ligand binding to ER (tamoxifen and other selective ER modulators), inhibiting the peripheral production of estrogen (aromatase inhibitors) or by degrading and downregulating ER (fulvestrant).

However, a substantial number of ER+ breast cancer patients will not respond to initial hormonal therapy (primary or "de novo" resistance). Other patients will progress during therapy despite showing an initial response (secondary or acquired resistance). Either "de novo" or acquired endocrine resistance is a major limiting factor to the use of endocrine therapy and has been the focus of much research both in vitro and in vivo. Multiple mechanisms of endocrine resistance have been proposed, including the deregulation of the ER pathway, alterations in the cell cycle and cell survival signaling molecules and the activation of escape pathways. A thorough understanding the molecular mechanisms regulating the hormone sensitivity or resistance is important to improve the efficacy of and overcome the resistance to endocrine therapy. Over the past years, a number of trials have been carried out incorporating many targeted agents into endocrine therapy, such as EGFR inhibitors, HER2 inhibitors, PI3K/Akt/mTor inhibitors, histone deacetylases (HDAC) inhibitors, Src inhibitors, CDK4/6 inhibitors in order to overcome endocrine resistance for ER positive advanced or metastatic breast cancer patients. I will present the current options for endocrine therapy in ER+ advanced or metastatic breast cancer, proposed mechanisms of endocrine resistance, and ongoing clinical trials of novel targeted agents combined with hormonal therapy as a means of overcoming resistance.

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[Indication] 1 Breast Cancer • Metastatic and locally advanced breast cancer 1) 1st line treatment of patients with locally advanced or metastatic breast cancer in combination with doxorubicin, 2) In combination with trastuzumab, treatment of patients with HER2 overexpressed (IHC 3+ or FISH positive) and chemotherapy naive metastatic breast cancer which is overexpressed HER2 (IHC 3+ or FISH positive) and have not treated with chemotherapy, 3) Treatment of patients with locally advanced or metastatic breast cancer in whom previous chemotherapy has failed, 4) In combination with capecitabine, treatment of patients with locally advanced or metastatic breast cancer in whom previous chemotherapy has failed. Previous therapy should have included an anthracycline. • Adjuvant breast cancer 1) Adjuvant treatment in combination with doxorubicin and cyclophosphamide is indicated for the adjuvant treatment of patients with operable node-positive breast cancer • operable node-negative breast cancer with one or more high risk factors. (tumor size ≥2 cm, age <35 years, hormone receptor status negative, tumor grade 2 or 3) 2) Doxorubicin and cyclophosphamide followed by TPM® in combination with trastuzumab is indicated for the adjuvant treatment of patients with operable breast cancer whose tumors overexpress HER2 (ACTH regimen) 3) Taxotere in combination with trastuzumab, and carboplatin is indicated for the adjuvant treatment of patients with operable breast cancer whose tumors overexpress HER2 (TCH regimen) 4) Taxotere in combination with cyclophosphamide is indicated for the adjuvant treatment of patients with operable breast cancer (primary tumour of ≥1 cm and <7 cm) (TC regimen) **2 Non-Small Cell Lung Cancer :** Treatment of patients with locally advanced or metastatic non-small cell lung cancer, including those who have failed platinum-based chemotherapy. **3 Prostate Cancer :** Treatment of patients with androgen independent (hormone refractory) metastatic prostate cancer in combination with prednisolone. **4 Ovarian Cancer :** 1st line therapy for the treatment of patients with advanced or metastatic epithelial ovarian cancer in combination with carboplatin. **5 Head and Neck Cancer :** In combination with cisplatin and fluorouracil, induction treatment of patients with locally advanced squamous cell carcinoma of the head and neck. **6 Gastric cancer :** Advanced and metastatic or locally recurrent gastric cancer. **7 Esophageal cancer :** Advanced or recurrent squamous esophageal cancer. **[Dosage and Administration] 1 Breast Cancer** • Metastatic and locally advanced breast cancer 1) For the 1st line treatment of breast cancer, docetaxel 75mg /m² is given in combination therapy with doxorubicin (50mg/m²) 2) In combination with trastuzumab for the treatment of HER2 overexpressed and chemotherapy naive metastatic breast cancer, the recommended dose of docetaxel is 100 mg/m² as a 60-minute infusion every three weeks. Initial docetaxel infusion can be started the day following the first dose of trastuzumab. If docetaxel doses can be administered immediately after completion of the trastuzumab infusion, if the preceding dose of trastuzumab was well tolerated. * The recommended initial dose of trastuzumab is 4mg/kg as 90-minute intravenous infusion. The recommended weekly dose of Herceptin is 2 mg/kg, beginning one week after the initial dose. (Refer to the product information of trastuzumab.) 3) For the treatment of breast cancer in whom previous chemotherapy has failed, docetaxel 75~100 mg/m² is administered as a one-hour infusion every three weeks. 4) In combination with capecitabine, for the treatment of locally advanced or metastatic breast cancer in whom previous chemotherapy including anthracyclines has failed, the recommended dose of docetaxel is 75mg/m² every three weeks, administered twice daily (within 30 minutes after a meal) for 2 weeks followed by 1-week rest period. For capecitabine dose calculation according to body surface area, see capecitabine package insert. • Adjuvant breast cancer 1) In the adjuvant treatment of operable node-positive and node-negative breast cancer, the recommended dose of docetaxel is 75 mg /m² administered 1-hour after doxorubicin 50 mg/m² and cyclophosphamide 500 mg/m² every 3 weeks for 6 cycles (AC regimen). Prophylactic G-CSF may be used to mitigate the risk of hematological toxicities (see Dosage adjustments during treatment). 2) AC-TH regimen (1) AC cycles 1~4) doxorubicin (A) 60 mg/m² followed by cyclophosphamide (C) 600 mg/m² administered every three weeks for 4 cycles. (2) TH cycles 5~8) docetaxel (T) 100 mg/m² administered every three weeks for 4 cycles, and trastuzumab (H) administered weekly according the following schedule - Cycle 5 (starting three weeks after the last cycle of AC): Day 1: trastuzumab 4 mg/kg (loading dose) Day 2: docetaxel 100 mg/m² Days 8 and 15: trastuzumab 2 mg/kg - Cycles 6~8: Day 1: docetaxel 100 mg/m² and trastuzumab 2 mg/kg Days 8 and 15: trastuzumab 2 mg/kg Three weeks after day 1 of cycle 8, trastuzumab is administered for a total duration of 1 year. 3) TCH regimen (1) Docetaxel (T) 75 mg/m² for 1 hour and carboplatin (C) at AUC of 6 mg/mL/min administration over 30 to 60 min every three weeks, Day 2 of cycle 1, Day 1 of cycle 2~6 (2) Trastuzumab (H) 4 mg/kg for 90 min in day 1 as loading dose, then weekly administered 2 mg/kg for 30 min as maintenance dose. (3) Trastuzumab 6 mg/kg for 30 min is given every three weeks after completion of adjuvant chemotherapy. Trastuzumab is administered for a total duration of 1 year. 4) TC regimen TAXOTERE 75mg/m² over 1 hour and cyclophosphamide 600mg/m² as an intravenous administration over 30 to 60 minutes on day 1 of a 21 day cycle for a total of four cycles. Premedication with oral dexamethasone 8mg twice daily is administered commencing 1 day before administering TAXOTERE and continuing for 1 total of five doses. **2 Non-Small Cell Lung Cancer :** The recommended dosage of Docetaxel is 75 mg/m² administered as a one-hour infusion every 3 week. Maximum dosage is 75mg/m² at platinum-combined chemotherapy. **3 Prostate Cancer :** The recommended dosage of docetaxel is 75 mg/m² administered as a one-hour infusion every 3 week. Prednisolone 5 mg oral twice daily is administered continuously. **4 Ovarian Cancer :** As the first line therapy for advanced or metastatic ovarian cancer, docetaxel is 75 mg/m² administered as a one-hour infusion every three week. Then carboplatin 6.0 mg/ml/min (AUC) is intravenously administered during 30~60 min. **5 Head and Neck Cancer :** 1) Induction chemotherapy followed by radiotherapy For the induction treatment of inoperable locally advanced squamous cell carcinoma of the head neck (SCCHN), the recommended dose of docetaxel is 75 mg/m² as a 1 hour infusion followed by cisplatin 75 mg/m² over 1 hour, on day one, followed by fluorouracil as a continuous infusion at 750 mg/m² per day for five days. this regimen is administered every 3 weeks for 4 cycles. Following chemotherapy, patients should receive radiotherapy. 2) Induction chemotherapy followed by chemoradiotherapy For the induction treatment of patients with locally advanced (technically unresectable, low probability of surgical cure, and aiming at organ preservation) squamous cell carcinoma of the head and neck (SCCHN), the recommended dose of docetaxel is 75 mg/m² as a 1 hour intravenous infusion on day 1, followed by cisplatin 100 mg/m² administered as a 30-minute to 3-hour infusion, followed by fluorouracil 1000 mg/m²/day as a continuous infusion (from day 1 to day 4). This regimen is administered every 3 weeks for 3 cycles. Following chemotherapy, patients should receive chemoradiotherapy. **6 Gastric Cancer :** 1) As single agent, the recommended dosage of docetaxel is 75mg/m² administered as a one-hour infusion every three weeks. 2) The recommended dose of docetaxel is 75 mg/m² as a 1-to 3-hour infusion, followed by cisplatin 75 mg/m², as a 1-to 3-hour infusion (both on day 1 only), followed by fluorouracil 750 mg/m² per day given as a 24-hour continuous infusion for 5 days, starting at the end of the cisplatin infusion. Treatment is repeated every three weeks. Patients must receive premedication with antiemetics and appropriate hydration for cisplatin administration. Prophylactic G-CSF should be used to mitigate the risk of haematological toxicities. **7 Esophageal Cancer :** The recommended dosage of docetaxel is 70mg/m² administered as one-hour infusion every 3~4 weeks, and the dosage may be reduced or increased depending on the condition of patients **<Premedication Regimen>** All patients should be premedicated prior to TAXOTERE administration in order to minimize fluid retention and severe hypersensitivity reaction. Such premedication consisting of oral corticosteroids such as dexamethasone 16 mg per day (ex. 8mg bid) for 3 days starting one day prior to TAXOTERE administration, should be used unless it is contraindication. Prophylactic G-CSF may be used to mitigate the risk of hematological toxicities. **<Dosage adjustments during treatment>** Frequent monitoring of neutrophil counts should be performed during TAXOTERE therapy. Dosage should be adjusted if necessary depending on neutrophil count. **[Precautions] <Contraindications>** 1) Hypersensitivity reactions to TAXOTERE or Polysorbate 80. 2) Patients with baseline neutrophil count of <1,500 cells/mm³. 3) Patients with severe liver impairment. 4) When combined with other medicinal products, contraindications for those products also apply. (severe renal impairment, hypersensitivity to paraplatin, Pheromgrods and/or mermitidae etc.) 5) Patients with complications of infections (infections could be worsened or fatal) 6) Patients who are suspected to have infectious fever (infections could be worsened or fatal) 7) Patients who have severe myelosuppression (severe infection could be occur or fatal) **<Special Precautions in Use>** 1) Patients with myelosuppression 2) Patients with liver impairment (See ☜ General precautions') 3) Patients with renal impairment 4) Patients with pneumonia interstitialis or pulmonary fibrosis 5) Patients with edema 6) Patients with pregnant potential (both men and women) (Effective contraceptive measures must be taken during treatment, and for men at least 6 months after cessation of therapy.)

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Adjuvant Non-Anthracycline Regimen in Operable Breast Cancer-Changing the Standard of Care (Non-Anthracycline Regimens in Node Negative Early Stage Breast Cancer)

Yeesoo Chae

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Since 1990 anthracyclines have been a key component of adjuvant chemotherapeutic regimens for early breast cancer in particular node positive tumors. However, anthracyclines have major concern related to acute toxicities including severe emesis and extravasation necrosis and moreover there is increased understanding of the long-term, irreversible toxicities associated with anthracyclines, including cardiac failure and secondary leukemia. These concerns about cardiac toxicity were reinforced with the emergence of trastuzumab for the treatment of HER2-positive breast cancer.

As the international guidelines recommend adjuvant chemotherapy for the patients with small sized node-negative breast cancer based on the recent meta-analysis results, the debate has been triggered when using anthracycline-containing regimens. Although adding taxane into anthracycline was identified to reduce relapse in node negative breast cancer, no definitive evidence for breast cancer death or only marginal if any. Therefore, taxane without anthracycline was expected as alternative regimens as a substitute for anthracycline-based regimens.

Although there has been no large clinical data yet for non-anthracycline taxane-based regimen in patients with node negative early breast cancer, US oncology 9735 trials demonstrated promising results because almost 50% of patients were node negative. Based on the results, Taxotere and cyclophosphamide became the most common regimen used for patients with node negative in the USA and Europe. For HER2 positive tumor, BCIRG006 trial showed that non-anthracycline regimen has similar outcome but less toxicity compared with the standard AC followed by docetaxel + trastuzumab. Currently, as some promising non-anthracycline regimens are under investigation, the wider availability of these regimens may increase options when deciding upon adjuvant chemotherapy for patients with early breast cancer, especially in patients with a high risk of cardiac toxicity.

This review outlines the evidence for the use of non-anthracycline adjuvant regi-

mens in EBC, including cyclophosphamide/docetaxel (TC) and trastuzumab/docetaxel/carboplatin (TCH), which have demonstrated equivalent efficacy and reduced toxicity compared to anthracycline-based regimens in various trials.

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효능・효과

【 유방암 】

• 전이성 유방암

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

• 조기 유방암

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

용법・용량

투여 전 투여하려는 제형(정맥 또는 피하주사)이 환자에 처방된 것이 맞는지 제품라벨을 확인하여야 한다. 이 약은 정맥주사용이 아니다.
환자의 체중에 관계없이 이 약 600mg을 투여한다. 부하용량이 필요하지 않으며, 매 3주마다 권장용량을 2–5분간 피하 주사한다.
조기 유방암 환자를 대상으로 이 약과 수술 전 화학요법으로 도세탁셀(75mg/m2) 투여 후 FEC(5FU, 에피루비신, 사이클로포스파미드)를 표준용량으로 투여한 임상시험을 수행하였다.

치료기간

전이성 유방암 환자는 질병의 진행이 있을 때까지 이 약을 투여한다. 조기 유방암의 경우는 1년 동안 또는 질병재발까지 이 약을 투여해야한다. 조기 유방암 치료를 1년 넘게 지속하는 것은 권장되지 않는다.

감량투여

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

투약일이 지났을 경우

가능한 한 빨리 이 약 600mg을 투여하고, 이후 3주 간격으로 투여를 지속한다.

주입방법

이 약 600mg 용량을 2–5분간 피하주사 한다. 좌우 허벅지에 번갈아 가며 주사한다. 새로 주사하는 곳은 이전에 주사했던 곳과 2.5 cm이상 떨어져 있어야 하고, 붉거나 멍들었거나 아프거나 딱딱한 피부에는 절대 주사하지 않는다. 이 약 치료 중 다른 피하주사약물을 투여할 경우, 이 약 주사 장소와 다른 곳에 주사하는 것이 바람직하다. 처음 주사한 경우 주사 후 6시간, 이후로는 주사 후 2시간 동안 주입 관련 반응의 징후나 증상이 있는지 환자를 관찰해야 한다.

사용상 주의사항

1. 경고

1) 심기능 장애(Cardiac dysfunction)
허셉틴 투여 시 울혈성 심부전[뉴욕심장학회(NYHA)등급 2–4등급] 또는 무증상 심기능 장애의 위험이 증가할 수 있다. 특히, 안트라싸이클린(독소루비신이나 에피루비신)을 포함한 화학요법후, 허셉틴 단독 또는 파클리탁셀이나 도세탁셀과 병용투여 받은 환자에서 이러한 사례가 관찰되었다. 그 정도는 중등도–중증이었으며 사망과 관련이 있었다. 또한 심질환 위험성이 큰 환자(고혈압, 입증된 관상동맥질환, 울혈성 심부전, 이완기 장애, 55% 미만 LVEF, 고령자)에 투여 시 주의를 기울여야 한다. 허셉틴의 치료대상환자, 특히 이전에 안트라싸이클린 및 사이클로포스파미드를 투여 받은 환자는 치료개시 전에 병력 및 신체검사와 ECG, 심초음파도, MUGA scan 또는 MRI 등의 심기능을 평가해야 한다. 허셉틴 투여를 결정하기 전에 주의 깊게 위험–유익성에 대한 평가를 내려야 한다.
트라스투주맙의 반감기는 약 28–38일이므로, 허셉틴 투여 중단 후 27주까지 트라스투주맙이 순환계에 존재할 수 있다. 허셉틴 투여 중단 후 안트라싸이클린을 투여 받은 환자에서 심기능장애가 증가될 수 있다. 가능하다면 전문의는 허셉틴 투여 중단일로부터 27주까지 안트라싸이클린이 포함된 치료요법을 피하도록 해야 하며, 안트라싸이클린을 투여하는 경우 심장기능을 주의 깊게 모니터해야 한다.
치료 전 검사시 심혈관계 문제가 있는 환자의 경우 일반적인 심장 평가가 고려되어야 하며, 치료 중에는 심장기능을 모니터해야 한다(예, 매 3개월마다). 모니터링을 통해 심기능장애를 나타내는 환자를 발견할 수 있다. 무증후성 심기능장애를 더 빈번한 모니터링을 통해 알아낼 수 있다(예, 매 6–8주마다). 좌심박출률(LVEF)이 지속적으로 감소된 환자가 계속 무증후성일 경우 허셉틴의 임상적 이점이 없다면 전문의는 허셉틴의 투여 중지를 고려해야 한다. 조기유방암 환자에서 LVEF가 55% 이하인 경우 치료시 주의를 기울여야 한다.
LVEF가 치료 전 수치에서 10 ejection point 및 50%미만으로 떨어졌을 때, 허셉틴 투여를 중단하고 약 3주 이내에 LVEF를 다시 평가해야한다. LVEF가 개선되지 않을 경우 또는 감소할 경우 치료상 유익성이 위험을 상회하지 않는 한 허셉틴의 투여 중단을 심각하게 고려해야 한다. 이러한 환자의 경우 심장 전문의에 진료를 의뢰해야 하며 계속 관리되어야 한다.
허셉틴 투여 중 증후성 심부전이 발생할 경우, 표준 요법으로 치료되어야 한다. 임상적으로 유의한 심부전이 발생한 환자에서 유익성이 위험을 상회하지 않는 한 허셉틴의 투여 중단을 심각하게 고려해야 한다.
심기능 장애를 경험한 환자에서 허셉틴 투여의 지속 또는 재투여에 대한 안전성은 전향적으로 연구되지 않았다. 그러나 임상시험에서 심부전을 겪은 대부분의 환자는 표준 요법으로 개선되었다. 표준요법은 ACE 억제제 또는 안지오텐신 수용체 차단제(ARB) 및 베타차단제를 포함하였다. 심장 증상과 허셉틴 치료의 임상적 유익성을 나타낸 환자의 대부분은 추가 심장 증상 없이 허셉틴 투여를 계속 실시하였다.

– 전이성 유방암

허셉틴과 안트라싸이클린은 전이성 유방암에서 동시에 투여하지 않는다. 기존에 안트라싸이클린을 투여 받았던 전이성 유방암환자의 경우에도 허셉틴과 안트라싸이클린을 병용 투여 했을 때 보다는 그 위험도가 낮으나 허셉틴의 투여로 인한 심기능장애의 위험이 있다.

– 조기 유방암

조기유방암 환자의 경우 치료 전, 치료 중 매 3개월마다, 치료 종료 후 매 6개월마다 24개월까지 심장평가를 실시해야 한다. 안트라싸이클린을 함유한 화학요법제를 투여 받는 환자는 추가적인 모니터링이 요구되고, 지속적인 LVEF 감소가 있는 경우 허셉틴의 치료 종료로부터 5년 이상 해마다 모니터링 해야 한다.
조기 유방암환자를 대상으로 한 임상시험에서, 심근경색 병력이 있는 환자, 약물치료가 필요한 협심증환자, 울혈성 심부전(NYHA Ⅱ–Ⅳ)이 있거나 병력이 있는 환자, 55% 미만 LVEF, 기타 심근병증, 약물치료가 필요한 부정맥환자, 임상적으로 유의한 판막질환환자, 조절이 어려운 고혈압환자(단, 표준 약물 치료로 조절 가능할 경우 임상시험 참여 가능), 혈역학적 심낭삼출환자(Hemodynamic effective pericardial effusion)는 제외되었기 때문에 이 환자들에 대한 유익성/위험비율에 대한 자료가 없다. 따라서 이러한 환자에 허셉틴 투여는 권장되지 않는다.

– 보조요법 치료

허셉틴과 안트라싸이클린 약물은 보조요법 치료에서 동시에 투여하지 않는다.
조기 유방암 환자에서 도세탁셀과 카보플라틴의 비-안트라싸이클린 요법과 허셉틴 정맥주사 병용투여 시에 비해 안트라싸이클린 포함 요법 후 허셉틴 정맥주사 병용투여 시 증후성 및 무증상성 심장 이상반응의 발생률 증가가 관찰되었으며 이러한 증가는 탁산계 약물에 이어 순차적으로 투여시보다 탁산계 약물과 병용투여 시 더욱 현저했다. 사용된 요법에 상관없이, 대부분의 증후성 심장 이상반응은 첫 18개월 이내에 발생하였다. 중앙 추적조사기간이 5.5년이었던 3개 주요 임상시험 중 하나(BCIRG006)에서 증후성 심장 이상반응이나 LVEF 이상반응의 누적 발생율의 지속적인 증가가 나머지 두 대조군 (안트라싸이클린+싸이클로포스파미드 투여 후 탁산 투여, 탁산+카보플라틴+허셉틴)에서 약 1%에 비해 안트라싸이클린 투여 후 탁산과 허셉틴을 병용한 군에서 최대 2.37%로 관찰되었다.
보조요법에 관한 임상시험에서 확인된 심장 이상반응의 위험 요인은 고령(〉50세), 허셉틴 투여 전 낮은 LVEF(〈55%) 또는 LVEF의 감소(10–15 point), 파클리탁셀 투여 시작 전/후 낮은 LVEF(〈55%), 허셉틴 투여, 항고혈압 약물 이전 투여 또는 병용투여였다. 보조요법이 끝난 후 허셉틴을 투여하는 환자에서, 허셉틴 투여 전 축적된 안트라싸이클린 및 체질량지수(BMI)가 25kg/m²을 넘는 경우 심기능 장애의 위험이 있었다.

– 수술전 보조요법/수술후 보조요법

수술전 보조요법/수술후 보조요법 치료에 적합한 조기 유방암 환자에서, 허셉틴은 화학요법제 치료를 받지 않은 환자에 대해 저용량의 안트라싸이클린 요법과 동시 투여할 수 있다(최대 누적용량 : 독소루비신 180mg/m², 에피루비신 : 360mg/m²).
수술전 보조요법 치료에서 저용량의 안트라싸이클린과 허셉틴을 동시에 투여 받은 환자는 수술후에 추가적인 세포독성 화학요법제를 투여하지 않는다. 기타 상황에서 추가적인 세포독성 화학요법제의 필요성은 개개 요인에 따라 결정한다.
현재 저용량의 안트라싸이클린과 허셉틴을 동시에 투여한 경험은 제한적이다. NOAH 임상시험에서, 허셉틴은 수술전 보조요법으로 안트라싸이클린(독소루비신의 누적 용량 180mg/m² 또는 에피루비신 300mg/m²) 3–4주기 투여를 포함한 수술전 보조 화학요법제와 병용투여 하였다. 증후성의 심장 기능 장애는 허셉틴 투여 군에서 낮았다(115명 중 2명, 1.7%).
NOAH 임상시험에서 65세 이상인 환자는 적었다. 65세 이상 그룹의 임상 경험이 제한적이기 때문에 수술전/수술후 보조요법 치료에서 65세 이상인 환자에게는 권장하지 않는다.
2) 주입관련 반응, 알러지양 반응 및 과민반응 : 이 약 투여 시 주입관련반응이 발생하는 것으로 알려져 있다. 주입관련 반응의 발생 위험을 감소시키기 위해 전 처치를 할 수도 있다. 이 약 투여 시 중대한 주입관련반응(호흡곤란, 저혈압, 천명, 기관지연축, 빈맥, 산소 포화도 감소, 호흡곤란증후군 포함)이 보고되지 않았으나 이러한 주입관련반응이 허셉틴 정맥주사와 연관이 있으므로 주의하도록 한다. 처음 주사한 경우 주사 후 6시간, 이후로는 주사 후 2시간 동안 주입 관련 반응의 징후나 증상이 있는지 환자를 관찰해야 한다. 주입관련 반응이 나타나면 허셉틴의 주입을 중단시키거나 주입속도를 감소시키고 증상이 소실될 때까지 환자를 모니터링 해야 한다. 대부분의 환자에서 증상이 소실되었고 이후 허셉틴의 주입을 재개하였다.
중대한 이상반응은 산소, 베타작용제, 코르티코스테로이드와 같은 보조 치료를 통해 성공적으로 치료되었다. 드물게 이러한 반응은 치명적인 결과를 초래하는 임상 경과와 관련이 있었다. 진행성 종양의 합병증 및 동반질환으로 인해 안정 시 호흡곤란인 환자는 치명적인 주입관련 반응의 위험이 증가될 수 있으므로 이러한 환자들에게는 허셉틴을 투여하지 않는다. 초기 개선 후 임상적 악화 및 급격한 임상적 악화를 동반한 지연 반응이 보고되었다. 주입 후 수 시간에서 일주일 이내에 사망이 발생하기도 했다. 매우 드물게 허셉틴 주입 시작으로부터 6시간 이상 지난 후 주입반응 또는 폐 증상이 발생하기도 했다. 환자에게 이러한 지연성 반응의 가능성을 경고해야 하며 증상이 발생되었을 경우 전문의에게 연락하도록 해야 한다.
3) 폐이상반응 : 드물게 중증 폐이상반응이 허셉틴 정맥주사의 시판후조사에서 보고되었으므로 이 약 투여 시 주의한다. 이는 때때로 치명적일 수도 있다. 이러한 이상반응으로 폐침윤을 포함한 간질성 폐질환, 급성 호흡곤란 증후군, 폐렴, 간질성 폐렴, 흉막 삼출, 호흡곤란, 급성 폐부종 및 호흡부전 등이 보고되었다.
간질성 폐질환과 연관된 위험 요소로는 탁산계약물, 젬시타빈, 비노렐빈, 방사선 요법과 같이 이러한 질환과 연관이 있는 것으로 알려진 여타의 항종양약물 요법을 이전에 투여 받았거나 동시에 투여하는 경우가 있다. 이는 주입관련 이상반응의 일부분이거나 지연형 이상반응과 함께 나타날 수 있다. 전이성 악성종양과 그에 따른 합병증의 발병으로 인해 안정 시 호흡곤란을 나타내는 환자는 폐질환의 위험성이 증가할 수 있다. 따라서 이러한 환자에 허셉틴을 투여하지 않는다. 폐렴환자, 특히 탁산계 약물을 병용 투여하는 경우 주의해야 한다.

2. 다음 환자에는 투여하지 말 것

1) 트라스투주맙, 설치류 유래 단백, 히알루로니다제 또는 이 약의 구성성분에 과민반응 병력이 있는 환자
2) 진행성 악성종양에 의한 중증 안정시 호흡곤란 또는 산소보충이 필요한 환자

3. 다음 환자에는 신중히 투여할 것

1) 안트라싸이클린계 약물을 투여 중인 환자 또는 이전에 치료경험이 있는 환자(심부전 등의 심장장애가 나타나기 쉽다)
2) 흉부로 방사능을 조사 중인 환자(심부전 등의 심장장애가 나타나기 쉽다)
3) 심부전증상이 있는 환자(증상이 악화될 우려가 있다)
4) 관상동맥질환(심근경색, 협심증 등)환자 또는 그 병력이 있는 환자(증상이 악화될 우려가 있다. 또는 심부전 등의 심장장애가 나타나기 쉽다)
5) 고혈압환자 또는 그 병력이 있는 환자(심부전 등의 심장장애가 나타나기 쉽다)
6) 안정시 호흡곤란(폐전이, 순환계질환 등에 의한)이 있는 환자 또는 그 병력이 있는 환자 (점적주입관련 반응이 중증화 되기 쉽다)

4. 임부 및 수유부에 대한 투여

1) 생식독성시험은 허셉틴 정맥주사의 사람 유지용량인 주 2mg/kg에 25배 용량을 암컷 cynomolgus 원숭이에 투여하여 실시하였으며 수태능력의 손상 또는 태자에 대한 악영향은 나타나지 않았다. 태자발달 초기(임신 20–50일째) 및 말기(임신 120–150일째) 중 트라스투주맙의 태반이행이 나타났다. 임신 여성에 투여 시 허셉틴이 태아독성을 유발하거나 수태능력에 영향을 미치는지는 알려진 바 없다. 동물생식시험에서 사람의 반응을 항상 예측할 수는 없지만, 허셉틴 투여의 유익성이 태아에 대한 위험성을 상회할 때만 허셉틴을 투여해야 한다.
시판 후 조사에서 허셉틴을 투여 받은 임부에서 폐형성저하증을 초래하는 양수과소증과 관련 있는 태아의 신장 발달과/혹은 기능 장애가 보고되었다. 임신할 가능성이 있는 여성은 허셉틴 치료기간 중 및 치료 종료 후 최소 7개월 동안 효과적인 피임이 요구된다. 임신한 여성에게는 태아에 대한 유해한 영향의 가능성을 알려야 한다. 만약 임부가 허셉틴으로 치료 받았을 시에는 다학제적 팀에 의한 주의 깊은 모니터링이 필요하다.
2) 수유기 cynomolgus 원숭이를 대상으로 허셉틴 정맥주사의 사람유지용량인 주 2mg/kg의 25배 용량을 투여하여 실시한 시험에서 트라스투주맙은 모유 중으로 이행되는 것으로 입증되었다. 신생원숭이의 혈청 중 트라스투주맙의 존재가 출생에서 1개월 령에 이르기까지 이들의 성장 및 발생에 어떠한 부정적 영향을 미치지는 않았다. 트라스투주맙이 사람의 모유에 분비되는지는 알려져 있지 않다. 사람 IgG는 사람 모유 중으로 이행되며, 신생아에 대한 위해 가능성은 알려져 있지 않기 때문에 허셉틴 치료기간 중 및 치료종료 후 7개월 동안은 수유를피해야 한다.

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Current and Future Perspectives in Treatment of Metastatic TNBC

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Triple negative breast cancer (TNBC) is a heterogeneous disease at molecular, pathologic, and clinical levels. Stratification of TNBC into subclasses, using new markers, will identify new screening methods, prognostic factors, methodologies, and perhaps targets for personalized therapies. A lot of new targeted therapies are actually under study, but the efforts are not reaching the hoped results.

Bevacizumab showed encouraging results in several trials, as suggested by the meta-analysis of O'Shaughnessy et al. Unfortunately, progression free survival (PFS) advantage was not confirmed also by an advantage in overall survival (OS); this may be due to the several currently available post-progression therapies. However, bevacizumab is a well-known drug with a manageable toxicity profile, so it could be useful to further evaluate its action in this difficult patient setting. Meanwhile other anti-VEGF therapies, like tyrosine kinase inhibitors (TKIs), which have good results in other diseases, have shown all their limits in TNBC; therefore, because TNBC is only a part of a larger BC population, results have been limited to subgroup analysis in the majority of clinical trials.

Regarding the anti-EGFR therapies, there was a strong rationale for their use in TNBC treatment, particularly because of the correlation between EGFR hyper-expression and negative prognosis in this disease. Furthermore, in some trials cetuximab showed a positive trend to an OS advantage in this setting, even if those trials enrolled only a small number of patients. From these results, it seems that the subpopulation of TNBC appears to be more sensitive to these therapies; moreover, many efforts are under way to identify TNBC patients who benefit from cetuximab treatment, which may be correlated with lower expression of alpha-crystallin B chain, higher expression of PTEN homologue, and lack of KRAS expression in patients with basal-like breast cancer (BLBC). In addition, erlotinib and gefitinib showed some actions in TNBC, but the experiences are too small to consider these results conclusive at all. The mTOR inhibitor everolimus also needs further evaluation to clarify its real action in this clinical setting.

On the basis of preclinical studies, there was a lot expected from PARP inhibitors.

Until now, olaparib has not been studied in a Phase III trial, while iniparib activity, which in a Phase II study seemed very promising, was not confirmed in the Phase III study. However, the BRCA-mutated population seems to be the target of this drug family, so future clinical trials should be based on this class of TNBC.

Other target agents, even if based on fascinating theories, at the moment have not shown impressive achievement in the Phase I and Phase II trials in which they have been evaluated. Further investigations are needed, above all in translational studies involving the evaluation of predictive response biomarkers.

Expression profiling and genomic studies are changing our view about the molecular biology of BC, which is currently considered as a group of distinct diseases from the molecular point of view. However, the detailed molecular characterization of TNBC is ongoing, both to better understand the different biology and clinical outcome, and to identify specific diagnostic, prognostic, and therapeutic targets. In particular, one important goal is the identification of prognostic factors and markers to reliably select high- and low-risk subsets of patients with TN disease, in order to explore different biologically based treatments and to tailor the therapeutic approaches to the single patient.

However, TNBC is clearly a complex disease; indeed the genetic heterogeneity is present not only in differently affected individuals, but also among tumors occurring at different sites within the same patient. As such, it is likely that its biology involves multiple redundancies and pathway cross-talk. If only one pathway is selectively inhibited, the efficacy of the therapeutic strategy would likely be undermined by activation of a compensatory pathway. Therefore, it is not surprising that, to date, not a single targeted therapy has been approved for the treatment of TNBC, for which cytotoxic chemotherapy remains the standard treatment. Combining two or more targeted agents may be required for a more rational and optimal approach to TNBC treatment.

Importantly, intratumoral infiltration by lymphocytes was associated with good prognosis in patients with TNBC treated with adjuvant chemotherapy. This body of evidence suggests that assessing immune infiltration and activation could be useful in the future to stratify triple negative breast cancer patients. In addition, they provide evidence for the development of immunotherapies in BCs, such as immune check-point blockade. It may open new perspectives for TNBC management.

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DS01

Clinical Impacts of Primary Prophylaxis for Febrile Neutropenia in Breast Cancer Patients

Young Jin Suh

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Chemotherapy-induced neutropenia (CIN) is a common toxicity caused by the administration of chemotherapeutic drugs. This side effect can lead to life-threatening infections and may alter the chemotherapy schedule, thus impacting on early as well as long-term outcomes. There is good evidence to suggest that dose intensity is important when considering the effectiveness of adjuvant chemotherapy in patients with breast cancer. However, the development of chemotherapy-induced febrile neutropenia can lead to reduction in dose intensity and other treatment modifications, which may negatively affect patient outcomes. Elderly breast cancer patients with impaired health status or advanced disease as well as patients undergoing dose-dense anthracycline/taxane- or docetaxel-based regimens have the highest risk of CIN. Neutropenic cancer patients may develop febrile neutropenia and CIN-related severe medical complications. Febrile neutropenia can be prevented by the use of primary prophylactic treatment, notably with granulocyte colony-stimulating factors (G-CSF). This practice is supported by international guidelines, all of which recommend that primary prophylaxis with granulocyte colony-stimulating factors should be used with chemotherapy where the risk of febrile neutropenia is 20% or greater. A careful assessment of the baseline risk for CIN allows the selection of patients who need primary prophylaxis with granulocyte colony-stimulating factor and/or antimicrobial agents. Specific risk assessment tools, along with thorough and comprehensive clinical evaluation, are able to define a subset of febrile patients with low risk for complications who can be safely treated as outpatients. Conversely, patients with higher risk of severe complications should be hospitalized and should receive intravenous antibiotic therapy with or without G-CSF.

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BS02

The Role of The Everolimus in the Treatment Landscape for ER+ Advanced Breast Cancer Patients

Fabrice Andre

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Oral Presentation

GBCC 2015 & 4th IBCS
Abstract Book

Prognostic Value of Tumor-to-Breast Volume Ratio *vs.* Tumor Size Revision of TNM

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Background/Purpose: A combination of factors, from the biological characteristics of the tumor itself, the body and the adequacy of diagnosis, treatment, management of patients affects the development and outcome of cancer. One of the important biological characteristics of tumor is the size, which is reflected in the diagnosis according to the TNM system. However, this system does not consider the size of affected organs and its correlation with tumor volume.

Methods: The effect of T index on the forecast was examined and monitored in 47 patients with breast cancer T2N0M0. The tumor-to-breast volume ratio was also studied. Tumor volume was measured using ultrasound, mammography and magnetic resonance imaging magnetic resonance studies. The volume of breast has been studied with manual method MRI study before the operation and the Archimedes procedure. Patients depending on the tumor-to-breast volume ratio were divided into the following groups: group I (T2 / 1)- tumor-to breast volume ratio was 1/1 to 1/3, group II (T2 /2)- 1/3 and 1/4, group III (T2/3) - > 1/4.

Results: Progression of the disease were different depending on tumor-to on tumor-to-breast volume ratio: in group I -25 months, in group II - 31.5 months, in group III - 55.3 months. The 5 years-recurrence-free survival was 72.3% (34 patients). The survival of patients in the group I (T2/1) was 33.3% in the group II (T2/2) of 57.1%, the best results were when the tumor-to-breast volume ratio were more than (T3/3) 1/4 81.1% ($p = 0.249$). ($\chi^2 = 2.53$ 3rd degree of freedom $p < 0.05$).

Conclusion: Thus, tumor-to-breast volume ratio has a statistically significant impact on the outcome of breast cancer. In order to obtain reliable data a study of a large sample of patients have to be carried out.

OP01-2

Does Internal Mammary Node Irradiation Affect Treatment Outcome in Clinical Stage II-III Breast Cancer Patients Receiving Neoadjuvant Chemotherapy?

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Background/Purpose: Data on the efficacy of internal mammary node irradiation (IMNI) in breast cancer patients receiving neoadjuvant chemotherapy are lacking, causing ongoing controversy regarding its application. We herein assess the value of IMNI in patients receiving postoperative radiotherapy after neoadjuvant chemotherapy.

Methods: Between 2001 and 2009, 521 consecutive patients with clinical stage II-III breast cancer received neoadjuvant chemotherapy and postoperative radiotherapy. With a consistent policy, the treating radiation oncologist either included (n = 284) or excluded (n = 237) the internal mammary node in the treatment volume. Anthracycline- and taxane-based chemotherapy was provided to 482 (92.5%) patients.

Results: At a median follow-up of 71 months, the 5-year disease-free survival with and without IMNI was 81.8% and 72.7%, respectively ($p = 0.019$). The benefit of IMNI varied according to patient characteristics such that it was more apparent in patients with N1-2 disease, inner/central location, and triple negative subtype. In multivariate analysis, IMNI was an independently significant factor for disease-free survival (DFS) ($p = 0.039$).

Conclusion: Our results indicated that IMNI was associated with a significant improvement in DFS with low toxicity rate for breast cancer patients receivingneoadjuvant chemotherapy. Further prospective studies are warranted to confirm the effect of IMNI in the neoadjuvant chemotherapy setting.

TAU and HER2 Predict Pathologic Complete Response for Estrogen Receptor-Positive Breast Cancer

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Background/Purpose: Pathological complete response (pCR) after neoadjuvant chemotherapy is an independent predictive factor. This study was to evaluate the correlation between multimolecular markers and pCR rates after neoadjuvant chemotherapy.

Methods: Patients with previously untreated, non-metastatic, stage I-III breast cancer were enrolled. We used immunohistochemistry to examine multimolecular markers expression in breast cancer biopsies. Patients were treated for 4 cycles with paclitaxel (175 mg/m^2 biweekly) and carboplatin(area under the curve (AUC) 5 biweekly). Patients with human epidermal growth factor 2 (HER2)-positive disease received simultaneous trastuzumab (6 mg/kg initial dose with subsequent doses of 4 mg/kg biweekly). The primary end point was Pathological complete response. We evaluate the correlation between multimolecular markers and pCR rates on multivariate analysis.

Results: Between January 2009 and February 2014, 131 patients enrolled. And 89 patients were estrogen receptor (ER) positive, 50 were HER2 positive. The overall pCR rate was 34.4% (45 out of 131). In univariate analysis, ER, progesterone receptor (PgR), HER2, ki67 and tau were found to be significantly predictive of a pCR ($p<0.01$, <0.01, <0.01, 0.048, 0.003 respectively).ER-negative [OR = 0.207,95%CL (0.087-0.493), $p=0.01$], and HER2-positive [OR = 5.451,95% CL (2.312-12.850), $p=0.01$] achieved higher pCR on multivariate analysis. HER2 [OR = 5.746, 95% CL (1.669-19.778), $p=0.006$] and tau [OR = 0.154, 95% CI (0.038-0.627), $p=0.01$]were significant for PCR on multivariate analysis in ER-positive tumors.

Conclusion: In univariate analysis, patients with ER negative, PgR negative, HER2 positive, high level of ki67 and tau were more likely to achieve pCR after neoadjuvant chemotherapy. ER-negative and HER2-positive achieved higher pCR on multivariate analysis. Higher pCR rates occurs in HER2-positive and tau-negative in patients with ER-positive tumors. Additional study about the postoperative follow-up of this regimen is warranted.

Survival Outcome of Concurrent GnRH Agonist Plus Tamoxifen is Comparable to That of Sequential Adriamycin and Cyclophosphamide Chemotherapy Plus Tamoxifen in Premenopausal, Lymph Node-Negative, Hormone-Responsive, HER2-Negative, T1-2 Breast Cancer Patients

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Background/Purpose: The purpose of this study was to compare treatment outcomes between gonadotropin-releasing hormone (GnRH) agonist plus tamoxifen and adriamycin and cyclophosphamide (AC)-containing chemotherapy plus tamoxifen in hormone-responsive, premenopausal, node-negative, breast cancer patients.

Methods: A total of 994 premenopausal women with node-negative, hormone receptor-positive, human epidermal growth factor receptor (HER2)-negative, breast cancer were included in this retrospective cohort study: 608 patients (61.2%) were treated with GnRH agonist together with tamoxifen, and 386 patients (38.8%) were treated with AC-containing chemotherapy with tamoxifen.

Results: The median follow-up period was 7.4 years. In premenopausal, lymph node-negative, hormone-responsive, HER2-negative, T1-2, breast cancer patients, an age younger than 39 years and a higher T stage were independent negative prognostic factors ($p = 0.013$ and 0.047, respectively). In subgroup analysis, patients were divided into four groups according to their T stage and age. In each subgroup, there were no survival differences for disease-free survival, cancer-specific survival, and overall survival between the two treatment groups.

Conclusion: Adding GnRH agonist to tamoxifen is a reasonable alternative to adding AC chemotherapy to tamoxifen in premenopausal, hormone-responsive, HER2-negative, lymph node-negative, T1-2, breast cancer patients.

OP01-5

A Phase II Study of Neoadjuvant Chemotherapy Using Combined Taxane, Anthracycline, and Cyclophosphamide in High Risk HER2-Negative Locally Advanced Breast Cancer

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Background/Purpose: The standard neoadjuvant chemotherapy (NAC) for HER2-negative breast cancer usually consists of sequential taxane and anthracyclin-based regimen. In high-risk patients, a more intensive regimen conceivably would derive more clinical benefit but there is limited data to support such practice. This study explored the feasibility and response of a 'risk stratified and response guided' approach using the third generation combined chemotherapy taxane, anthracycline, and cyclophosphamide (TAC) in high risk locally advanced breast cancer (LABC).

Methods: This is a phase II prospectively study of the regimen TAC in LABC with high risk features, defined as either estrogen receptor (ER)/progesterone receptor (PR)+ human epidermal growth factor receptor 2 (HER2) negative with highly proliferative index (Ki67 > 30% or > 10 active mitosis per HPF), triple negative (TN; ER/PR/HER2-) or poor responder to standard sequential regimen within first 2 cycles of treatment. Each patient received 6-8 cycles of TAC (docetaxel 75 mg/m^2; doxorubicin 50 mg/m^2 or epirubicin 75 mg/m^2; cyclophosphamide 500 mg/m^2) every 3 weeks with G-CSF support. Treatment response was evaluated by positron emission tomography or magnetic resonance imaging at the end of treatment.

Results: Since April 2012, 19 patients were enrolled. Mean age was 48 and 74% were pre-menopausal. All patients had LABC (Stage IIB 21%, IIIA 16%, IIIB 11%, IIIC 52%). The proportion of ER/PR+, TN and poor responder were 53%, 31% and 16% respectively. All poor responders had ER/PR+ HER2 negative tumor, and had received paclitaxel prior to TAC. The median cycles of TAC delivered was 6. There was no treatment

related mortality. Overall radiological response rate by RECIST was 95% (partial response 53%; completed response 42%) and pathological response rate (pCR) was 32%. Breast conservation therapy (BCT) was performed in 16% of patients. The actual rate of surgical assessed feasible BCT will be presented in the meeting.

Conclusion: TAC is well tolerated in neoadjuvant setting when appropriate supportive treatment is given. 'Risk stratified and response guided' approach is feasible, with high response rate and can potentially increase the rate of BCT. LABC is a heterogeneous disease. Customised approach should be considered for high risk patients.

Prediction of the Benefit of Radiation Therapy After Breast-Conserving Surgery in Elderly Breast Cancer Patients: Nomogram Leads the Way.

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Background/Purpose: Radiotherapy (RT) may be omitted for elderly (age >70 years) breast cancer patients with favorable disease (CALGB criteria: stage I and ER-positive with endocrine therapy). This study sought to develop a nomogram to predict the survival benefit of RT in elderly patients who do not meet the CALGB criteria (with stage I & ER-negative, or stage II/III (regardless of ER status) disease).

Methods: We used Surveillance, Epidemiology and End Results data to identify 9,079 patients (age ≥70 years) with stage I & ER-negative, or stage II/III (regardless of ER status) disease who received breast-conserving surgery between 1990 and 2005. We used competing-risk regression and logistic regression to develop a nomogram to predict the Cancer Specific Survival (CSS) and validated it using bootstrapped technique. We hypothesized that in patients with 'good prognosis' predicted by our nomogram, there will be no survival benefit of RT.

Results: With a median follow-up of 83 months, the overall 10- and 15-year CSS of the included population were 82.1% and 75.8%, respectively. RT was significantly associated with improved CSS in the multivariate analysis. A nomogram was developed for the prediction of 10-year CSS and showed a bootstrapped-corrected area under the curve (AUC) value of 0.679. RT did not deliver any survival benefit to patients with predicted CSS > 90%. In addition, RT significantly increased the 10-year CSS by 3.6% and 10.1% in patients with predicted CSS from 0.8-0.9, 0.8, respectively. The traditional TNM stages failed to identify a subgroup of patients in which the RT did not bring any survival benefit.

Conclusion: This nomogram is a useful tool to predict the 10-year CSS in elderly breast cancer patients who do not meet the CALGB criteria (with stage I & ER-negative, or stage II/III (regardless of ER status) disease). The benefit of RT varied among patients with different predicted CSS. In patients with predicted CSS > 90%, RT did not deliver any survival benefit and could be spare in these patients.

OP01-7

Early Cardiac Toxicity with Concurrent Trastuzumab and Left-Sided Adjuvant Radiotherapy

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Background/Purpose: Trastuzumab and adjuvant radiotherapy (RT) are usually given concurrently. The aim of this study was to evaluate cardiotoxicity risk with concurrent trastuzumab and left-sided RT.

Methods: The medical records of 64 patients treated with concurrent trastuzumab and RT and 73 patients treated with RT alone for left-sided breast cancer were retrospectively reviewed. Detail information of doses delivered to cardiac structures was collected. Cardiac event (grade ≥ 1) was assessed according to CTC 2.0.

Results: Median follow-up was 6 months. The median absolute left ventricular ejection fraction (LVEF) decrease was 3% (-7% to 15%) and 1% (-13% to 13%) in patients treated with concurrent trastuzumab and those with RT alone, respectively. Grade 1 LVEF dysfunction was observed in 5 (7.8%) patients treated with concurrent trastuzumab and 3 (4.1%) patients treated with RT alone. Univariate analysis showed that trastuzumab was the only risk factor for LVEF dysfunction. For patients treated with concurrent treatment, the mean heart dose was significantly higher in those with LVEF dysfunction compared to those without cardiotoxicity (9.4 ± 3.3 Gy versus 6.1 ± 2.6 Gy; $p = 0.01$). Further analysis showed that D10-D30, D50-D55, V5-V20 of the heart and D30-D45, D65-D75, V6-V15 of the LV were significantly higher in patients who developed LVEF dysfunction.

Conclusion: Concurrent treatment of trastuzumab and left-sided RT appeared cardiac safety. In the meantime, minimize the irradiation of cardiac structure might still provide further protection for heart in the setting of trastuzumab and left-sided RT.

Neoadjuvant Letrozole and Lapatinib in Asian Postmenopausal Women With Estrogen Receptor and Human Epidermal Growth Factor Receptor-2 Positive Breast Cancer (Neo-All-In): First Efficacy and Safety Report

Ji Hyun Park[1], Myung Joo Kang[1], Jin-Hee Ahn[1], Jeong Eun Kim[1], Kyung Hae Jung[1], Gyung-Yub Gong[2], Hee Jin Lee[2], Byung-Ho Son[3], Hak-Hee Kim[4], Hee Jung Shin[4], Sei-Hyun Ahn[3], Dae-Hyuk Moon[5], Sung-Bae Kim[1]*

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Background/Purpose: Neo-ALL-In (NCT 01275859) is a single center, prospective study aimed to evaluate the recruitment feasibility, efficacy and safety profiles as well as biologic features of neoadjuvant letrozole plus lapatinib in postmenopausal women with estrogen receptor (ER) and human epidermal growth factor receptor 2 (HER2) positive breast cancer.

Methods: Postmenopausal women with stage IIA to IIIB ER and HER2 positive breast cancer were eligible. Patients received combination therapy of letrozole 2.5 mg orally daily plus lapatinib 1,500 mg orally daily for 18-21 weeks before surgery. Clinical responses were assessed by clinical palpation, ultrasonography (US), mammogram and/or MRI. Tissue and/or blood samples were collected for analysis of biomarkers at three time points (baseline, day 15, and before surgery). Baseline Fluorine-18 Fluorodeoxyglucose (18F-FDG) and Fluorine-18 Fluoroestradiol (18F-FES) PET-CT imaging were obtained.

Results: Among 24 patients initially enrolled, all underwent surgery. Seventeen patients (70.8%) completed planned neoadjuvant letrozole and lapatinib, whereas 4 patients (13.6%) prematurely terminated the treatment and proceeded to surgery due to minimal clinical response or progression. Except grade 3 liver toxicities revealed in 3 patients (12.5%), which resulted in sequential dose reduction and discontinuation, toxicities were mainly grades 1/2 (Skin, 83%; GI, 79%), which were generally tolerable with

excellent compliance. Overall clinical response rates was 70.8% (n = 17), and pathologic complete response in breast (ypT0-is) was 4.2% (n = 1) (Table 1). In univiariate analyses of biomarkers thus far, baseline TIL ≥ 20%, SUVmax in FES-PET < 5.5, and decreased ER Allred score after surgery were significantly associated with unfavorable overall response.

Conclusion: This chemo-free combination neoadjuvant therapy was feasible, with comparable efficacy outcomes and manageable toxicities profiles. Updated data on 18F-FES PET-CT and biomarkers will be provided. However, considering that pathologic response rate was still low and liver toxicities was non- negligible, further investigation of biomarkers, particularly in Asain women, is urgently requested Updated data on 18F-FES PET-CT and biomarkers will be provided.

OP02-1

Oral Presentation

Psychosocial Characteristics of Hong Kong Chinese Females Undertaking Genetic Counselling and Testing for Hereditary Breast and Ovarian Cancers

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Background/Purpose: Genetic counselling and testing of hereditary breast and ovarian cancer syndromes (HBOC) can facilitate more precise risk estimations, guide the choices of surveillance regimes, prophylactic procedures, and has become standard of care. The present study focused on the characteristics of individuals and psychosocial factors affecting decisions on undertaking genetic testing of HBOC among at-risk Southern Chinese females residing in Hong Kong.

Methods: Hong Kong Chinese female residents, with personal or family breast and/or ovarian cancer history who met the selection criterion were offered free genetic counselling and testing service sponsored by The Hong Kong Hereditary Breast Cancer Family Registry. They were surveyed at the pre-testing stage by a face-to-face interview at a multidisciplinary breast clinic before they received their first genetic counselling consultation. Socio-demographic information, medical history, pre-testing knowledge, attitudes and perceptions on HBOC were also obtained.

Results: 120 females (75.8% with breast or ovarian cancer history) were recruited. 88.4% of them completed high school education or above. Better pre-testing knowledge on HBOC was significantly associated with higher educational level and younger age. Cancer survivors were less likely to adopt passive coping strategies when facing adversities ($p < 0.01$), and more likely to cope by pursuing sports or relaxation ($p = 0.07$). Cancer survivors anticipated that they would experience greater positive changes and post-traumatic growth if they were proven to be gene-carriers comparing with their unaffected counterparts at pre-testing stage ($p < 0.01$).

Conclusion: Results showed that high risk Hong Kong Chinese females with cancer history, higher educational level, and younger age were either more receptive to breast cancer risk assessment, likely to find it useful for cancer prevention, or relevant to them.

One postulation is that the cancer survivors of this study adopted an active coping pattern in face of life adversities and their self-perceived resilience was higher in terms of facing a possible positive genetic testing result. Older, less educated, and unaffected mutation carriers may need assistance in coping with the condition.

Epithelial-Mesenchymal Transition Induced by IL-6/Stat3 Pathway Activation in Residual Tumor Predict Outcome in Triple Negative Breast Cancer Patients After Neoadjuvant Chemotherapy

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Background/Purpose: Among triple negative breast cancer (TNBC) patients receiving neoadjuvant chemotherapy, only those with pathological complete response (pCR) have improved survival. In contrast, in patients lacking a pCR, neoadjuvant chemotherapy enriches a subpopulation of chemotherapy-resistant tumor cells. This study sought to investigate whether IL-6/Stat3 pathway activation could induce epithelial-mesenchymal transition (EMT) of cancer cells in residual tumor and predict worse survival for TNBC patients with neoadjuvant chemotherapy.

Methods: We selected consecutive 112 TNBC patients who did not achieve pCR with neoadjuvant chemotherapy between 2009 and 2011. Expression of IL-6 in residual tumor was evaluated with immunohistochemistry and expression of p-STAT3, Vimentin and E-cadherin was tested with immunofluorescence staining. The relationship between IL-6 expression and p-STAT3, Vimentin, and E-cadherin expression in the cancer tissue was analyzed. The relationship between IL-6 expression and patient disease-free survival (DFS) was assessed using univariate and multivariate analysis.

Results: Majority of patients presented in stage IIb to stage IIIb and IL-6 was expressed in 76% of the residual tumor tissues after neoadjuvant chemotherapy. Furthermore, IL-6 expression correlated positively to p-STAT3 and Vimentin expression, but correlated inversely to E-cadherin expression. The patients with IL-6 high expression had a worse DFS ($p = 0.007$). In multivariate-analysis, the interleukin (IL)-6 expression was an independent and worse prognostic marker for DFS ($p = 0.020$).

Conclusion: IL-6/STAT3 activation may lead to acquired resistance to chemotherapy by promoting EMT and serve as a predictor for worse DFS and a potential therapeutic target in TNBC patients with residual tumor after neoadjuvant chemotherapy.

OP02-3

Oral Presentation

Common Genetic Variants Associated with Breast Cancer and a New Mammographic Density Measure, Cirrocumulus, that Better Predicts Disease

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Background/Purpose: After adjusting for age and body mass index, mammographic density defined by the "white or bright" areas on a mammogram and measured using the computer-assisted method CUMULUS, is a breast cancer risk factor. At least one of 12 common single nucleotide polymorphisms (SNPs) are associated with this mammographic density breast cancer risk-predicting measure, in particular rs3817198 (LSP1). We have developed a new measure based on defining mammographic density by the "brighter" areas of the mammogram, called Cirrocumulus, and found that it is a better predictor of breast cancer risk.

Methods: This study comprised 497 monozygotic pairs, 327 dizygotic pairs and 634 non-twin sisters from the Australian Mammographic Density Twins and Sisters Study genotyped for the 12 SNPs. We measured Cirrocumulus measures of mammographic density. We used multilevel mixed-effects linear regression and multivariate Gaussian regression to estimate the associations with the SNPs. We tested the null hypothesis that none of n SNPs was associated with mammographic density by seeing if the distribution of p-values was consistent with a uniform distribution.

Results: The observer repeatability for transformed dense area within set and between set for Cirrocumulus were 0.88 and 0.84, respectively. After transforming and adjusting for age and BMI, Cirrocumulus was most strongly associated with rs3817198 (LSP1) ($p = 0.005$), rs21443621 (H19) ($p = 0.002$), rs981782 (HCN1) ($p = 0.030$) and rs889312 (MAP3K1) ($p = 0.080$). When considering all 12 SNPs, the distribution of p values was not uniform ($p = 0.003$), and after deleting rs3817198 (LSP1), the deviation was marginal ($p = 0.020$).

Conclusion: Mammographic density measured by Cirrocumulus was associated with

at least one common breast cancer susceptibility variant, rs3817198, in the region of the LSP1 gene. We are further investigating the association of 77 breast cancer susceptibility SNPs with Cirrocumulus using the Melbourne Collaborative Cohort Study.

OP02-4

Oral Presentation

Comparing Strengths of Breast Cancer Risk Factors Measured on Different Scales Using Odds PER Adjusted Standard Deviation (OPERA)

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Background/Purpose: How can the 'strengths' of risk factors, in the sense of how well they discriminate cases from controls, be compared when they are measured on different scales such as continuous, binary, and integer? Given risk estimates take into account other fitted and design-related factors - and that is how risk gradients are interpreted - so should the presentation of risk gradients.

Methods: For each risk factor X0, use appropriate regression techniques to derive from population data the best fitting relationship between the mean of X0 and all other covariates fitted in the model or adjusted for by design, (X1, X2, …, Xn). The Odds PER Adjusted standard deviation (OPERA) presents the risk association for X0 in terms of the change in risk per standard deviation of X0 after adjusting for X1, X2, …, Xn, rather than of X0 itself. If risk increases let RR be the increased risk over A standard deviations. Then OPERA = exp[ln(RR)/A]-fold over A adjusted standard deviations, OPERA = exp [ln(RR)/A].

Results: For breast cancer, after gender and age, familial factors rank highly. The currently known 'high risk' genes and the established common markers of risk account for half this gradient in risk, and less for early-onset disease despite having a stronger familial risk component. Within a western population, number of child births is not strong, but is more important in some other populations. The currently known common genetic markers rank on a par with the current measures of mammographic density (adjusted for age, body mass index and other risk factors).

Conclusion: OPERA estimates are by definition independent, and can be used to compare the predictive strengths of risk factors across diseases and populations. For breast cancer, the risk gradient with measured genetic risk factors will likely increase as

new markers are discovered and better and more sophisticated risk prediction models are developed. New measures of risk, such as markers of methylation and novel approaches to extracting information on risk from mammograms, are proving to be even better risk predictors, as judged by OPERA.

A Proposal for a New Classification of T4 Breast Cancer as Stage IIIC: A Report From the Korean Breast Cancer Society

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Background/Purpose: We compared the survival of patients with Stage IIIB and Stage IIIC tumors and evaluated the prognosis of N3 and T4 to determine the criteria for an update of the classification system

Methods: Using information from two databases, including the nationwide Korean Breast Cancer Registry (KBCR), three cohorts composed of patients from the ASAN Medical Center from 1989 to 2002 (cohort I), from 2003 to 2008 (cohort II), and KBCR from 2003 to 2005 (cohort III) were assembled. New classifications were suggested that rearranged Stage IIIB as T1-3N3 disease and Stage IIIC as T4 any N disease.

Results: A joint analysis of 9640 invasive breast cancer patients from cohorts I and II showed Stage IIIB had significantly poorer disease-free survival (DFS) and breast cancer-specific survival (CSS) compared with Stage IIIC. These findings were validated by an analysis of 14281 cohort III data. The hazard ratio (HR) of CSS for Stage IIIC cancers was 17.1 (range, 11.9 to 24.6), but 14.1 (range, 11.4 to 17.3) for Stage IIIB cancers. Using our new staging system the new Stage IIIB showed a better DFS (HR 6.5; range, 5.3 to 7.9) and CSS (HR 12.59; range, 9.62 to 16.50) compared with the new Stage IIIC (HR 14.07 for DFS; range, 10. 35 to 19.11; HR 28.95 for CSS; range, 20.22 to 41.44).

Conclusion: T4 disease shows a poorer survival outcome than N3T1-3 disease. Reclassification of any T4 disease as Stage IIIC and N3T1-3 disease as Stage IIIB is appropriate.

Concurrent GnRH Agonist with Chemotherapy Improve Response of Neoadjuvant Chemotherapy

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Background/Purpose: Gonadotropin-releasing hormone agonists (GnRHa) with concurrent chemotherapy is evaluated for the fertility preservation for young breast cancer patients. But oncologic effect of GnRHa with concurrent chemotherapy is not clear. Ki-67 expression was evaluated for the oncologic efficacy between the patients with neoadjuvant chemotherapy alone (chemotherapy alone group) and GnRHa concurrent with chemotherapy (GnRHa group).

Methods: A retrospective analysis was performed on 331 invasive breast cancer patients who were below the age of 40 at diagnosis and received neoadjuvant chemotherapy at ASAN Medical Center from December 2010 to September 2014. Pathologic complete response rate (pCR) and Ki-67 changes were evaluated between two groups. A change in Ki-67 index values were divided into 4 groups, namely increased, < 20 decreased, ≥ 20 decreased, and $\geq 50\%$ decreased.

Results: 117 patients were received GnRHa concurrent with chemotherapy and 214 patients were received neoadjuvant chemotherapy alone. Chemotherapy alone group had more progesterone receptor (PR) positive tumor (49.8%) compared with GnRHa group (37.6%, $p = 0.022$). GnRHa group showed high pCR rate (17.9%) compared with chemotherapy alone group (10.2%, $p = 0.035$). For hormone receptor negative tumor, pCR rate of GnRHa group was 30.9% compared with 18.4% in chemotherapy alone group ($p = 0.06$). The changes of Ki-67 index between GnRHa group and chemotherapy alone group were 25.4 ± 32.8 and 18.6 ± 30.4 ($p = 0.061$), respectively. Ki-67 index had improved significantly on GnRHa group compared to chemotherapy alone group ($p = 0.01$). Moreover, a decrease in Ki-67 index over 20 was 47.9% in GnRHa group and 31.3% in chemotherapy alone group, respectively ($p = 0.002$).

Conclusion: Concurrent administration of GnRHa during neoadjuvant chemotherapy treatment improved pCR rate and suppressed Ki 67 expression.

The Impact of Ras/MAPK/S6K Signaling Pathway on Prediction of Clinical Outcome in Metastatic HER2 Positive Breast Cancer Patients Treated with Trastuzumab

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Background/Purpose: The overexpression of human epidermal growth factor receptor 2 (HER2) in breast cancer is associated with poor prognosis, tumor recurrence and shortened survival. The administration of the trastuzumab significantly improves patients prognosis. However, in spite of these successful results, trastuzumab is effective only in 30-50% of cases. PI3K/Akt and Ras/MAPK signaling pathways are activated through HER2 receptor and other growth factors' receptors and both play important role in tumor behavior.

Methods: The study included 76 women with verified HER2 metastatic breast cancer (MBC) who were treated with trastuzumab based palliative chemotherapy. Immunohistochemistry was performed on formalin fixed, paraffin embedded tissue sections with antibodies against S6K, p-S6K-Ser235/236, MAPK, p-MAPK-Thr202/Tyr204, GSK3β, p-GSK3β-Ser9, mTOR, p-mTOR-Ser2448. The cytoplasmatic and nuclear fractions of the staining were assessed separately.

Results: Patients whose tumors showed cytoplasmic (c) and nuclear (n) expression of p-GSK3β-Ser9 exhibited worse progression free survival (PFS) compared to tumors with negative p-GSK3β-Ser9 (PFS 5.1 *vs* 9.1 months; $p = 0.006$). Similar results were also found in p-S6K kinase activity, with the difference that it was possible to observe the dependence on the p-S6K kinase compartmentalization. Patients whose tumors showed p-S6K-Ser235/236 expression accompanied with only cytoplasmatic (c) or nuclear and cytoplasmatic (n+c) staining exhibited worse PFS compared to tumors with negative p-S6K-Ser235/236 expression (negat) (c *vs* negat: 6.3 *vs* 16.1 months, $p = 0.006$; n+c *vs* negat: 7.8 *vs* 16.1 months, $p = 0.025$). Of the remaining kinases, we

showed no effect of their expression on treatment outcome.

Conclusion: This study confirms that prediction of the response or resistance to trastuzumab treatment depends on the S6K and GSK3β kinase activity. Patients, whose tumors had high level of p-S6K or p-GSK3β, had poorer benefit from trastuzumab based therapy. These patients are candidates for targeted blockade of PI3K/Akt and/or RAS/MAPK signaling pathways.

Fibroblast Growth Factor Receptor 4 Expression is Associated with Resistance to Docetaxel During Neoadjuvant Chemotherapy in Triple Negative Breast Cancer

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Background/Purpose: Preoperative doxorubicin plus cyclophosphamide (AC) followed by docetaxel (D) have been widely applied as a standard neoadjuvant therapy (NAC). While initial response to NAC may be related to high rate of pathological complete remission (pCR), some patients suffered from initial response to AC and progression on docetaxel (dPD). We wanted to find out the difference of molecular characteristics between pCR and dPD tumors.

Methods: We reviewed medical records, pathologic specimens and reports to select the cases that primary breast tissue before any NAC was stored in our institute. All patients underwent a subsequent image work-up at during NAC and before definitive surgery. dPD was defined that progression during docetaxel, initially had response to AC. Nanostring® nCounter® Analysis was performed in initial tumor samples before NAC. We also confirm the result with immunohistochemically in tissue microarrays.

Results: We tested initial tumor samples of 9 pCR and 8 dPD patients. In a total 536 kinase gene in nCounter® panel, we found that 23 genes had statistically difference between pCR and dPD patients ($p < 0.05$). After control the family-wise error rate using single step procedure, Fibroblast Growth Factor Receptor 4 (FGFR4) gene still had statistically significant difference ($p < 0.01$) and highly expressed in dPD group ($p = 0.010$). We also demonstrated that difference of FGFR4 expression by FGFR4-antibody immunohistochemistry stain in primary breast tissue. dPD had relatively high score in cytoplasmatic FGFR4 immunostating.

Conclusion: FGFR4 is a marker for resistance in patient with NAC, especially progression during docetaxel regimen in triple negative breast cancer. FGFR4 expression may generate a clue when we make a decision to choose NAC regimens for these patients.

OP03-1

Oral Presentation

A Novel Potential Prognostic Marker SIRT1 on Tumor Invasion and Metastasis, and Tumor Recurrence in Triple Negative Breast Cancer

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Background/Purpose: Silent mating type information regulation 2 homolog 1 (SIRT1) is a histone deacetylase that regulates a variety of cellular and physiological events. But it is not well recognized how SIRT1 act on breast cancer. In this study, we investigated the prognostic role of SIRT1 expression on tumor invasion and lymph node metastasis, and disease related recurrence survival in triple negative breast cancer (TNBC).

Methods: 344 patients who received surgical resection of TNBC from January 2003 to December 2006 at Seoul National University were enrolled in this study. Clinicopathologic information was obtained by reviewing electronic medical records. Tissue microarray was used for SIRT1 immunohistochemistry. To study cancer cell invasion ability, western blot and invasion assay was carried out with Human TNBC cell line (MDA-MB-231), following SIRT1-siRNA transfection.

Results: The expression of SIRT1 significantly correlated with lymph node metastasis ($p = 0.008$). In multivariate analysis, SIRT1 ($p = 0.011$), T stage ($p = 0.014$) and lymphatic invasion ($p < 0.001$) was revealed independent prognostic factors. On receiver operating characteristics curves analysis, the value of areas under the curves was 0.69. SIRT1 expression correlated with shorter disease free survival ($p = 0.003$), but it did not show statistical significance on overall survival. On invasion assay, SIRT1-silenced TNBC cell line showed significantly reduced invasion ability.

Conclusion: In TNBC, SIRT1 may have an important role on invasion and tumor progression, and could be used as a prognostic indicator as well as a potential chemotherapeutic target.

OP03-2

Oral Presentation

Opposing Role of miRNA-155 in Tumor Microenvironment and Tumor Cells Compensate Each Other in Mouse Breast Cancer Model

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Background/Purpose: microRNA-155 (miRNA-155) has diverse roles in normal immune function, as verified by knockout mouse study. On the other hand, it is a well-known oncogenic miRNA in various cancers including B, T-cell lymphoma, colon, lung and breast tumor. Here we report a first analysis of miR-155 deficient, spontaneous mouse breast tumor model and demonstrate its opposing roles in two different tumor contexts.

Methods: To elucidate the role of miR-155 in breast cancer model, the *BRCA1*;Trp53 conditional Knockout (KO) mouse model driven by K14-Cre was crossed with miR-155 KO mouse. For the analysis of immune cells in breast tumor microenvironment, we used FACS and immunofluorescence. For the mechanism study, we performed cytokine PCR array of WT and miR-155 knockout breast cancer cells co-cultured with adipocytes.

Results: We observed the deficiency of miR-155 in recipient mouse allow faster xenograft growth, suggesting a compromised immune surveillance in miR-155 KO tumor microenvironment. Indeed, FACS analysis of the tumor-infiltrated immune cells revealed an increased Myeloid-derived Suppressor Cells (MDSC) infiltration in miR-155 knockout tumors. IL-4, IL-6 and CXCL9, known to recruit MDSC cells, were confirmed to be increased in KO cells, through up-regulated CEBP-beta.

Conclusion: Altogether, our data demonstrate dual role of miR-155 in vivo. In tumor microenvironment, the miR-155 exerts an anti-tumoral effect by supporting normal immune cell function. In contrast, the miR-155 plays an oncogenic role in cancer cells, as shown by proliferation defects in KO cells. This finding suggests a systemic inhibition of miR-155 for cancer therapy could cause an adverse effect.

Mitochondrial ERβ Interacting with Hsp70, Enhances the Aanti-Cancer Activity of Tamoxifen via Improvement of Mitochondrial Function in Breast Cancer

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Background/Purpose: Estrogens play an important role for the development and progression of breast cancer and their receptors have been identified estrogen receptor (ER) α and ERβ. ERα play major role in the estrogen-mediated genomic actions and ERβ is still unclear. Moreover, ERα and ERβ were localized to the mitochondria. However, their function and mechanism to translocation in mitochondria is not fully identified. Here, we demonstrate that ERβ localizes to the mitochondria via the interaction with mitochondrial Hsp70 (mitoHsp70) protein and improves mitochondrial oxygen consumption (OCR) rate and ATP production in breast cancer cells.

Methods: The author used western blot analysis and immunoprecipitation studies to find binding proteins for ERβ. Small interfering RNA used for knocking down mitoHsp70. Expression of ERβ isotype was identified in cancer tissue and adjacent tissue from patients with breast cancer.

Results: In immunoprecipitation studies, ERβ was interacted with mitoHsp70 and localized at matrix in mitochondria. Depletion of mitoHsp70 using small interfering RNA resulted in decrease of translocation of ERβ protein into mitochondria. Conversely, overexpression of Hsp70 was increased the translocation of ERβ protein into mitochondria. The translocated ERβ into mitochondria induced the improvement of mitochondrial function, such as OCR and ATP production and finally enhanced the cell death by tamoxifen treatment. Besides, ERβ expression was significantly decreased in cancer tissue compared with adjacent normal tissue in patients with breast cancer.

Conclusion: Taken together, this study demonstrated that ERβ is localized to mitochondria via the interaction with mitoHsp70, suggesting a role for mitochondrial ERβ in tamoxifen effects. Therefore, mitochondrial ERβ protein may prove useful to the development of novel strategies for the treatment of breast cancer patients.

OP03-4

Oral Presentation

Exploration of Molecular Marker Candidates Predicting Axillary Lymph Node Metastasis by Cap Analysis of Gene Expression

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Background/Purpose: Cap Analysis of Gene Expression (CAGE) is a method to quantify promoter activities (or gene expression) across the genome at one base-pair resolution by sequencing 5'ends of mRNA molecules, based on a combination of next generation sequencer and a cap-trapping method that captures 5'-end complete cDNAs. Axillary lymph node metastasis is one of the most important prognostic factors in breast cancer, and we tackled to find potential promoters which activities are associated with the metastatic status by using CAGE.

Methods: A series of 81 primary invasive breast cancer tissues without systemic drug therapy before operation were collected from Kanagawa Cancer Center. The 81 tumors were classified into 24 triple negative type (ER-/HER2-), 16 HER2 type(ER-/HER2+), 41 luminal type (ER+/HER2+or-) with immunohistochemistry. We obtained CAGE profiles from them by using Illumina HiSeq sequencer.

Results: We confirmed that the CAGE profiles are consistent with the breast cancer subtypes based on immunostaining. Within each of the subtypes, we examined individual promoters if they could be useful to predict lymph node positive cancer or negative one. We found that transcription of a gene encoding glycoprotein is highly elevated in the negative group of lymph node metastasis in HER2 type breast cancer.

Conclusion: This result indicates a possibility that the gene expression levels are associated with axillary lymph node metastatic status. A series of questions remain such as if it can be confirmed at the level of protein, and/or in larger patient groups. An intriguing question would be why it is found only in HER2 subtype. We are going to discuss the result and also report our progress of its follow -up experiments.

OP03-5

Oral Presentation

Synergistic Induction of Apoptosis by DCA and S6K1 Inhibition in Breast Cancer Cells via Downregulation of HK2

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Background/Purpose: The unique metabolic profile of cancer (aerobic glycolysis) is an attractive therapeutic target for cancer. Dichloroacetate (DCA), an inhibitor of pyruvate dehydrogenase kinase (PDK), has been shown to reverse glycolytic phenotype and induce mitochondrion-dependent apoptosis. In the present study, we investigated the effects of S6 kinase 1 (S6K1) inhibition on DCA-induced cell death and the underlying mechanisms in breast cancer cells.

Methods: Cell death was evaluated by annexin V and PI staining. The synergistic effects of DCA and PF4708671 were assessed by isobologram analysis. Small interfering RNA (siRNA) was used for suppressing gene expression. The mRNA and protein levels were measured by RT-PCR and western blot analysis, respectively.

Results: PF4708671, a selective inhibitor of S6K1, and knockdown of S6K1 with specific siRNA enhanced DCA-induced cell death. Interestingly, a combination of DCA/PF4708671 markedly reduced protein expression of a glycolytic enzyme, hexokinase 2 (HK2). Suppression of HK2 activity using specific siRNA and 2-deoxyglucose (2-DG) further enhanced cell sensitivity to DCA/PF4708671. Overexpression of Myc-tagged HK2 rescued cell death induced by DCA/PF4708671.

Conclusion: Based on these findings, we propose that inhibition of S6K1, in combination with the glycolytic inhibitor, DCA, provides effective cancer therapy.

OP03-6

Lyn Plays an Important Role in Acquiring Tamoxifen-Resistance on MCF7 Breast Cancer Cells.

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Background/Purpose: Tamoxifen is effective for treating estrogen receptor-alpha positive breast cancers. However, few molecular mediators of tamoxifen resistance have been elucidated. There are needed to establish the molecular mechanisms of tamoxifen resistance in breast cancer.

Methods: We established tamoxifen resistant cell lines by maintaining in tamoxifen-containing medium. We performed gene array analyses and identified 414 genes with altered expression in TamR cell lines compared to parental tamoxifen-sensitive MCF7 cell lines (parental).

Results: Among these genes, Lyn is a member of the Src family of protein tyrosine kinases and plays a role in cell proliferation, differentiation, apoptosis, migration and metabolism. We found that both mRNA and protein levels of Lyn were overexpressed in TamR cell lines. Knockdown of Lyn using specific small interfering RNA resulted in reduced cell growth of TamR cell lines. In addition, Lyn knockdown potentiated sensitivity to tamoxifen in TamR. The Src family kinase inhibitor also enhanced tamoxifen-induced cell death.

Conclusion: These results suggest that Lyn is a key mediator to acquire tamoxifen resistance, as well as a potential target to overcome resistance to antiestrogen therapy.

Progesterone Receptor-Lacking Tumor in Hormone Receptor-Positive and HER2-Negative Breast Cancer: High Rate of TP53 Mutation and Increased Glycolytic Activity

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Background/Purpose: Prognostic significance of progesterone receptor (PR) is robust in hormone receptor (HR)-positive breast cancer. To know biologic alterations in tumors lacking PR, we investigated the rate of TP53 mutation and the level of glucose uptake in relation to PR among HR+/human epidermal growth factor receptor 2 (HER2) breast cancer patients.

Methods: Three hundred and thirty-eight patients who underwent *TP53* gene sequencing using Sanger direct sequencing were identified. Mutational analysis of exon 5 to exon 9 of the *p53* gene was carried out. Among them, 217 underwent preoperative FDG-PET (n = 291), and in whom maximum SUV was obtained. Low PR was defined by low Allred score (≤ 4). Recurrence-free survival (RFS) was estimated.

Results: PR level classified 82 women as the low PR-group and 256 women as the high PR-group. The RFS was significantly prolonged in the high PR-patients than in the low PR-patients ($p = 0.039$). Also, women with low PR tumor had higher rate of *TP53* mutation ($p = 0.002$) or *TP53* missense-mutation ($p = 0.022$). Finally, average SUV was significantly higher in low PR tumor than in high PR tumor ($p = 0.001$).

Conclusion: We provide evidence that a genetic alteration of *TP53* gene and dysregulated glucose metabolism involve in PR-lacking tumors, even if those are HR-positive and HER2 negative.

Establishment and Characterization of Patient-Derived Human Breast Cancer Xenograft Models

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Background/Purpose: Triple negative breast cancer (TNBC) has a worse prognosis than other subtypes and has a high level of intertumoral heterogeneity. We established the patient-derived human breast cancer xenograft (PDX) models from TNBC and characterized them. With these PDX tumors, we wanted to identify if those tumors have homology with the original tumors, to find out if late passaged PDX tumors still keep the homology. We also wanted to search for any targetable mutation in those PDX models.

Methods: Tumor specimens were transplanted into the mammary fat pad of the immunocompromised mice. When tumors were grown to about 1 cm3, those were serially passaged in vivo. We analyzed the relationship between the patients' prognosis and PDX establishment. To test the homology between human tumors and PDX tumors, we performed H&E stain, short tandem repeat (STR) genotyping, and array comparative genomic hybridization (aCGH) analysis. We compared two long-term maintained PDX tumors to their original tumors (P2, P5, P8). We analyzed PDX tumors with CancerScan®, a novel targeted next generation sequencing tool.

Results: We established 16 PDX models from 69 TNBC patient tumors with a success rate of 23.2%. There was a correlation between PDX establishment and recurrence of the patients. STR genotyping and aCGH showed that high rate of homology maintained between patient tumors and PDX tumors, even in long term maintained PDX tumors of P8. We could not find any shared mutation sites among PDX tumors, and p53 mutation was the most frequently found mutation in CancerScan® analysis.

Conclusion: We could set up PDX tumors from TNBC patients' tumors with the high rates of homology. PDX establishment was correlated to worse prognosis of the original tumor bearer. We could verify the high rate of intertumoral heterogeneity in TNBC

PDX tumors. Since long-term maintained PDX tumors still have high rate of homology to their original tumors, PDX tumors may be used to characterize the original tumors and provide solution for the personalized treatment.

OP04-1

Oral Presentation

The Transition to Next Generation Sequencing from Conventional Sanger Sequencing for Breast Cancer Genetic Study

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Background/Purpose: The incidence of breast cancer is on the rise in Asia including Hong Kong. 40% of the breast cancer patients are diagnosed before age of 50 in Hong Kong. From clinical aspect, it is important to distinguish patients with inherited predisposition to breast cancer from sporadic cases, particularly in early-onset patients (< 45 years old). *BRCA*1/2 have been widely investigated and frequently implicated in familial predisposition to breast cancer. Conventional Sanger sequencing has long been used and proved to be a reliable method, although it is relatively labour intensive and expensive.

Methods: An alternative high efficiency method is much desired, thus more patients will benefit from screening. Harnessing the advantage of Polymerase Chain Reaction (PCR) array and next generation sequencing (NGS), we expand the *BRCA* gene panel to include *TP53* and *PTEN*. The sensitivity of the NGS platform was validated by over hundred Sanger detectable mutations. We have also provided a solution to overcome the challenges in the analysis of homopolymer regions by in-house bioinformatics algorithm.

Results: The NGS approach to mutation detection was applied to 464 high-risk index patients. Altogether 1,092 index patients were examined by either Sanger or NGS approach, germline mutation has been identified in 10% of the families. Overall, 24.1%, 19.4% and 17% of the mutation carriers presented with multiple cancers, triple negative breast cancer and family history of breast and/or ovarian cancer respectively.

Conclusion: These findings may provide information for adaptation of NGS in the diagnostic molecular pathology service and revolutionize laboratory strategies for mutation screening.

OP04-2

Clinical Application of Color Map Pattern on Shear Wave Elastography (SWE) in Invasive Breast Cancer

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Background/Purpose: The purpose of this study is to classify the color map pattern on shear wave elastography (SWE) and to verify the association of the three color map patterns and clinicopathologic factors of invasive breast cancer.

Methods: A total of 103 invasive breast cancers were imaged by B-mode ultrasonography (US) and SWE before surgery. We could classify the color map pattern on the SWE into three categories as followings: type 1 - increased stiffness in the surrounding stroma and the interior lesion itself; type 2 - marked peri-tumoral stiffness at anterior and lateral portions with no or minor stiffness at posterior portion; type 3 - marked peri-tumoral stiffness at anterior and posterior portion with no or minor stiffness at both lateral portions.

Results: In the three color map patterns, type 1 and 2 tumors had a trend that 'the extent of the synchronous non-invasive cancer' had a 1.6-2.0 times wider distribution than the size of the tumor measured by preoperative US or MRI. In histopathologic factor, histologic grade (HG), differentiation, presence of necrosis, degree of Ki-67 expression, and molecular subtype of invasive cancer were associated with the color map pattern on SWE ($p < 0.05$). Type 3 tumor showed high HG, poor cell differentiation, presence of necrosis, high Ki-67, and high percentage of triple negative cancer ($p < 0.05$).

Conclusion: We could find out the association between the color map pattern on SWE and the clinicopathologic factors of invasive breast cancer. We also expect that the color map pattern on SWE will help to decide therapeutic plan and to predict prognosis in breast cancer patients.

Hyperbaric Oxygen Treatment in Reducing Side-Effects of Radiation Therapy of the Breast

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Background/Purpose: We examine patient reported outcome (PRO) of breast cancer patients treated with hyperbaric oxygen treatment (HBOT).

Methods: Breast cancer patients treated with HBOT were interviewed (2009-2013) and quality of life was assessed using validated European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 and (specific breast-related)QLQ-BR23 questionnaires, Numeric Rating Scale (NRS-11), and Patient Global Impression of Change (PGIC) (2014). HBOT treatment consisted of on average 40 sessions, 5 days a week. In total 80 minutes of 100% O2 is delivered during a 115 minutes hyperbaric session.

Results: A total of 111 patients were available for evaluation. Regarding 82 interviewed patients, 66% were satisfied with HBOT results. For severe fibrosis, 55% scored > 3 and for shoulder complaints 45% > 3. In total 83% of these patients experienced improvement after HBOT. Regarding the 29 patients receiving the questionnaires post-HBOT mild to no complaints were seen regarding "pain in arm" (59%), "swollen arm" (79%), "arm movements" (72%), "painful area" (76%), "Swollen area"(83%), "oversensitive area" (72%), "skin problems" (79%), NRS-11 (63%), and PGIC (85%).

Conclusion: PRO in patients receiving hyperbaric oxygen treatment is positive , on average 70-80% mild to no complaints of DRI. HBOT is a well-tolerated treatment for DRI of breast cancer patients. Side-effects are minimal and reversible. A prospective trial regarding the optimal time frame of hyperbaric treatment is warranted and on the way in our medical center.

OP04-4

The Basic Facts of Korean Breast Cancer in 2012: Results of a Nationwide Survey and Breast Cancer Registry Database

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Background/Purpose: Breast cancer is the 2nd most frequent malignancies among Korean women, and the incidence is rising annually. The Korean Breast Cancer Society has constructed a nationwide breast cancer database using an online registration program. The aim of present study was to report the basic facts of Korean breast cancer of 2012, and to analyze the changing patterns in clinical characteristics and management of Korean breast cancer over the past ten years.

Methods: Data on number of newly-diagnosed breast cancer patients, age, stage, and type of surgery of year 2012 were collected from 97 hospitals and clinics, using a questionnaire survey. Additional data such as changing patterns of breast cancer were collected and analyzed utilizing the online breast cancer registry database.

Results: A total of 17,788 patients were newly diagnosed with breast cancer in 2012. The survey data and registry data showed equivalent results. The rate of increase of new breast cancer cases has slowed from 17.9% in 2010 to 4.8% in 2012. estrogen receptor (ER) positive breast cancer steadily increased from 58.2% in 2002 to 73.0% in 2012. The proportion of stage 0 and I breast cancer increased continuously for 10 years (56.4% in 2012), and breast conserving surgery (67.2%) was performed more frequently than total mastectomy (32.3%).

Conclusion: The clinical characteristics of Korean breast cancer changed over the last

decade, and the management of breast cancer has changed, accordingly. The nationwide registry data will contribute to a better understanding of changing clinical characteristics of Korean breast cancer.

Who are Sexually Active During and After Breast Cancer Treatment? Patterns of Sexual Functioning Changes in Breast Cancer Patients from Diagnosis to 3 Year Follow-Up

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Background/Purpose: Breast cancer and its treatment have impacts on sexual life, and breast cancer patients reported lowered sexual functioning resulting in poor quality of life. Moreover, some patients have difficulties to be sexually active for a longer period whereas others regain some normalcy after recovery. The goal of this study was to evaluate changing pattern of sexual functioning of breast cancer patients from diagnosis to 3 year follow-up and find factors associated with low sexual functioning.

Methods: Between July 2010 and July 2011, we recruited 432 stage 1 to 3 patients before surgery from two hospitals in Seoul, Korea. Sexual functioning was assessed using EORTC-BR 23 at diagnosis (before any treatment), 2 weeks, 3, 6, 12, 24 and 36 months after surgery. We also measured self-esteem, body image, appearance distress and reasons for sexual difficulties. Growth mixture models was used to find distinct patterns of sexual functioning changes and multivariate analysis was performed to find risk factors using STATA 13.

Results: Five SF distinct patterns were identified: constantly high (CH): 22.7%, constantly increase (CI): 15.1%, decrease and recover (DR): 22.8%, decreased, recovered and decreased (DRD): 16.5% and constant low (CL): 22.9%. There was no statistically different with stage at diagnosis, surgery, and hormone therapy among 5 groups. While CL was little older and lower sexual desire, DRD had high level of stressed and concern due to altered appearance. Overall, higher SF associated with higher self-esteem

($p < 0.001$) and body image ($p < 0.001$).

Conclusion: While breast cancer patients' sexual functioning decreased during active treatment (chemo- and radio-therapy), patients regain sexual functioning and became active over time. Patients with high altered appearance distress, lower body image and self-esteem were less likely to be sexually active after treatment. Appropriate education and supportive care during and beyond breast cancer treatment is necessary to intervene appearance distress and body image.

OP04-6

Oral Presentation

Prospective Study of Internal Mammary Sentinel Lymph Node Biopsy in Patients with Clinically Positive Axillary Lymph Nodes

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Background/Purpose: Current research of sentinel lymph node biopsy (SLNB, both axillary and internal mammary) was limited to patients with clinically negative axillary lymph nodes (ALN). As internal mammary lymph node metastases are mostly found concomitantly with ALN metastases, patients with positive ALN would more likely benefit from internal mammary sentinel lymph node biopsy (IM-SLNB) because of its impact to staging and accurate indication of radiation to the internal mammary area. The aim of this prospective study is to evaluate the roles of IM-SLNB in breast cancer patients with clinically positive ALN.

Methods: From June 2013 to December 2014, 89 breast cancer patients with clinical positive ALN from Shandong Cancer Hospital were enrolled into this study. All patients underwent axillary lymph node dissection. Meanwhile, IM-SLNB would be performed for patients with visualized IM-SLN. Modified injection method of radiotracer was used which could significantly improve the visualization rate of the IM-SLN in clinically negative ALN (77.2%, 223/289, the latest data).

Results: The visualization rate of internal mammary lymph node was 68.5% (61/89), and IM-SLNB had been performed in 59 of the 61 patients. The detection rate was 94.9% (56/59) and the incidence of complications was 5.1% (3/59). The metastasis rate of IM-SLN was 19.6% (11/59). Patients with the upper inner quadrant tumors and with more number of ALN metastasis had significantly higher chances of metastasis ($p < 0.001$ and $p = 0.017$, respectively).

Conclusion: As a minimally invasive staging technique for the evaluation of the status of Internal mammary lymph node with high safety and feasibility, IM-SLNB should be performed routinely in all patients with clinically positive ALN. Since radiotherapy of the Internal mammary lymph node chain carries increased cardiac and pulmonary side effects, the appropriate identification of patients who might benefit from adjuvant

radiotherapy is essential and should be based on the tumor-positive results of IM-SL-NB rather than the high-risk estimation only.

OP04-7

Oral Presentation

Breast-Specific Gamma Imaging versus Magnetic Resonance Imaging in Ductal Carcinoma *In Situ*: A Prospective Head-to-Head Trial

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Background/Purpose: Ductal carcinoma *in situ* (DCIS) is very early cancer that is highly treatable, but accurate determination of the size or extent of the lesion is difficult. Breast magnetic resonance imaging (MRI) may provide an accurate assessment of tumor size. But there are limited data on the utility of breast-specific gamma imaging (BSGI) in DCIS. The aim of the study was to prospectively compare the accuracy of BSGI to MRI for the assessment of the size of DCIS.

Methods: This single-center prospective study conducted from Jun 2013 to December 2014 at the ASAN Medical Center included 135 patients with a histologically proven DCIS or DCIS with microinvasion (DCISM) by needle biopsy, who all underwent BSGI and MRI. Each longest diameter (LD) measurements were compared to histopathological LD. The measurements were validated using Bland and Altman analysis and Pearson's correlation. Bland and Altman agreement plot methodology resulting in dimensionless mean difference and 95% limits of agreement (LOA).

Results: Pathologic tumor size of the DCIS ranged from 0.2 to 12.0 cm (median 2.2 cm). Of 142 cases of biopsy-proven DCIS or DCISM in 135 women, 76.3% were detected with BSGI, and 95.0% were detected with MRI. Bland-Altman agreement plot analysis for the whole cohort revealed mean difference between MRI and histopathology (0.2901), 95% LOA (-2.6447 to 3.2249) compared with BSGI and histopathology (mean difference 0.2863), 95% LOA (2.9585 to 2.3860). Overall, Pearson's correlation

of the size between BSGI and histopathology was 0.801 versus 0.777 between MRI and histopathology.

Conclusion: Although MRI is thought to be more sensitive than BSGI for detecting DCIS, BSGI comparable to MRI in the assessment of tumor size.

OP04-8

Depression and Anxiety After Adjuvant Ovarian Suppresion in Premenopausal Breast Cancer

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Background/Purpose: The results of the Suppression of Ovarian Function Trial (SOFT) and the Tamoxifen and Exemestane Trial (TEXT) showed that ovarian suppression in premenopausal early breast cancer patients without chemotherapy improves disease outcome. However, mood swings after medication is one of the chief complaints to make patients stop undergoing endocrine therapy. Studies about the complications of ovarian suppression in breast cancer patients are not designed to examine the mental status or retrospective. We designed this randomized controlled trial to evaluate psychological functioning of patients after undergoing adjuvant ovarian suppression by goserelin.

Methods: We randomly assigned 64 premenopausal women with hormone receptor positive early breast cancer to the tamoxifen or tamoxifen plus gorserelin for a period of 1 year. Participants are screened for depression and generalized anxiety disorder using Hamilton Rating Scale for Depression (HAMD), Hamilton Rating Scale for Anxiety (HAM-A), Anxiety Sensitivity Index-revised (ASI-R) and State and Trait Anxiety Inventory (STAI) in addition to assessing Brain-derived Neurotrophic Factor (BDNF) level at baseline, one month and 12 months after adjuvant endocrine treatment. The results were analysed using statistical tests and correlation analysis..

Results: Sixty-four women aged 23 to 48 (average: 43.8) years were followed up. Each group consisted of 32 women. There was no difference in baseline characteristics. No woman was diagnosed with depression or generalized anxiety disorder by the scale we used. Measured HAM-D, HAM-A and STAI didn't show any significant difference between groups at any moment. However, scale for anxiety, ASI-R, showed the significant correlation in repeated measured Analysis of variance (ANOVA) ($p = 0.032$). It was found that the average of ASI-R for tamoxifen group was higher than for tamoxifen with goserelin group in 12 months (18.35 ± 2.59 vs 11.71 ± 2.06, $p = 0.025$). There was no significant correlation in BDNF level.

Conclusion: The obtained research results on the correlation of anxiety and depression after goserelin didn't show consistent outcome. We could assume that tamoxifen group could be more anxious by the average in ASI-R score. The mood fluctuation by the augmented menstrual cycle is postulated as the cause comparing to no menstrual cycle in tamoxifen with goserelin group. When we consider the depression or anxiety in both groups, adjuvant ovarian suppression by goserelin is a safe and recommendable choice.

Poster Exhibition

GBCC 2015 & 4th IBCS
Abstract Book

PO001

Reliability of Estrogen Receptor, Progesterone Receptor, HER2 Status, and Ki67 Level in Core Needle Biopsy in Breast Cancer Patients

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Background/Purpose: It has become increasingly important in the preoperative work up of breast cancer patients to analyze estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor 2 (HER2), and Ki67 in core needle biopsy (CNB). For accuracy of ER, PR, HER2, and Ki67 in CNB, we compared the results of CNB and those of surgical specimen.

Methods: We retrospectively reviewed data from 161 breast cancer patients whose ER, PR, HER2, and Ki67 were analyzed in both CNB and surgical specimen between 2013 and 2014. ER, PR, and Ki67 were determined immunohistochemistry (IHC) and reported as percentage. HER2 was determined by IHC and/or fluorescence in situ hybridization (FISH).

Results: Pearson's correlation coefficient for ER, PR, HER2 and Ki67 between CNB and surgical specimen were 0.911, 0.793, 0.836, and 0.768, respectively ($p = 0.001$ for all). However, the false positive rates of ER, PR, HER2 and Ki67 were 26.9%, 18.2%, 0%, and 31.6%. The false negative rates of ER, PR, HER2 and Ki67 were 4.7%, 7.0%, 5.6%, and 11.6%.

Conclusion: Despite the good correlation of ER, PR, HER2 and Ki67 between CNB and surgical specimen, we need to be aware of the possibility of false positive and false negative results in CNB.

PO002

Comparison of Hormone Receptor and HER2 Assay Results Between Core Needle Biopsy and Mastectomy Specimen from the Same Patients

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Background/Purpose: In the treatment of breast cancer, hormone receptor (HR) expression and human epidermal growth factor receptor 2 (HER2) gene expression are the most important biomarkers. Therefore, the accuracy of their results is critical.

Methods: We studied the results of HR expression and HER2 gene expression of 153 consecutive patients between March 2009 and February 2014. Estrogen receptor(ER), progesterone receptor (PgR) and HER2 gene immunohistochemical (IHC) assay of tissues from mastectomy specimens were compared with their previous core needle biopsy (CNB) ER, PgR and HER2 gene IHC assay results.

Results: The tumors of 112 (73.2%) out of the 153 patients are positive HR (ER and/or PgR) in CNB specimens and 107 (69.9%) are positive HR in mastectomy specimens. 33 (21.6%) patients are positive HER2 in CNB specimens and 34 (22.2%) are positive HER2 in mastectomy specimens. ER positivity decreased from 71.9% in the CNB to 68.0% in mastectomy specimens, while PgR positivity increased from 60.8%

Conclusion: There are CNB negative and mastectomy positive disagreements in HR and HER2 cases. Proper hormonal therapy depends on accurate hormone receptor assay results, as well as target therapy depends on HER2 assay results. Both assays of CNB and mastectomy specimens are very helpful in accurate ER, PgR and HER2 assay results.

PO003

Magnetic Resonance Imaging After Completion of Neoadjuvant Chemotherapy Can Accurately Discriminate Between No Residual Carcinoma and Residual Ductal Carcinoma *In Situ* in Patients with Triple-Negative Breast Cancer

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Background/Purpose: To investigate independent clinicopathological and radiological predictors for discriminating no residual invasive or *in situ* carcinoma (ypT0) from residual ductal carcinoma *in situ* (ypTis) in breast cancer patients received neoadjuvant chemotherapy (NCT).

Methods: Parameters of 117 patients attaining pathological complete response (CR) in breast after NCT between January 2010 and December 2013 were retrospectively evaluated by univariate and multivariate analyses. All patients examined mammography, ultrasound, and magnetic resonance imaging (MRI) before and after NCT.

Results: Patients with ypT0 were 67 (57.3%) and associated with hormone receptors-negative, HER2-negative tumor and higher proportion of breast-conservation surgery. Baseline mammographic and MRI presentation of main lesion, presence of associated microcalcification, and shape, posterior echo pattern and presence of calcification in ultrasound were significantly associated with ypT0. CR in mammography, ultrasound, or MRI after NCT was also related to ypT0. By multivariate analysis, independent predictors of ypT0 were triple-negative subtype [Odds ratio (OR), 4.234; 95% confidence interval (CI), 1.114-16.087] and CR in MRI after NCT (OR, 5.230; 95% CI, 1.532-17.852). Stratified analysis by breast cancer subtype demonstrated MRI well predicted ypT0 in all subtypes except HER2-positive subtype. Especially, of 40 triple-negative breast cancers, 22 showed CR in MRI and 21 (95.5%) were ypT0 after NCT.

Conclusion: MRI accurately discriminates between ypT0 and ypTis after NCT, especially in triple-negative breast cancers. Breast MRI can be useful for evaluating tumor response to NCT and planning surgical treatment of patients with all subtypes other than HER2-enriched tumors after NCT.

PO004

Utility of Bone Scintigraphy in Breast Cancer Patients Undergoing PET/CT

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Background/Purpose: We have compared PET/CT with bone scintigraphy to determine if bone scintigraphy adds any additional utility in terms of clinical management in patients with breast cancer.

Methods: Subjects were selected for inclusion if they had a F-18 FDG PET/CT scan for initial staging of malignant neoplasm of the female breast and a Tc-99m MDP whole body bone scintigraphy within 30 days of each other. The interpretation of the both PET/CT and bone scintigraphy regarding the presence of bone metastases was recorded and compared with follow-up imaging or histologically proven metastasis.

Results: A total 235 examinations in 47 female patients were reviewed. 171 studies were negative on both examinations, 13 positive on PET/CT only, 15 positive on bone scintigraphy only, and 36 positive on both. Of the studies proved positive on bone scintigraphy alone, only two later turned out to represent actual metastasis.

Conclusion: Our findings suggest that bone scintigraphy may not be superior to F-18 FDG PET/CT for the detection of osseous metastasis for staging, and may not affect on treatment strategy significantly in breast cancer patients.

PO005

Usefulness of Optical Diffusion Imaging in Differentiating Malignant Breast Masses from Benign Masses

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Background/Purpose: The aim of this study is evaluate the diagnostic accuracy of optical diffusion breast imaging in differentiating malignant breast lesions from benign lesions.

Methods: Optical imaging obtained at 155 breast masses(126 benign and 29 malignant) in 155 female patients(mean age, 46 years; range, 16-86 years) who scheduled Ultrasound-guided biopsy using commercially available unit (Optimus®). We compared the diagnostic accuracy of total hemoglobin (HB) level or oxygen saturation level for discrimination benign and manlignant breast mass.

Results: The mean total HB levels ± SD were 0.2390 ± 0.08643 mmol/L (95% confidence interval [CI], 0.2061-0.2718) in malignant masses and 0.1264 ± 0.1022 mmol/L (95% CI, 0.1084-0.1444) in benign masses ($p < 0.0001$). The mean oxygen saturation levels were 0.9977 ± 0.05731 mmol/L (95% CI, 0.9759-1.0195) in malignant masses and 0.9878 ± 0.05645 mmol/L in benign masses ($p = 0.39$).

Conclusion: The total hemoglobin level is statistically different between benign and malignant breast masses, thus optical diffusion imaging might be a good supplemental tool to increase the diagnostic accuracy of conventional breast ultrasound.

PO006

Diagnostic Value of Ultrasonography, Contrast-Enhanced Magnetic Resonance Imaging, F-18 Fluorodeoxyglucose Positron Tomography in Breast Cancer Patients for Detection of Axillary Lymph Node Metastasis

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Background/Purpose: Axillary lymph node metastasis is an important factor of breast cancer recurrence, treatment and survival rate for breast cancer patients. Preoperative detection of axillary lymph node metastasis reduces complication of axillary dissection. In this study we evaluate the diagnostic performance of ultrasonography, Contrast-Enhanced Magnetic Resonance Imaging (cMRI), and F-18 Fluorodeoxyglucose Positron Tomography (PET-CT) in breast cancer patients.

Methods: Between January 2013 and December 2013, 148 patients with histopathologically confirmed breast cancer were included in this study. All patients underwent breast US, breast cMRI and PET-CT before surgery. Sensitivity, specificity, accuracy, positive predictive value, negative predictive value of each modality were obtained taking histopathological results of axillary lymph node dissection or sentinel lymph node biopsy as the reference standard.

Results: Axillary lymph node metastasis was confirmed in 88 patients by histopathological studies. The sensitivity, specificity, positive predicition value, negative prediction value and accuracy of ultrasonography were 72%, 73%, 50%, 87% and 73% respectively. For cMRI it was 70%, 72%, 40%, 90%, 72% and for PET-CT it was 67%, 75%, 57% 82%, 72% respectively. There were no significant differences between three modalities.

Conclusion: Diagnostic performances of PET-CT was not superior to that of ultrasonography and cMRI. So multimodal imaging in combination are useful for preoperative axillary staging and each modality cannot replace sentinel lymph node biopsy up to now.

PO007

Papillary Lesions of the Breast: Outcomes of Management by Vacuum Assisted Excision

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Background/Purpose: Intraductal papilloma (IP) is a commonly identified breast lesion with variable clinical presentations. The management of benign papilloma (BP) without atypia identified on breast core needle biopsy (CNB) is controversial because of their heterogeneity and possibility of hidden malignancy. In published studies, the upgrade rate to carcinoma with a diagnosis of BP without atypia on CNB ranges from 0% to 29%. The aim of this study was to assess the value of vacuum assisted excision (VAE) in the diagnosis and treatment of intraductal papillomas of the breast.

Methods: From 2004 to 2014, a total of 1,328 VAE were performed. We identified 80 patients (6%) with IPs, of which 22 was confirmed by VAE without previous CNB and its selection criteria was detection only by ultrasonography without clinical symptoms and small mass (< 1 cm). During the same period, a total 100 patients underwent surgical resection for IP. Patients were stratified as follows: CNB followed by VAE (n = 58, group 1), VAE alone (n = 22, group 2), CNB followed by surgical excision (n = 34, group 3) and surgical excision alone (n = 66, group 4)

Results: In VAE groups, we found 64 BPs and 16 atypical IPs. Among 16 atypical IPs (all in group 1), ductal carcinoma *in situ* (DCIS) was seen in 4 (upgrade 25%). In 64 BPs and in group 2, there was no cancer from pathology and during follow-up. In group 3, 1 of 4 atypical IPs was upgrade to DCIS (25%) and 30 BPs upgrade to 2 DCIS (6.6%). In group 4, 1 of 6 atypical IPs was upgrade to invasive cancer (16.6%) after 5 months. In the remaining 60 BPs, no cancer was found.

Conclusion: Our findings suggest that selective approach for IP by VAE may be safe and alternative to surgical excision. Our proposed criteria include nonsymptomatic patient with ultrasound detected mass which was smaller than 1 cm.

PO008

Next-Generation Sequencing of *BRCA1/2* in Breast Cancer Patients: Potential Effects on Clinical Decision-Making Using Rapid, High-Accuracy Genetic Results

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Background/Purpose: We evaluated the clinical role of rapid next-generation sequencing (NGS) for identifying *BRCA1/2* mutations compared to traditional Sanger sequencing.

Methods: Twenty-four paired samples from twelve patients were analyzed in this prospective study to compare the performance of NGS to the Sanger method. Both NGS and Sanger sequencing were performed in two different laboratories using blood samples from patients with breast cancer. We then analyzed the accuracy of NGS in terms of variant calling and determining concordance rates of *BRCA1/2* mutation detection.

Results: The overall concordance rate of *BRCA1/2* mutation identification was 100%. Variants of unknown significance (VUS) were reported in two cases of *BRCA1* and three cases of *BRCA2* after Sanger sequencing, whereas NGS reported only one case of *BRCA1* VUS, likely due to differences in reference databases used for mutation identification. The median turnaround time of Sanger sequencing was 22 days (range 14-26 days), while the median time of NGS was only 6 days (range 3-21 days).

Conclusion: NGS yielded more accurate and rapid results than Sanger sequencing with respect to *BRCA1/2* mutation identification. The shorter turnaround time and higher accuracy of NGS may help clinicians make more timely and informed decisions regarding surgery or neoadjuvant chemotherapy in patients with breast cancer.

PO009

Validation of HER2 Expression in Cell Lines by Immunofluorescence and SISH

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Background/Purpose: Circulating tumor cell has been studied for clinical meaning in many cancers including breast cancer. In breast cancer, it has also been investigated for understanding the heterogeneity of breast cancer. Particularly, discordance of human epidermal growth factor receptor (HER2) expression between primary tumor tissue and circulating tumor cell is debate for clinical significance and treatment for anti-HER2 therapy. Therefore we validated HER2 expression level by checking the immunofluroscence staining which used by detecting the HER2 -stained circulating tumor cell.

Methods: We used 6 cell-lines (MCF-7, BT20, MDA-MB 468, ZR-75-1, BT474 and SK-BR-3). All cell-lines were cultured according to the supplier's protocols (American Type Culture Collection). In order to immunofluorscense staining, all cells were attached to slide and fixed followed by staining, for which was done by using antibodies HER2, CD45 and 4',6-diamidino-2-phenylindole (DAPI). And then SMART Cytogen viewer software program ver 3.28 (CytoGen, Seoul, Korea) was used for the measurement of intensity of HER2 positive images. At the same time, all cell lines of the amplification of HER2 gene were checked.

Results: In HER2-expressed SKBR3 and BT474, HER2 average intensity by using SMART Cytogen viewer software program ver 3.28 were 241.4 and 221.28 respectively and the silver in situ hybridization (SISH) result were 12.7 and 12.15. In HER2-negative cell lines such as ZR-75-1, BT20, MCF-7, MDA-MB 468, HER2 average intensity were 139.7, 152.12, 90.2 and 36. And their SISH results were 1.56, 1.4, 1.03 and 1.13. Therefore HER2 average intensity must be over 200 if the HER2 expression is positive by immunofluorescence using SMART Cytogen viewer software program ver 3.28.

Conclusion: This study showed the feasibility of immunofluorescence staining on HER2 protein compared with SISH. Using this method, we will be able to calibrate the HER2 status of circulating tumor cell more precisely.

PO010

A Case of Breast Poroid Hidradenoma Mimicking Papillary Neoplasm

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Background/Purpose: Poroid hidradenoma is a rare cutaneous neoplasm, most frequently situated on head and neck. We report a case of poroid hidradenoma arising on the breast mimicking papillary neoplasm. A 68-year-old female presented with an enlarging cystic mass on right lower inner quadrant of breast. Initially, she had visited the hospital 3 years ago because of a 1.5 cm size slowly growing cystic mass in right breast.

Methods: The ultrasound finding was suggestive of papilloma. The pathologic result of biopsy was suggestive of intraductal papilloma. We recommended local excision of lesion but follow-up was lost. 3 years later, she visited our office because the mass increased and caused painful sensation. Physical examination revealed a dark bluish, ovoid cystic mass, 4.6 cm in size, on the right inner quadrant of breast. About 30cc needle aspiration was done every week for symptom relief. Meanwhile, the solid portion had been significantly increased on ultrasound.

Results: The pathologic result of biopsy was papilloma neoplasm too. Wide excision was performed under general anesthesia. Histopathological result was poroid hidradenoma, 2.8 cm, clear resection margin. Immunohistochemical stains showed that C-erb-B2 was 0, CK 5/6 was positive, E-cadherin was positive, EGFR was positive (3+), Ki-67 was from less than 1% to up to 5% positive, P63 was strongly positive. CK5/6 positive was suggestive of poroma.

Conclusion: The poroid hidradenoma will be listed up in the differential of breast adnexal neoplasm mimicking papillary neoplasm. Treatment is based on surgical resection, in order to prevent a possible recurrence or a rare malignant transformation.

PO011

Core Needle Biopsy Specimen is More Appropriate for Evaluation of Phosphorylated S6 Kinase-1 than Surgical Specimen in Invasive Breast Cancer

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Background/Purpose: Phosphorylation of ribosomal protein S6 Kinase 1 (p-S6K1), a surrogate marker of mTOR inhibitor, is associated with poor prognosis. Theoretically, core needle biopsy (CNB) could be better choice for evaluation of phosphorylated maker because of the shorter time interval from the tissue obtain to the fixation than surgical specimen. We investigate the difference of expression rate of p-S6K1 between surgical specimen and CNB specimen.

Methods: A total of 99 invasive breast cancer patient who treated with surgical procedure between Jan 2012 and Jul 2013 were included in this retrospective analysis. Clinicopathological information were reviewed from medical record. Estrogen receptor (ER), progesterone recept β or (PR), human epidermal growth factor receptor 2 (HER2) and p-S6K1 were assessed with both CNB specimen and surgical specimen by immunohistochemistry.

Results: The expression rate of p-S6K1 on CNB specimen and surgical specimen were 77.8% and 59.6%, respectively. On CNB specimen, p-S6K1 expression has tendency to positively related with histologic grade, which is classical poor prognostic pathologic parameter ($p = 0.068$). In contrast, the expression of p-S6K1 on surgical specimen showed no significant correlation with histologic grade ($p = 0.190$).

Conclusion: The expression rate of p-S6K1 was higher in CNB specimen compared to surgical specimen. CNB specimen is more appropriate for evaluation of p-S6K1 than surgical specimen.

PO012

The Reliability of Core Needle Biopsy in the Diagnosis of Benign Proliferative Breast Lesions without Atypia

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Background/Purpose: To evaluate the accuracy of ultrasound-guided core biopsy in the diagnosis of benign proliferative breast lesions without atypia, with definitive pathological diagnosis obtained after surgical excision or with radiologic follow-up, and to assess clinicopathological factors that can possibly predict occult atypia and malignancy in such lesions.

Methods: We evaluated 428 core biopsies diagnosed with proliferative breast lesions without atypia, consecutively performed on 422 patients. The histopathologic findings were 179 lesions with sclerosing adenosis, 111 lesions with florid ductal, 6 lesions with radial scars and 132 lesions with papillary lesions. All patients underwent ultrasound-guided core biopsies using 14-gauge automated core biopsy needles with free-hand technique. A total of 330 lesions (77%) underwent surgical excision, whereas 98 lesions were followed-up with ultrasound.

Results: Among the core biopsied lesions, there were 31 lesions with underestimation of diagnosis. With definite surgical excision, 6 lesions were diagnosed with atypical ductal hyperplasia (ADH), 17 lesions with ductal carcinoma *in situ* (DCIS) and 8 lesion with invasive ductal carcinoma. When clinicopathological factors were compared between the diagnostically underestimated group and stationary group, size was found to be significantly different. (16.0 mm ± 8.9 vs 10.9 ± 6.2, $p = 0.028$)

Conclusion: Diagnosis of benign proliferative disease of the breast can be difficult with clinical, radiological, and even histopathological examination. The rate of diagnostic underestimation (31/428, 7.2%) provides support for the recommendation of further excision in lesions diagnosed as benign proliferative breast lesions without atypia by core needle biopsy. Even though there is no typical criterion for the prediction of hidden atypical or malignant features in such core biopsy samples, size of the lesion could influence the decision for further surgical excision.

PO013

Value of Breast MRI for Predicting Axillary Lymph Node Metastasis in Breast Cancer Patients According to Histologic Subtype

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Background/Purpose: To predict the state of the axillary lymph node prior to surgery, may help in the treatment strategies. The purpose of this study was to compare the ultrasonography (US), contrast-enhanced magnetic resonance imaging (MRI), and 18F-fluorodeoxyglucose positron emission tomography/computed tomography (PET/CT) and to evaluate the diagnostic efficacy of MRI according to histologic subtype.

Methods: Between January 2013 and December 2014, 305 patients with T1 and T2 Breast cancer patients who were preoperatively evaluated using US, MRI, PET/CT were enrolled in this study. All patients underwent primary surgery. A retrospective chart review was conducted and analyzed.

Results: Mean age of patients was 52.6 years. The axillary lymph node metastases (ALNM) in 107 (35.1%) patients were pathologically confirmed. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of US for determining ALNM were 27.1%, 91.4%, 63.0%, 69.9%, and 68.9%, respectively. MRI was 43.0%, 84.6%, 63.0%, 73.7%, 71.1% and those of PET/CT were 51.4%, 88.4%, 70.5%, 77.1%, and 75.4%, respectively. The comparison between the subtypes with MRI, PPV in HER2 type was only significantly lower than that of luminal A subtype.

Conclusion: When classified according to histological subtype, was in HER2 group, specificity, PPV, NPV, ACC is low, especially PPV showed a significant difference. Therefore, Patients with HER2 subtype will be helpful to compare with other diagnostic tools predict whether ALNM.

PO014

Effects of Wire Localization Performer in the Localized Excision Biopsy of Mammographic Microcalcification

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Background/Purpose: This study aims to investigate whether the operator's execution allows doing more accurate and faster excision of the wire localization regarding to mammographic microcalcifacation than radiologist's.

Methods: Medical records of patients who have undergone diagnostic excision biopsy for mammographic microcalcification between May 2011 and December 2014 are reviewed. 43 cases of localized excision biopsy have been performed in all 41 patients during the period. We compares the group in which wire localization is performed by operator and the group by radiologist in the operation time, the specimen size for the target cluster size, and re-excision rates.

Results: The median operation time of the group by the operator is 64 minutes, which is compared to 79 minutes by radiologist. And the difference is not statistically significant ($p = 0.11$).But the median detection time which is between start of incision and verification for the final specimen mammography is 42 minutes by operator's localization, which is statistically significantly shorter in univariate and multivariate analyses than 59 minutes by radiologist's ($p = 0.04$, 0.018 respectively). There is no significant difference in the specimen size for the target cluster size, and re-excision rates.

Conclusion: The operator's execution of wire localization for microcalcification may contributes to shorten the operation time through the reduction of detection time without increasing the extent of the resection or the re-excision rate.

PO015

Lectin-Based Approach for Detecting Carcinogenesis in Breast Tissue

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Background/Purpose: It has been suggested that diversity in structure and sensitivity in response to the cancer progression of the glycosylation can provide great potential for cancer screening. However, most efforts have paid into development of protein or nucleotide marker in breast cancer research field. In the present study, we investigated the glycosylation change in the breast cancer tissue using enzyme-linked lectin assay (ELLA) which has potential for high-throughput assay.

Methods: Cancer tissues (CCs) and normal tissues (CNs) were collected from women with breast cancer stage 0 to IIIA. The specimens were divided into two groups, stage 0 to I (stage 0-I) and stage II to III (stage II-III), and the values of CCs and CNs in stage 0-I or stage II-III were compared in ELLA using four types of lectins. The statistical significance of differences between groups was determined by two-tailed Student's t-tests.

Results: The CCs showed markedly enhanced level of mannosylation (stage 0-I: $p < 0.001$; stage II-III: $p < 0.001$) galactosylation (stage 0-I: $p < 0.05$; stage II-III: $p < 0.001$), sialylation (stage 0-I: $p < 0.001$; stage II-III: $p < 0.01$) and fucosylation (stage 0-I: $p < 0.01$; stage II-III: $p < 0.01$). Moreover, CCs of stage II-III showed significantly increased levels of mannosylation ($p < 0.01$) and galactosylation ($p < 0.05$).

Conclusion: Our results demonstrate that the enhanced glycosylation levels in the ELLAs indicate breast carcinogenesis and suggest that the ELLA system have extraordinarily superior sensitivity and specificity in detecting the breast cancer.

PO016

BRAF Mutation in Korean Thyroid and Breast Cancer Patients: A Pilot Study

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Background/Purpose: In Korean population, papillary thyroid carcinoma is the most commonly occurring malignancy affecting women and the risk of breast cancer as the second primary malignancy is relatively high due to diagnosis at a young age. The V600E mutation of the *B-type Raf kinase* (*BRAF*) is the most common genetic alteration in thyroid cancer and is detected at a relatively high prevalence in Korea. The aim of this study was to evaluate the frequency of the *BRAF* mutation in Korean patients possessing both thyroid and breast cancers.

Methods: A total of 16 patients with both thyroid and breast cancers from March 2010 to February 2014 were included in this study. We analyzed the frequency of the *BRAF* V600E mutations on both thyroid and breast tissues by performing dual priming oligonucleotide-based multiplex real-time polymerase chain reaction to isolate and to purify the DNA from the formalin-fixed and paraffin-embedded tumors. Also, clinicopathologic variables including the size, histologic type, lymph node status, estrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor-2 (HER2) were evaluated.

Results: The incidence of the *BRAF* V600E mutation in patients with Korean thyroid cancer was 56.3%. However, our preliminary results showed that the *BRAF* V600E mutation was not detected in any of the patients with breast cancer (0%). On the other hand, the ER, PR and HER2 expressions were all negative in papillary thryoid carcinomas. The clinicopathologic evaluations showed that there was significant difference in *BRAF* mutations between thyroid and breast cancer tissues ($p = 0.016$).

Conclusion: We analyzed the frequency of the *BRAF* V600E mutation as the *BRAF* V600E mutation accounts for the highest frequency among all types of *BRAF* mutation. However, different genes that act as a secondary hit may have roles in the development of disease. Although out results showed a significant difference in *BRAF* muta-

tion between thyroid and breast tissue, further multicenter study with larger pool is needed to confirm the results of our study.

PO017

HER2 Stained Circulating Tumor Cells in HER2-Negative Breast Cancer

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Background/Purpose: Circulating tumor cells (CTCs) can provide the basis for a liquid biopsy and may guide the use of targeted therapies, even they are useful as an indicator of prognosis. Recently, some reports present the discordance between HER2 expression on CTCs in peripheral blood and the primary tumor. Here, we evaluate the result of HER2 stained CTCs in HER2-negative breast cancer and analyze the pathological factors associated with this discordancy.

Methods: We assessed HER2 status on CTCs from blood samples of breast cancer patients. CTCs were separated and stained using the microfluidic method (CytoGen Co., Ltd®). HER2 status was assessed by immunofluorescence. Blood samples were obtained from 72 patients before anti-cancer therapy. The pathological factors of primary tumor were from the tissue with core needle biopsy. Statistical analysis was performed using the SPSS software for Windows.

Results: Thirty two patients had a discordancy between CTC sample and primary tissue. We found non-concordant results in 55% of cases (n = 40). There was no difference between the two groups; age, tumor size, nodal status, level of tumor marker and hormone receptor status. The mean level of serum HER2/neu was 9.907 versus 10.543 ($p = 0.186$). Among the patiens who underwent operation, a residual cancer burden (RCB) score was calculated and no significant difference was found in the two groups.

Conclusion: A subset of patients with HER2 negative primary breast cancer had HER2 positive CTCs at the time of initial sampling. The pathological characteristics of primary tissue associated the discordance of HER2 expression were not clear in our analysis.

PO018

The Role of Radiologic Evaluation for Detection of Axillary Lymph Node Metastasis in Early Breast Cancer

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Background/Purpose: Axillary lymph node metastasis (ALNM) is a key prognostic factor of breast cancer, thus, diagnostically accurate methods for determining ALNM are very important. The purpose of this study was to evaluate the availability of preoperative breast ultrasonography (US), contrast-enhanced magnetic resonance imaging (MRI), and 18F-fluorodeoxyglucose positron emission tomography-computed tomography (PET-CT) for detection of ALNM in early breast cancer (tumor size ≤ 5cm).

Methods: The medical records of patients with breast cancer who underwent sentinel lymph node biopsy (SLNB) or axillary lymph node dissection (ALND) after preoperative breast US, MRI and PET-CT between January 1, 2012 and October 31, 2014, were retrospectively reviewed. We analyzed positive predictive value (PPV), negative predictive value (NPV), sensitivity and specificity of each radiologic modality.

Results: Of 105 patients with early breast cancer underwent axillary surgery, 71 patients evaluated all radiologic modalities preoperatively. The mean age of patients was 50.7 ± 11.0 years (range 30-80 years). 55 patients underwent planned SLNB and 16 patients underwent planned ALND. 8 patients underwent SLNB needed additional ALND after frozen biopsy. 28.2% (20/71) of patients exhibited ALNM on pathologic report. The PPV was 52.2%, 61.9%, and 92.3%, and the NPV was 83.3%, 86.0%, and 86.2%, respectively. The sensitivity was 60.0%, 65.0%, and 60.0%, and specificity was 78.4%, 84.3%, and 98.0%, respectively.

Conclusion: There are no definitive modalities for detecting ALNM in early breast cancers to replace SLNB. However, PET-CT seems to be a predictive radiologic modality for detection of ALNM considering higher PPV and specificity. If ALNM is suspected based on PET-CT, ALND without SLNB might be a better option.

PO019

Axillary Siliconomas Mimicking Metastatic Lymphadenopathy

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Background/Purpose: Siliconomas in the axillary lymph nodes are rare complications of silicone gel filled breast implants. They can be mistaken for metastatic lymphadenopathy, especially where there is definite lymph node enhancement on contrast-enhanced computed tomography.

Methods: A 43-year-old woman presented with multiple palpable masses in her right axillary area. She reported having undergone bilateral breast augmentation with a silicone prosthesis 12 years previously. Well-circumscribed firm nontender lumps were palpable in the right axillary area. On precontrast chest CT scans, multiple well-circumscribed oval masses of 3.5 cm in maximal size were found in the right axillary area. On postcontrast scans, these oval masses were enhanced homogeneously. Sonography showed multiple hyperechoic lesions with dense posterior shadowing in the right axillary area.

Results: A core needle biopsy of the right axillary mass was performed under sonographic guidance using a 14-gauge automated core biopsy needle. A histologic analysis identified lymph nodes that had largely been replaced by foreign material masses, along with a pronounced foreign body response. The right axillary lymph nodes, including the right outer quadrant masses, were excised, and the breast implant was removed. The implant showed bilateral intracapsular ruptures without extracapsular damage. Pathologic examination identified infiltration of histiocytes as well as multinucleated giant cells with vacuoles and refractive materials, consistent with silicone lymphadenopathy.

Conclusion: Siliconomas can present as well-defined homogeneously enhanced masses on contrast-enhanced CT. In such cases, malignancy is the most important differential diagnosis, but siliconomas should also be considered on the basis of their characteristic sonographic findings and any history of silicone-based breast augmentation.

PO020

Uncommon Tumor-Like Proliferative Feature of the Breast; Case Report of the Diabetic Mastopathy

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Background/Purpose: Diabetic mastopathy or sclerosing lymphocytic lobulitis, as it is known to pathologists, is a very rare benign breast disease. It has been reported in premenopausal woman with long standing type 1 diabetes. Recently few cases of diabetic mastopathy in type 2 diabetes and thyroid disease is reported. Clinical features present single or multiple, hard, non-tender palpable breast masses, so that mimicking malignancy. We report a case of diabetic mastopathy, its diagnosis and progress.

Methods: A 32-year-old woman presented with a palpable mass in the right breast, recognized 2 months ago. She had type I diabetes, diagnosed 15 years ago and diabetic retinopathy, neuropathy and nephropathy. She was on insulin therapy and hemodialysis. And she was affected by Grave's disease in treatment with hormone medication. Physical examination, ultrasonography, magnetic resonance image and core needle biopsy was underwent for making diagnosis about her breast mass.

Results: Physical examination revealed a hard, movable mass in the lower inner quadrant of the right breast. Ultrasonography revealed a focal hypoechoic lesion in the right breast and bilateral tissue distorsion. Core needle biopsy was performed showing fibrosis not combined with malignancy. On 3 month follow up, very hard mass was shown in the both breast and ultrasonography revealed hypoechogenicity with posterior acoustic shadowing. So magnetic resonance imaging was performed. Her blood HbA1c was 9.0% at first visit, and increased to 12.0% at 3 month follow up.

Conclusion: Diabetic mastopathy is an uncommon diabetic complication, but should be managed with other complication of diabetes. Because its finding by physical examination, ultrasonography are non-specific and mimick those of breast cancer, magnetic resonance image and core needle biopsy can helpful for diagnosis. And the presenting

that progression of diabetes related reversible progression of the breast lesion, is expected for help to manage diabetic mastopathy. But further study about relationship between diabetes progression and reversible changes of the breast lesion is necessary.

PO021

Not All Breast Cysts are Benign; Huge Atypical Cyst Diagnosed as a Triple Negative Breast Cancer

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Background/Purpose: Breast cysts are the most common breast benign disease and are usually found in diagnostic examinations. However, malignancy does occur in breast cysts with an incidence ranging from 0.1% to 1.2%. Atypical breast cyst is classified by the presence of internal echoes, thin septations, an intracystic mass, a perceptible wall or by the absence of definitive posterior wall enhancement. Atypical breast cysts are estimated to be reported in approximately 6% of all breast ultrasound examinations. We report a huge atypical cyst diagnosed as a triple negative breast cancer.

Methods: A 59-year-old, unmarried woman with no remarkable medical history arrived at our institution for the initial evaluation of a left breast mass that had enlarged during the past two months. This was the first breast screening for her. The patient reported no family history of cancer. Physical examination revealed a palpable, large (about 8x6cm), protruding, ill-defined dense area associated skin redness that filled the entire left lower outer quadrant. No nipple discharge was noted. Mammogram showed a huge 7 cm sized mass with segmental distributed microcalcifications and pleomorphic calcifications.

Results: Sonography revealed a huge 7 cm sized cystic mass with wall microcalcification and some nodularity is noted with an enlarged lymph node in axillary portion. The warm, bloody, and serous fluid was drained immediate after incision on skin redness area. The pathologic results from cytology and incisional biopsy of cystic capsule were invasive carcinoma. Preoperative radiologic evaluations showed the lesion localized area of drained cystic wall as scattered pleomorphic calcification and no additional other systemic lesion. The surgical treatment of choice was a quadrantectomy including skin area of previous incision site with axillary lymph node dissection. Pathological examination revealed a triple negative breast cancer and no positive lymph nodes were seen. There was skin invasion but clear margin has been secured.

Conclusion: Because of breast cysts are the most common breast benign disease, may

have difficulty during the diagnostic process in the case of breast cancer as a cyst. The accurate sonographic characterization of atypical breast cysts and adequate assessment are important for early and accurate diagnosis and treatment of breast cancer.

PO022

When We Meet a Case of Clinico-Pathologic Discrepancy; Adenoid Cystic Carcinoma Diagnosed as Fibroadenoma by Core Needle Biopsy

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Background/Purpose: Adenoid cystic carcinoma is a rare and morphologically distinct form of other invasive carcinoma. These tumors compromise 0.1% of all breast cancers, and are associated with an excellent prognosis. Adenoid cystic carcinoma consists of a mixture of proliferating glands (adenoid component) and stromal or basement membrane elements. Because of this intratumoral heterogeneity, adenoid cystic carcinoma may be difficult to recognize in core needle biopsy. We report an adenoid cystic carcinoma diagnosed as a fibroadenoma by core needle biopsy.

Methods: A 43-year-old, premenopausal woman with no medical history arrived at our medical center for right mastalgia during several months. The patient reported no family history of cancer. Physical examination revealed a palpable, ill-defined dense area at right 7H, 3 cm distance from nipple (cT1cN0, suspicious of malignancy). Sonography revealed an irregular shape, spiculated margin, and parallel, about $1.9 \times 1.5 \times 1.0$ cm sized hypoechoic mass Breast Imaging Reporting And Data system category 4C.

Results: Because of suspicion of malignancy immediate core needle biopsy performed. Pathological diagnosis was a fibroadenoma. Because of clinico-pathological discordance, vacuum-assisted breast biopsy performed to obtain of enough amount of specimen. The pathologic result from vacuum-assisted biopsy (VAB) revealed as an Adenoid Cystic Carcinoma. We were able to find the presence of adenoid cystic carcinoma component from retrospective review of core needle biopsy specimen.

Conclusion: It is not uncommon that experience of benign pathologic result despite of suspicious malignant finding from physical examination and radiologic study (clinico-pathologic discrepancy). We should review of pathologic result and consider of procedure that can obtain sufficient amount of specimen, especially the case of suspicious of malignancy.

PO023

Solitary Left Axillary Mass without Interval Change During Two Years, What is Your Differential Diagnosis?

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Background/Purpose: The axilla is a triangular shape that contains mesenchymal tissues such as fat, vessels, nerves and lymph nodes, from which various diseases can develop. The most common axillary masses are lymph node metastases from breast cancer. On the other hand, axillary lymph nodes drainage system have a characteristic developmental asymmetry; contrast to left axillary lymphatic flow, right axillary lymph nodes can be drained from only right upper body, right breast and right upper limb.

Methods: So in the case of left axillary mass without breast lesions, we should be considered for more various causes rather than right side. We report a left axillary mass diagnosed as a neurogenic tumor. A 52-year-old, peri-menopausal woman with hypertension history arrived at our medical center for the routine breast cancer screening. The patient reported no family history of cancer. Physical examination revealed no specific finding of both breast and axilla.

Results: Mammogram showed an oval shape mass on left axillary area thought as an enlarged lymph node, but no definite lesion of breast observed. Sonography revealed a solitary, well circumscribed, 2.3 cm sized hypoechoic mass not associated with breast lesion. By the way, this mass was observed from two years ago breast sonography and showed no interval change. At that time, any additional study was not performed. Core needle biopsy performed on left axillary mass. Pathological diagnosis was a neurogenic tumor and no evidence of lymph node.

Conclusion: In the case of the axillary mass without breast lesion is observed, we will first consider the possibility of occult breast cancer and metastatic lymph node from other organs. It is not easy to consider of axillary mass from soft tissue other than lymph node. Awareness of the characteristic imaging findings of disease entities that causes axillary masses and axillary lymphadenopathies important for accurate diagnosis of axillary lesions. Also if possible, to compare with previous radiologic study is helpful for finding clues of diagnosis.

PO024

Adenoid Cystic Carcinoma Combined with Invasive Ductal Carcinoma Arising in an Irradiated Breast: Carcinosarcoma Recurrence? Or New Primary?: A Case Report

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Background/Purpose: Adenoid cystic carcinoma (ACC) is a rare breast malignancy accounts for less than 0.1% of all primary carcinomas of breast. ACC consists of epithelial and myoepithelial components and resembles a well known tumor of salivary gland. Also ACC combined with invasive ductal carcinoma (IDC) is much rare. Metaplastic breast carcinoma (MBC) is also rare that constitutes less than 1% of all breast cancers and among these, carcinosarcoma (mixed epithelial and mesenchymal metaplastic carcinoma) is very rare.

Methods: We report a case of a 50-year-old female who had an ACC combined with IDC arising in an irradiated breast. She was diagnosed as carcinosarcoma of breast 5 years ago and breast conserving surgery, adjuvant radiation and chemotherapy was done at that time.

Results: Wargots and Norris suggested that carcinosarcoma of breast, in which an epithelial mesenchymal transition zone does not exist, should be distinguished from other metaplastic carcinoma. Management of MBC has paralled that of IDC. However traditional adjuvant chemotherapy for IDC and radiation is known ineffective against MBC.

Conclusion: Whether ACC of this patient is recurrence of carcinosarcoma or new primary is debatable. Clinically ACC of the breast is a subgroup of low-grade tumors with indolent clinical behavior that also displays a triple-negative, basal like phenotype. On the other hand, MBC including carcinosarcoma is aggressive clinical behavior which show a basal-like phenotype and as these frequently overexpress epidermal growth factor receptor (EGFR), patients with metastatic breast cancer (MBC) may be benefit from anti- EGFR treatment. We hopefully this case and review lead to personalized therapy for these rare breast tumors.

PO025

Detection of Circulating Tumor Cells by Single Cell Picking and Target Sequencing of Epithelial Cell Adhesion Molecule Attached Cells

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Background/Purpose: Circulating tumor cell (CTC) enumeration provides prognostic information for chemotherapy in metastatic breast cancer. However, due to its rarity and heterogeneity, it is difficult to characterize the detected CTCs individually and utilize the information for therapeutic strategies. The aim of this study was to evaluate the feasibility of single cell picking and target sequencing of epithelial cell adhesion molecule (EpCAM)-positive cells for detecting CTCs.

Methods: Whole blood sampled from metastatic breast cancer patients who were newly diagnosed with metastasis or who had disease progression during palliative treatment were used for this study. After applying IsoFlux Circulating Tumor Cell Enrichment Kit (Fluxion, South San Francisco, CA, USA), single CTC candidates were picked from a pool of EpCAM-positive cells. Genomic Deoxyribonucleic acid (DNA) from the picked cells was whole genome amplified and target sequencing was performed using Ion AmpliSeq™ Cancer Hotspot Panel. Somatic mutation profile of the single cells were analyzed.

Results: Seven EpCAM-positive cells were selected according to size and EpCAM status, and the remaining cells were grouped into a pooled sample from 6 mL of whole blood from each of two patients. A mean 12.38 variants were detected from 14 single cells and two pooled samples. In the first patient, four single cells carried variants not detected in the pooled sample. Three of the four single cells carried a variation in NOTCH1, and one single cell carried variations in HNF1A, IDH2, MET, FGFR2, and PIK3CA. In the second patient, one single cell carried variations in CDKN2A and MET, which were not detected in the pooled sample.

Conclusion: Potential CTCs were successfully identified by single cell picking and target sequencing of EpCAM-positive cells from whole blood of metastatic breast cancer patients. These potential CTCs carry unique mutations not detected in other picked single cells and pooled samples. Genomic profiling of corresponding primary tumor and metastatic site biopsy is warranted to verify the CTCs and investigate their role in disease progression.

PO026

Pathologic Correlation of Sonographically Suspicious Lymph Node with Sentinel Lymph Node Using Preoperatively Tattooing in Breast Cancer Patients

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Background/Purpose: The purpose of this study was to evaluate the efficiency of preoperative ultrasound-guided tattooing of axillary lymph node with activated charcoal and to correlate the sonographically suspicious lymph node with final histologic result through performing node-to-node analysis. And another purpose was to determine the concordance rate between tattooed lymph node and sentinel lymph node.

Methods: Axillary ultrasound was undergone before sentinel node biopsy. The detected lymph nodes in ultrasound were classified as positive or negative finding for metastases based on their shape, cortical morphology and echogenicity. Ultrasound-guided tattooing for sonographically suspicious or enlarged axillary lymph node was performed preoperatively by injection of 3 cc of Charcotrace™ (activated charcoal 120 mg and sodium chloride in water for injections to 3 mL) into the cortex of lymph node and the adjacent soft tissue. Identification of black pigment and concordance between sentinel and tattooed nodes was evaluated.

Results: 40 patients were tattooed, 10 in group I (enlarged but sonographically benign node) and 30 in group II (sonographically suspicious node). Eight cases had evidence of metastases in final histology, 2 in group I and 6 in group II. Black tattoo ink was visualized intraoperatively in all cases. Sentinel nodes corresponded to tattooed nodes in all except one patient with a tattooed non-sentinel node.

Conclusion: Tattooing is a feasible and low-cost method for marking biopsied nodes. The black pigment can be discerned by surgeons from blue dye. In addition, this study demonstrates that sampled, tattooed lymph nodes correlate well with sentinel nodes, which add to the accuracy of surgical axillary staging.

PO027

Spectrum of Genetic Variations in Korean Patients with Non-*BRCA1/2* High-Risk Breast Cancer: Sequence Analyses of *BRIP1* and *NBS1* Genes

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Background/Purpose: The current study was aimed at assessing the spectrum of genetic variations in *BRCA1* interacting protein C-terminal helicase 1 (*BRIP1*) and Mre11 complex subunit *Nbs1* (*NBS1*) genes among Korean patients with non- *BRCA1/2* high-risk breast cancer.

Methods: We screened 235 non-*BRCA1/2* Korean patients with high-risk breast cancer for *BRIP1* and *NBS1* mutations. The entire *BRIP1* and *NBS1* gene were sequenced using fluorescent-conformation sensitive capillary electrophoresis. In silico analysis of *BRIP1* and *NBS1* variants were performed using PolyPhen-2 and SIFT algorithms. For *NBS1*, frequencies of variant which is predicted to be deleterious by in silico analysis were compared between the patients and controls. Blood samples from 281 healthy females were selected as the control group.

Results: In *BRIP1*, 20 sequence alterations (12 exonic and 8 intronic) were found. There were 10 missense variants, and 4 (p.L263F, p.L340F, p.L474P, and p.R848H) were predicted to be pathogenic by in silico analysis. These variants were found in 5 patients. For *NBS1*, 28 variants (9 exonic and 19 intronic) were identified. There were 5 missense variants, and p.I171V (c.511A > G) was the only variant predicted to be deleterious by in silico analysis. The frequency of the p.I171V was not significantly different between the patient and control groups (1.7% vs. 1.06%, $p = 0.7$).

Conclusion: Protein truncating mutation was not found among the tested patients. Sequence variations in *BRIP1* and *NBS1* account for a small proportion of the Korean patients with non-*BRCA1/2* high risk breast cancer.

PO028

Clinical Predictors of Early Cancer-Related Mortality for T1 to T2 Node-Negative Breast Cancer: A Result from the Korean Breast Cancer Society Cancer Registry

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

Methods: We used a 9 year (1999 to 2007) retrospective review of the Korean Breast Cancer Society cancer registry. A total of 13,289 patients were examined. All patients had T1/T2 breast lesions and negative axillary lymph node (N0) pathologically. Patient demographics, clinical, and pathologic variables were analyzed. We then defined 'early cancer-related mortality' group confirmed death within 5 years of their date of operation.

Results: The median follow-up period was 87.0 (58-144) months. Overall 217 of 13,289 patients (1.6%) died from breast cancer during a median follow-up of 87 months. The median age at diagnosis was 40 years. Clinical predictors of early cancer-related mortality within 5 years by multivariate analysis included Age > 50 years (HR 1.721; CI 1.046-2.831), Estrogen receptor negative (HR 2.808; CI 0.111-3.734), No hormonal treatment (HR 1.881; CI 1.058-3.344). Operation type, body mass index, tumor size, progesterone receptor status, HER2 status were not associated with early cancer-related mortality.

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

PO029

Daily Physical Activity Helps to Control Arm Symptoms Among Breast Cancer Patients: 3 Year Longitudinal Prospective Study

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Background/Purpose: Arm symptoms are one of commonly reported breast cancer side effect that lowers patients' quality of life and limits daily activities. Although physical activity would help to reduce arm symptom, little is known about possible effects of daily physical activities on preventing arm symptoms among breast cancer patients. We evaluated patterns of daily physical activities of breast cancer patients from diagnosis to 3 year after surgery and its impact on arm symptom.

Methods: Pre-menopause non-metastatic breast cancer patients (N = 278) were recruited from two cancer hospitals in Seoul, Korea from July 2010 and July 2011. Moderate to vigorous physical activity ((MVPA), metabolic equivalent, (MET) level ≥ 3.0) and sedentary time was assessed using minesota leisure time physical activity questionnaire (MLTPAQ) before surgery, 2 weeks, 3-, 6-, 12-, 24- and 36-months after surgery. Arm symptoms were measured using EORTC-BR23. Growth mixture models were used to identify trajectory classes of physical activity pattern. Multivariate analysis was used to find impact of MVPA on arm symptoms using STATA 13.

Results: Three physical activity distinct groups were identified according to 3-year change patterns: little increase (LI): 49.9%, continuous decrease (CD): 27.3% and sharply increase (SI): 22.8%. MVPA decreased during active treatment and returned to the baseline level around 6 months after surgery. However, MVPA of the CD group did not return to the baseline level until 3 year after surgery ($p < 0.001$). Compared to the CD, the CL and SI experienced 12.5 (95% CI = -2.7, -22.3) and 11.1(95% CI = -2.7,

-19.5) lower arm symptoms at 3 years after surgery.

Conclusion: Breast cancer patients who regain baseline (before cancer treatment) MVPA after completion of active treatment were less likely to have arm symptoms compared to who did not. It is necessary to promote tailored physical activity to cancer patients considering their daily MVPA before treatment.

PO030

A Comparison of the Clinical Outcomes of Patients with Invasive Lobular Carcinoma and Invasive Ductal Carcinoma of the Breast According to Molecular Subtype in a Korean Population

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Background/Purpose: The importance of molecular subtype in the prognosis of Invasive ductal carcinoma (IDC) has been increasingly emphasized. However, relatively little is known about Invasive lobular carcinoma (ILC) despite its increasing incidence. Therefore, we aimed to compare the association between the molecular subtype and the clinical outcomes of IDC and ILC in Korea using patient information from the nationwide Korean Breast Cancer Registry (KBCR) database.

Methods: We analyzed characteristic differences and survival outcomes of 14,547 IDC and 528 ILC patients diagnosed between January 1995 and December 2006.

Results: The ILC presented with a larger tumor size, more advanced cancer stage, increased rate of hormonal receptor positivity, human epidermal growth factor 2 (HER2) negativity and mastectomy than the IDC. The ILC patients more frequently presented with the luminal A subtype, whereas the IDC patients more frequently presented with the luminal B, HER2-overexpression, or triple negative subtype. The Breast cancer specific survival and Overall servival were not significantly different between the IDC and ILC for each molecular subtype.

Conclusion: This is the first report comparing the differences in survival outcome be-

tween IDC and ILC according to molecular subtype within an Asian population. Despite some characteristic differences, our study demonstrated a similar survival outcome for ILC patients among all molecular subtypes compared to IDC patients. This study indicates that similar to IDC patients, molecular subtype should be considered for prognostic prediction and treatment decisions for ILC patients.

PO031

Distribution of Subtypes and Treatment Patterns in Early or Locally Advanced Breast Cancer: Single Center Experience

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Background/Purpose: Breast cancer is a heterogenous disease, encompassing a large number of entities showing different morphological features and having clinical behaviors. We explored the distribution of subtype and treatment patterns in early or locally advanced breast cancer.

Methods: This is retrospective analysis of 133 early or locally advanced breast cancer patients. The pathological variables included tumor type, the presence of ductal carcinoma in situ, lymphovascular invasion, and expression of estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor 2 (HER2) receptors and Ki-67 by immunohistochemical (IHC) analysis. ER, PR, HER2 IHC staining, if need, and subsequent fluorescent in situ hybridization studies were performed to categorize breast cancer subtypes.

Results: All patients are female and mean age of patients is 55 (range: 33-76) years old. We identified 51% of luminal A, 23% of lumimal B, 9% of HER2 enriched, and 18% of basal like. Of total, 25% patients received mastectomy and 75% received breast conserving surgery. Neoadjuvant and adjuvant chemotherapy administered respectively 10% and 71% of patients. Of total, 22% received adjuvant. Trastuzumab for one year. About 75% received adjuvant hormone therapy. Mean Ki-67 expression is high in basal like, followed by HER2 enriched and luminal B.

Conclusion: IHC staining is the most commonly used tool in dividing breast cancer subtype and can help physicians make a plan for adjuvant therapy of patients with early or locally advanced breast cancer. Further studies to reveal the relation between IHC subtype and molecular subtype are warranted.

Association Between Alterations in the Serum 25-hydroxyvitamin D Status During Follow-Up and Breast Cancer Patient Prognosis

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Background/Purpose: Serum vitamin D status can affect the prognosis of breast cancer patients. Our aim was to determine the association between the 25-dihydroxyvitamin D [25(OH)D] status alterations during follow-up and the prognosis of breast cancer patients. Additionally, we evaluated the association between the 25(OH)D status at diagnosis and prognosis using detailed age, and stage categorization.

Methods: 469 patients were included. We collected the patients' serum 25(OH)D concentration at diagnosis and at the annual follow-up until 4 years after diagnosis. The patients were divided according to their 25(OH)D status at diagnosis into a deficient and a non-deficient group. At follow-up, patients were categorized into the four following groups-"persistently deficient", "improved", "deteriorated", and "persistently non-deficient".

Results: After a median follow-up period of 85.79 ± 31.01 months, the patients with advanced-stage disease or an older age in the non-deficient group showed a significantly better survival compared with the deficient group. Furthermore, at the 1-year follow-up, the persistently non-deficient group and the improved group had better survival compared with the other two groups.

Conclusion: Our results suggest that maintaining an optimal 25(OH)D status at diagnosis and at the 1-year follow-up period is important for improving breast cancer patient survival.

18F-FDG/PET May Help to Identify a Subgroup of Patients with T1-T2 Breast Cancer and 1-3 Positive Lymph Nodes Who are at a High Risk of Recurrence After Mastectomy

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Background/Purpose: Current international consensus does not routinely recommend post-mastectomy radiotherapy (PMRT) for patients with T1/2N1 disease unless there are additional adverse features. However, indications for PMRT have varied significantly across institutions. The objective of this study was to assess efficacy of 18F-FDG PET for identifying a high risk of recurrence among this subset of patients with mastectomy and standard adjuvant therapies.

Methods: Of 712 patients who consecutively underwent upfront mastectomy and were diagnosed with T1-T2 N1 breast cancer between 2003 and 2012, 109 had undergone preoperative 18F-FDG PET and were included in this study. Metabolic (maximum standardized uptake value, SUVmax), volumetric (metabolic tumor volume, MTV), and combined (total lesion glycolysis, TLG) indices were measured. The median follow-up time was 40 months.

Results: SUVmax (area under curve, 0.824) was more informative than either MTV or TLG as means of identifying high-risk for progression. Increase of SUVmax was associated with decreased disease-free survival (adjusted hazard ratio 1.77, $p = 0.004$). The SUVmax threshold that showed the best predictive performance was 5.36. PET-defined high-risk subgroup (SUVmax ≥ 5.36) included more T2, high-grade, and hormone-receptor negative tumors (all $p < 0.05$).

Conclusion: High SUVmax on preoperative PET was associated with elevated risks of recurrence. The high-SUVmax subgroup included a mixture of T2, high-grade and hormone receptor negative tumors. These characteristics could not be represented by any single known clinicopathologic factor. Pre-treatment PET may improve assessments of recurrence risk in patients with T1-2 N1 breast cancer, clarifying the indications for post-mastectomy radiotherapy.

The Expression of Estrogen Receptor and Insulin Receptor Substrate 1 as Prognostic Factor of Breast Cancer Patients

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Background/Purpose: Insulin receptor substrate 1 (IRS-1) has been known as an associated factor of breast cancer progression. Many studies reported that IRS-1 is involved in breast cancer development and progression, and there were authors who insisted on the relationship between IRS-1 and hormone receptors. This study was designed to evaluate the impact of estrogen receptor (ER) and IRS-1 on prognosis of breast cancer.

Methods: We analyzed the pathologic finding of 376 tissue samples from breast cancer patients who received proper treatments between Jan. 1990 and Dec. 2006 by using the tissue microarray. We measured the expression of ER and IRS-1 by immunohistochemistry staining and analyzed the difference of recurrence and survival rate in each subgroup of ER and IRS-1.

Results: Of 376 patients, the recurrence rate was 30.6% and median disease free survival was 69.5 months. Our results showed that ER(+)/IRS-1(+) subgroup had a more favorable prognosis than other subgroups in multivariate analysis of recurrence ($p = 0.01$). But we could not find a difference of survival between each subgroup of ER and IRS-1 in multivariate analysis ($p = 0.07$).

Conclusion: ER and IRS-1 appears to be a critical factor for prediction of breast cancer recurrence. Especially, we suggest that the patients who have ER negative and IRS-1 positive breast cancer take more aggressive treatment for preventing recurrence.

Potential Prognostic Value of HDAC6 and Acetylated HSP90 in Early Stage Breast Cancer

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Background/Purpose: Histone deacetylase 6 (HDAC6) is known as a deacetylase of heat shock protein 90 (HSP90). Many studies have investigated the role of HDAC6 and HSP90 in tumorigenesis and their association with the prognosis of cancer patients. This study aimed to evaluate the prognostic value of HDAC6 and acetylated HSP90 in the cohort of breast cancer patients.

Methods: The 314 surgical specimens of patients with invasive breast cancer were stained immunohistochemically to assess the expression of HDAC6 and acetylated HSP90 in addition to the standard pathologic factors. Statistical analyses were performed to assess the association among HDAC6, HSP90 and conventional clinicopathologic factors and the prognostic values of these factors were evaluated.

Results: HDAC6 did not show any correlation with other clinico-pathologic factors but acetylated HSP90 showed significant correlation with histologic grade ($p = 0.001$) and Ki-67 index ($p = 0.015$). HDAC6 and acetylated HSP90 were significantly associated with each other ($p = 0.047$). Although HDAC6 was not prognostic for disease free survival (DFS) but patients with high expression of HDAC6 showed continued recurrence after 5 years of diagnosis in contrast with no recurrence of low expression group. Acetylated HSP90 was significantly associated with DFS in total patients ($p = 0.016$) and in patient with HDAC6 high expression ($p = 0.017$).

Conclusion: HDAC6 and acetylated HSP90 were correlated with each other. HDAC6 is suggested as a predictive marker for late recurrence and acetylated HSP90 has prognostic value for predicting DFS in total patients and HDAC6 high expression group.

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Relationship Between Body Mass Index and the Expression of Hormone Receptors or Human Epidermal Growth Factor Receptor 2 with Respect to Breast Cancer Survival

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Background/Purpose: The association between body mass index (BMI) at the time of breast cancer diagnosis and the prognosis of breast cancer patients remains controversial. Furthermore, the association between BMI and prognosis with respect to different breast cancer subtypes is not clearly defined.

Methods: We analyzed data from 41,021 invasive breast cancer patients between January 1988 and February 2008 from the Korean Breast Cancer Registry (KBCR) database. Overall survival (OS) and breast cancer-specific survival (BCSS) were analyzed among all patients and specific breast cancer subtypes with respect to BMI categories.

Results: A U-shaped association between BMI and mortality was observed in the total cohort. Underweight and obese individuals exhibited worse OS (HR 1.23 [1.05 to 1.44] and 1.29 [1.13 to 1.48], respectively) and BCSS (1.26 [1.03 to 1.54] and 1.21 [1.02 to 1.43], respectively) than normal-weight individuals. In the hormone receptor (HR)+/human epidermal growth factor receptor (HER2)- subgroup, obese individuals exhibited worse OS (1.48 [1.18 to 1.85]) and BCSS (1.31 [1.13 to 1.52]) than normal-weight individuals. Conversely, in the HR-/HER2+ subgroup, underweight individuals exhibited worse OS (1.68 [1.12 to 2.47]) and BCSS (1.79 [1.11 to 2.90]) than normal-weight.

Conclusion: We observed a U-shaped relationship between BMI at diagnosis and poor OS and BCSS among all breast cancer patients. However, obesity in the HR+/HER2- subgroup and underweight in the HR-/HER2+ subgroup were poor prognostic factors. Therefore, BMI at diagnosis and breast cancer subtype should be considered simultaneously in various treatment decision processes and surveillance schedules.

Prognostic Effect of Progesterone Receptor in Luminal Type Breast Cancer

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Background/Purpose: Progesterone receptor (PgR) is synthesized by tumor cells that are stimulated by estrogens through an interaction with estrogen receptor (ER). In theory, the presence of PgR might be a better indicator of hormonal dependence than ER because ER may be present but not functional in some patients.
Positive PgR assay identifies a more tamoxifen-responsive subgroup of patients even when patients have ER-negative tumors. The aim of the present study was to evaluate the prognostic significance of semiquantitative measurement of PgR expression in the IHC-based luminal subtype of breast cancer.

Methods: 1327 consecutive patients with ER and/or PgR+ human epidermal growth factor receptor 2 (HER2)- invasive breast cancer treated with surgery and adjuvant treatment at the Seoul National University Hospital from July 2009 to December 2011 were reviewed. ER, PgR, HER2, and Ki-67 were determined from surgically resected tumor tissue. The RFS and OS in Kaplan-Meier plots for the PgR high and low ($>, \leq 20\%$) expression groups was compared using the log-rank test. Multivariate analyses of survival in relation to various factors were performed with a Cox proportional hazards model, which yielded the HR and 95% of CI.

Results: Patients were separated into two groups with PgR percentage cutoff 20%. 665 (48.5%) showed high and 707 (51.5%) showed low PgR expression. PgR expression was relatively high in patients under 50 years old. Higher PgR expression was related to low Ki-67 expression ($p = 0.003$), and low cancer stage ($p < 0.001$). High PgR subset showed better survival than the low PgR subset only in patients under 50 years old ($p = 0.005$ and 0.037). Cox analysis showed that low PgR expression (HR, 3.06; 95% CI, 1.44-6.47) and negative ER expression (HR, 19.68; 95% CI, 5.89-65.80) were significant independent risk factors for patients' survival.

Conclusion: We were able to demonstrate that high PgR expression is associated with a better prognosis for luminal type breast cancer. The semiquantitative determination of PgR expression might thus improve the accuracy of the IHC-based classification of luminal A and luminal B breast cancer, especially for premenopausal patients.

Prognostically Distinctive Biologic Subgroup in Stage IIIc Breast Cancer

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Background/Purpose: We often encounter patients who show discordance between TNM stage and prognosis. Especially, in high nodal stage group (N3), we clinically face some patients who are in disease-free status for long periods. We investigated whether there are prognostically different subgroups among patients with stage IIIc (anyT-N3M0) breast cancer.

Methods: The records of 180 patients who operated for stage IIIc breast cancer from January 2002 to September 2009 were reviewed. Excluded were patients who received neoadjuvant therapy. All patients received adjuvant therapy planned according to standard protocols. The primary outcome was recurrence-free survival (RFS). We calculated the cumulative incidence of events and performed multivariate analysis using the Cox proportional hazards model.

Results: Tumor biologic subtype was most significant predictive factor of recurrence. (Wald = 13.13, highest among relating factors) Age, neutrophil/lymphocyte ratio, nodal ratio (ratio of positive over excised lymph node) and were also relating factors with prognosis. According to St. Gallen 2013' updated definition of intrinsic molecular subtypes, patients who were grouped as HER2 negative Luminal B (ER or PR positive, 'high' (≥ 14%) Ki67 level, HER2 negative) type showed far better outcome (5-year RFS 90%) while patients in group with triple negative phenotype showed poorer outcome (5-year RFS 37%).

Conclusion: Patients with N3 but HER2 negative Luminal B subtype tumor had similar clinical outcomes as those with stage II breast cancer. High level Ki67 is presumed to be good responder to adjuvant chemotherapy to be 'down staging' effect in high nodal stage breast cancer, especially HER2 negative Luminal B subtype. The current results show that intrinsic subtype has a greater prognostic impact in predicting clinical outcomes, in addition, different patient subgroups may be offered different treatment strategies.

Prognostic Effect of Serum Anti-Mullerian Hormone and Inhibin B Level in Premenopausal Hormone Receptor Positive Breast Cancer Patients Treated by Neoadjuvant Chemotherapy

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Background/Purpose: The value of serum anti-mullerian hormone (AMH) or inhibin B (InhB) level to predict the ovarian function restoration after chemotherapy is currently interested in gynecologic field. However, the prognostic role of AMH or InhB in breast cancer patients is unclear. We investigated the prognostic importance of AMH and InhB level in premenopausal hormone receptor (HR)-positive breast cancer patients treated by neoadjuvant chemotherapy (NCT).

Methods: The specimens were obtained at the time of the completion of NCT. A total of 32 premenopausal women with clinical stage III HR+ invasive ductal breast cancer were included in this analysis. All patients were treated by NCT between 2007 and 2010. The level of AMH, InhB, follicular stimulating hormone (FSH), and estradiol (E2) were measured by enzyme-linked immunosorbent assays. The median follow-up period was 57.7 months (6-79 months).

Results: The median age of patients was 41.5 years old. Thirty-one patients were treated by neoadjuvant anthracycline-docetaxel regimen. The median level of AMH, InhB, FSH, and E2 were 1150.40 pg/mL, 18.50 pg/mL, 59.45 mIU/mL, and 5.0 pg/mL respectively. The level of AMH, InhB and E2 was significantly related with each other ($p < 0.05$). Kaplan-Meier analysis using a cut-off of 1,000 pg/mL (AMH) and 30 pg/mL (InhB) showed that patients with higher AMH and InhB level showed significantly poorer disease-free survival ($p = 0.043$).

Conclusion: Higher serum AMH and InhB level examined after NCT had a negative prognostic effect in premenopausal women with HR-positive breast cancer.

The Relationship Between Tumor-Free Axillary Lymph Node Morphology and Clinicopathologic Features in Invasive Breast Cancer

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Background/Purpose: Enlargement of the cortex of a lymph node is known to indicate an early change of metastasis and this has been suggested as a criterion for differentiation of suspicious lymph nodes in breast cancer. Despite the high positive predictive value of these classifications, some tumor-free lymph nodes present with thick cortex or loss of fatty hilum. The purpose of this study is to examine the relationship between preoperative sonographic lymph node classification and clinicopathologic features in breast cancer with no axillary lymph node metastasis.

Methods: Patients who received primary surgery for invasive breast cancer between November 2005 and December 2009 were retrospectively reviewed. Preoperative sonographic classification of axillary lymph nodes (ALN sono grade) was performed for all patients, one day before surgery. Maximum thickness of cortex and appearance of fatty hilum were evaluated and classified: grade 1, $\leq$ 1.5 mm; grade 2, $>$1.5 mm, $\leq$ 2.5 mm; grade 3, $>$2.5 mm, $\leq$ 3.5 mm; grade 4, $>$3.5 mm, intact fatty hilum; grade 5, $>$3.5 mm, loss of fatty hilum. This classification has been previously validated (Cho et al., Am J Roentgenol, 2009)

Results: A total of 1,827 patients were proven of having no axillary lymph node metastasis. Younger age, larger tumor size, high nuclear grade, high histologic grade, strong Ki-67 expression, hormone receptor negative and triple-negative breast cancer were all significantly related to having ALN sono grade $\geq$3. Patients with ALN sono grade $\geq$3 presented with significantly worse disease-free survival compared to patients with benign looking axillary lymph nodes. But after adjusting for prognostic factors (age, tumor size, histologic grade, Ki-67 expression and hormone receptor status) there was no survival difference.

Conclusion: Thick cortex or loss of fatty hilum in tumor-free axillary lymph nodes is related to adverse clinicopathologic features in primary invasive breast cancer. The immunologic configuration of these suspicious-looking tumor-free lymph nodes will be investigated in future studies

Phosphorylated S6 Kinase-1 as Predictive Marker of Lapatinib Efficacy in HER2-Positive Metastatic Breast Cancer Patients

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Background/Purpose: The 40S ribosomal protein S6 kinase-1 (S6K1) is a crucial downstream effector of PI3K/AKT/mTOR pathway. The overexpression of S6K1 is found in 10-30% of breast cancers and associated with aggressive disease and poor prognosis. We investigated the relationship between expression of phosphorylated S6K1 (p-S6K1) and efficacy of lapatinib in patients with human epidermal growth factor receptor-2 (HER2) positive metastatic breast cancer.

Methods: We retrospectively analyzed the data of 36 patients with HER2 positive metastatic breast cancer treated with lapatinib between January 2010 and September 2014. The p-S6K1 expression status of the primary tumor was assessed by immunohistochemistry with the mouse monoclonal antibody.

Results: Fourteen of the 36 patients (38.9%) had a p-S6K1 positive tumor. The median progression free survival (PFS) of patients with p-S6K1 positive tumor was significantly longer than that of patients with p-S6K1 negative tumor (13.4 vs. 7.1 months, $p = 0.025$). There was also a trend toward higher rate of clinical benefit and overall response in patients with a positive expression of p-S6K1 ($p = 0.062$ and $p = 0.073$). In multivariate analysis, p-S6K1 positivity remained an independent, favorable predictive factor for PFS (hazard ratio, 0.374; 95% confidence interval, 0.154-0.908; $p = 0.03$).

Conclusion: The high expression of p-S6K1 was significantly associated with prolonged PFS, suggesting that a p-S6K1 could be a potential biomarker for prediction of lapatinib efficacy in HER2 positive metastatic breast cancer patients.

Analysis of p95 HER2 and PTEN in HER2 Positive Breast Cancer: Relation of Trastuzumab Resistance in Primary Breast Cancer

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Background/Purpose: Expression of p95 human epidermal growth factor receptor (p95HER2) and phosphatase and tensin homolog (PTEN) loss is well known to relate to trastuzumab resistance and they could be used as biomarker for trastuzumab resistance. In the literature, identification of p95HER2 by immunohistochemistry (IHC) using anti-HER2 cytoplasmic/extracellular domain antibodies could be predicting trastuzumab resistance.

Methods: Total 213 HER2 positive breast cancer was enrolled and histologic features are reviewed. Expression of p95 HER2 is defined as decreased anti-extracelluar domain of HER2 antibody IHC than intracellular domain antibody IHC. Loss of PTEN expression confirmed by decreased staining intensity compared to internal positive control.

Results: Hormone receptor (HR)(-)/HER2(+) group showed significantly older age, higher nuclear grade, poor tubule formation, higher histologic grade, and higher rate of trastuzumab resistance than HR(+)/HER2(+) tumors. The tumors with decreased extracellular domain (ECD) IHC (possible p95HER2 expression tumors) are not related to trastuzumab resistance. But, the tumors of well-preserved ECD IHC showed longer progression free period than decreased ECD IHC tumors in trastuzumab resistant group. PTEN loss was found in up to 55.8% in HER2 positive breast cancer which is consistent with previous reports but PTEN loss was not correlated to trastuzumab resistance.

Conclusion: We confirm the HR(+)/HER2(+) tumors and HR(-)/HER2(+) tumors have different histologic features and clinical outcome. But investigate the expression of

p95HER2 in HER2 positive breast cancer using two antibody analysis is need further evaluation to confirm the p95HER2 existence. In this study, PTEN expression loss rate is similar to previous study but IHC analysis alone is not related to trastuzumab resistance.

Predictive Value of Tumor Response Ratio in Neoadjuvant Chemotherapy for Breast Cancer

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Background/Purpose: Neoadjuvant chemotherapy has been preferred treatment method in locally advanced breast cancer. The purpose of chemotherapy is to shrinkage the primary tumor. In neoadjuvant setting, the discrepancy between clinical stage and pathologic staging could be happen. Pathologic complete response has been shown to predict improved overall survival. However, prognosis of patient with partial response is not unclear. Several methods which predict the prognosis of patients with of the partial response have been proposed. We validate the tumor response ratio method which predict the prognosis after neoadjuvant chemotherapy.

Methods: We retrospectively reviewed the hospital's electronic database. One hundred seventy one patients were eligible in this study. The patients underwent breast surgery after neoadjuvant chemotherapy. Tumor response ratio (TRR) was calculated as residual invasive lesion size divided by size on initial imaging. The overall survival rate and disease free survival were compared for four groups predefined by TRR groups: TRR 0: pCR; TRR > 0-0.4: strong partial response (SPR); TRR > 0.4-1.0: weak partial response (WPR); TRR > 1.0: tumor growth (TG).

Results: Mean age of total patients was 48.3 years. Mean follow up period was 44.7 months. Fourteen patients (5.9%) had pCR, 66 (27.6%) SPR, 70 (29.3%) WPR, and 21 (8.8%) TG. Overall survival and disease free survival were increased with the response ratio. However, only pCR group showed statistically significant survival benefit compared with other TRR group. Moreover, clinical staging was significant in disease free survival and overall survival.

Conclusion: In our study, pCR group is the only cohort who showed statistical significant benefit. And the TRR could not prove the superiority to pathologic and clinical staging at predicting the prognosis of patient with partial response. Therefore, more accurate and readily available prognostic tools for partial responder is needed.

Prognostic Impact of AJCC Response Criteria for Neoadjuvant Chemotherapy in Stage II/III Breast Cancer Patients: Breast Cancer Subtype Analyses

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Background/Purpose: Neoadjuvant chemotherapy (NAC) is a standard therapy for stage II/III breast cancer patients and response to the NAC is a useful prognostic marker for them. To improve the outcome of NAC, 6-8 cycles of NAC was introduced and became the standard treatment. The purpose of this study is to evaluate the prognostic impact of American Joint Committee on Cancer (AJCC) response criteria and its usefulness in four different breast cancer subtypes.

Methods: Clinical stage II/III breast cancer patients who received NAC of ≥ 6 cycles were enrolled. Response after NAC and the clinicopathological factors were reviewed retrospectively. AJCC response criteria for NAC were adopted from the AJCC 7th edition: complete response (CR), partial response (PR), and no response (NR).

Results: From Jan 2009 to Dec 2010, 183 patients were enrolled. CR, PR, and NR were consisted of 22 (12.0%), 123 (67.2%), and 38 (20.8%) respectively. AJCC response was significantly associated with relapse free survival (RFS) ($p < 0.001$), whereas pathologic CR which is a current gold standard for response evaluation for NAC was not ($p = 0.140$). AJCC response was a significant prognostic factor for RFS in all four breast cancer subtypes, luminal A ($p = 0.006$), luminal B ($p = 0.001$), HER2 enriched ($p = 0.039$) and triple negative breast cancer ($p = 0.035$).

Conclusion: In conclusion, AJCC response criteria is a simple and easily reproducible tool for response evaluation in NAC setting and a useful clinical prognostic marker for

RFS. It also has a prognostic impact in all four breast cancer subtypes, including luminal A in which pCR has a limited role.

The Prognostic Role of 18F-Fluorodeoxyglucose PET/CT in Operable Invasive Breast Carcinoma

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Background/Purpose: We evaluated whether 18F- fluorodeoxyglucose (FDG) uptake on tumor or axillary lymph node (ALN) in preoperative PET/CT could be prognostic factor in patients who had curative surgery for invasive breast carcinoma.

Methods: Retrospectively, we reviewed 244 patients who conducted preoperative 18F-FDG PET/CT and curative surgery for breast cancer in our institute between 2008 and 2009. We searched the parameters of 18F-FDG PET/CT and the clinicopathological factors related with prognosis. We also investigated the recurrence and survival after surgery. Finally, 5year-disease-free survival rate (DFSR) and 5year-overall-survival rate(OSR) were calculated by Kaplan-Meier survival analysis, and the factors related with recurrence and survival were investigated by Cox proportional hazard model.

Results: Mean follow-up time was 62.7 ± 13.0 months (range, 7.9-82.8). 5year-DFSR was 93.2%. 5year-OSR was 97.5%. In 124 (84.8%) patients, there was 18F-FDG uptake in tumor. Fifty four patients (22.1%) had 18F-FDG uptake in ALN. In receiver operating characteristics curve about 18F-FDG uptake on tumor and recurrence, the cut-off value of the maximum standardized uptake (SUVmax) value of tumor for recurrence was 3.0. The 18F-FDG uptakes on tumor ($p = 0.034$, OR 4.150, 95% CI 1.114-15.454) or ALN ($p = 0.023$, OR 3.133, 95% CI 1.170-8.388) were independent significant risk factors of DFSR.

Conclusion: Over 3.0 of SUVmax on tumor or 18F-FDG uptake on ALN in preoperative PET/CT are risk factors of recurrence after the curative operation for invasive breast carcinoma.

Poor Prognosis of the Young Breast Cancer is due to Late Recurrence in Hormone Responsive Breast Cancer

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Background/Purpose: To evaluate the trend of prognosis and treatment response of very young breast cancer patients (age ≤ 35 years)

Methods: We analyzed data from 9,633 breast cancer patients who were part of the ASAN Medical Center Breast Cancer Center database between 1990 to 2008. The disease free survival (DFS) was evaluated between age group according to the time periods and subtype

Results: 778 patients (8.1%) were below than 35 years old and 8,855 (91.9%) patients were older than 35 years old. On annual hazard ratio plot, DFS of breast cancer increased over time but DFS of very young breast cancer was not improved from 1990 to 2008. On multivariate analysis adjusted by tumor size, node metastasis and grade, reference as 50 years old patients, HR decreased significantly from below 35 years old in hormone receptor positive, HER2 negative breast cancer. Higher recurrence rate of very young age group was prominent in late recurrence (after 5 years) (HR 2.2, 95%CI 1.5 to 3.1) compared with early recurrence (before 5 years) (HR 1.2 95%CI 0.9 to 1.5)

Conclusion: Survival of very young breast cancer patients did not improved over time. In hormone responsive breast cancer, late recurrence is the cause of the poor survival in very young breast cancer patients

Neutrophil Lymphocyte Ratio Change After Systemic Therapy is Predictive of Cancer Specific Survival in Stage lV Breast Cancer

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Background/Purpose: Inflammatory response exacerbate mechanisms linked to tumor growth and dissemination. It is also known to be associated with response to systemic chemotherapy. As an index of systemic inflammatory status, neutrophil lymphocyte ratio(NLR) may be a predictive biomarker of both prognosis and response to therapy. We evaluated initial pre-treatment NLR and post-treatment NLR change to assess whether initial and change in NLR would be predictive of disease outcome in stage lV breast cancer patients.

Methods: This study included 297 stage IV breast cancer patients diagnosed at ASAN Medical Center between 1997 and 2012. Among these patients, 250 patients were available white blood cell counts. The NLR was calculated by dividing neutrophil by lymphocyte. All initial(pre-treatment) NLR was evaluated at the first visit day in ASAN medical center. Post-treatment NLR was obtained at the first follow-up visit at the outpatient department after first treatment (chemotherapy first:about after 3weeks/endocrine therapy:after 3~6 months). We evaluated prognostic value of NLR by comparison with CSS.

Results: There was no statistical difference in Cancer Specific Survival (CSS) between higher pretreatment NLR (≥ 4) group and lower NLR (< 4) group (log rank $p = 0.864$). Increased NLR group (post NLR/pre NLR ≥ 1.2) compared with the other group, CSS was lower (log rank $p = 0.052$) and median follow-up months was shortened (35.8 ± 2.9 vs 27.4 ± 3.3). In a multivariate analysis, higher pretreatment NLR was not prognostic factor for CSS (hazard ratio/95% CI = 1.015/0.541-1.905), on the other hand, increased NLR was independent prognostic factor for CSS (hazard ratio/95% CI = 1.628/1.018-2.604).

Conclusion: Higher pre-treatment NLR is not a prognostic factor in stage IV breast cancer. After start of treatment, increased NLR has a predictive value for poor CSS in stage IV breast cancer.

Discordance of Hormone Receptor and Human Epidermal Growth Factor Receptor2 as a Prognostic Factor of Survival Between Primary Breast Cancer and Recurrent Breast Cancer

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Background/Purpose: The aim of this study was to compare the hormone receptor (HR) and human epidermal growth factor receptor2 (HER2) status between primary and metastatic breast cancer and also to evaluate the impact of discordance and other clinicopathologic factors on survival.

Methods: This study retrospectively reviewed 427 recurrent breast cancer patients who were confirmed by histological sampling of loco-regional relapse site from Jan 1999 to Dec 2008. Estrogen receptor (ER), Progesterone receptor (PR) and HER2 assessment were performed on the primary and recurred specimen at the same laboratory.

Results: Discordance rates of ER, PR and HER2 were 15.0%, 30.4% and 17.8% respectively. Concordant positive group of ER or PR had statistically significant better cancer specific survival (CSS) and post-recurrence survival (PRS). Switch of ER or PR from positive to negative resulted worse CSS and PRS ($p = 0.002$ for ER, $p = 0.059$ for PR). On multivariate analysis adjusted by tumor size, lymph node metastasis, grade, ER discordance was found to be an independent prognostic factor for CSS. (HR = 3.4 95% CI) Radiation therapy is the only suspected factor that affected to alteration of ER ($p = 0.004$).

Conclusion: Hormone receptor changing from positive to negative is worse prognostic factor. Also, radiation therapy might be the key of finding alteration mechanism of hormone receptor.

Correlation of Breast Cancer Subtypes, Prognostic Factors and Survival Outcome with Functional Imaging Parameters from FDG-PET/CT

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Background/Purpose: The objective of this study was to evaluate the clinical significance and prognostic relevance of glucose metabolism using maximum standardized uptake value (SUVmax) on fluorodeoxyglucose positron emission tomography/computed tomography (FDG-PET/CT) in breast cancer.

Methods: Clinicopathological characteristics and molecular subtypes were assessed in 210 patients with invasive ductal carcinoma between October 2006 and July 2014. Subtypes were defined as luminal A, luminal B, triple negative (TN) and human epidermal growth factor receptor 2 type. SUVmax was measured on FDG-PET/CT preoperatively, 90 minutes after injection of a 5 MBq/kg of 18F-FDG. Correlations of SUVmax with clinicopathological characteristics, subtypes and survival were evaluated.

Results: There was positive relationship between mean of primary tumor SUVmax and AJCC stage showed statistically significant correlation ($p < 0.01$). The mean of primary tumor SUVmax of TN subtype (7.37 ± 5.91) was higher than of luminal A subtype (4.56 ± 3.33) ($p < 0.01$). In overall survival there was a statistically significant level of primary tumor SUVmax affecting survival in luminal A subtype (5.50 ± 0.09, $p < 0.01$).

Conclusion: 18F-FDG uptake reflected tumor metabolism and high SUVmax level was associated with aggressive features in breast cancer. High uptake of 18F-FDG (SUVmax) on FDG-PET/CT may have potential value for predicting poor prognosis in breast cancer.

Tumor-Infilterating Lymphocytes in Patients with Early Triple-Negative Breast Cancer: Validation to Recommendations by an International Tumor Infiltrating Lymphocytes Working Group 2014

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Background/Purpose: The aim of the study was to evaluate the clinical utility of tumor-infiltrating lymphocytes (TILs) that were reviewed by recommendations by an international TILs working group (TILs IWG) 2014 in patients with early triple-negative breast cancer (TNBC).

Methods: 133 patients with early TNBC who underwent surgery between 2008 and 2010 were retrospectively reviewed. 121 of 133 formalin-fixed, paraffin-embedded tumor samples were available and reviewed according to the recommendations by TILs IWG. Stromal, intratumoral TILs, and TILS at the invasive edge in the context of TILs expressions of TILs IWG were reviewed. With cut-off of 10% threshold of stromal TILs, survival outcomes including recurrence-free survival and overall survival were calculated. Both univariate and multivariate analyses were performed to investigate the implication of TILs expressions as prognostic factors.

Results: Most patients had node-negative T1-2 tumors and received adjuvant chemotherapy; T1-2 tumors were 117 of 121 cases, node-negative diseases were 106 cases, and 117 patients received adjuvant chemotherapy, respectively. Seventy-five patients, 62%, had more than 10% of stromal TILs. Intratumoral TILs and lymphocyte-predominent breast cancer (LPBC) were observed in 72% and 19% of patients, respectively. However, there was no significant difference according to the presence of stromal TILs, intratumoral TILs, TILs at the invasive edge, and LPBC in terms of recurrence-free and overall survival (all $p > 0.05$). Furthermore, stromal TILs, intratumoral TILs, TILs at the invasive edge, and LPBC were not associated with survival outcomes in multivariate analysis adjusted for T and N stage, grade, adjuvant chemotherapy, and various TILs parameters.

Conclusion: TILs evaluations according to the recommendations by TILs IWG may be not useful to predict survival outcomes in patients with early TNBC. Further validations to the recommendations by TILs IWG should be needed to confirm the prognostic and predictive values of TILs in patients with early TNBC.

Survival Analysis According to Period and Analysis of the Factors Influencing Survival Changes in Breast Cancer Patients with Recurrence

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Background/Purpose: We performed this study to analyze the changing survival patterns of recurrent breast cancer in Korea during the last 20 years (1993-2008). We also sought to determine factors possibly influencing outcomes and changes over time in the duration of survival after a recurrence.

Methods: We retrospectively analyzed a total of 10,988 patients with breast cancer who were treated at the ASAN Medical Center between January 1993 and December 2008. We divided the study period into 3 periods (period I: 1993-1997, period II: 1998-2002, period III: 2003-2008). Then, we reviewed the collected database including the age at diagnosis, clinical manifestations, pathology report, surgical methods, types of adjuvant treatment modalities, type of recurrence, and follow-up period.

Results: Among the 10,988 patients, recurrences were 2,015 cases (18.3%). With a median follow-up of 28.8 months (range, 0-228.0 months) from the time of relapse, the median survival rate was 36.0 months. There was a significant improvement in survival after recurrence rate according to period. The median survival time increased from 27.6 months in period I to 42.3 months in period III ($p=0.001$). The 3-year survival rate increased from 41% in period I to 55% in period III, and the 5-year survival rate increased from 29% in period I to 39% in period III. Factors related to survival after the first recurrence by multivariate analysis were age at diagnosis, stage, tumor grade, progesterone receptor status, chemotherapy, and disease-free interval.

Conclusion: The outcomes of breast cancer have been improving recently, and survival time after the first recurrence of breast cancer has steadily increased in recent decades. We confirmed that advances in treatments have contributed to this improvement in survival after the first recurrence.

Level Changes of CA15-3 Can Predict Recurrence in Breast Cancer Patients

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Background/Purpose: The most widely used serum tumor markers in breast cancer are CA 15-3 and carcinoembryonic antigen (CEA). While the level of CA 15-3 is rarely elevated in patients with early stage or localized cancer, the majority of patients with metastatic breast carcinoma have elevated serum level of CA 15-3. So we evaluated the wave line made by several regularly checked values of CA15-3.

Methods: From 2001 01 to 2014 01, 153 breast cancer cases with metastasis or without metastasis were enrolled in our study. CA15-3 was evaluated by patient record retrospectively. Wave of CA15-5 were made by Microsoft Excel programe. We analysed the type of wave, the average duration between shoulder sign and the date of defined as metastasis at imaging study. Wave one is up and wave two is down correcting W1, wave 3 again move upward and the bottoms of wave2 is higher than the start of wave one.

Results: 21.5% (33/153) were defined as up wave. 28.1% (43/153) were defined as W wave 28.2% (43/153) were defined as down wave 22.2% (34/153) were defined as zigzag wave.

Conclusion: If the level of CA15-3 is continously increased through 18months without decreasing, the rate of recurrent cancer is about 49.6%.

The Impact of 21-Gene Recurrence Score on Treatment Decisions for Patients with Hormone Receptor-Positive Node-Positive Breast Cancer

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Background/Purpose: The addition of adjuvant chemotherapy to hormonal therapy is recommended for patients with hormone receptor-positive node-positive breast cancer. Some of these patients, however, are not likely to benefit from treatment and may be overtreated. This retrospective study evaluated the usefulness of 21-gene Recurrence score (RS) on treatment decisions in hormone receptor-positive node-positive (up to 3 positive nodes) breast cancer patients.

Methods: The retrospective analysis included 125 patients with results of 21-gene RS. The patients had hormone receptor-positive, HER2-negative breast cancer and 1 to 3 positive nodes. The results of RS and the presence of any recurrence for short-term follow-up period were reviewed.

Results: Among the 125 patients, 70 (56%) had a low RS of < 18, 44 (35.2%) had an intermediate RS of 18-30, and 11 (8.8%) had a high RS of ≥ 31. Sixty-two patients (49.6%) received endocrine therapy alone and 63 (50.4%) received endocrine therapy with chemotherapy. At a median follow-up of 15 months, only one patient, who refused radiotherapy, had a local recurrence and remaining 124 had not any recurrence. The RS of patients with a single positive node was not significantly different with that of patients with 2-3 positive nodes ($p = 0.465$).

Conclusion: The 21-gene RS could help guide treatment decisions for patients with hormone receptor-positive, node-positive breast cancer. The RS results showed low risk in more than half of node positive patients who could avoid adjuvant chemotherapy. Prospective studies are warranted to evaluate the role of 21-gene RS for hormone receptor-positive node-positive breast cancer patients.

Dual Expression of Aquaporin 3 and 5 in Patients with Early Breast Cancer

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Background/Purpose: We reported separately that Aquaporin (AQP)5 or AQP3 expression in tumor tissue may predict survival after surgery for the specific types of early breast cancer (EBC). However, there is no definitive evidence for the role of dual expression of the two AQPs. Therefore, the current study focused the association and its prognostic impact of their tumoral expressions in the same patients.

Methods: AQP3 and AQP5 expressions were investigated on the basis of the immunohistochemistry of tissue microarray specimens from 447 EBC patients who underwent surgery between 2003 and 2008 as described in previous studies. Patients were divided into 4 subgroups based on AQP3 and AQP5 expressions: group1 for (-/-), group2 for (-/+), group 3 for (+/-), and group 4 for (+/+), respectively.

Results: Among 477 patients, the number of patients for each group was as follows: group 1 (n = 193, 43.2%), group 2 (n = 74, 16.6%), group3 (n = 110, 24.6%) and group 4 (n = 70, 15.7%), respectively. In the current study a positive correlation was identified between AQP3 and 5 expressions ($p = 0.017$ by a χ^2- test) in particular for human epidermal growth factor receptor 2 (HER2)-overexpressing and estrogen receptor positive tumors ($p = 0.009$ and 0.044, respectively). Multivariate survival analysis showed that dual expression of AQP3 and AQP5 was a negative prognostic factor for relapse-free or distant disease-free survival for patients with HER2-overexpressing EBC (HR = 3.107 and 3.683; $p = 0.043$ and 0.027, respectively), statistically more prominent compared in case with AQP3 expression alone (HR = 3.137 and 2.784; $p = 0.036$ and 0.070, respectively).

Conclusion: Dual expression of AQP3 and AQP5 in tumor tissue may be considered as a potential prognostic marker in patients with HER2-overexpressing EBC after curative surgery.

Clinicopathological Characteristics and Prognosis in Old Age Breast Cancer

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Background/Purpose: Aging is one of the greatest risk factors for development of breast cancer. Elderly population of Korea is growing very fast. However, research on breast cancer in elderly patients was insufficient. We performed this study to asses the clinical characteristics of elderly women with breast cancer and evaluated the determinants and effects of treatment choice for breast cancer prognosis among elderly patients.

Methods: We reviewed medical record of 1580 patients who diagnosed and treated invasive ductal carcinoma at Gachon University Gil Medical Center between 2002 and 2012. Patients were classified according to the age ≥ 60 and < 60 years. Tumor characteristics, surgical method, adjuvant therapy were taken into consideration.

Results: The number of childbirth and the proportion of postmenopausal women were higher in elderly patients. There were no differences between two age groups in family history, tumor size, and the number of metastatic lymph nodes. 130(47.1%) of elderly patients had a mastectomy. The elderly showed higher proportion of negative progesterone receptor. Adjuvant chemotherapy was effective on patient with positive hormone receptor and no lymph nodal invasion but did not affect survival rate of patients with negative hormone receptor. Postoperative radiation therapy is effective in young patient with breast conserving surgery and elderly patients with mastectomy. Poor prognostic factors in elderly patients were lymph nodal invasion, recurrence, triple negative, negative for progesterone receptor and negative for p53.

Conclusion: The key prognostic factors of elderly breast cancer patients are hormone receptor status and lymph nodal invasion. Triple negative status is more critical to old age patients. Adjuvant therapy showed a similar effect to elderly and young patients. Therefore appropriate surgical method and adjuvant treatment considering comorbidity and adverse effect should be given to elderly patients

Prognostic Abilities of B-Cell Lymphoma 2 (BCL2) Protein Expression in Primary Breast Cancers:Why BCL2 Cannot Explain the Prognosis of the Patients with Breast Cancer?

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Background/Purpose: The *B-cell chronic lymphocytic leukemia/lymphoma 2* (BCL2) gene family encodes pro- and anti-apoptotic proteins that are critical regulators of programmed cell death. Although Higher levels of BCL2 expression has occasionally been suggested as a candidate prognostic factor for breast cancer, it is still not accepted as a prognostic factor. We attempted to validate the role of BCL2 as a prognostic factor of breast cancer.

Methods: This study data on 232 breast cancer patients from Yonsei wonju severance christian hospital, department of surgery in 2005-2014 were analyzed. The prognostic value of BCL2 expression was evaluated studying correlations with clinicopathologic features (histologic grade, tumor size, lymph node status, estrogen receptor, HER2 receptor and age group) and their prediction of survival. The BCL2 expression and clinical feature, recurrence related free survival and overall survival (OS) were estimated by statistical analysis.

Results: BCL2 expression Positive group (n = 165) and Negative group (n = 67) were estimated by analysis for clinicopathologic feature. Significant relationships between BCL2 expression and histologic grades ($p < 01001$), estrogen receptor ($p < 0.001$), HER2 receptor ($p < 0.001$) were observed. BCL2 were significantly associated with OS but only in the first 36 months ($p = 0.018$), whereas DFS analysis were not significantly correlation for the BCL2 expression but were representing to tendancy for good outcome ($p = 0.060$). Cox univariate analyses indicated that BCL2-like 2 (BCL2L12) expression is associated with tumor size (HR = 1.436, $p < 0.001$), lymph node status (HR = 1.113,

$p < 0.001$) and estrogen receptor status (HR = 73,185, $p = 0.002$).

Conclusion: We conclude that BCL2 expression were predictive biomarkers for better and worse survival respectively, but only in the first to 36 months after diagnosis. This study is a limitation as it is a small patients groups performed at a single institution. But, this study represents a significant attempt at assessing the role of BCL2 as a potential tumor marker in breast cancer and future studies are needed for validation of our results and to further demonstrate its role in clinical practice.

Risk Factors Associated with Recurrence in Ductal Carcinoma *In Situ* or Small Breast Cancer

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Background/Purpose: The purpose of this study was to evaluate the risk factor of recurrence in patients with ductal carcinoma *in situ* (DCIS) or small breast cancer with tumor size ≤ 1cm.

Methods: We retrospectively identified patients with DCIS or small breast cancers who received surgery between 2000 and 2010. Kaplan-Meier analysis was used to estimate recurrence-free survival and Cox regression analysis was performed to identify independent prognostic factors.

Results: In total 528 patients were diagnosed with DCIS or small breast cancer (DCIS: 255, T1mi: 68, T1a: 47, T1b: 158). During 48 months (4-167 months) of median follow up period, 16 patients (3%) experienced recurrence. In univariate analysis, age and lymph node metastasis were significant factors associated with recurrence ($p = 0.006$, $p = 0.011$, respectively) and human epidermal growth factor receptor 2 (HER2) overexpression was shown marginally significance associated with recurrence ($p = 0.07$). In multivariate analysis, young age (under 35 years) and lymph node metastasis were independent factors associated with recurrence, corresponding to adjust odds ratios of 4.06 (95% CI: 1.10-14.98, $p = 0.035$), 3.48 (95% CI: 1.07-11.37, $p = 0.039$), respectively.

Conclusion: Young age (under 35 years) or initial lymph node metastasis patients have a relatively higher risk of recurrence.

PO059

Association of Basal Epithelial Phenotype and *BRCA1/2* Germline Mutations in Korean Breast Cancer Patients

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Background/Purpose: A basal epithelial phenotype accounts for 15% of all invasive breast cancers. We investigated the association between *BRCA1/2* germline mutations and histologic features of basal-like breast cancer. We also identified *BRCA1/2* mutation prevalence according to age and family history in triple negative breast cancer (TNBC) patients.

Methods: We performed a retrospective review of 411 breast cancer patients who underwent *BRCA* genetic testing at Seoul National University Bundang Hospital between July 2003 and September 2012. We obtained information of immunohistochemistry including ER, PR, HER2, CK5/6, EGFR and p53.

Results: In total, 50 patients (12.2%) have *BRCA1/2* mutations. Among 95 TNBC patients, *BRCA1/2* mutations were identified in 26 patients. CK5/6, EGFR, ER, PR, and TNBC were related to *BRCA1* mutation in univariable analysis, but only TNBC was significant in multivariable analysis. Among non-familial breast cancer patients, *BRCA1* mutations prevalence in TNBC-group (11.8%) was higher than that in non-TNBC-group (1.7%).

Conclusion: In our study, only TNBC is an independent predictor of *BRCA1* mutation in patients with high-risk for hereditary breast and ovarian cancer. Other histologic features of basal-like breast cancer did not help to refine *BRCA1* mutation risk estimates.

PO060

Percent Mammographic Density Refines Conventional Breast Cancer Risk Predicting Model; A Case-Control Study in 4413 Korean Women

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Background/Purpose: Mammographic density is a well-known risk factor of breast cancer. Few studies have evaluated percent mammographic density (PD) with conventional risk predicting model quantitatively. To confirm density as a risk factor also in Korean women and whether the risk varies by *BRCA* mutation status, we performed a case-control study of 1980 breast cancer patients and 2,433 healthy controls among whom 869 had *BRCA* tested

Methods: Risk of developing cancer was calculated using modified Gail, Asian-Gail and KOREAN model (Park et al. PLosOne 2013). Factors associated with percent density were analyzed. 'Residual density' was calculated to eliminate the possible effect of the risk factors on PD by using linear regression analysis. Incremental discrimination power was measured by adding 'residual density' to the three conventional risk predicting models. Percent density (PD, dense area/breast area, %) was measured of the unaffected contralateral CC view using computer-assisted method Cumulus by single observer

Results: Younger age, premenopause and absence of breastfeeding were independently associated with high PD. PD was significantly higher in cancer patients compared to controls. This finding was consistent after matching the case-control by 1) age, 2) BMI, 3) menopause, 4) history of breast biopsy and family history of breast cancer (49.35% ± 15.45 vs 40.07% ± 15.73, $p < 0.001$). Modified Gail, Asian-Gail model failed to discriminate cancer-control group. The AUC value of 1) KOREAN model, 2) PD, 3)

KOREAN model with residual PD were 0.600, 0.769 and 0.780 respectively ($p < 0.001$, Delong's method). Distribution of PD did not differ by *BRCA* mutation status

Conclusion: PD is a strong risk factor of breast cancer in Korean women. Although PD was affected by known risk factors of breast cancer, PD alone discriminated cancer-control group better than the existing risk assessment models. PD should be included into the conventional risk predicting models to better stratify risk of developing breast cancer leading to personalized screening. The underlying mechanism of how dense mammary tissue may contribute to tumorigenesis should further be addressed

PO061

Risk-Benefit Index of Tamoxifen and Raloxifene for Chemoprevention of Korean Breast Cancer

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Background/Purpose: According to the NSABP-P1 and P2 studies, tamoxifen and raloxifene can protect breast cancer and hip fracture, but they can induce endometrial cancer, stroke, and pulmonary embolism. We estimated the risks and benefits of tamoxifen and raloxifene using a Korean database in order to evaluate the feasibility of using tamoxifen and raloxifene for breast cancer chemoprevention in Korean women.

Methods: Data were reviewed on the incidences of breast cancer, hip fracture, endometrial cancer and stroke in the absence of tamoxifen and raloxifene treatment in Korean women. We also reviewed NSABP-P1 and P2 data on the effects of tamoxifen and raloxifene on these outcomes. A risk-benefit index was calculated according to age and specific risk of breast cancer. Sensitivity analyses were performed of assumptions regarding the effects of tamoxifen and raloxifene.

Results: Compared to U.S., the numbers of hip fractures and endometrial cancers were lower, but the number of strokes was much higher. The net benefit of tamoxifen and raloxifene were reduced with increasing age because of a high risk of stroke in older women. Older Korean women had more risk than benefit from tamoxifen and raloxifene chemoprevention. Only women younger than age 40 had a positive risk-benefit index of tamoxifen with an average 5-year risk of breast cancer in Korea. Raloxifene has more favorable index in postmenopausal women with a uterus.

Conclusion: Women under the age 40 had more benefit than risk from tamoxifen chemoprevention. In the postmenopausal women with a uterus, raloxifene has more favorable risk-benefit index than tamoxifen.

PO062

Impact of Increased Physical Activities After Diagnosis on Fatigue and Overall Pain During Cancer Treatment: A Prospective Cohort Study

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Background/Purpose: Existing evidence strongly suggests that exercise is not only safe but also feasible during cancer treatment. Physical activity is recommended for improving multiple post-treatment adverse effects on bone health, muscle strength, and other quality-of-life measures. Yet, limited evidence exists regarding effect of increased physical activity after diagnosis on symptoms management of breast cancer patients.

Methods: A total of 422 patients were recruited from July 2010 to July 2011 at two cancer hospitals Seoul, Korea. Physical activity in sports (PAS) was assessed using Minnesota Leisure Time Physical Activity Questionnaire before and 2 weeks, 3-, 6-, 12-, 24- and 36-months after diagnosis. Physical symptoms including fatigue, pain, systemic therapy side effects, and breast symptoms were measured using EORTC-C30 and BR23. Growth mixture models were used to identify trajectory classes of physical activity patterns. Multivariate analysis was used to find impact of PAS on symptoms using SAS 9.3.

Results: Three distinct PAS groups were identified according to 3-year change patterns: moderate to moderate (MM): 40.8%, none to moderate (NM): 31.1% and moderate to vigorous (MV): 28.1%. The NM and MV group increased PAS from diagnosis but it began to decrease from 1 year after diagnosis. Compared to the MM, the NM and MV reported significantly lower level of fatigue (MM:40.7, NM:32.2, MV:33.7), pain (MM:28.0, NM:25.6, MV:20.6), systemic therapy side effects (MM:26.9, NM:22.6, MV:21.8), and breast symptoms (MM:25.4, NM:21.7, MV:20.2) during active treatment (6 months after diagnosis).

Conclusion: The results of the study confirm that increased physical activity after diagnosis, even with patients who did not exercise at all before diagnosis, helps to control fatigue, pain, systemic side effects, and breast symptoms during treatment. It is necessary to find ways to promote physical activity after diagnosis and help patients to stay active during treatment.

PO063

Outcome of High Risk Breast Cancer Patients; A Retrospective Review of 1213 *BRCA* Tested and 7590 Sporadic Breast Cancer Patients

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Poster Exhibition

Background/Purpose: Breast cancer outcome of high risk patients was evaluated by comparing *BRCA* mutated, wild type and sporadic cancers. Risk of local/regional/systemic recurrence and death owing to primary tumor were analyzed. Risk of developing secondary malignancies including contralateral breast cancer and ovarian cancer were assessed to find evidence in risk-stratified preventive intervention and surveillance after adjuvant treatment of the primary tumor among the high risk population.

Methods: A retrospective review of breast cancer patients undergone surgery between 1989 and 2008 in ASAN Medical Center was performed. Among the 11,233 total patients, 2,430 high risk patients without *BRCA* testing were excluded and 8,803 were included. *BRCA* testing was done as indicated 1) < 40 yr, 2) family history of breast/ovarian cancer, 3) bilateral breast cancer, 4) history of ovarian cancer or other primary cancer. Analysis was done by comparing the three group; *BRCA* wild type, *BRCA* mutated and 7,590 sporadic tumors.

Results: Among the 1,213 *BRCA* tested patients, 133 (11%) had pathogenic mutation (67 *BRCA1*, 66 *BRCA2*). *BRCA* mutated tumors were less likely to be hormone receptor positive than WT (45.9% vs 65.3%, $p < 0.001$). No differences of tumor size, LN metastasis nor performed surgery was observed. Recurrence free and overall survival was similar and patients undergone breast conserving surgery had more ipsilateral breast cancer (IBC) events but only in *BRCA* mutated patients. Contralateral breast cancer (CBC) was associated with younger age (< 35 yr) and not taking tamoxifen in univariate analysis and *BRCA* mutation was the only independent risk factor with 5 yr cumulative incidence 4.4% vs 9.3% (10 yr; 9.7% *vs* 20.1%). 27.8% (37/133) among *BRCA* mutated

patients undergone bilateral salpingo-oophorectomy (BSO) but was not significantly associated with risk reduction.

Conclusion: Risk of IBC was higher when conserving surgery was performed in *BRCA* mutated tumors and risk of CBC was higher. But neither affected risk of death that *BRCA* mutation was not associated with breast cancer specific nor overall survival. Tamoxifen may lower risk of CBC but future analyses are necessary to provide evidence for applying as a preventive strategy and the benefit of BSO should further be re-addressed.

PO064

Can the Elderly Stay Safer than Younger Counterpart?: Reality of the Older Patient with Breast Cancer

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Background/Purpose: Korean researchers have focused on the young patients, because young age remains a risk factor for poorer survival, although improvements in treatment and earlier detection have reduced mortality in all age groups. However, epidemiologic studies reported changing patterns that the median age at diagnosis increased over time. Another important feature of poor prognosis of young patients comes from the papers, where analyzing survival difference according to a certain age such as 35 or 45 including peri-menopausal women. We compared patients ≥ 65-years to patients ≤ 45-years and evaluated the exact feature of elderly patients.

Methods: We included patients with Primary Breast cancer between April 2001 and December 2014 at Wonju Severance Christian Hospital (WSCH) and completed all phases of their primary treatment. We obtained follow-up data from the breast cancer database of WSCH and the Korean National Cancer Center database. We set the age of Elderly as ≥ 65 years, and younger as ≤ 45 years. We analyzed the clinicopathologic factors such as tumor size, nodal status, hormonal receptor status, human epidermal growth factor receptor 2 (HER2) and TNM stage according to AJCC, type of surgery between two groups and survival data.

Results: We identified 364 patients are eligible in this study, 108 elderly patients (65 to 89, Mean age = 70.87 ± 0.88, CI = 95%) and 256 younger patients (22 to 45, Mean age = 39.52 ± 0.56, CI = 95%) were included. When compared elderly to younger patient, T stage, estrogen receptor, progesterone receptor, HER2 show no statistical difference. But N stage and Type of surgery were significantly associated with age group. Elderly shows higher N stage and modified radical mastectomy rate ($p = 0.007$, $p < 0.002$). The 10-year disease free survival was significantly associated with age group that elderly shows poorer outcome ($p < 0.002$).

Conclusion: We can find the disparities in breast cancer outcome of older women.

Survival disparities appear to be pronounces with higher stage, higher risk disease and risk for less than standard management, such as cerebrovascular disease, cardiac disease. We found that the detection of early stage disease in older women, therefore is important. And elderly also require careful consideration not to be under-treated.

PO065

Hormonal Risk Factors of Each Subtype of Breast Cancer

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Background/Purpose: The prognosis and behaviour of breast cancer depends on subtypes classified by hormone receptors such as estrogen receptor (ER), progesteron receptor (PR), human receptor tyrosine-protein kinase erbB-2 (HER2) as well as the stage of the cancer. Female sex hormones are well known risk factors of breast cancer and the hormones may affect differently the several subtypes of breast cancer. We can predict the effect of female sex hormones on breast cancer behaviour and prognosis more precisely by evaluating the effect of sex hormones on different subtypes of breast cancer.

Methods: This is a case-control study. The cases are 34,400 breast cancer patients who were enrolled in Korean Breast Cancer Society patient database and the controls are 68,800 individually age-matched female participants from Korean Genome and Epidemiology Study (KoGES). The cases were classified to 6 groups (Group1: total breast cancer, Group2: ER+PR+HER2-, Group3: ER+ or PR+ HER2-, Group4: ER+PR+ HER2+, Group5: ER-PR-HER+, Group6: ER-PR-HER2-). Logistic regression model was build with BMI, menstruation age, parity, breast feeding, hormonal replacement, oral contraceptive, surgery and family history. We used R 3.1.

Results: After adjusted with body mass index, menstruation at age 14-16 increased the breast cancer risk by 1.23-1.39 times in group1-6 and menstruation after age 17 increased the breast cancer risk by 1.18-1.62 times in group1-6 compared to early menstruation (age < 14). Each delivery decreased the risk by 0.88-0.92 times in group1-4 and increased risk by 1.02 times in group 5. Family history of breast cancer increased the risk by 3.88-5.40 times in group1-6. Short period of breast feeding (< 6 months) increased the risk by 1.52-1.69 times in group1-6 compared to longer period of breastfeeding (> 6 months). Oophorectomy increased the risk by 1.80-2.56 times in group1-6 and hysterectomy decreased the risk by 0.61-0.80 times in group 1-6. Oral contraceptive use or hormone replacement therepy didn't show significant risk changes.

Conclusion: Nulliparity and short breast feeding period increased the risk in all subtypes. Early menstruation showed protection effect and we couldn't prove significant relationships between oral contraceptive, hormone replacement and breast cancer due to high missing rate. Since oral contraceptive usage showed a trend to increase risk, we may consider imputation of the data or subgroup analysis. Each risk factor showed different odds ratio in each subtype of breast cancer, we may develop a more precise breast cancer risk prediction model by predicting the risk of each subtype of breast cancer.

PO066

Do Ductal Carcinoma *In Situ*-Specific Knowledge Affect Survivors' Psychological Burden?

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Background/Purpose: Advanced detection technology yielded increasing number of ductal carcinoma *in situ* (DCIS) patients, yet there is limited DCIS-specific information. How much they know may affect survivors' psychological health. Also, it is unnecessary for DCIS survivors to carry psychological burden when over 99% of them survive. The purpose of the study is to address correlation of DCIS survivors' knowledge level with their overall psychological health.

Methods: We reached DCIS survivors who completed treatment and have had at least one surveillance exam. Survivors were asked to participation in a cross-sectional survey at two breast cancer clinics of university-based hospitals in Seoul, Korea from August through October, 2013. Participants' clinical information was collected by the electronic medical records. Knowledge about DCIS, scanxiety- anxiety due to scan or surveillance exams, experience from surveillance check-up, anxiety, depression, fear of cancer recurrence, and quality of life were assessed along with socio-demographic information.

Results: Total 111 DCIS survivors participated in the study. Of all, 90.8% were married, 54.7% were housewives, and 55.7% were at least college graduates. Mean time since diagnosis was 3.7 years and mean age was 51.6 years. About half (57.7%) received lumpectomy. About 90% carried fear of second cancer, recurrence, and metastasis. More than 75% believed 'DCIS is as severe as invasive breast cancer (IBC)'. Participants who considered 'DCIS as severe type of cancer' expressed higher anxiety (2.64, SE = 0.86) and scanxiety (0.29, SE = 0.13). Most participants (91%) believed 'DCIS survivors need as much surveillance as IBC survivors'. Participants with better DCIS-knowledge were more likely to believe surveillance is helpful to keep healthy life-style and they were willing to manage healthy life-style.

Conclusion: Still, most DCIS survivors suffer from fear of cancer and consider DCIS as severe cancer. The survivors are also at high risk of psychological burden and they are less likely to put efforts for healthy life-style especially when they know little about their disease. Therefore, DCIS survivors need more tailored information to understand their disease and to avoid unnecessary psychological burden.

PO067

Genetic Susceptibility Loci Associated with Early Onset *BRCA1/2*-Negative Breast Cancer

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Background/Purpose: Genetic variants in *BRCA1/2*, the most well-established cause of hereditary breast cancer, account for around 15% of familial relative risk (FRR) of breast cancer. Although numerous other genetic loci with varying degree of penetrance were reported to be associated with breast cancer risk, none of them have explained such a substantial proportion of genetic burdens yet . Because breast cancer epidemiology in Asian women shows different characteristics from that of Westerners, we attempted to identify new genetic loci that might fill the gap of expected genetic burden and known genetic variants.

Methods: Breast and/or ovarian cancer patients who have been proved to be free of clinically significant mutation or clinically unverified mutation in *BRCA1/2* were selected from the Korean Hereditary Breast Cancer (KOHBRA) study according to onset age, menopausal status when diagnosed, and family history of breast/ovarian cancer. 1,522 individuals were genotyped using Illumina HumanCore Beadchip and imputation was performed with IMPUTE2. After stringent QC and imputation, over 4 million markers were analyzed. Age-matched 1,020 individuals from population cohort were used as control data. Genome-wide association study was conducted using PLINK software.

Results: Several genetic loci showed association with breast cancer in *BRCA*-negative cases. One of the strong signals was observed in a 6q25.1 region (the lowest *p*-value in this region: 2.4×10^{-7}), which has been reported before. This Simple (or Single) Nucleotide Polymorphism (SNP) is common with minor allele frequency (MAF) of 0.36 and odds ratio of 1.34, explaining 3.6% of FRR when assuming FRR = 1.8. When when including estrogen receptor negative cases only, it showed more significant result (*p*-value: 4.2×10^{-8}). Other loci showing significant results have been reported in previous

studies: 11q24.1 (4.9×10^{-6}), 18q12.3 (5.3×10^{-6}), while novel loci has also been found: 3q13.2 (9.0×10^{-9}).

Conclusion: This study has found several genetic susceptibility loci including novel variants associated with breast cancer beyond *BRCA1* and *BRCA2* genes, which might account for an unexplained part of breast cancer risk. Further analyses are needed including rare variants when whole-exome sequencing data are available, and using larger samples of control data. Further studies, together with results of this study, may help unraveling the genetic basis of breast cancer.

PO068

Setup Error and Effectiveness of Weekly Image-Guided Radiation Therapy of TomoDirect for Early Breast Cancer

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Background/Purpose: The aim of this study was to investigate setup error and effectiveness of weekly image-guided radiotherapy (IGRT) of TomoDirect for early breast cancer.

Methods: From 2012 to 2013, 151 breasts of 147 consecutive patients who underwent breast conserving surgery, followed by whole breast irradiation using TomoDirect, were evaluated. All patients recieved weekly IGRT. The weekly setup errors from simulation to each treatment in reference to chest wall and surgical clips were measured. Random, systemic, and 3-dimensional setup errors were acquired. Extensive setup error was defined as 5 mm above the margin in any directions.

Results: All mean errors were within 3 mm of all directions. The mean angle of gantry shifts was 0.6 °. The mean value of absolute 3-dimensional setup error was 4.67 mm. In multivariate analysis, breast size (OR = 2.82, 95% of CI: 1.00-7.90, $p = 0.049$) was a significant factor for extensive error. The largest significant deviation of setup error was observed in the first week of radiotherapy ($p < 0.001$) and the deviations gradually decreased with time. The deviation of setup error was 5.68 mm and within 5 mm, in the first week and after the second week, respectively.

Conclusion: In this study, there was a significant correlation between breast size and significant setup error in breast cancer patients who received TomoDirect. The largest deviation occurred in the first week of treatment. Therefore, patients with a large breast should be closely observed on every fraction and fastidious attention is required in the first fraction of IGRT.

PO069

Tumor Resection Using Near-Infrared Indocyanine Green Fluorescence in Benign Breast Mass and Early Breast Cancer

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Background/Purpose: Near-infrared fluorescence imaging and lymph node mapping using indocyanine green (ICG) has been reported to provide feasible and safe real time observation of lymph node signaling in breast cancer. We report that near-infrared ICG fluorescence can be successfully applied for imaging of the resection margins by direct injection into nonpalpable breast tumors,making possible to accurately identify resection lines.

Methods: Between March and November 2014, 20 patients diagnosed with early breast cancer or non-palpable benign breast tumors were enrolled in the study. Prior to the operation, we injected ICG intratumorally 1 cm from the tumor margin under the guidance of ultrasonography. Resection was monitored using a specially designed near-infrared ICG camera. We reviewed specimens for tumor size, resection margin, operation time.

Results: Among the 20 patients, 6 patients were diagnosed with early breast cancer and 14 patients with benign tumors. In cancer, all cases had negative resection margins. The median operation time was 98 minutes. The median of resection margin size was 2.2/2.4/2.0/0.5 cm. For the benign cases, the median operation time was 37 minutes. The median of specimen to tumor size was $2.7 \times 1.9 \times 0.5$ cm.

Conclusion: Near-infrared ICG fluorescence detection of breast tumor margins was successful in both non-palpable masses and early breast cancer. It was shown to be an efficient method of obtaining a high proportion of negative margins and optimum resection volumes in patients undergoing breast conserving surgery.

PO070

Is Ductal Carcinoma *In Situ* Component of Excisional Specimens Related with Primary Tumor's Surgical Resection Margin Status?

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Background/Purpose: The margin status of excisional specimens after breast conserving therapy (BCT) is the most important predictive factor for local recurrence. This study aims to investigate whether the ductal carcinoma *in situ* (DCIS) component affects closed margin status and to evaluate the clinicopathologic factors that are associated with the DCIS component in patients undergoing BCT for invasive ductal carcinoma.

Methods: From January 2012 to December 2013, 514 patients who initially underwent a BCT at Seoul St. Mary's Hospital, were retrospectively analyzed. Data included tumor characteristics, size and site of DCIS, and final pathologic results. We excluded all pure DCIS at the final pathology of primary breast tumor, insufficient data, and re-operation cases by positive margin from permanent pathologic results.

Results: In the univariate analysis, multifocality ($p = 0.025$), axillary procedure method ($p = 0.025$), lymphatic invasion (L-I) ($p < 0.001$), human epidermal growth factor receptor 2 status ($p = 0.009$), and existence of DCIS ($p = 0.018$) were significantly associated with margin status. In a multivariable Logistic regression analysis, multifocality ($p < 0.001$)) and L-I ($p = 0.01$) were the only statistically significant factors related to closed margin status.

Conclusion: In conclusion, the existence of DCIS component is significantly related with the closed margin. There was no significant correlation between DCIS component size and close margin status.

PO071

The Optimal Timing and Duration of Daily Primary G-CSF Prophylaxis After Adjuvant TAC (docetaxel/doxorubicin/cyclophosphamide) Chemotherapy in Node Positive Breast Cancer Patients: Multicenter Randomized Open-Label Phase IV Study

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Background/Purpose: Docetaxel/doxorubicin/cyclophosphamide (TAC) regimen is associated with high incidence of febrile neutropenia (FN). This prospective randomized trial compared the timing and duration of primary granulocyte colony-stimulating factor(G-CSF) prophylaxis for FN and related toxic effects in breast cancer patients receiving adjuvant TAC.

Methods: Node positive breast cancer patients with adjuvant TAC chemotherapy were randomly assigned to receive daily G-CSF (filgrastim 5 μg/kg/day) from day 2 (group 1, n = 30) or from day 5 (group 2, n = 30). The primary outcome was the incidence of FN. The secondary outcome was to compare the duration of neutropenia, incidence of neutropenic infection, and hematomogic toxicities between the two groups.

Results: Daily primary G-CSF prophylaxis from day 2 was more effective than from day 5 in preventing FN (8.1% *vs.* 18.8%, $p = 0.004$). The incidence of grade 4 neutropenia (100% *vs.* 100%), mean duration of grade 4 neutropenia (3.1 day *vs.* 3 day, $p = 0.593$), and mean Absolute neutrophil count nadir (38 *vs.* 27, $p = 0.961$) during cycle 1 were similar between the two groups.

Conclusion: Daily primary G-CSF prophylaxis from day 2 provided optimal protection against FN in patients receiving TAC. This was the first study to provide evidence on the timing of primary G-CSF prophylaxis after adjuvant TAC in breast cancer patients.

PO072

Huge Bilateral Breast Hamartoma with Ectopic Breast Hamartoma Mistaken for Phyllodes Tumor

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Background/Purpose: Breast hamartoma is an uncommon neoplasm, accounting for 1.2% of all benign breast masses, which is easily confused with other well circumscribed, benign diseases such as phyllodes tumors and fibroadenomas. Hamartomas are diagnosed by both radiologic and pathologic studies, but because of indefinite diagnostic criteria, they are often misdiagnosed.

Methods: It is usually presented unilaterally; very few cases have reported of bilateral breast hamartomas, and no case to date has reported of hamartoma in ectopic breast tissue accompanied with bilateral breast hamartoma. Herein, we report a case of huge bilateral breast hamartoma with ectopic hamartoma in unilateral axilla.

Results: A 34 year-old woman visited our breast center, presented with bilateral breast mass sized 25 cm on the right and 18 cm on the left. The patient's previous breast size was around A cup, but her breast gradually enlarged to the aforementioned size in only 6 months. She also had a mass on her left axilla.

Conclusion: Final pathologic report was hamartoma associated with focal pseudoangiomatous stromal hyperplasia and macromastia. Another interesting finding was that that the excised accessory breast mass of left axilla was also hamartoma. This is first case report of bilateral breast hamartoma accompanied with hamartoma in ectopic breast tissue, which is the largest one ever reported.

PO073

Contralateral Pectoralis Major Myomammary Nipple Areolar Complex Flap as an Oncoplastic Breast Surgery: Report of 10 Cases

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Background/Purpose: Despite of some limitations, many reconstruction methods have being performed when breast or nipple-areolar complex preserving was impossible because of nipple invasion or advanced stage. Authors report the initial experience of contralateral myomammary nipple-areolar complex flap as a nipple reconstruction method in patients breast cancer with nipple invasion and breast ptosis (grade III).

Methods: The retrospective review of ten patients who undergone contralateral myomammary nipple-areolar complex flap with mastectomy was done. The criteria was determined when the patient refused radiotherapy, had breast ptosis, and the contraindication of nipple-areolar preservation. The flap is composed of contralateral pectoralis major muscle and half of nipple-areolar complex with supplying vessels. The cosmetic result was assessed by patient herself.

Results: In postoperative complication, seroma formation and partial necrosis of nipple-areolar complex occurred in 2 cases each. The cosmetic result showed good in 2 patients, fair and poor in 6 and 2 patients, respectively.

Conclusion: The consmetic outcomes of contralateral myomammary nipple-areolar complex flap are not satisfactory up to now. The nipple reconstruction with contralateral nipple-areolar complex, however, would be another method using normal breast tissue and nipple-areolar complex when additional operation of contralateral breast may needed to resolve the breast ptosis (grade III).

PO074

Which Factors were Related to Severe Skin Reaction After Adjuvant Whole Breast Irradiation Using Field-In-Field Technique?

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Background/Purpose: To know the risk factors for severe skin reaction of adjuvant whole breast irradiation applying field-in-field technique, the relations of various radiation dosimetric parameters for radiotherapy planning, anatomical characteristics and clinical factors with severe skin reaction were evaluated.

Methods: Total 127 patients took both whole breast irradiation and boost to tumor bed. Skin reaction was measured on the first day of boost based on the photography of radiation field. For each axilla and inferior fold, the score of intensity of erythema (1-5) and extent (0-1) were summed and the severe skin reaction was defined as score 5 or 6.

Results: Total 41 (32.3%) and 37 (29.1%) patients showed the severe skin reaction to axilla and inferior fold, respectively. In multivariate analyses, age ($p = 0.019$ (Exp (B) = 0.938, 0.889-0.990) for axilla and $p = 0.024$ (Exp (B) = 0.937, 0.886-0.991) for inferior fold) and V100 ($p = 0.001$ (Exp (B) = 1.005, 1.002-1.008) for axilla and $p < 0.001$ (Exp (B) = 1.006, 1.003-1.009) for inferior fold) were the significant factors for severe skin reaction.

Conclusion: Young age and huge V100 could be one of prognostic factor for severe skin reaction during the modern adjuvant whole breast irradiation after conserving surgery.

PO075

The Clinical Usefulness of Adjuvant Treatment of Tamoxifen Plus Gonadotropin-Releasing Hormone Analogue in Premenopausal Patients with Early Breast Cancer

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Background/Purpose: The adjuvant treatment of premenopausal women with hormone receptor positive early breast cancer today include chemotherapy and/or tamoxifen and ovarian suppression therapy by gonadotropin-releasing hormone analogue (GHRHa). The purpose of our study was to compare the efficacy of tamoxifen plus GHRHa and anthracycline-based chemotherapy followed by tamoxifen plus GHRHa, and identify whether tamoxifen plus GHRHa may be used as substitute.

Methods: We conducted a retrospective review of 538 premenopausal patients who were diagnosed with invasive ductal carcinoma between November 2006 and November 2009. Of these, 110 were treated with tamoxifen (20 mg/day) plus GHRHa (Zoladex, 3.6 mg/kg every 28 days) (TZ group), and 11 were treated with anthracycline-based chemotherapy (Doxorubicin and Cyclophosphamide, 4 cycle every 21 days) followed by tamoxifen (20 mg/day) plus GHRHa (Zoladex, 3.6 mg/kg every 28 days) (AC-TZ group).

Results: 117 (96.7%) were stage I-II and well to moderately histologic grade of Invasive ductal carcinoma. With a median follow-up of 63 months, 12 (9.8%) of patients in TZ group developed relapse (Locoregional vs. distant, 6 vs. 7). There was no relapse in AC-TZ group. There were no significant differences in relapse free survival and overall survival between TZ group and AC-TZ group.

Conclusion: There was no additional beneficial effect in anthracycline-based chemotherapy (AC) followed by tamoxifen plus GHRHa group. The adverse events occurred more frequently in chemotherapy, so the treatment of tamoxifen plus GHRHa is more tolerable. The combination treatment of tamoxifen plus GHRHa can be considered for premonopausal women with early stage (stage I-II), hormone receptor positive breast cancer in the adjuvant management.

PO076

Silibinin Controls TGF-β Signaling Pathway in Triple Negative Breast Cancer Cells

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Background/Purpose: Transforming growth factor-β (TGF-β) is a pleiotropic cytokine that has crucial roles in tumor progression, formation and metastasis. TGF-β signaling promotes tumor promotion changes, such as increasing cell motility, loss of cell polarity and epithelial to mesenchymal transition. Silibinin may affect therapeutic drug for preventing TNBC cells migration throught regulation of TGF-β2 in triple negative breast cancer (TNBC) cells.

Methods: The human breast cancer cell lines MCF-7 and HCC-1806 were grown in DMEM supplemented with 10% FBS. The cell lysates were used in the immunoblot analysis for analyzing of protein expression and isolated RNA samples were used for RT-PCR. To analyze of MMP-9 and MMP-2 expression, zymography was used for the semi-quantitative analysis of gelatinase levels and HCC1806 TNBC cells migration were analyzed by wound healing assay.

Results: The basal level of TGF-β2 mRNA expression more highly expressed in TNBC than non TNBC cells. TGF-β2 induced fibronectin, matrix metalloproteinase (MMP) 2 and MMP-9 expression is reduced by TGF-β2 inhibitors in HCC1806 TNBC cells. Silibinin also suppresses the TGF-β2 induced HCC1806 TNBC cell migration thought regulation of fibronectin, MMP-2 and MMP-9 expression.

Conclusion: Our study demonstrated the first time that the TGF-β2 more highly expressed in TNBC cells than non-TNBC cells and TGF-β2 promote breast cancer cells metastasis related genes such as fibronectin, MMP-2 and MMP-9 expression. Interestingly, TGF-β2 induced fibronectin, MMP-2 and MMP-9 protein and mRNA levels and HCC1806 TNBC cells migration are inhibited by silibinin.

PO077

A Study of the Impact of the 21-Gene Breast Cancer Assay on Adjuvant Chemotherapy

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

Methods: The 21-gene assay was performed on 10 patients with estrogen receptor-positive early breast cancer in Dong-A University Hospital. Ten patients with human epidermal growth factor receptor 2 negative, N0/N1 node-positive breast cancer from our hospital were eligible for the study. The primary endpoint was the overall change in treatment recommendations after receiving the assay

Results: Among the 10 patients, 4 (40.0%) had a low RS of < 18, 5 (50.0%) had an intermediate RS of 18-30, and 1 (10.0%) had a high RS of ≥ 31. Treatment decisions were changed in 6 of 10 patients (60.0%) from chemotherapy plus hormone therapy to hormone therapy.

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

PO078

Implication of Adjuvant Chemotherapy in T1b-c N0 Luminal Breast Cancer

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Background/Purpose: The benefit of adjuvant chemotherapy to patient with small hormone receptor positive (HR+) node negative breast cancer is questioned. The aim of this study was to evaluate the effect of adjuvant chemotherapy on small node negative luminal breast cancer.

Methods: A total of 1111 women with HR+ T1b-c node negative breast cancer who underwent definitive surgery from 2001 to 2010 were retrospectively reviewed. Clinicopathological characteristics and clinical outcomes were analyzed.

Results: T1b and T1c tumors were 319 (28.7%) and 792 (71.3%) cases. Recurrence free survival (RFS) between patients with and without adjuvant chemotherapy in both groups were not significantly different. The overall survival (OS) of T1c patients with adjuvant chemotherapy tended to be better than those without adjuvant chemotherapy, however, the OS in T1b groups were not significantly different. In multivariate analyses of T1b group, adjuvant chemotherapy was not a significant risk factor for RFS and OS. However, adjuvant chemotherapy had marginal significance to improve the overall survival in T1c group.

Conclusion: Over 1cm sized HR+ tumor tended to have survival benefit from adjuvant chemotherapy, however, smaller HR+ tumor may not have survival benefit from adjuvant chemotherapy.

PO079

The Clinical Effectiveness of Immunotherapy Using Viscum Album as an Adjuvant Treatment in Invasive Breast Cancer

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Background/Purpose: Viscum album, also known as European Mistletoe, is as powerful medicinal herb which is used for treatment of many cancers including breast cancer. The effect of Viscum album is to enhance macrophage phagocytic and cytotoxic medicated abilities, and the prominent extracts like viscotoxins and lectins have cytotoxic and growth-inhibiting effects on cancer cells. In this study, we evaluate survival benefit of adjuvant immunotherapy in invasive breast cancer compared to patients who have not undergone immunotherapy.

Methods: Of 754 female patients who underwent curative surgery followed by standard adjuvant therapies in Hallym Sacred Heart Hospital from 2003 to 2011, 162 patients underwent immunotherapy with Viscum album, which is a species of mistletoe, as an adjuvant therapy. In order to analyze survival benefit, 31 patients who were taken immunotherapy for less than 12 months were excluded. We compared disease free survival (DFS) and overall survival (OS) of immunotherapy group (n = 131) with those of non-immunotherapy group (n = 592) using Kaplan-Meier survival curve.

Results: The mean age of all patients was 50.14 ± 0.41 (range, 23-85) years and the median follow-up period was 61 months (range 7-137). In survival analysis for all patients, there was no significant survival benefit in immunotherapy group, statistically. In subgroup analysis by hormonal receptor (HR) status, however, immunotherapy group had significant DFS benefit (5-year DFS: 96.5% *vs.* 88.4%, $p = 0.005$). Of 201 HR negative patients, recurrence was related to lymph node status ($p = 0.023$), TNM stage ($p = 0.030$), and adjuvant immunotherap ($p = 0.020$), in univariate analysis. However, adjuvant immunotherapy was only statistically significant factor that was related recurrence in multivariate analysis ($p = 0.018$).

PO079

Conclusion: In this study, additional immunotherapy after standard treatment without endocrine therapy showed survival benefit in HR negative group, even though immunotherapy group had more poor prognostic factors. Therefore, we suggested that adjuvant immunotherapy might be a therapeutic option for HR negative patients.

PO080

A Case Report of Breast Cancer Patients with Ipsilateral Supraclavicular Lymph Node Dissection

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Background/Purpose: The ipsilateral supraclavicular lymph node metastasis in breast cancer patients is a difficult problem to manage. It was considered as an inevitable signal of micrometastasis due to poor prognosis and was thus classified as M1 disease in 1998. However, supraclavicular metastasis was again categorized as N3 in the current sixth version of AJCC staging system 2003, based on the finding that aggressive treatment of patients with locally advanced breast cancer without distant metastasis. Selective patients with supraclavicular lymph node metastasis should be treated with a curative intent rather than palliative.

Methods: In 2010, a 52-year-old female presented with a painless palpable mass on the Lt. breast. Physical examination showed a non-tender, fixed mass. The ultrasonographic examination of the tumor showed 5 cm hypoechoic lesion with irregular margin and multiple axillary lymph node enlargement. The preoperative PET-CT scan showed increased uptake of multiple axillary and ipsilateral supraclavicular lymph node. We suggested a preoperative chemotherapy to patient. But she wanted operation. She received modified radical mastectomy and supraclavicular lymph node dissection.

Results: Histologic examination revealed invasive ductal carcinoma of histologic grade 2 and lymph node metastasis was found (113/139). Number of involved axillary lymph nodes was 50 (50/55). Number of involved supraclavicular lymph nodes was 63 (63/84). Hormonal status was ER negative and PR negative. HER2 receptor was weakly positive. She received docetaxel/doxorubicin/cyclophosphamide chemotherapy and radiation therapy. She has no recurrence during fifty-six months after surgery.

Conclusion: Although there are no specific guidelines for treatment of patients with ipsilateral supraclavicular lymph node metastasis. But, in some individual patients, supraclavicular lymph node dissection with combined modality, including systemic therapy and radiation therapy, might get a good prognosis.

PO081

Efficacy of an Aromatase Inhibitor Plus a Luteinizing Hormone-Releasing Hormone Agonist in Premenopausal Patients with Hormone Receptor-Positive Metastatic Breast Cancer

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Background/Purpose: In hormone receptor (HR) positive metastatic breast cancer (MBC), endocrine therapy has become the most preferred treatment option, unless there is need for rapid disease control. We investigated the efficacy of combination therapy using aromatase inhibitor (AI) and luteinizing hormone-releasing hormone (LHRH) agonist as first or second-line therapy in premenopausal patients with HR-positive MBC.

Methods: We retrospectively analyzed the medical records of 22 patients with HR-positive MBC treated with AI plus LHRH agonist between December 2007 and August 2014. All patients received goserelin 3.6 mg by subcutaneous injection every 4 weeks. The co-administered AIs were letrozole 2.5 mg (n = 20), anastrozole 1 mg (n = 1) or exemestane 25 mg (n = 1) daily.

Results: The median age at the time of treatment was 41.5 years old (range 29-50).The overall response rate was 36.4%, with 2 complete response (9.1%) and 6 partial response (27.3%). Stable disease lasting more than 6 months was achieved by 11 patients (50.0%). Thus, the combination of AI and LHRH agonist conferred clinical benefit in 19 women (86.4%). The median time to progression was 45.4 months (95% CI, 32.5-58.4 months). No patient experienced grade 3 or 4 toxicity.

Conclusion: The combination of AI and LHRH agonist safely and effectively induced remissions or prolonged disease stabilization, suggesting that it could be a promising treatment option for premenopausal patients with HR-positive MBC.

PO082

The Significance of Negative Sentinel Lymph Node Biopsy After Neoadjuvant Chemotherapy in Breast Cancer Patients with Clinically Positive Axillary Lymph Nodes at Presentation

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Background/Purpose: It is still controversial whether axillary lymph node dissection (ALND) can be omitted after negative sentinel lymph node biopsy (SLNB) in breast cancer patients with clinically positive axillary lymph node (ALNs) at presentation treated with neoadjuvant chemotherapy (NAC). The aim of study was to evaluate whether the negative result of SLNB could be reliable in these patients.

Methods: In a retrospective study, eligible patients were women with invasive breast cancer with clinically positive ALNs at presentation treated with NAC. They underwent total or partial mastectomy with SLNB followed by ALND regardless of result of SLNB. We compared with the results of SLNB and ALND, and analyzed clinical factor for predicting of ALN status.

Results: Overall, the median number of sentinel lymph nodes retrieved was 6 (range 1-11). In 61 women with breast cancer, 41 (67.2%) had at least 2 SLN-metastasis and 18 patients showed the negative SLN. Two patients of 20 patients with negative SLN had 1 ALN metastases after ALND. The false-negative rate and accuracy of SLNB were 10.0%, and 96.7%, respectively. In 20 patients with negative SLN, 19 patients revealed clinically negative ALN and 1 patient still had clinically positive ALN. Pathologic tumor response after NAC was significantly associated with negative ALN ($p = 0.045$).

Conclusion: Although it was considered carefully that negative SLN could be used for predicting of ALN status in breast cancer patients with clinically positive ALN at presentation treated with NAC, ALND could be omitted after the negative results of SLNB in the patients with clinically negative ALN and pathologic tumor response of breast cancer after NAC.

PO083

Immediate Nipple Reconstruction as Oncoplastic Breast Surgery: The 'Cigar Roll' Flap with Inner Dermal Core

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Background/Purpose: A wide variety of techniques have been described in the creation of a new nipple, which means that no single technique is entirely satisfactory. The most common problem following reconstruction is a postoperative loss of projection, which result in flattening of the reconstructed nipple. Despite various techniques available for nipple reconstruction, a simple and reliable method that maintains nipple projection remains elusive. We introduce a simple and feasible method for immediate nipple reconstruction 'cigar roll flap with inner dermal core technique', which expected to maintain long-term nipple projection.

Methods: Rectangular shaped "V" flap are raised at the superficial subcutaneous level. The overlying epidermis on the both ends of the V flap(long and short arm) was deepithelialized very thinly. The free end of deepithelialized long arm was holded with a atraumatic tissue forcep then was wound around the forcep. Then deepithelialized portion of the short arm was folded into the nipple center, inside of the rolled dermis. As a result, two arms of the V flap created a foundation and dermal core of the new nipple.

Results: Mean nipple projection at the time of surgery was 1.1 cm (range, 0.9-1.5 cm). After radiation therapy (average 8 months postoperatively), the mean projection was 1.0 cm (range, 0.7-1.2 cm). The preservation of nipple projection is the percentage of projection at average 8 months in relation to the projection immediately after the reconstruction. Mean maintenance of nipple projection was 83.7% (range, 75.0-92.3%). In our series, no immediate or delayed postop erative major complications. Our patients have been satisfied with the 3-dimensional projection of the nipple.

Conclusion: The 'cigar roll flap with inner dermal core technique' is a simple and reliable method for immediate nipple reconstruction. This technique maintains constant projection without major complication or any donor-site morbidity.

PO084

Arm Node Preserving Surgery in Axilla: 3 Year Experience

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Background/Purpose: We hypothesize arm node preserving surgery using axillary reverse mapping (ARM) during axillary lymph node dissection (ALND) reduce the incidence of lymphedema without increasing risk of recurrence.

Methods: From January 2009 to May 2014, 135 breast cancer patients were underwent ARM. 121 patients had their arm node preserved (ANP) and 14 patients had their arm node removed (ANR). The ipsilateral and contralateral upper arm circumference were measured pre- and post-operatively for 2 years. Circumference difference (CD) between ipsilateral and contralateral upper arm of ≥ 2 cm was defined as lymphedema. Follow-up studies were checked every 6 months for 5 years and then annually using ultrasound, mammography and/or PET.

Results: The mean follow-up period was 41.10 ± 20.13 months. The last measured CD was 0.168 ± 0.65 cm in ANP group and 0.85 ± 0.87 cm in ANR group ($p = 0.001$). Three cases of lymphedema were developed, only in ANR group (0% *vs.* 21.4%, $p = 0.001$). There were 7 patients complained whether they had lymphedema or not, 3 patients in ANP group and 4 patients in ANR group (2.5% *vs.* 28.6%, $p = 0.002$). But except 3 patients in ANR group, the others were below objective criteria of lymphedema. There were 10 cases of distant metastasis, 8 cases in ANP group, 2 cases in ANR group (6.6% *vs.* 14.29%, $p = 0.277$). Only one patient in ANP group had distant metastasis and ipsilateral axillary recurrence simultaneously, but TNM stage was already IIIc at the diagnosis. There was no solitary axillary recurrence.

Conclusion: Arm node preserving surgery during ALND can reduce the incidence of lymphedema and it simultaneously has oncological safety.

PO085

Retrospective Study of Immediate One-Stage Implant Breast Reconstruction

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Background/Purpose: As incidence rate of breast cancer has recently increased, more attention has been paid to breast reconstruction. Most patients want breast reconstruction after mastectomy. The authors studied morbidity and safty of implant breast reconstruction, retrospectively.

Methods: From July 2011 to December 2014, 53 patients were underwent one stage immediate breast reconstruction. Among the patients, 51 patients were underwent reconstruction using cohesive silicone gel-filled breast implant and 2 patients were underwent reconstruction using latissimus dorsi muscle flap. Among 51 patients who underwent implant breast reconstruion, 19 patients were treated nipple-saving mastectomy and 13 patients needed contralateral breast reduction or matopexy. We studied compliation and additional operation time due to reconstruction

Results: The mean implant volume was 245.97 g (range 120-435 g). Including contralateral breast reduction or mastopexy, the mean additional operation time due to reconstruction was 24.85 minutes (range, 10-150 minutes). The mean operation time of implant breast reconstruction only was 14.82 minutes (range, 10-20 minutes). Complication were developed in 6 patients. Nipple necrosis was most common complication and were developed in 4 patients. 1 patient developed infection and 1patient complained pain. Because complication, no one was delayed chemotherapy.

Conclusion: The incidence rate of complication was low and additional operation time due to reconstruction was acceptable. But, additional long-term safty studies are needed.

PO086

Patterns of Breast Reconstruction and Oncologic Outcomes of Breast Cancer Patients: Single Institute Analysis

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Background/Purpose: Breast reconstruction has cosmetic advantage and also oncologic safety to breast cancer patients who need mastectomy. We aimed to analysis the patterns of breast reconstruction and prognosis.

Methods: We performed retrospective review of breast cancer patients who had breast reconstruction from 2003 to March 2014 in our institute. We excluded the oncoplastic surgery for the partial breast resection and reconstruction for the non-epithelial originated breast tumor.

Results: Total patients were 85 cases; immediate reconstruction was 67 cases (78.2%) and delayed reconstruction was 18 cases (21.8%). Among immediate reconstruction group, 41 patients had reconstruction with transverse rectus abdominis myocutaneous (TRAM) flap, 19 patients had lattisimus dorsi (LD) flap, 6 had implants, 1 had LD with implant. Post-operative complications were occurred in 8 patients, which included flap necrosis, hematoma, seroma, ventral hernia and capsule formation. In patients who had adjuvant chemotherapy, only 4 had post-operative complications and all these patients started chemotherapy within 3 weeks. Mean duration between operation and chemotherapy was 27.7 days. Recurrences were noted in 3 patients; two were distant metastases, one was axillary nodal recurrence. Five year-disease free survival for immediate reconstruction was 93.8%.

Conclusion: Immediate reconstruction using autologous graft is commonly used after mastectomy in our institute and did not affect the initiation of chemotherapy. Further evaluation of cosmetic result after long term follow-up would be needed.

PO087

Our Experience of Surgical Treatment for Metastatic Breast Cancers

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Background/Purpose: The prognosis of patients with metastatic breast cancer is in general very poor, despite of the improvement of the diagnostic modalities and chemotherapy. The 5 year survival rate from the national cancer database has been reported to be 15% and the median survival rate is 8-24 months. The "toilette" mastectomy on the metastatic breast cancers after palliative chemotherapy is still controversial. Thus, we present the surgical treatment outcomes for the metastatic breast cancers.

Methods: We analyzed 7 patients with metastatic breast cancers underwent chemotherapy and surgery between August 2000 and October 2013. We analyzed characteristics, hormonal receptors status, relapse, and overall survival among those patients. We evaluated the treatment outcomes based on relapse-free survival and overall survival. The surgical interventions were undertaken to stable disease and remission of distant metastasis after chemotherapy for control local results. In other words, the mastectomy was undertaken only when the initial metastatic lesions regressed by chemotherapy.

Results: A total of 7 cases were included, and mean age of this group was 50.4 years old (range 34-73). The mean follow up is 51.8 months, and the average size of mass was 3.77 cm. On immunohistochemistry, there were 2 negative hormonal receptors, 2 overexpressions of HER2, and 1 triple-negative feature. The median relapse free survival was 36.1 months (range 10-68). The overall survival is 51.8 months (range 11-90). In this study, most common metastatic sites (n = 7) were the bone, and there were 1 liver metastasis and 1 multiple metastasis including lung, brain, and bone metastasis.

Conclusion: The treatment for the metastatic breast cancers is that palliative chemotherapy, and breast surgery (mastectomy) is performed only if stable disease. When the palliation with systemic therapy produced the remission of the metastatic lesions or maintained the minimal metastatic lesion (bone metastasis), aggressive local therapy provided survival advantages, such as mean relapse free survival and overall survival.

PO087

In this study, the aggressive local therapy (mastectomy) could be improved the quality of life as well as the survival despite of the overall prognosis of the metastatic breast cancers is still poor.

PO088

Long-Term Follow Up Results and Recurrent Pattern of Nipple-Areolar Complex Skin Sparing Mastectomy

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Background/Purpose: Preservation of nipple-areolar complex (NAC) is helpful to keep more natural breast shape, but, can cause anxiety about local recurrence. This study reviewed long term follow-up result of nipple-areolar skin sparing mastectomy (NASSM) compared with skin sparing mastectomy (SSM), retrospectively.

Methods: This study included 272 primary breast cancer patients who received NASSM (178 patients) or SSM (94 patients) except bilateral breast cancer from September 1996 to December 2008. Frozen section was conducted for analysis of NAC resection margin status. In case of positive resection margin, NAC was sacrificed. The mean follow-up was 94.9 months.

Results: The patients in NASSM group tended to have more worse disease free survival than those in SSM group (75.3% *vs.* 86.2%, $p = 0.087$). But, in analysis of only local recurrence including NAC, there were 24 cases (13.5%, 7 in skin flap and 17 in NAC) of local recurrence in NASSM group and 8 (8.5%) in SSM group. There was no cliniopathologic differences between skin flap recurrent patients and NAC recurrent patients in NASSM groups. Young age (≤ 35) was the only factor affecting recurrence in NASSM group ($p = 0.001$). There was no distant recurrence after surgical treatment for local relapse in NASSM group. There was no significant difference for the overall survival between NASSM and SSM group (97.8% *vs.* 96.8%, $p = 0.556$).

Conclusion: In this study, result of long term follow up showed that patients in NASSM group tend to have more local recurrence than patients in SSM group, even if there is no statistically significance. However, surgically well-controlled local recurrence of skin flap and/or NAC did not affect on overall survival. NASSM is alternative method for SSM with oncological safety and better cosmetic outcome.

PO089

Idiopathic Granulomatous Mastitis: A Report of 8 Cases Successfully Treated by Vacuum Assisted Biopsy Method

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Background/Purpose: Idiopathic granulomatous mastitis (IGM) is apprised of a rare chronic inflammatory breast disease with unknown etiology. But, practically we face with young women including pregnant women with IGM at local clinic, infrequently. Besides, treatment of IGM remains obscure, controversy. Commonly known treatment of IGM is corticosteroids, immunosuppressant, antibiotics, abscess drainage, surgical excision. Particularly, steroids and surgical excision are known with effective treatment among others but both have weakness. Steroids demonstrates several side effects and require long periods, while surgical treatment has been reported recurrence rates of 5-50% and cosmetic fault.

Methods: Considering to majority of patients are young women of childbearing age, treatment of IGM needs to ensure good cosmetic result, low recurrence rate and safety. Eight patients with a mean age of 33 years (range 23-44) were treated by vacuum assisted biopsy (Mammotome) from Jan to July 2014 ,5 cases of them had been in addition to steroids treatment before and after. 1 patient was 7 month pregnancy in treatment periods. All cases were pathologic diagnosed by core needle biopsy before treatment. Six cases presented with palpable lesion, 2 cases only painful lesion.

Results: Treatment periods ranged from 2 weeks from 34 months. Clinical manifestation is variable from a single mass like abscess pocket to multicentric abscess pockets. In 2 cases tried to only vacuum assisted excision, one case is a painful small focus abscess like mass and other case is three masses with 3 cm abscess pockets. One pregnant women experienced frequent relapse for all steroid treatment and surgical drainage duration 30 months .During pregnant periods 4th relapse was attacked, surgical drainage was not effective and finally vacuum assisted excision was tried and good results. Totally 4 cases were treated to steroids addition to after vacuum assisted excision duration from 1 months to 3months. All cases were no symptomatic duraion observation periods (4-12month).

Conclusion: We tried to find a way to conserve a breast safely. So we suppose carefully that Vacuum assisted excision method is useful in some IGM cases.Thoroughly Mammotome is a minimal invasive procedure method under local anteshsia. It is probable that complete resection of abscess pocket without unnecessary damage. Proper surgical management is shortening the steroids dosage and periods. Therefore, steroids side effects is minimized and patient life quality is enhanced. In early IGM case, vacumm assisted excision can be a single perfect method and in pregnant women selectively available.

PO090

Effects of Full Quilting in Preventing Seroma After Latissimus Dorsi Musculocutaneous Flap

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Background/Purpose: Latissimus dorsi musculocutaneous flap (LDMCF) is a commonly used technique for breast reconstruction following breast-conserving surgery, but in conventional surgery, it was hard to make full quilting. However, 1you can perform full quilting at donor site, if you put out the latissimus dorsi muscle (LD) through axillary incision. The aim of this study is to evaluate the effect of full quilting at donor site on seroma formation.

Methods: Between July 2014 and December 2014, a total of 72 patients with breast cancer underwent immediate breast reconstruction with LDMCF. Patients were divided into Group A, in which full quilting and a closed suction drain were used, and Group B, in which half quilting and a closed suction drain were used. We compared age, BMI, drain removal time and incidence of postoperative aspiration.

Results: In Group A, duration of drain were significantly reduced ($p < 0.05$). However, the incidence of postoperative aspiration was not different between Group A and Group B ($p = 0.11$).

Conclusion: The full quilting technique reduces the duration of drain and may help prevent of seroma after LDMCF.

PO091

Patterns of Management and Outcome of Elderly Breast Cancer Patients Aged ≥ 70 Years

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Background/Purpose: The population of breast cancer patients over the age of 70 has been increased as elderly people increasing. The management of breast cancer in the elderly has not been properly provided with reasons like comorbidities and short remaining life. There is little research regarding the decision support needs of older patients faced with this choice. The aim of this study was to review given treatment and the outcomes in elderly breast cancer patients, as useful data to make an appropriate decision of treatment.

Methods: We identified consecutively 377 women with primary invasive breast cancer who underwent surgical resection at the National Cancer Center (Goyang, Korea) between April 2001 to November 2014. Clinicopathologic data obtained from prospective collecting medical database of our institution were analyzed retrospectively. We evaluated the disease free survival and overall survival after surgical treatment.

Results: Median follow up time was 66 months. During this period, 55 patients had died. Among them, breast cancer specific mortality was in 22 patients. Another five women had died with other primary malignancies. We could find disease relapse in the last medical records of ten patients who died with unknown cause, but they or their family wanted no further treatment or transfer to other hospital. During follow-up loss period after their last visit, they would have died with breast cancer related cause. Chemotherapy was performed in 37.7% of patients. Total relapse was in 19 cases (4 local recurrences, 15 systemic metastasis). 5 year disease free survival was 79 months (rate 62.1%) and the 5 year overall survival was 84 months (rate 68.6%).

Conclusion: Compared to the young patients, although the overall survival of elderly breast cancer patients was not good and the rate of recurrence or death related with breast cancer was high. But they could not receive proper disease management for various reasons, especially their old age. Even if evidences about the treatment of breast

cancer in elderly are still controversial, each patient deserves a multidisciplinary approach to discuss the best treatment option.

PO092

Planned Skin Incision of Non-Reconstructive Skin Sparing Mastectomy for Advanced Breast Cancer

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Background/Purpose: One of the causes that have been reluctant to initially consider surgery in locally advanced breast cancer was the concern of the become unnecessarily extensive surgery. In classic modified radical mastectomy (MRM) design, resection area was excessively large not only for primary lesion with safe margin, but also was the included skin within elliptical design. We propose non-reconstructive skin sparing mastectomy (NR-SSM) to minimize the incidence of additional skin graft or flap surgery through modification of incision design, measurement of objective length and it's adjustment.

Methods: Three clinical parameter, breast circumference, chest circumference and Breast height were measured on sitting position. Available skin length was calculated by using the Pythagorean Theorem. Three steps of Adjustment protocol were applied.

Results: We compared skin incision of steward method and our method in classic MRM cases for its reliability in 60 cases. We are 95% confident that the mean difference between measurement by classic & calculated method is between 1.7 to 2.46cm would be wider at calculated method. We presented how we applied our method in Planned Skin Incision

Conclusion: New method using calculation offers more available skin length resulting in minimized additional skin graft or myocutaneous flap (MCF) incidence for pure defect coverage by adjusting skin incision design. This method also has other benefit in deciding skin islet size for inevitable skin graft or MCF in far advanced cases.

PO093

What's New in the 6th Korean Breast Cancer Treatment Guideline?

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Background/Purpose: A guideline is a statement by which to determine a course of action. A guideline aims to streamline particular processes according to a set routine or sound practice. Guidelines could lose, however, their clinical relevance as they age and newer research emerges. The purpose of this presentation is to review, evaluate and discuss if the new findings are appropriate for 6th revised edition of KBCS guideline.

Methods: Korean Breast Cancer Guideline Working Group has 5 sub-committee. Each subcommittee has multi-professional members. Each subcommittee selected topics with a systematic, independent and transparent fashion and send manuscripts to executive committee. Executive committee prioritize topics based on epidemiology of health problems, emergence of new technologies or other factors creating needs for high quality, updated information after 5th edition was announced, the year 2013.

Results: 1th subcommittee for in situ carcinoma found that there are considerable evidence for the patient with lobular carcinoma and interesting report about radiation therapy for ductal carcinoma *in situ*. 2nd subcommittee for early breast cancer found substantial new data about the surgery of the axilla in case of primary breast cancer and after preoperative chemotherapy. In addition, they also found informative data about systemic therapy and radiotherapy 3rd subcommittee for advanced breast cancer, 4th committee for metastatic breast cancer and 5th subcommittee for hereditary breast

cancer found practice changing evidence for patient with breast cancer and the new findings will be discussed in detail.

Conclusion: We respect the clinician's choice after careful consideration of all possibilities, because statistically correct treatment standards could be wrong for a minority of patients and that some knowledgeable physicians may choose to vary their care away from advised standards in a way that may benefit particular patients. What we guard physicians against is straying from accepted norms because of incomplete knowledge of state-of-the-art standards, which we, members of 6th Korean Breast cancer treatment guideline wish to help physicians to stay in.

PO094

Cosmetic Outcomes and Patients' Satisfaction of Oncoplastic Surgery in Korean Patient with Breast Cancer

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Background/Purpose: Oncoplastic surgery (OPS) has emerged as the latest ideal surgery in treatment of breast cancer. The goal of modern OPS is to maintain postoperative breast contour as normal looking as possible. The purpose of this study is to evaluate the cosmetic outcome of volume displacement surgery and patients' satisfaction in Korean women with relatively small breast size.

Methods: This is a retrospective study of 173 patients who had volume displacement of OPS at Busan Paik Hospital, Inje University during 2008-2013. Cosmetic outcome was evaluated by a doctor who didn't participate in the actual surgery. He inspected the operation site either at the outpatient clinic during the patients' follow-up or via photographs. The evaluation was recorded on a scale of good, fair and poor. The level of patients' satisfaction was assessed by a questionnaire divided into four categories; cosmetic satisfaction, satisfaction on operative method, femininity, and side effects.

Results: 57% of patients were cosmetically satisfied; only 5% were unsatisfied. The satisfaction rate on operative method was 65% in comparison with 9% unsatisfied patients. Femininity showed 34% of confidence and 17% with less confidence. The rate of side effect was 81% of very little side effect and 10% with considerable side effects. The cosmetic score by the doctor was 72% as good, 25% as fair and 3% as poor. Most patients preferred good contour over short scar regardless of age and marital status (good contour 54% vs short scar 21%).

Conclusion: Volume displacement of OPS brings both the best possible cosmetic outcome and high patient satisfaction for Korean women with a small size of breast in breast cancer surgery. It is highly suggestive that Korean women considers good contour more than the size of scar; therefore, volume displacement of OPS is a recommendable means of breast cancer surgery for Korean women.

PO095

Methods in Defining Margin Outside of Skin in IMRT for Breast Cancer

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Background: Patient movement, inaccurate patient positioning, and respiratory organ motion cause uncertainty of target position during the course of radiation therapy. Conventionally, 2.5 cm margin from the skin needed for whole breast radiation therapy to compensate the uncertainty of target position. In order to perform the Intensive Modulation Radiation Therapy (IMRT), adequate margin should be defined outside of the breast. But there is a limitation on fluence map optimization in IMRT, when we define the margin in the air. In this study, the practical methods to overcome the limitation are introduced and evaluated to apply IMRT for breast cancer.

Methods: Computed tomography (CT) images of a case of breast cancer were selected to compare the plan results. Various IMRT plans with the same gantry angles were created. There are two methods to define the margin in IMRT planning. One is expanding the fluence map manually to the outside of the skin. The other is generating fluence map from virtual target to the outside of the skin. The plans with/without intentional setup errors were created and compared each other.

Results: The conformity index of the dose distribution for the IMRT plans with enough margins were greater than with no margins to the outside when intentional setup errors were applied.

Conclusion: Due to respiratory motion-range the skin margin of breast is required greater than 1 cm to minimize the dosimetric errors in IMRT. The both methods for defining margin for IMRT planning in this study were feasible.

PO096

Memory Loss and Menopause Symptoms Among Pre-Menopause Breast Cancer Patients

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Background/Purpose: Pre-menopausal young breast cancer survivors are vulnerable to short term memory loss due to cancer therapy. Moreover, this cognitive impairment lasts for a long time resulting in depression, anxiety, and sleep disturbance. We examined changing patterns of cognitive functions from diagnosis to 3 year after surgery in pre-menopause breast cancer patients. We compared menopause symptoms between patients who regain cognitive function after completion of active treatment and who did not.

Methods: Between July 2010 and July 2011, 278 non-metastatic pre-menopausal breast cancer patients were recruited from two cancer hospitals in Seoul, Korea. Memory loss were assessed as a part of quality of life using European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-C30 (EORTC QLQ-C30) and menopause symptoms was evaluated using menopause symptoms scale (MRS) before surgery, 2 weeks, 3, 6, 12, 24, and 36 months after surgery. Multivariate analysis was performed to find association between patterns of cognitive impairment and MRS using STATA 13.

Results: Of total, 170 (61.2%) were followed up to 3 years after surgery, and their mean age was 42.7 Among them, 41.1% of the patients' cognitive function was not recovered at 3 years after surgery compared to 6 months after surgery when patients' cognitive function was most deteriorated. Clinical characteristics of patients' whose cognitive

function was not recovered (NR) were similar to patients whose cognitive function was recovered (R). The NR were more likely to experience menopause symptoms ($p = 0.04$) compared to the R. There was statistical difference with psychological symptoms between the groups ($p < 0.01$).

Conclusion: Almost half of young breast cancer patients experience cognitive impairment due to cancer treatment, and it is associated with severer menopause related psychological symptoms such as depression, anxiety and sleep disturbance. It is necessary to develop tailored intervention for young breast cancer patients who would experience both cognitive impairment and menopause related psychological distress.

PO097

Effect of Postmastectomy Radiotherapy in Breast Cancer Patients with One to Three Positive Lymph Nodes

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Background/Purpose: Postmastectomy radiotherapy (PMRT) was known to reduce the risks of both recurrence and mortality in breast cancer patients with more than or equal to four positive axillary lymph nodes. However, the effect of PMRT in breast cancer patients with pT1-2 and pN1 is still controversial. We aimed to examine the benefit of PMRT for patients with pT1-2 and pN1.

Methods: We conducted propensity score matching with eligible 1244 patients receiving mastectomy during 1991-2010 in Severance Hospital and Gangnam Severance Hospital. Propensity scoring was based on age, tumor stage, number of positive axillary nodes, estrogen receptor, progesterone receptor, and histologic grades. Kaplan-Meier survival analysis and Cox-regression analysis were used to compare locoregional recurrence free survival (LRFS), relapse free survival (RFS), breast cancer specific survival (BCSS), and overall survival (OS) according to PMRT.

Results: After propensity scoring, each group according to PMRT was allocated 196 patients with median follow-up 75 months (Range 6-227 months). PMRT improved LRFS (HR = 0.30; 95% CI, 0.13-0.70; $p = 0.005$), but did not significantly improve RFS, BCSS, and OS. In multivariate analysis, PMRT was an independent factor for LRFS. In subgroup analysis, the benefit of PMRT for LRFS was in patients with two to three positive axillary nodes.

Conclusion: We showed that improved LRFS by PMRT did not confer significant survival benefit regarding BCSS and OS for breast cancer patients with pT1-2 and pN1 after propensity score matching. However, PMRT can be used to reduce locoregional recurrence in breast cancer patients with 2-3 positive axillary nodes.

PO098

Incidence of Febrile Neutropenia in Asian Female Patients with Breast Cancer Receiving Pre- or Postoperative AC Followed by Docetaxel Chemotherapy

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Background/Purpose: Based on the chemotherapy regimen and patient-related risk factors, many guidelines recommend prophylactic use of Granulocyte-colony stimulating factor (G-CSF) for overall high-risk group (incidence of febrile neutropenia greater than 20%). Pre- or post-operative doxorubicin/cyclophosphamide for 4 cycles followed by docetaxel for 4 cycles are frequent used regimen in worldwide. National Comprehensive Cancer Network (NCCN) guideline categorized this regimen as "intermediate risk of febrile neutropenia", but the incidence of febrile neutropenia is various from 5% as much to 40%. So we investigated the incidence of febrile neutropenia in Asian women patients who received this regimen.

Methods: From Sep 2010 and Feb 2013, 200 female breast cancer patients who received preoperative or postoperative AC followed by docetaxel chemotherapy were enrolled (100 patients in preoperative and 100 patients in postoperative chemotherapy). Febrile neutropenia is defined as neutropenia (< 500 neutrophils/mcl or < 1,000 neutrophils/mcl over the next 48 hr) with febrile event (> = 38.3°C orally or > = 38.0°C over 1 hr). Incidence of protocol-defined febrile neutropenia in each cycle, febrile neutropenia related hospitalization requiring intravenous antibiotics, febrile neutropenia with shock and death during chemotherapy were analyzed.

Results: Among 200 patients, 53 patients (26.5%) experienced febrile neutropenia including 27 patients in preoperative chemotherapy (27%) and 26 patients in postoperative chemotherapy (26%). Febrile neutropenia requiring hospitalization with usage of intravenous antibiotics occurred in 31 patients (15.5%; 15 patients from preoperative chemotherapy and 16 patients from postoperative chemotherapy). Febrile neutropenia with shock occurred in 5 patients (2.5%; 3 patients from preoperative chemotherapy and 2 patients from postoperative chemotherapy). No chemotherapy related death was de-

tected. Disease free survival and overall survival by experience of febrile neutropenia and relative dose intensity will be updated.

Conclusion: NCCN guideline recommends individualized consideration of G-CSF use in conventional AC followed by docetaxel chemotherapy. However, the incidence of febrile neutropenia in this regimen was analyzed mostly in Western breast cancer patients and there are few data in Asia patients. Experience of febrile neutropenia can result in reduction of relative dose intensity leading to increased risk of recurrence and disease related death. Thus, large prospective study is required to assess the accurate incidence of febrile neutropenia in Asia patients and validity of prophylactic G-CSF usage for maintaining relative dose intensity.

SPARC Expression in Phyllodes Tumors of the Breast

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Background/Purpose: Secreted protein acidic and rich in cysteine (SPARC) plays a crucial role in the process of tumor invasion and metastasis in some tumors. Our aim was to assess the expression of SPARC in phyllodes tumors (PTs) and to determine its association with the grade, clinical behavior, and matrix metalloproteinase (MMP)-2 and -9 expression of PTs.

Methods: Eighty-two PTs (50 benign, 22 borderline, and 10 malignant) were analyzed. Automated immunohistochemical staining for SPARC, MMP-2, and MMP-9 was performed using tissue microarray blocks, and their expression was assessed in the stromal components.

Results: Stromal SPARC expression was positive in 19 (38.0%) benign PTs, 18 (81.8%) borderline PTs, and 9 (90.0%) malignant PTs. The percentage of recurrence was higher in the SPARC-positive group (17.4%) than in the SPARC-negative group (2.8%), however, the difference was not statistically significant. Expression of SPARC correlated with MMP-2 and MMP-9 expression ($p < 0.05$ and $p < 0.01$, respectively).

Conclusion: SPARC expression in PTs was associated with the grade, and correlated with MMP-2 and MMP-9 expression. These results indicate that SPARC-mediated degradation of the extracellular matrix, and its possible association with MMPs, may contribute to the progression of PTs.

PO100

Myofibroblast Activated by SPIN90 Deficiency Promotes Cancer Invasion and Metastasis by Remodelling Microenvironment

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Background/Purpose: Cancer stroma is remodeled by a cancer-associated fibroblast, which is an 'activated' fibroblast stimulated by cancer cells. Tumor-stroma interactions play a crucial role in cancer progression but it has not been fully understood yet. we demonstrate the novel function of SH3 Protein Interacting with Nck(SPIN90) which inhibits activation of fibroblast in 3D collagen matrices and modulates cancer metastasis by remodeling extra cellular (ECM) composition

Methods: Mouse embryo fibroblast (MEF) cells were embedded in collagen matrix and MDA-MB-231 cells were seeded on the matrix. Images of H&E staining were displayed. Invasion of MDA-MB-231 cells into collagen gel matrix was quantified by Metamorph program and Invasion index was calculated. Conditioned media of SPIN90+/+ and SPIN90-/- MEFs was analyzed by Mass

Results: SPIN90-/-MEFs displayed prominent enlargement of vinculin positive focal adhesions and increased expression and activation of focal adhesion kinase (FAK). SPIN90-/-MEFs highly expressed a smooth muscle actin (SMA). SPIN90 deficient myofibroblasts promoted ivasion of MDA-MB-231 cells and long distant metastasis of B16F10 mouse melanoma to lung was increased in SPIN90-/- mice. extra domain A-containing fibronectin increased by SPIN90 deficiencywas an essential modulator of invasion of cancer cells.

Conclusion: that SPIN90 may play a critical role in the myofibroblast differentiation and negatively regulates cancer progression, which may provide the insight for understanding the mechanism of cancer progression in cancer microenvironment.

PO101

Relationship Between Inflammation and Breast Cancer Stem Cell Phenotype

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Background/Purpose: There is increasing evidence that inflammation and cancer stem cells mediate tumor growth and metastasis. Recently some immune mediators have been reported to influence breast cancer stem cell biology. However, most of previous studies were pre-clinical studies. In this study, we evaluated relationship between inflammation and breast cancer stem cell phenotype in human breast cancer tissue.

Methods: Immunohistochemical staining for CD24, CD44, CD4, CD8 and CD68 was performed using tissue microarray blocks. Breast cancer stem cell was defined as CD44+/CD24- tumor cell. The levels of inflammatory modulators and cytokines including TNF-α, IL-2, IL-4, IL-6 and interferon-γ were assessed by the levels of RNA transcripts in frozen tissue using RT-PCR. Intratumoral or peritumoral lymphocyte infiltration was also assessed.

Results: The CD44+/CD24- phenotype was inversely associated with lymph node metastasis. The CD44+/CD24- phenotype was associated with molecular subtype of breast cancer and especially more abundant in basal-like subtype. The prevalence of CD44+/CD24- tumor cells was associated with intratumoral inflammation and tumor-infiltrating CD4+ T cell counts. Tumor-infiltrating CD4+ T cells were increased in patients with basal-like subtype of breast cancer.

Conclusion: In this study, significant associations were found between inflammation and stem cell phenotype in breast cancer. The results suggest that the interaction between inflammation and cancer stem cells may affect tumorigenesis and progression along the stages of breast cancer. Further studies are needed to clarify the role of inflammation and cancer stem cells in breast cancer.

PO102

Aurora Kinase is Essential for Protein Kinase C Induced Invasion and Matrix Metalloproteinase-9 Expression in MCF-7 Breast Cancer Cells

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Poster Exhibition

Background/Purpose: The Aurora kinase family of serine/threonine kinases has been known to be crucial for cell cycle control. And Aurora kinases recently have been focused as a target of anticancer drugs. However, few studies have assessed the effect of Aurora kinases in breast cancer. This study investigated that the molecular mechanisms of Aurora kinases on carcinogenesis using breast cancer.

Methods: We used MCF-7 breast cancer cell line and cell viability assay was performed by using MTT assay. Phosphorylation and expression of Aurora kinases were assessed by Western blotting. We performed electrophoretic mobility shift assay (EMSA), Reverse transcription-Polymerase chain reaction (RT-PCR), invasion, and migration assay for elucidating the regulatory mechanisms of Aurora kinases.

Results: Treatment of MCF-7 cells with 12-O-tetradecanoyl phorbol-13-acetate (TPA) induced up-regulation and phosphorylation of Aurora kinases via mitogen activated protein kinase (MAPK) signaling pathway. And the inhibition of Aurora kinases by their siRNAs and inhibitors suppressed TPA-induced cell invasion and expression of Matrix metalloproteinase-9 (MMP-9) through inhibiting activation of NF-κB/AP-1 in MCF-7 cells.

Conclusion: These results suggest that Aurora kinases mediate PKC-MAPK signal to NF-κB/AP-1 with increasing MMP-9 expression and invasion of MCF-7 cells. This is the first study showing that Aurora kinases are key molecules in protein kinase c (PKC) induced invasion in breast cancer cells.

Radiosensitization with Combined Use of Olaparib and PI-103 and Underlying Mechanism in Triple-Negative Breast Cancer

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Background/Purpose: Triple-negative breast cancer (TNBC) shows aggressive clinical behavior, but the treatment options are limited due to lack of a specific target. Recent study showed that phosphoinositide 3-kinase (PI3K) inhibition impairs *BRCA1/2* expression and sensitizes *BRCA*-proficient TNBC to poly (ADP-ribose) polymerase (PARP) inhibition. Therefore, we assessed the radiosensitizing effect, and the underlying mechanism of combination treatment with PARP inhibitor and PI3K inhibitor in *BRCA*-proficient TNBC cells.

Methods: MDA-MB-435S cells were divided into four treatment groups, irradiation (IR) alone, olaparib plus IR, PI-103 plus IR, and olaparib plus PI-103 plus IR. The cell survival curve was obtained using a clonogenic assay. Western blotting and immunofluorescent detection of γH2AX foci were performed. Xenograft and bioluminescence imaging were carried out to assess in vivo radiosensitivity.

Results: Combined use of olaparib and PI-103 enhanced radiation-induced death of MDA-MB-435S (sensitizer enhancement ratio [SER] 0.05, 1.7) and MDA-MB-231-BR (SER0.05, 2.1) cells and significantly reduced tumor volume in a xenograft models ($p < 0.001$). Treatment with PI-103 showed persistent γH2AX foci, indicating delayed repair of DNA strand breaks. PI-103 alone increased levels of poly (ADP-ribose) and phosphorylated extracellular signal-regulated kinase, and downregulated *BRCA1*.

Conclusion: Combined use of olaparib and PI-103 enhanced radiation-induced cell death in cells and xenografts. Targeting of the PI3K signaling pathway combined with PARP inhibition maybe a feasible approach to enhance effects of radiation in *BRCA*-proficient TNBC.

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uPA and PAI-1 Expression in Breast Cancer

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Background/Purpose: The ain evaluate urokinase-type plasminogen activator (uPA) and plasminogen Activator Inhibitor-1(PAI-1) expression as reliable prognostic markers for breast cancer patients.

Methods: We analyzed the demographic and clinicopathological parameters of 214 breast cancer patients diagnosed and treated from 2006 to 2010 at Kangbuk Samsung Hospital. We used immunohistochemistry as a detection method.

Results: Age at diagnosis, history of hormone replacement therapy, radiation therapy, skin/chest wall invasion, Paget disease, lymphovascular invasion, estrogen receptor positivity and triple negative subtype had statistically significant influence on patients' prognosis. Ductal carcinoma *in situ* (DCIS) group had higher PAI-1 expression than invasive ductal carcinoma group, respectively, 94% and 63%. Positive correlation between uPA and PAI-1 was observed.

Conclusion: In conclusion, it is possible that PAI-1 could play some role in tumor progression in early stage of breast cancer such as DCIS. A statistical correlation between lymph node metastasis implies that uPA/PAI-1 by immunohistochemical evaluation could be used for prognostic factor in breast cancer patients.

PO105

Synergistic Effect Between Celecoxib and Luteolin is Dependent on Estrogen Receptor in Human Breast Cancer Cells

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Background/Purpose: The anticancer effects of celecoxib and luteolin are well known. Although our previous study demonstrated that the combination of celecoxib and luteolin synergistically inhibits breast tumor growth compared with each of the treatments alone, we did not uncover the molecular mechanisms of these effects. The aims of our present study were to compare the effects of a celecoxib and luteolin combination treatment in four different human breast call lines and to determine the mechanisms of action *in vitro* and in vivo.

Methods: We analyzed cell proliferation, cell death, apoptosis, and changes in protein expression by performing cell survival assays, apoptosis assays and Western blotting in vitro. Furthermore, we used a nude mouse xenograft model to assess the anticancer efficacy of celecoxib and luteolin as mono-therapies or as a combined therapy *in vivo*.

Results: The synergistic effects of a celecoxib and luteolin combination treatment yielded significantly greater cell growth inhibition in all four breast cancer cell lines compared with the single agents alone. In particular, combined celecoxib and luteolin treatment significantly decreased the growth of MDA-MB-231 cancer cells in vivo compared with either agent alone. The celecoxib and luteolin combination treatment induced synergistic effects via Akt inactivation and ERK signaling inhibition in MCF-7 and MCF7/HER18 cells and via Akt inactivation and ERK signaling activation in MDA-MB-231 and SkBr3 cells.

Conclusion: These results demonstrate the synergistic antitumor effect of the celecoxib and luteolin combination treatment in different four breast cancer cell lines, thus introducing the possibility of this combination as a new treatment modality.

PO106

Elevated TGF- β1 and - β2 Expression Accelerates the Epithelial to Mesenchymal Transition in Triple-Negative Breast Cancer Cells

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Background/Purpose: The epithelial-mesenchymal transition (EMT) is a key process in tumor invasion and migration. Transforming growth factor-βs (TGF-βs) are multifunctional growth factors and powerful modulators of the EMT. Here, we investigated the relationship between TGF-β expression and invasion by treated triple-negative breast cancer (TNBC) cells.

Methods: MCF-7, MDA-MB231, and Hs578T human breast cancer cells were grown in a humidified atmosphere of 95% air and 5% CO_2 at 37°C in DMEM supplemented with 10% FBS, 2 mM glutamine, 100 IU/mL penicillin and 100 mg/mL streptomycin. BT474 human breast cancer cells were grown in RPMI1640 media under the same conditions. To evaluate invasiveness of breast cancer cells, we analyzed the rates of invasion using the boyden chamber assay. Migratory cells were analyzed by wound healing assay. All proteins and mRNAs expression was analyzed by western blotting and real-time PCR, respectively.

Results: Invasion capacity of TNBC cells was markedly higher than that of non-TNBC cells. In addition, EMT-related gene signatures, including vimentin (vim), fibronectin (FN), snail, and slug were highly expressed in TNBC cells. Interestingly, TGF-β1 and β2 mRNA expression levels were higher in TNBC cells than those in non-TNBC cells. Thus, our data show that vim, FN, and slug mRNA expression levels dose-dependently decreased by LY2109761, TGF-β receptor I/II inhibitor. TNBC cell motility also decreased in response to LY2109761.

Conclusion: Taken together, we demonstrated that elevated TGF-β1 expression triggers invasion and migration by TNBCs through the EMT process. Inhibiting the TGF-β1 signaling pathway is considered a promising therapeutic strategy for treating TNBC.

A Combination of Metformin and Lapatinib Synergistically Induces Apoptosis in Human Breast Cancer Cells

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Background/Purpose: Metformin, a biguanide, is a widely used pharmaceutical agent in the management of type-2 diabetes. Moreover, metformin has been shown to have strong anti-cancer effect in many breast cancer cells. Lapatinib is a potent and selective oral dual receptor tyrosine kinase inhibitor of both epidermal growth factor receptor (EGFR) and human epidermal growth factor receptor 2 (HER2). In the present study, we show that a combination of metformin and lapatinib induces more extensive apoptosis than either drug alone in breast cancer cells.

Methods: The cellular glycolysis level was determined by measuring the lactate production. Cell viability and cell death were assessed by MTT assay and Annexin V-FITC/PI staining, respectively. Loss of mitochondrial membrane potential was examined by flow cytometry with JC-1 staining. Small interfering RNA (siRNA) was used for suppressing gene expression. The protein levels were measured by western blot analysis.

Results: Cell viability was reduced by metformin or lapatinib, in a dose-dependent manner. However, Cell death at 5 mM metformin or 10 μM lapatinib was about 15% and 10%, respectively. Combination of metformin and lapatinib drastically increased apoptotic cell death via loss of mitochondrial membrane potential. In addition, Metformin slightly increased AMPKα activity, whereas combination of metformin/lapatinib further increased AMPKα activity. Knockdown of AMPKα by siRNAs resulted in decreased cell death by metformin and lapatinib. These results indicate that AMPK plays a role during metformin/lapatinib - induced apoptosis in breast cancer cells.

Conclusion: Based on these findings, we propose that combination of metformin and lapatinib may be an effective strategy for sensitizing breast cancer cells.

PO108

Piperlongumine Regulates AKT/mTOR Signaling Pathway and Induces Apoptosis via Increased ROS

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Background/Purpose: Piperlongumine (PL) has been shown to selectively induce apoptosis in cancer cells via reactive oxygen species (ROS) accumulation. In this study, we investigated the regulatory mechanism of PL-induced apoptosis through regulation of Akt/mTOR signaling pathway.

Methods: Cell viability and cell death were assessed by MTT assay and Annexin V-FITC/PI staining, respectively. ROS generation was measured using the H2DCFDA. Small interfering RNA (siRNA) was used for suppressing gene expression. The mRNA and protein expression were analyzed by RT-PCR and western blot analysis, respectively.

Results: PL induces a dose and time dependent decrease in Akt and mTOR activity in breast cancer cells. Pretreatment with the ROS scavenger N-acetyl-cysteine resulted in a recovery of decreased Akt/mTOR activity and induced cell death by PL. Inhibition of Akt/mTOR by PL led to a marked decrease in the expression levels of the anti-apoptotic proteins Mcl-1 and survivin. Overexpression of Mcl-1 and survivin reduced PL-induced cell death, suggesting that down-regulation of Mcl-1 and survivin is involved in PL-induced cell death.

Conclusion: We suggested that PL-induced apoptosis involved AKT/mTOR pathway, which was regulated by increased intracellular ROS by PL.

A Case of a Breast Cancer with Pericardial Metastasis

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Background/Purpose: Primary tumours of the heart are rare. However, secondary or metastatic tumours of the heart are more common than primary tumours. The clinical diagnosis of malignant pericardial effusion is difficult because cardiac metastasis may be totally asymptomatic, or the symptomatology may be attributed to general manifestations of a widespread disease. Malignant pleural or pericardial effusion occurs in about a half of patients with breast cancer. We present a case of breast cancer with symptomatic pericardial metastasis 6 years after breast conserving surgery (BCS).

Methods: The patient's past medical history was significant for a left-sided breast conserving surgery (BCS) with left axillary lymph node dissection for invasive ductal carcinoma of the breast in 2009.The patient was staged as T3N2M0. Sentinel and axillary lymph nodes were positive. After operation, the patient was treated with TAC regimen (Taxane,anthracycline,cyclophosphamide), radiation therapy and hormone therapy. In March 2013, she was diagnosed the bone metastasis in the left ala of sacrum and started zometa therapy. In 2014, bone metastasis was progressed, zometa therapy was stopped and started afinito+aromasin therapy.

Results: In January 2015, 6 years after BCS, a 42-year-old woman with dyspnea and both leg edema was admitted to our hospital. On admission, the patient was afebrile and in a moderate degree of respiratory distress. Chest radiography revealed an cardiomegaly with both effusion. 2D-echo revealed large pericardial effusion with tamponade physiology. The patient was treated with pericardiocenteis and percutaneous catheter drainage (PCD) insertion.There was detected adenocarcinama in the pericardial fluid and she was made pericardiotomy operation in January 2015.

Conclusion: Metastatic diseases of the pericardium resulting from the breast are in unusual. This remarkable rarity makes successful treatment of breast cancer metastases to pericardium all the more challenging. Obviously, it is important to know that in cancer patients with symptoms of metastatic pericardial deposits must be considered in the

differential diagnosis. Clinicians should be concerned to the possibility of pericardial metastasis in a patient with and even without clinical symptoms. This case demonstrates that BCS, other oncological and surgical procedures are implemented for many years, but regular medical lifelong follow-up is mandatory.

PO110

Stem Cell Markers $CD44^{+}CD24^{-}$ and ALDH1 in Primary Breast Cancers and Metastatic Sentinel and Non-Sentinel Lymph Nodes

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Background/Purpose: Studies of Aldehyde dehydrogenase 1 (ALDH-1) and $CD44^{+}/24^{-}$ have suggested them as cancer stem cell (CSC) markers in breast cancers and the clinicopathologic and prognostic significance of these CSC markers have been widely investigated. However, expressions of CSC in metastatic axillary lymph nodes (ALN) of breast cancers seems not yet been the center of interest. Therefore, the object of this study is to explore breast CSC markers $CD44^{+}CD24^{-}$ and ALDH-1 in the primary breast tumor and metastatic ALNs by retrospectively analyzing their expressions on metastatic tumor cells within ALN.

Methods: 180 surgically resected breast cancers were selected and among them 165 cases had undergone sentinel lymph node (SLN) with or without non-sentinel lymph node (NSLN) dissections. 50 SLNs (30.3%) and 43 NSLNs (30.9%) had metastatic tumor cells and total of 74 cases were involved with ALN metastasis. Double immunohistochemistry of CD44/CD24 and single immunohistochemistry of ALDH-1 were applied on paraffin embedded breast tissue specimens and lymph node specimens to evaluate the CSC phenotypes of primary tumor and metastatic lymph nodes.

Results: The prevalence of CD44+/CD24- and ALDH-1(+) tumor cells in primary breast cancer was 76.7% and 45.0%. In triple negative breast cancers contained significantly higher percentage (49.2%) of ALDH-1 positive tumor cells ($p = 0.001$). CD44+/CD24- phenotype was present in 65.2% and 40.0% in metastatic SLNs and NSLNs, respectively. The analysis of metastatic SLN and breast cancers with CSCs indicated that there are significant relationships with ALDH-1(+) ($p < 0.001$) and CD44+/CD24- ($p < 0.001$) phenotypes. CSC expression in metastatic NSLNs and breast tumors also showed significant association ($p = 0.001$).

Conclusion: This study investigated the impact of the stem/progenitor phenotype de-

fined by CD44 positivity/CD24 negativity and ALDH-1 positivity in SLN on NSLN metastases. CSC phenotypes expressed in metastatic SLNs and NSLNs, independently showed significant association with the primary breast tumors. However, in future, the authors recommend that the exploration of a much larger study including a vast amount of pool will provide a more reliable result.

PO111

Dichloroacetate Potentiates Tamoxifen-Induced Cell Death through Epidermal Growth Factor Receptor Downregulation

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Background/Purpose: Cancer cells are characterized by reprogrammed glucose metabolism known as the Warburg effect or aerobic glycolysis, which is glucose converted to lactate even under sufficient oxygen tension. The generic drug dichloroacetate (DCA) is an orally available small molecule that, by inhibiting the pyruvate dehydrogenase kinase, increases the flux of pyruvate into the mitochondria, promoting glucose oxidation over glycolysis. Recently, several researches suggest that DCA might be a potential anticancer drug to a large number of diverse tumors. However, direct preclinical evidence of anticancer effects of DCA still has been investigating.

Methods: MCF7 breast cancer cell lines were grown in DMEM medium. We performed MTT assay, FACS anaylsis, siRNA transfection and Western blotting for individual purpose.

Results: In the present study, we unexpectedly found that DCA sensitized tamoxifen-induced cell death in MCF7 breast cancer cells by suppressing epidermal growth factor receptor expression. Furthermore, combined treatment of DCA and tamoxifen resulted in loss of cancer stem cells population of MCF7 cells accompanied with reduced nanog and c-myc protein levels.

Conclusion: In summary, our results show demonstrated that DCA is an attractive and potential drug to sensitize tamoxifen-induced cell death and overcome the tamoxifen resistance in breast cancer cells.

PO112

Expression of Metalloproteinases and Their Inhibitors in Different Molecular Subtypes of Breast Cancer

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Background/Purpose: Metalloproteinases (MMPs) and their tissue inhibitors of metalloproteinases (TIMPs) are involved in several key pathways of tumor growth, invasion and metastasis, but little is known about their expression according to different molecular subtypes of breast cancer. The aims of this study were to assess the prevalence and clinical significance of MMP and TIMP expression in invasive breast cancer and to determine its association with immunohistochemical-based molecular classification.

Methods: Tissue microarray sections were immunostained for estrogen receptor-α (ER-α), progesterone receptor (PR), human epidermal growth factor receptor 2 (HER2), cytokeratin (CK) 5/6, epidermal growth factor receptor (EGFR) and with specific antibodies against MMP-1, 2, 7, 9, 11, 13, and 14 and TIMP-1, 2, and 3. Based on the immunostaining data from five of the markers used (ER-α, PR, HER2, EGFR and CK5/6), three major subtypes (123 luminal A, 31 basal-like, and 17 HER2-overexpressing) were selected.

Results: Statistically significant differences among three subtypes were found in tumoral MMP7 ($p = 0.005$), tumoral MMP-9 ($p = 0.000$), tumoral MMP-13 ($p = 0.016$) and stromal MMP-13 ($p = 0.016$). The incidence of tumoral MMP-9 expression in HER2-subtype was significantly higher than in luminal-A subtype ($p = 0.021$). Tumoral MMP-9 and stromal MMP-13 expression were significantly higher in HER2-subtype than in basal-like subtype ($p = 0.000$ and $p = 0.016$). Tumoral MMP-7 expression was significantly higher in basal-like subtype compared to luminal-A ($p = 0.007$) and HER2-subtype ($p = 0.004$). Tumoral MMP-13 showed a higher expression in basal-like subtype than in HER2-subtype ($p = 0.010$). In multivariate analysis, stage and stromal MMP-1 expression were significantly related to overall survival.

Conclusion: We found some variations in MMP and TIMP expression among the immunohistochemical-based molecular subtypes of breast carcinomas, suggesting differences in their tumor pathophysiology. Additional studies are needed to determine the mechanisms underlying the differences of MMP and TIMP expression in the molecular subtypes for the development of specific therapeutic targets for breast cancer subtypes.

Characteristics of Mammography-Negative Tumors in Breast Cancer Patients

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Background/Purpose: The aim of this study was to investigate the clinicopathologic characteristics of mammography-negative (MN) tumors in breast cancer patients.

Methods: We retrospectively reviewed both of mammography and breast ultrasound from a cohort of patients diagnosed with breast cancer between 2003 and 2014. Patients with ductal carcinoma in situ or microinvasive cancer were also included. Among a total of 2005 patients, 112 (5.6%) patients revealed to have MN tumors. Logistic regression analysis was used to identify factors associate with MN tumors, compared to mammography-positive tumors.

Results: In univariate analysis, age < 50, Breast Imaging-Reporting and Data System (BI-RADS) category III or IV dense breast, low grade tumor, small tumor, endocrine receptor (ER) or progesterone receptor (PR) negative and human epidermal growth factor receptor 2 (HER2)-positive tumor were associated with MN tumors. In multivariate analysis, only density and tumor size were independent predictive factors for MN tumors. Comparison of BI-RADs type I or II with III and IV gave adjusted odds ratio of 7.85 (95% CI: 1.86-33.08) and 30.25 (95% CI: 6.77-135.07), respectively. Compared with T1a, adjusted odds ratio of T1b, T1c, and ≥ T2 were 0.75 (95% CI: 0.33-1.71), 0.29 (95% CI: 0.13-0.64), and 0.08 (95% CI: 0.03-0.19), respectively. Among 225 patients with extremely dense breast, 39 (17.3%) patients had MN tumors, and only 16 (1.8%) out of 891 patients with tumor ≥ 2 cm did.

Conclusion: The present study showed that MN tumors were associated with highly dense breast and small tumor regardless of tumor biology. We suggest that ultrasound should be considered in patients with extremely dense breast in mammography.

PO114

A Novel Sentinel Lymph Node Model to Predict Axillary Burden in Early Breast Cancer

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Background/Purpose: The Z11 trial advocates axillary lymph node dissection (ALND) be avoided in patients with low axillary burden. Our group propose a standardisation of sentinel lymph node biopsy (SLNB), incorporating 2 novel sentinel nodal stations (SNS). By increasing the specificity and positive predictive value of SLNB, we aim to identify a subgroup of mastectomy patients who can be spared from ALND.

Methods: A prospective study was performed on patients with breast cancer who underwent SLNB at the National Cancer Centre Singapore from February 2012 to December 2013. 325 cases (313 patients, 12 bilateral) were performed using a specific surgical technique to identify SLN at the 2 SNS. The intercostal brachial (ICB) and median pectoral (MP) SLN were identified in 313 (96.3%) and 258 (79.4%) cases respectively.

Results: An axillary clearance was performed for ≥ 1 positive ICB/MP SLN (n = 55), and 49.1% had further axillary involvement. The sensitivity of ≤ 2 positive SLNs in predicting further axillary lymph node involvement is low (29.6%). The MP SLN is specific (85.7%), has a high positive predictive value (76.5%) and is significant (OR 5.57, $p = 0.006$) for non-sentinel axillary nodal involvement.

Conclusion: SLNs are consistently localised at 2 SNS above the ICB nerve (96.3%) and deep to the MP neurovascular bundle (79.4%). A sequential lymphatic drainage is observed, namely from the breast to the ICB to the MP nodal stations. The MP SLN may help stratify patients, allowing those with low disease burden to avoid an ALND and their associated complications.

PO115

Utility of Second-Look Ultrasound for Enhancing Lesions Detected Initially on Breast MR Imaging

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Background/Purpose: Increasing studies suggests that for many women breast magnetic resonance imaging (MRI) provides the best possible accuracy, superior to both mammography and ultrasound (US). However, there is a large overlap in the MR findings of enhancing breast lesions, which often makes decisions regarding patient management difficult. Tissue diagnosis is gaining popularity for lesions with suspicious or indeterminate features on MR imaging. Significant advances have been made in biopsy needles and localization systems for MRI-guided biopsies. However, it still has several disadvantages and is not as widely available as US-guided interventions. Re-evaluation with ultrasound, also named second-look ultrasound for the breast is performed after review of breast MR findings can offer the possibility of identifying the MRI-detected lesions that were not previously detected at mammography or US, thereby permitting immediate biopsy.

Methods: Between January 2011 and December 2012, 133 patients with 147 enhancing lesions were detected only at MRI images initially, and MRI-directed second-look ultrasound was performed for these lesions with MRI examination. The MRI and second-look US findings were studied according to the lexicon of breast imaging reporting and data system (BI-RADS) recommended by American College of Radiology (ACR). The management was imaging-guided biopsy or surgical excision for BI-RADS 4 or 5 lesions classified by MRI or second-look US, and clinical and imaging follow-up for BI-RADS 2.

Results: Second-look US identified 124 out of 147 (84.3%) enhancing lesions initially detected by MRI. 94 lesions identified by second-look US were underwent US-guided biopsy or were excised, and the outcome were benign in 45 and malignancy in 49 findings. The other 9 enhancing lesions at MRI without identified by second-look US were also excised, the outcome were benign in 3 and malignancy in 6. The detection rate of second-look US was higher for mass-like MRI lesions (89.9%, 71/79) than non mass-like lesions (77.9%, 53/68), with statistical difference ($p = 0.047$).

Conclusion: Second-look US is a valuable procedure in identifying most incidental MRI findings. The detection rate of second-look US was higher for mass-like MRI lesions than non mass-like lesions. Histopathology of surgical specimen is necessary for most non mass-like lesions.

PO116

Axillary Dissection in Breast Cancer - A Diminishing Role?

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Background/Purpose: Morbidity of surgery in breast cancer is due to mastectomy and axillary dissection. In our study sentinel lymph nodes (SLNs) were retrieved using an anatomical approach without technology (blue dye or radioactive colloid). Axillary dissection was deferred in all patients, to study the impact of arm morbidity. Chemotherapy and/or radiotherapy was administered as indicated.

Methods: 400 patients with invasive breast cancer T1,2 N0 were studied. Mastectomy performed in 240 patients and breast conservation surgery (BCS) in 160 patients. SLN's 2.8 ± 0.77 were retrieved with an anatomical approach. Axillary dissection was omitted in all patients. SLNs positive patients and T2 lesions, estrogen receptor/progesterone receptor negative and human epidermal growth factor receptor 2 positive received chemotherapy (350 patients) and patients with BCS received radiation (160 patients).

Results: Five year Follow up of 4.7 ± 0.33 years, 2 patients developed with negative SLN developed axillary node metastasis. These could be skip metastasis. The morbidity of axillary dissection, lymphoedema, seroma and neuralgias were avoided.

Conclusion: Based on our study we believe that chemotherapy and tangential radiation is effective in controlling and eradicating metastatic lymph nodes and avoiding morbidities due to axillary dissection. Axillary dissection is a staging procedure which is rarely indicated now, except in heavy axillary node burden or chemo-resistant group.

PO117

Feasibility of the Use of Tumour Marker Velocity in the Prediction of Breast Cancer Recurrence

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Background/Purpose: Tumour marker velocity, defined as the rate of change in tumour marker level over time, has been established to be of significant use in the surveillance of prostate cancer, using prostate specific antigen (PSA). There is a lack of evidence in the similar use of cancer antigen 15-3 (CA 15-3) and carcinoembryonic antigen (CEA) to monitor breast cancer relapse. Our study aims to evaluate the predictive value of Ca 15-3 and CEA velocity in detecting breast cancer recurrence.

Methods: Consecutive patients from a prospectively collected database over a 15-year period (1998-2013) with available serial CA 15-3 and CEA measurements at recurrence were reviewed. Eligible patients with no recurrence were matched and included as a control group.

Results: This study included 137 patients (67 patients with recurrence and control group of 70 patients). A minimum rise in serum CA 15-3 and CEA velocity by 2.5 U/ml/year and 1.2 μg/L/year respectively is highly predictive of recurrence. Both tumour marker velocities had a combined sensitivity of 93.4%, specificity of 74.3%, positive prediction value of 0.83 and negative prediction value of 0.88. Logistic regression analysis was performed to investigate the association between tumour characteristics and disease recurrence and both CA 15-3 and CEA velocity remained as highly significant predictors ($p = 0.01$). Axillary lymph node status and the grade of the tumour were found to be predictive for breast cancer recurrence.

Conclusion: Measurement of tumour marker velocity (CA 15-3 and CEA) offers a novel method of utilizing tumour markers and sets the stage for its routine use in breast cancer surveillance.

PO118

Measured Environmental Determinants of the Cirrocumulus Mammographic Density Measure that Predicts Breast Cancer Risk: A Twins and Sisters Study

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Background/Purpose: Current methods for measuring mammographic density use the computer-assisted thresholding technique CUMULUS, and the "white or bright" areas of the mammogram. We call these measures Cumulus, and they are negatively associated with age and body mass index (BMI) and therefore confounders of breast cancer risk. We have developed a new measure based on the "brighter" areas of the mammogram, called Cirrocumulus, and found it is a better predictor of breast cancer risk. In this study, we investigated associations between measured environmental risk factors and the Cirrocumulus measure of mammographic density.

Methods: This study of 1,159 independent families comprised 525 monozygotic pairs, 324 dizygotic pairs and 768 non-twin sisters from the Australian Mammographic Density Twins and Sisters Study. We measured both the Cumulus and Cirrocumulus measures of mammographic density using CUMULUS. We conducted multivariable multilevel mixed-effects linear regression models and multivariate Gaussian regression using the software FISHER to estimate associations with measured environmental risk factors.

Results: The correlation between Cumulus and Cirrocumulus measures was 0.5. For Cirrocumulus, log dense area was associated with age (-0.039; 95% CI -0.049 to -0.028 per year), log BMI (-1.285; -1.539 to -1.031 per log kg/m^2) (-1.285; -1.539 to -1.031 per log kg/cm^2), and number of live births (-0.044; -0.078 to -0.010). These explained 9% of variance. There was no evidence of association with other measured factors. For Cumulus, cube root dense area was associated with age, log BMI and number of live births (7% of variance), but also menopausal status and other factors (1% of variance).

Conclusion: In terms of measured environmental risk factors, the determinants of the new Cirrocumulus measure are similar to those of the gold standard Cumulus measure. Further studies will address the issue of measured genetic factors, and unmeasured genetic and environmental factors.

PO119

Common Genetic Variants and Breast Cancer Susceptibility

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Background/Purpose: Breast cancer is a complex disease with many lifestyle-related and genetic factors contributing to susceptibility. To date, almost 100 common genetic susceptibility variants have been identified using genome-wide association studies (GWAS) that include replication of associations in very large combined studies. Together, these common variants explain 15% of the familial aggregation of breast cancer; and it has been estimated this percentage could be doubled if further studies with sufficient sample size were carried out. Here I present a summary of GWAS and related findings, and the direction of future work.

Methods: This review is based predominantly on the work of the Breast Cancer Association Consortium (BCAC), which aims to combine data from many studies, and to provide a reliable assessment of the risks associated with these genes. BCAC has genetic and other risk factor data for more than 100,000 women from studies carried out over the world, mostly of white European origin. BCAC has carried out GWAS and replications studies, plus complementary studies, including fine-mapping of identified susceptibility loci, comprehensive evaluations of genetic and gene-environment interactions and more recently risk modelling.

Results: BCAC has identified or replicated associations with vast majority of the common breast cancer susceptibility variants identified to date. Most are non-coding and unlikely to be causal, and not even the gene(s) through which they act can be easily established. Fine-mapping studies have identified some causal variants and genes, and discovered additional variants independently associated with disease risk. Most susceptibility variants are more strongly associated with ER-positive disease. Extensive analyses of interactions between established genetic and lifestyle risk factors for breast cancer have consistently found little evidence of departure from multiplicative relative risks, which has important implications for risk modelling. There is emerging evidence that genetic interactions are unlikely to explain a substantial part of the familial aggregation of disease.

Conclusion: GWAS have been successful in identifying common breast cancer susceptibility loci. Very large sample sizes are required for replication of these findings and even larger sample sizes will be required to discover additional variants. Larger studies of less common variants, of disease subtypes and of women of other ethnicities are also likely to be fruitful. Future work will include the development and evaluation of risk prediction models that incorporate these established and newly discovered susceptibility variants.

PO120

Improvement Activities Linked with Customer Journey Map of Breast Cancer Patients

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Background/Purpose: The number of patients visiting hospitals for breast cancer is continuously increasing and the treatment process for breast cancer becomes complicated depending on cancer phase, hormone receptor, and human epidermal growth factor receptor 2. There is no customer journey map for treatment of breast cancer that shows the overall treatment flow of patients at a glance, employees at hospitals have difficulty in sharing the diagnostic and treatment processes for breast cancer. This results in failure to efficiently link processes of different medical departments and leads to customer complaints.

Methods: The overall flow of breast cancer treatment and processes of different medical department for diagnosis and treatment are examined to develop a customer journey map for treatment of breast cancer. This customer journey map can help employees better understand the treatment process and be able to offer consistent explanation on the treatment process, allowing for efficient linkage of processes between different departments.

Results: When the customer journey map for treatment of breast cancer was shared with employees, 33.3% responded as 'Agree' and 66.7% as 'Strongly agree' to the question of whether the map helped understand the treatment process of breast cancer. 33.3% of employees responded as 'Agree' and 66.7% as 'Strongly agree' to the question of whether the customer journey map is helpful for their duties, verifying that the improvement activities provided support on duties of employees.

Conclusion: These improvement activities were implemented to develop a customer journey map for treatment of breast cancer that shows the overall flow of the treatment process from the first hospital visit of breast cancer patients and to increase understanding of the treatment process by sharing the process with employees. The meaning of these activities can be found in the fact that a customer journey map was developed

based on the necessity to increase understanding of the treatment processes in different medical departments and help employees with their duties.

PO121

Psychosocial Adjustment and Associated Factors in Korean Younger Breast Cancer Survivors

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Background/Purpose: Younger women with breast cancer (age < 50) have higher psychological stress scores related to their breast cancer diagnosis and exhibit a greater fear of body image changes, sexual dysfunction and cancer recurrence than older women with breast cancer (age ≥ 50). Much attention is required with regard to the unique issue of age-related psychosocial adjustment withstood by younger breast cancer survivors. The aim of this study was to identify factors affecting psychosocial adjustment in younger breast cancer survivors.

Methods: Younger breast cancer survivors (n = 112) between the ages of 20 to 49 years were included in the study. Data were collected through self-report questionnaires which were constructed to include clinical characteristics items, Symptom Experience Scale (SES), Mishel Uncertainty Illness Scale (MUIS), Social Support (SS), Life Orientation Test-Revised (LOT-R), and Psychosocial Adjustment to Illness Scale-Self Report Korean version (PAIS-SR). Data were analyzed using SPSS/WIN 21.0 for descriptive statistics, t-test, ANOVA, Scheffe' test, Pearson's correlation coefficients, and stepwise multiple regression.

Results: The mean score of psychosocial adjustment was 26.32 (SD = 4.85). Based on the forward stepwise multiple regression, the most significant factor of psychosocial adjustment was symptom experience ($\beta = 0.487$, $p < 0.001$), social support ($\beta = -0.330$, $p < 0.001$), immune therapy ($\beta = -0.295$, $p < 0.001$), uncertainty ($\beta = 0.211$, $p = 0.004$) , and body mass index ($\beta = 0.165$, $p = 0.008$). These variables was accounted for 63.4% of sexual dysfunction ($F = 25.75$, $p < 0.001$).

Conclusion: The findings indicate the importance of counseling and educational programs to improve the psychosocial adjustment according to breast cancer survivors' age. Furthermore, there is strong demand for appropriate nursing interventions to counter factors related to maladjustment in the early stages and thus enhance the social-psychological adjustment of younger breast cancer survivors.

PO122

Sex Life Recovery Paradigm in Women with Breast Cancer: A Qualitative Study

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Background/Purpose: Effective sexual rehabilitation for women with breast cancer begins with an adequate understanding of the sex life recovery process these women are undergoing. The purpose of this study is to provide preliminary data for a sexual rehabilitation program for women with breast cancer by thoroughly examining the sex-life changes they experience during their cancer treatment and by taking a grounded theoretical approach to devise a theoretical model of the sexual rehabilitation process.

Methods: Ten women with breast cancer who had concluded aggressive cancer treatment at least 6 months prior to this study and who were members of a breast cancer support group participated in this study, which was carried out from February to October of 2014. Data were collected through in-depth interviews and analyzed using the grounded theory of Strauss and Cobin.

Results: The causal conditions were "physical changes due to the cancer treatment," "psychological stress due to the cancer treatment," "financial burden" and "conflict with spouse." The central phenomena were "lack of conversation," and "changes in sex life." The intervening conditions were "personal factors," "familial factors" and "social factors," and the interactive strategy was "efforts to restore a quality sex life." Finally, women with breast cancer were found to experience an "improved sex life" and "restoration of the marriage relationship" through the interactive strategy.

Conclusion: The analysis of the sex life recovery process in women with breast cancer revealed that recovery involves a four-step process that requires appropriate nursing intervention for each step. Moreover, as personal, social and familial factors are presumed to facilitate the recovery process, effective intervening strategies should be developed for those categories that can be manipulated.

PO123

Patient Adherence in Clinical Trials: The Role of Clinical Research Nurse

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Background/Purpose: Clinical research studies play an important role in development and establishing new treatment for patients' health improvement. Clinical trial studies are essential to generate evidence based data to guide medical practice and there by improving cancer patients' quality of life and survival. Well-trained clinical research nurse (CRN) with knowledge of clinical nursing skills and psychological care experiences can enhance nursing care and practice in clinical trials. With the professional training and management of research nurse,the adherence of patients recruited in this setting could be improved.

Methods: Nineteen international clinical research trials are conducted in our multidisciplinary breast centre, with 120 patients recruited in 2006-2014. We reviewed patients' participation rate and compliance level during participation throughout the study period. The scope and contribution of the role in CRN also reviewed in this study.

Results: Among the 120 patients were enrolled in international and investigator initiated research studies, approximately 90% of patients had completed all study procedures and follow up schedules. The 10% drop out rate was due to patients who died of breast cancer, had disease relapse during treatment period, immigration or left to follow up in the private sector. CRN with knowledge of The Declaration of Helsinki, Good Clinical Practice and ethical knowledge were more capable to enhance the patient adherence and compliance throughout the study.

Conclusion: These findings indicated that clinical research nurses can benefit in retaining patients in clinical trial studies and highlights the importance of their roles.With the increase in interest in trials conduction in Asia, training programs of CRN can improve clinical trials recruitment and quality.

Extent of Disease on Initial Bone Scan Predicts Survival Among Breast Cancer Patients with Bone Metastasis

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Background/Purpose: Despite advances in treatment of breast cancer, patients remain at risk for recurrence even after receiving standard treatment. It is important to distinguish subset of patients with aggressive disease resulted in cancer death. The present study attempts to evaluate quantitatively the initial bone scan appearance among breast cancer patients with bone metastasis, and to clarify the correlation with patients' outcome.

Methods: The subjects consisted of breast cancer patients with bone metastasis which developed after surgery. The cases recurred in other visceral sites at the same time of bone metastasis, were excluded from this series. On the basis of the extent of disease (EOD), the patients were divided into low-EOD and high-EOD groups, and their outcome was analyzed retrospectively.

Results: There was no significant difference between the groups concerning clinicopathological features and disease-free intervals after operation. However, 5-year survival rate after recurrence among low-EOD group was 50.8%, which was significantly higher than high-EOD cases (20.9%, $p = 0.001$).

Conclusion: The EOD grade on initial bone scan correlated with the survival after recurrence among breast cancer patients with bone metastasis. This information would be useful when considering follow-up schedules and when designing therapies targeting metastatic breast cancer.

Clinical Implications of iNOS Levels in Triple-Negative Breast Cancer Responding to Neoadjuvant Chemotherapy

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Background/Purpose: Triple-negative breast cancer (TNBC) is a high-risk breast cancer with poor survival rate. To date, there is a lack of targeted therapy for this type of cancer. One unique phenomenon is that inflammatory breast cancer is frequently triple negative. However, it is still ambiguous how inflammation influences TNBC growth and responding to chemotherapy.

Methods: We investigated the levels of inflammation-associated enzyme, iNOS, in 20 TNBC patients, and examined it correlation with patients' responses to platinum-based neoadjuvant chemotherapy.

Results: Our studies showed that the TNBC patients with attenuated inducible Nitric Oxide Synthase (iNOS) levels in tumor cells after treatment showed better responses to platinum-based neoadjuvant chemotherapy than other TNBC patients. Our further *in vitro* studies confirmed that induction of proper levels of NO increased the resistance to cisplatin in triple-negative MDA-MB-231 cells.

Conclusion: Our data suggest that aberrant high level of iNOS/Nitric Oxide are associated with less effectiveness of platinum-based neoadjuvant chemotherapy in TNBC. Therefore, we propose to monitor iNOS levels as a new predictor for TNBC patient's response to platinum-based neoadjuvant chemotherapy. Moreover, iNOS/NO is considered as a potential target for combination therapy with platinum drugs for TNBC.

Influence of Immediate Breast Reconstruction on Adjuvant Treatments and Prognosis of Patients with Stage 0 to III Breast Cancer

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Background/Purpose: Operation method of immediate breast reconstruction (IBR) spread globally for cosmetic reasons. However, very few studies have reported the influence of IBR on adjuvant treatments and prognosis of breast cancer.

Methods: Breast cancer register-based, case-control study. Breast cancer patients who received operation at Okayama University Hospital between October 2007 and December 2012, were reviewed and divided into two groups; IBR group and non-IBR group. Three major parameters were assessed to compare the two groups: time to initiation of adjuvant chemotherapy (TTC), implementation rate of postmastectomy radiotherapy (PMRT), and disease-free survival (DFS).

Results: Follow-up data from 513 consecutive patients was reviewed. Of the 513 patients, 98 underwent IBR. The mean age was 57-years. The median follow-up period was 39 months. The breast cancer stage was included from stage 0 to stage III. There was no significant difference between two groups in TTC, implementation rate of PMRT and the 3-year DFS.

Conclusion: In our single-institution cohort, IBR after mastectomy showed adequate results, which indicates that this method is oncologically safe for the prognosis of breast cancer.

Prevalence of *BRCA1* and *BRCA2* Mutations in Breast Cancer Patients from West China and the Impact of Mutations on Survival

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Background/Purpose: *BRCA1/2* mutation status shows increasing importance for treatment decision in patients with breast cancer. However, the reported *BRCA1/2* mutation frequency in Chinese breast cancer (BC) patients varies among studies largely due to differences in the pre-selected patient population and/or sequencing techniques. The influence of *BRCA1/2* mutation on survival of patients with BC has not been determined yet.

Methods: In our study, 507 not pre-selected patients diagnosed with breast cancer from West China between 2008-2014 were enrolled. Both somatic and germline mutations in the coding exons and the splice boundaries of *BRCA1* and *BRCA2* genes were detected using next-generation sequencing and confirmed by a second technology. 498 cases of non-metastatic breast cancer (median follow-up: 34.5 months) were assessable for survival analysis.

Results: *BRCA1/2* mutations were detected in 34.5% (175/507) of patients (germline: 29.4%; somatic: 3.2%; both: 1.8%). Among them, the deleterious mutations were found

in 9.5% of patients (germline: 7.1%; somatic: 1.2%; both: 1.2%), particularly high in triple-negative (21.4%) and Luminal B (9.0%) subtypes. *BRCA1/2* mutation carriers, regardless of pathogenicity classification, had a significantly higher disease free survival (DFS) rate than non-carriers (the adjusted HR = 0.315, 95% CI = 0.120-0.824, $p = 0.019$).

Conclusion: *BRCA1/2* mutations were present in one-third of Western Chinese breast cancer patients. The *BRCA1/2* mutation carriers had a better DFS, regardless of pathogenicity and mutation classification. Germline and somatic *BRCA1/2* testing should be recommended to all women diagnosed with breast cancer, especially subtypes of triple-negative and Luminal B.

Retrospective Audit to Assess the Prognostic Significance of Quadrant of Primary Tumor at Presentation in Women with Operable Breast Cancer

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Background/Purpose: Outer quadrant is the most common site of presentation of primary tumors in the breast with higher axillary lymph node (ALN) positivity than inner quadrant tumors (IQT). Despite which IQT have worse prognosis, possibly because the first echelon node is the internal mammary lymph node, which is not routinely addressed in early breast cancer (EBC). We analyzed the impact of tumor location on disease free survival (DFS) in women with EBC

Methods: A retrospective audit carried out in women with EBC treated at our center (1997-2009). Women with centrally located tumors or on neoadjuvant chemotherapy were excluded

Results: Total of 2,347 women with EBC analyzed. Of these 778 (33.2%) had IQT and 1,569 (66.9%) had outer quadrant tumors (OQT). Median age at presentation was 49 years, median tumor size 3 cm (1-5.5 cm). Estrogen receptor (ER)/progesterone receptor (PR) positivity was 57.4% and 46.2% patients were ALN positive (36.9% of IQT, 50.5 % of OQT). 5-years disease free survival for OQT was 83.9% *vs.* 79.4% for IQT ($p = 0.015$). Further analysis based on quadrant and lymph node status suggested that DFS for OQT node negative (N0) was 89.4%, IQT N0 was 84.1% ($p = 0.014$), OQT node positive (N+) was 78.6% and IQT N+ was 71.4% ($p = 0.011$). On multivariate analysis, ALN positivity (RR = 2.15), ER/PR negativity(RR = 1.65) and IQT (RR = 1.41) had worse prognosis

Conclusion: Tumors located in the inner quadrant fare relatively worse than those in the outer quadrant, especially if ALN positive.

Comparison Between Oncotype DX Recurrence Score Categories and Newly Proposed Immunohistochemically Defined Luminal Subtypes

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Background/Purpose: At the 13th St Gallen International Breast Cancer Conference in 2013, it was recognized that considerable progress has been made in the pathological characterization of breast cancer subtypes. In order to distinguish between luminal A-like and luminal B-like breast cancer, a useful surrogate definition was proposed, involving a combination of expressions of estrogen receptor (ER), progesterone receptor (PgR), and Ki-67. We examined the rate of concordance between the Oncotype DX recurrence score (RS) categories and the luminal A and B subtypes.

Methods: We examined 41 cases of T1-2 N0-1mi M0 (ER positive, human epidermal growth factor receptor 2 (HER2) negative) breast cancer to assess the relationship of both previously and newly proposed, immunohistochemically defined luminal subtypes to the Oncotype DX RS. First, we classified the 41 patients into previously proposed luminal subtypes, according to the level of Ki-67 as (≥ 14%), assessed by local pathologists. Next, we re-examined the Ki-67 by central review. Finally, by introducing PgR positivity (≥ 20%), we classified these patients to newly proposed luminal subtypes and compared them with the RS categories.

Results: The mean patient age was 54.7 years, 15 showed intermediate to high RS categories. In the previously proposed luminal subtypes, the concordance rate between luminal A and low RS category was 90.1% (10/11) by local pathologists and 76.5% (13/17) by central review and that between luminal B and intermediate to high RS category was 46.7% (14/30) and 45.8% (11/24), respectively. In newly proposed luminal subtypes, the concordance rate between luminal A and low RS category was 100% (13/13) and between luminal B and intermediate to high RS category was 53.6% (15/28).

Conclusion: Although this study was based on a retrospective chart review of a small number of patients, the newly proposed luminal subtypes, by inclusion of PgR positivity, seemed to improve the precision of selecting patients with intermediate to high RS categories.

PO130

Quality of Life and Symptom Experience in Women with Breast Cancer Before and After Chemotherapy

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Background/Purpose: Although chemotherapy improves overall survival, it is also associated with several side effects, such as decreased cardiac function, muscle wasting, reductions in physical and cognitive functioning, and fatigue. The aim of this longitudinal study was to examine the quality of life (QOL) and symptom experience over time in women with breast cancer, who received adjuvant chemotherapy.

Methods: 84 patients with breast cancer scheduled to receive chemotherapy (CTx group), and age- and menopause status-matched breast cancer who did not receive chemotherapy (comparison group). The Memorial symptom Assessment Scale-Short Form and Functional Assessment of Cancer Therapy-Breast questionnaire were administered before adjuvant therapy, toward the end of adjuvant therapy, as well as 6 months after the completion of adjuvant therapy.

Results: Compared to comparison group, CTx group reported lower QOL overall and lower physical well-being and breast cancer specific well-being, and had worse total and physical symptom distress at the end of adjuvant therapy. By 6 months, CTx group's QOL and symptom returned to baseline levels but were still worse than those of comparison group.

Conclusion: These results suggest that chemotherapy in breast cancer patients may be associated with worse symptom experience and QOL. Further studies are needed to explore factors which minimized symptom severity and improved QOL over time. Also nursing intervention for management and improvement of symptom experience and QOL should be developed and tested.

PO131

Objective Measurement of Cosmetic Outcomes of Breast Conserving Therapy Using BCCT.core

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Background/Purpose: To evaluate objective cosmetic outcomes and factors related to breast-conserving therapy (BCT) using the BCCT.core software.

Methods: Fifty-one patients who received BCT with informed consent were evaluated using the BCCT.core software. Patients were divided into two groups based on the BCCT score: excellent or good (n = 42) vs. fair or bad (n = 9). Clinical factors were analyzed to determine prognostic factors for cosmetic outcomes.

Results: The objective cosmetic outcome of BCT measured by the BCCT.core software was excellent in 10% of patients, good in 72%, and fair in 18%. Among factors of tumor characteristics, systemic adjuvant therapy, and radiation therapy, maximum dose within the breast was the only significant factor for breast cosmetic outcome with a risk ratio of 1.749 (95% confidence interval 1.041-2.939, $p = 0.035$).

Conclusion: Objective measurement of cosmetic outcome of BCT using the BCCT.core software was feasible. The cosmetic outcome of BCT may be affected by the maximum dose within the breast.

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PO132

Impact of Uncontrolled Menopause Symptoms on Fear of Recurrence Among Breast Cancer Survivors: A Prospective Cohort Study

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Background/Purpose: Breast cancer treatment-induced menopause symptoms resulted in poor quality of life and psychological well-being. This study aims to examine impact of uncontrolled menopause symptoms on fear of recurrence among breast cancer survivors. Between July 2010 and July 2011, non-metastatic breast cancer patients (n = 432) recruited from two cancer hospitals in Seoul, Korea.

Methods: Patients answered menopause symptoms scale (MRS) before surgery, 2 weeks, 3, 6, 12, 24, and 36 months after surgery. Fear of cancer recurrence (FCR) was measured at 24 and 36 months after surgery. Growth mixture models were used to identify trajectory classes and multivariate analysis was performed to find impact of uncontrolled menopause symptoms on FCR using STATA 13.

Results: Among 25.0 (58%) premenopausal patients at baseline, 3 MRS distinct groups were identified according to 3-year change patterns: constant low (CL): 29.3%, medium increase (MI): 48.7% and sharply increase (SI): 22.0%. Compared to the CL, the MI experienced 4.7 and 4.2 times higher FCR at 2 and 3 years after surgery. The SI experienced 16.5 and 21.15 times more likely to have FCR compared to the CL. It is statistically significant.

Conclusion: When the survivors experience more uncontrolled menopause symptoms, they had higher FCR. It is necessary to inform breast cancer patients about menopause symptoms are due to hormone therapy, not symptoms of cancer recurrence and help them to manage these symptoms during survivorship.

PO133

Patient Reporting Pain Intensity Immediately After Surgery Can be Associated with Underlying Depression in Women with Breast Cancer

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Background/Purpose: The aims of this study were to determine the prevalence of severe, definite depression symptoms, as measured using the Center for Epidemiological Studies Depression Scale (CES-D), and the association between high CES-D scores (i.e., ≥ 25) and sociodemographic and perioperative factors during perioperative period.

Methods: Among 1690 consecutive breast cancer patients who were admitted for definitive breast surgery during the study period, 1,499 patients were included in this study. Patients with a past medical history of psychiatric medication or support, a plan for elective surgery due to locoregional recurrence or any metastatic disease were excluded. The CES-D score was checked 1 day before definitive surgeries.

Results: The mean CES-D score was 18.5, with 24.1% (362/1,499) and 56.7% (850/1,499) having high CES-D scores of ≥ 25 and ≥ 16, respectively. Multivariate analysis revealed that the number of family members with any malignancy, sedative medication and postoperative numeric rating scale scores were significant associated factors for severe, definite depression symptoms.

Conclusion: Depression may increase the intensity of postoperative acute pain. Self-reporting of persistent postoperative pain intensity is potentially useful in detecting hidden depression symptoms in breast cancer patients awaiting definitive surgery.

PO134

Change of Health-Related Quality of Life in Survivors with Breast Cancer According to Time After Surgery Compared with Age-Matched General Population

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Background/Purpose: There were several studies that evaluated HRQoL in breast cancer. However, few studies conducted the comparison of HRQoL between breast cancer patients and age-matched general population (GP) group according to time after surgery.

Methods: 686 patients after a operation completed questionnaires at follow-up visit. According to time after surgery, breast cancer patients were divided into 5 groups. We used EQ-5D, a validated instrument for measuring HRQoL and then EQ-5D index score of each group was compared with that of age-matched GP groups.

Results: Mean index score was increased as time after surgery passed. Mean score of breast cancer group was similar to that of age-matched GP group after 5 years postoperatively (0.919 vs 0.928, $p = 0.305$). In category of motility, proportion of "problem" status of breast cancer (BC) groups was lower than that of matched GP group and in aspect of self-care and usual activities, there was similar proportion of "problem" status between two groups after 3 years postoperatively. However in pain/discomfort and anxiety/depression categories, high proportion of "problem" status was sustained over 5 years surgery ($p = 0.028$, $p < 0.001$)

Conclusion: HRQoL of breast cancer group was improved and became the similar status to that of matched GP group over 5 years after surgery. However, HRQoL related with pain/discomfort and anxiety/depression was restricted for a long time. Therefore, some tailored intervention programs according to time may be supposed for improvement of HRQoL in survivors with breast cancer.

How Do I Keep My Job?: Factors Associated with Maintaining Employment After Breast Cancer

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Background/Purpose: Returning to work and maintaining employment are critical for quality of life among breast cancer patients. The aim of this study was to explore various factors associated with maintaining employment after breast cancer.

Methods: This study used subgroup of 422 non-metastatic breast cancer cohort study conducted from July 2010 to July 2011 and followed at 2 weeks 3, 6, 12, 24 and 36 months after surgery. After excluding patients who did not work at baseline and did not report working status at each time point, total 123 were contacted at 3 years after surgery. To assess specific reasons for stop working, changing job, or maintaining working, telephone interview by a trained nurse was conducted. Descriptive statistics and thematic analysis were used to report outcomes.

Results: Among 123, 69.1% were contacted and all of them agree to have interview. Among them, 72.9% were working and 27.1% discontinued working at 3 years after surgery. Financial necessity (44.1%) was prior reason for patients to return to work following by self-satisfaction (23.7%) and company request (22%). Meanwhile, self-satisfaction (33.9%) and support from family (33.9%) and colleagues (25.4%) were the reasons to maintain the work. Yet, working patients experienced problems related to lack of social support (19.3%), altered appearance (17.7%), difficulties of gathering with coworkers (17.7%), and cognitive dysfunction (11.3%).

Conclusion: Further studies are necessary with larger sample and patients with vari-

ous occupations. Support from family and society is necessary for patients who are willing to return to work and maintain it after cancer treatment in a systematic way.

PO136

Changes in Working Status and Quality of Life Among Breast Cancer Survivors: A Prospective Cohort Study

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Background/Purpose: Advances in detecting and managing breast cancer led to the treatment of women who are more likely to be of working age. However, breast cancer survivors are less likely to be employed (maintaining work, returning to work, get a job) compared to healthy women of similar age resulting in financial difficulties and poor quality of life. We aim to evaluate longitudinal changes of working status among women with breast cancer and its impact on quality of life.

Methods: This is a cohort study with non-metastatic breast cancer patients (N = 422) from two cancer hospitals in Seoul, Korea. Patients were recruited before any treatment and followed at 2 weeks, 3, 6, 12, 24 and 36 months after surgery. Of total, 45% women (n = 190) were working at baseline and 88.4% of them reported about working status at 12, 24, and 36 months after surgery. Quality of life was assessed using EORTC-QLQ-C30 and QLQ-BR23. Mixed effect analysis was performed to examine changes overtime using STATA 12.

Results: Only 30.4% of women kept working at 3 year after diagnosis. While women working (WW) and not-working (WNW) reported similar pattern of poor functions and low quality of life until 6 months after surgery, WW showed improvement in role and social function, body image and future perspective compared to WNW ($p < 0.05$). In contrast, WNW kept reporting poorer physical function and more financial difficulties from 6 months after surgery than WW ($p < 0.05$). Specifically, WNW reported in-

creased fatigue and sleep disturbance over time and it was statistically different from WW.

Conclusion: Only one-third of breast cancer patients kept working 3 year after diagnosis. Working patients reported less symptom, better functioning, and less financial difficulties resulting in better quality of life during survivorship. It is necessary to help breast cancer patients to maintain their work during and after treatment as well as providing psychosocial support.

PO137

Effects of Intermittent Pneumatic Compression on Lower-Limb Edema During Chemotherapy of Breast Cancer Patients

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Background/Purpose: Current treatment protocols of decongestive therapy include limb elevation, massage and use of Intermittent Pneumatic Compression (IPC). IPC therapy provides non-invasive compression to the limbs for treatment of vascular and lymphatic conditions. This study is to clarify the effect of IPC on the lower-limb edema during chemotherapy of breast cancer patients.

Methods: The participants were thirty-two breast cancer patients who suffered the lower-limb edema during chemotherapy and prescribed IPC therapy. Calf circumference at 5 cm below knee joint, ankle circumference, and lower-limb range of motion were measured before and after IPC therapy. Quality of life was evaluated by The World Health Organization Quality of Life (WHOQOL) (26 questions; score range 1-5).

Results: All participants were women and their average age was 56.3 years. The median time since surgery was 1.7 years. After IPC therapy, the calf and ankle circumferences decreased. The scores of WHOQOL of the young group (less than 50 years old) significantly increased, but still lower than ones of the aged group.

Conclusion: These results suggest that IPC therapy is beneficial for lower-limb edema during chemotherapy of breast cancer patients. Nurses need to pay attention to the age of the patient when assessing the effects of the IPC therapy.

The Effects of Nurse-Led Telephone-Based Psychosocial Support in Breast Cancer Patients Care: Preliminary Analysis for Meta Analysis

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Background/Purpose: Psychosocial support is important in helping women adjust to breast cancer. This study aimed to explore the evidence on nurse-led telephone-based psychosocial intervention in breast cancer care.

Methods: We reviewed telephone-based intervention studies conducted over the last 20 years (1994-2015) in the area of breast cancer care. We used PubMed, Google Scholar, and Embase to search for articles indexed as "breast cancer," nurse," or "telephone."

Results: We searched a total of 1,334 published papers, out which 255 were extracted on breast cancer, and then out of which 5 were analyzed on nurse-led telephone-based psychosocial intervention employing randomized controlled trial. Breast cancer patients who underwent primary treatment were included in the analysis. Duration of intervention ranged from 11days to 13 months. Two studies employed self-regulation theory and the Roy adaptation model. The total sample sizes included in the analysis were 848. Patients were highly satisfied with psychosocial support intervention. The group intervened by nurses were more satisfied than the one by psychologists in dealing with somatic aspects, and reported positive outcomes such as reducing emotional distress and improving quality of life.

Conclusion: On the other hand, nurse-led telephone psychosocial intervention appeared to be as effective as a mailed educational resource. In addition, usual care also supported adjustment to breast cancer. The results on the effect of nurse-led telephone psychosocial intervention are controversial. There is a need for meta analysis to verify whether the nurse-led psychosocial intervention decreased side effect distress and increased psychological well-being among breast cancer patients.

PO139

The Relationship Between Four GWAS-Identified Single Nucleotide Polymorphisms and Female Breast Cancer in Henan Population

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Background/Purpose: The purpose of this study is to further verify the association between common breast cancer susceptibility loci which have been confirmed in European and Asian populations and breast cancer susceptibility in sporadic breast cancer among the Han nationality in Henan province, and analyse their genotypes in the internal type of breast cancer.

Methods: In 253 breast cancer case group and 343 healthy control group, rs2046210, rs298158, rs88931, rs3803662 are genotyped by single nucleotide polymorphism (SNP) improved multiple ligase detection reaction (LDR). According to estrogen receptor, progesterone receptor, human epidermal growth factor receptor 2 (HER2) and Ki67, breast cancer are divided into five types: Luminal A, Luminal B, HER2-enrich, Luminal HER2, Basal-like.

Results: rs2046210, rs2981582, rs889312 have no significant statistical differences with breast cancer, but rs3803662 in the case group and the control one are statistical difference. rs3803662 between the case group and control one are different in codominant inheritance and recessive genetic models, GG increased the risk of breast cancer. The four loci have no differences in different types of breast cancer.

Conclusion: Four common breast cancer susceptibility loci from GWAS are not entirely associated with breast cancer risk among the Han nationality in Henan province, only rs3803662 (TOX3/TNRC9) is confirmed to increase the risk of breast cancer. Different genotypes of four loci distribute equally in different types of breast cancer.

PO140

Current Status of the Management of Hereditary Breast and Ovarian Cancer in Asia: First Report by the Asian *BRCA* Consortium

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Background/Purpose: *BRCA1/2* mutation carriers possess an elevated lifetime risk for hereditary breast and ovarian cancer (HBOC), yet the availability of risk assessment and genetic testing for HBOC in Asians is far limited, thus limiting the chances for appropriate surveillance, clinical strategies and cancer management.

Methods: Current status of HBOC management in 14 Asian countries was reviewed. Data of genetic counseling and genetic testing uptake rates were collected, and were analyzed how economic factors, healthcare system, legal frameworks and cultural issues affect the genetic service availability in Asia.

Results: It was estimated that in 2012, of the 560,000 breast cancer patients in 14 Asian countries, only around 4,000 individuals were benefited from genetic counseling and 3,200 were tested, in which over 40% of the cases were from Korea. Economic factors

such as genetic service costs, and the lack of adoption into national healthcare systems (with the exception of Korea) are major barriers to genetic risk assessment in Asian countries. In addition, regional accredited laboratories, training programmes, and trained healthcare professionals are readily available only in half of the studied countries.

Conclusion: These limitations in healthcare system, combined with the lack of legal frameworks against genetic discrimination and lack of awareness among general public, remain the main challenges to HBOC management in Asia. The Asian *BRCA* (ABRCA) Consortium reports the current limitations in genetic counseling and testing for familial breast cancer in Asia, and urges the governments, healthcare sectors and researchers to address the disparities in HBOC management.

PO141

The Role of Pyruvate Kinase M2 Represented Aerobic Glycolysis

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Background/Purpose: About 80 years ago, a German biochemist Otto Warburg who got the Nobel Prize found that cancer cells obtain most of their energy by glycolysis even in the presence of adequate oxygen. This concept was called "aerobic glycolysis" or "Warburg effect", and it has been confirmed by many researchers after Warburg. Pyruvate kinase M2 which is one splice variant of *PKM* gene, is preferentially expressed in cancer, where complex regulation of its activity is important for control of cell metabolism.

Methods: Here we used Immunohistochemistry on paraffin-embedded sections to detect the expression of *PKM2* of 296 breast cancer patients, the median age of patients was 51 years (range, 23-83 years).

Results: We found the expression of *PKM2* was negatively correlated with Body Mass Index (BMI) ($p = 0.023$) and tumor size ($p = 0.008$), indicated that low expression of *PKM2* is associated with obesity and larger tumor size. While the expression of *PKM2* was positively correlated with lymph node stage ($p = 0.046$), showed that the high level of aerobic glycolysis might advance lymph node metastasis in human breast cancer.

Conclusion: The results encouraged us to expand the study to explore the significant effect of *PKM2* as a aerobic glycolysis factor in human breast cancer.

PO142

Relationship Between Single Nucleotide Polymorphisms of Zinc Finger Protein 350 Gene and Susceptibility of Early-Onset Breast Cancer of Uygur and Han Women in Xinjiang

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Background/Purpose: By detecting the mutations (variants) of zinc finger protein 350 (ZNF350) gene in exon, we investigated the relationship between single nucleotide polymorphisms (SNPs) of ZNF350 gene and susceptibility of early-onset breast cancer of Uygur and Han women in Xinjiang.

Methods: Exons region of ZNF350 gene of early-onset breast cancer of Uygur and Han women in Xinjiang (age 30 to 40 years, 80 cases, respectively) were detected via direct sequencing. Predicted the effects of mutations of ZNF350 on the protein function by using Polyphen and SIFT software, and then analyzed the relationships between SNPs and the clinical pathological features.

Results: Nine mutations were detected (Minor Allele Frequency (MAF) >1% referring to database) in ZNF350, including 5 missense mutations and 4 synonymous mutations, which located in exon 3, 4, and 5, respectively. Among them, 8 mutations in Uygur, and 7 mutations in Han, which includes 4 missense mutations respectively. The common mutations, rs4987241 and rs2278415, may affected the ZNF350 protein function by using Polyphen and SIFT software. Stratification analysis showed that there were different significant relationships between distribution of genotype on polymorphism loci and the clinical pathological features in Uygur and Han.

Conclusion: Mutations and polymorphisms of ZNF350 in exon region exist differences between Uygur and Han early-onset breast cancer in Xinjiang. There were different correlations between distributions of genotype on different polymorphism loci and the clinical pathological features in Uygur and Han, such as axillary lymph node status,

triple negative breast cancer and menarche age. These finds can guide high-risk population screening and clinical individualized treatment in Uygur and Han early-onset breast cancer in Xinjiang.

PO143

Relationship Between Single Nucleotide Polymorphisms of *BACH 1/BRIP 1* Gene and Susceptibility of Early-Onset Breast Cancer of Uygur and Han Women in Xinjiang

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Background/Purpose: By detecting the mutations (variants) of *BTB* and *CNC* homology 1 (*BACH 1*)/*BRCA1* interacting protein C-terminal helicase 1 (*BRIP 1*) gene in exon, we investigated the relationship between single nucleotide polymorphisms (SNPs) of *BACH 1/BRIP 1* gene and susceptibility of early-onset breast cancer of Uygur and Han women in Xinjiang.

Methods: Exons region of *BACH 1/BRIP 1* gene of early-onset breast cancer of Uygur and Han women in Xinjiang (age 30 to 40 years, 80 cases, respectively) were detected via direct sequencing. Predicted the effects of mutations of *BACH 1/BRIP 1* on the protein function by using Polyphen and SIFT software, and then analyzed the relationships between SNPs and clinical pathological features.

Results: Nine mutations were detected in *BACH 1/BRIP 1*, including 5 missense mutations, 2 synonymous mutations and 2 deletion mutations, which located in exon 6, 9, 19 and 20. Among them, 4 mutations in Uygur, and 9 mutations in Han, which includes 2 deletion mutations. Rs4986764 (the common mutations in Uygur and Han) and c.2593C > T (only in Han) were deleterious mutations by using Polyphen and SIFT software. Stratification analysis showed that there were significant different relationships between distribution of genotype on polymorphism loci and the clinical pathological features in Uygur and Han.

Conclusion: Mutations of *BACH 1/BRIP 1* in exon region exist significant differences between Uygur and Han early-onset breast cancer in Xinjiang. There were certain correlations between polymorphisms of *BACH 1/BRIP 1* gene and different clinical pathological features in Uygur and Han, such as Ki-67 status, family history of cancer and menarche age. These findings can guide high-risk population screening and clinical individualized treatment in Uygur and Han early-onset breast cancer in Xinjiang.

PO144

Attitude Towards the Risk-Reducing Strategies Uptake of Breast and Ovarian Cancers in Malaysian *BRCA* Mutation Carriers

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Background/Purpose: *BRCA* testing is projected to be more accessible and commonplace due to reduction in price and turnaround time. Little is known about the risk-reducing strategies (RRS) uptake in the Southeast Asian setting. In multi-ethnic Malaysia, there are many challenges faced in the provision of RRS to *BRCA* carriers.

Methods: We embarked upon a mixed-method study to investigate the RRS uptake by *BRCA* carriers identified from the Malaysian Breast Cancer (MyBrCa) study. A qualitative study to explore the psychosocial aspect behind the decision making was carried out. Information on *BRCA*-positive disclosure, attendance to genetic counselling and risk management clinic (RMC) and the RRS uptake were collected retrospectively. A topic guide was used to explore their experiences in RRS decision making. The interviews were audio-taped and transcribed verbatim. Thematic analysis and data management using NVivo 10 was performed.

Results: 129 affected *BRCA* carriers were identified. 62 carriers had attended RMC. Ten (20.4%) chose to have risk-reducing mastectomy. 37 (71.4%) chose breast screening while one also use tamoxifen for chemoprevention. Of the 49 carriers with intact ovaries, 24 (49%) chose to have risk-reducing salpingo-oophorectomy while 18 (36.7%) chose ovarian screening. In the qualitative study, eight carriers were interviewed. The emergent themes that motivates RRS were: Maximize survival for children, completed childbearing and not wanting to relive previous cancer experience. The barriers: Losing femininity and do not fix what is normal.

Conclusion: These findings will direct future research towards the development of intervention to assist RRS decision making in Malaysian *BRCA* carriers.

PO145

The Impact of *BRCA* Renetic Communication by Carriers to Relatives on the Uptake of Predictive Genetic Testing in Multiracial Malaysia

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Background/Purpose: There remain significant challenges in reaching the relatives in families with known *BRCA* mutations in Malaysia. In this study, we address these challenges which influence the uptake of *BRCA* genetic testing.

Methods: A survey was carried out to investigate the disclosure and communication pattern to relatives by the carriers who were identified in the Malaysian Breast Cancer (MyBrCa) study and the uptake of genetic counselling in these families.

Results: In this study, 64 *BRCA* carriers had result disclosure and 50 are still alive with a median follow up of 53 months (range 2 to 93). We report that of the 50 *BRCA* carriers, 44 (90%) responded to a counsellor-administered survey. 41 (93%) probands informed all of their 196 first degree relatives and 511 of 1,092 (47%) second/third degree relatives. 62 (32%) first degree and 32 (6%) second / third degree relatives from 25 (60%) informed families came forward for genetic counselling and testing. Notably, no relatives from 16 families (40%).

Conclusion: Our experience in Malaysian cohort indicates that 60% families have relatives coming forward but in 40% of families informed, none came forward. This could be due to the inherent stigma within the families about *BRCA* testing or the methodology and effectiveness of the probands' communication to their relatives. More research is necessary to aid the communication of genetic information to relatives and to overcome the stigma against the families as perceived by the probands to increase uptake of genetic counselling and genetic testing.

PO146

Impact of Angelina Jolie's Story on Genetic Referral and Testing and Uptake of Preventive Surgery in Asia

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Background/Purpose: In May 2014, Hollywood mega-star Angelina Jolie underwent preventive double mastectomy after she was found to be a *BRCA1* mutation carrier. Since then, there have been reports from Western institutions showing increase in referral for genetic counselling and testing and uptake of preventive surgery. The impact of the "Angelina Jolie effect" in Asia has not been reported.

Methods: We compared the number of patients referred, proportion of appropriate referrals, proportion of counseled patients who underwent genetic testing, and the number of mutation carriers undergoing preventive mastectomy and/or preventive salpingo-oophorectomy, 12 months before and after the Angelina Jolie story, from a cancer genetics clinic in a tertiary cancer centre in Singapore.

Results: Over a 12-month period immediately before and after the Angelina Jolie story, 49 *vs* 74 patients were referred for *BRCA1/2* counselling and testing, with 95.9% of referrals meeting testing criteria in both periods. Before the story, 9/47 (19.1%) patients fulfilling testing criteria underwent testing, compared to 35/71 (49.3%; $p = 0.001$) after. No mutation carrier identified before the story underwent preventive surgery. In contrast, after the story, 4/10 (40.0%) confirmed mutation carriers underwent preventive mastectomy and salpingo-oophorectomy, and 1/10 (10.0%) underwent salpingo-oophorectomy, at a median of 7 months (range 4-9) after diagnosis.

Conclusion: After the release of Angelina Jolie's story, genetic referrals and uptake of *BRCA1/2* genetic testing increased 1.5- and 2.5-fold respectively, and half of confirmed mutation carriers underwent preventive surgery within 9 months of diagnosis in Singapore, underscoring the impact of the "Angelina Jolie effect" even in Asia.

PO147

Review of the Clinical Characteristics and Surveillance Data for Hereditary Breast and Ovarian Cancer from a Single Institution in Japan

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Background/Purpose: Hereditary breast and ovarian cancer (HBOC) is a high-penetrance inherited disease. Characteristics such as bilateral breast cancer and early onset have been reported in the West. In this study, we reviewed the clinical characteristics and examined HBOC cases from a single institution in Japan.

Methods: Data on 47 *BRCA1/2* carriers and 140 non-carriers were collected at Showa University in Tokyo from September 2010 until the end of December 2014. Data regarding the age of breast cancer onset, pathological features, onset characteristics (e.g., unilateral, bilateral, or multiple breast cancer), second primary breast cancer age of onset, and anticipation symptoms were collected.

Results: Triple negative breast cancer was 84% in *BRCA1*. Nuclear Grade ≥ 2 was 92% in *BRCA2*. The age of onset was earlier for *BRCA1* than *BRCA2* breast cancer (38.8 *vs.* 41.6 years), and the periods until contralateral breast cancer onset (8.3 *vs.* 10.5 years) and recurrence in the conserved breast (5.8 *vs.* 7.3 years). Furthermore, when the age of onset was older than 10 years, there was a tendency of early development of *BRCA1* and *BRCA2* cancer in the subsequent generation (17.5 *vs.* 14.0 years).

Conclusion: Surveillance within ten years of the initial breast cancer was important in both *BRCA1* and *BRCA2* mutation carriers. We also considered anticipation symptoms and determined that earlier surveillance in the subsequent generation is necessary.

PO148

Utilization of Multi-Gene Panel Testing for Hereditary Breast and Ovarian Cancer Syndrome in a Cancer Genetics Clinic in Singapore

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Background/Purpose: Multi-gene panel testing using next generation sequencing is now widely available and affordable, and is increasingly used in clinical genetic testing in place of conventional single-gene testing. Multi-gene panel testing increases the likelihood of identifying causative mutations in genes other than *BRCA1/2* in patients suspected of having hereditary breast and ovarian cancer (HBOC) syndrome.

Methods: The national university cancer institute, singapore (NCIS) cancer genetic clinic started to offer multi-gene panel testing in July 2014. We compared the results from single-gene *BRCA1/2* and multi-gene testing among patients suspected of having HBOC syndrome at our clinic in the last 24 months. The multi-gene panel test comprises comprehensive sequencing and multiplex ligation-dependent probe amplification (MLPA) analysis of up to 29 genes including *BRCA1/2*, *PTEN*, *TP*53, *ATM*, *CDH*1, and the mismatch repair genes.

Results: From February 2013 to January 2015, 54 patients underwent single-gene testing. 11/54 (20.4%) carried deleterious mutations (*BRCA1* = 7, *BRCA2* = 4). 9/54 (16.7%) carried variants of uncertain significance (VUS). From July 2014 to January 2015, 21 patients underwent multi-gene testing. 4/21 (19.0%) patients carried deleterious mutations (*BRCA1/2* = 3, *TP53* = 1); the *TP53* mutation carrier had family history of breast/intestinal/nose cancer that did not fulfil testing criteria for Li-Fraumeni syndrome. A possibly deleterious *MSH2* mutation was identified in a young breast cancer patient with family history of stomach cancer. 3/21 (14.3%) patients carried VUS (*ATM* = 2, *MSH2* = 1).

Conclusion: Multi-gene panel testing is useful in identifying causative mutations in genes which may not have been predicted based on the patients' personal and family history of cancers.

PO149

Preliminary Screening of Variants of Uncertain Significance in *BRCA1* and *BRCA2*: A Malaysian Case-Control Study

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Background/Purpose: Estimation of breast cancer risk for variants of uncertain significance (VUS) in the *BRCA1* and *BRCA2* genes is a major challenge in genetic counseling and clinical management. Majority of VUS identified in Asians are unclassified. This study sought to evaluate the estimated risk of VUS identified in Malaysian Breast Cancer Genetic Study using a case-control approach.

Methods: From March 2003 to April 2014, 2,094 breast cancer patients and 1,464 unmatched healthy controls from University Malaya Medical Centre and Sime Darby Medical Centre in Kuala Lumpur, Malaysia were recruited to this study. Genotyping of the VUS was conducted using Sequenom MassARRAY iPLEX platform. Seventy VUS included in the genotyping assay were selected from literature search or identified from our study previously. The estimated risk of VUS was evaluated by calculating the variant frequency and odds ratio with logistic regression.

Results: Seven variants (*BRCA1* Y856H; *BRCA2* C315S, V950I, I1929V, R2108C, K2729N and I3412V) were likely benign as the variant frequency ranges from 1.0% to 3.8%. Two variants were likely to be associated with breast cancer risk, namely *BRCA1* P346S (OR = 3.0; 95% CI, 0.6-15.5; $p = 0.189$) and *BRCA1* R762S (OR = 7.2; 95% CI, 0.8-60.1; $p = 0.067$). Other variants (n = 61) in this study showed inconclusive results or cannot be evaluated because they were rare in our population.

Conclusion: The estimated breast cancer risk for 13% (9/70) of variants in this study

were evaluated. Future studies are needed to characterize these variants using other methods.

Prevention of Breast Cancer Among Women in Nigeria

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Background/Purpose: Breast cancer is an increasing public health problem in Nigeria among women due to lack of proper medical check up, and attitude toward taking proper precautions against factor that can cause breast cancers. Substantial advances have been made in the treatment of breast cancer, but the introduction of methods to predict women at elevated risk and prevent the disease has been less successful. It was revealed in recent data on newer approaches to risk prediction, available approaches to prevention, how new approaches may be made.

Methods: The methods which breast cancer can be effectively prevented and studies are divided in to four areas: (a) the prediction of breast cancer risk, (b) the evidence for the effectiveness of preventive therapy and lifestyle approaches to prevention, (c) how understanding the biology of the breast may lead to new targets for prevention, and (d) a summary of published guidelines for preventive approaches and measures required for their implementation.

Results: The Chi-square analysis was used in calculating the result, it was revealed if the Chi-square calculated is less than the chi-square tabulated, we accept the null hypothesis and reject the alternative hypothesis, but if the Chi-square calculated is greater than the chi-square tabulated we accept the alternative hypotheses and reject the Null hypothesis. The results level of significant is assumed to be 5% (0.05).

Conclusion: Overweight/obesity increases the risk for cancers of the oesophagus (adenocarcinoma), colorectum, breast (postmenopausal), endometrium and kidney; body weight should be maintained in the body mass index range of 18.5-25 kg/m^2, and weight gain in adulthood avoided. Alcohol causes cancers of the oral cavity, pharynx, oesophagus and liver, and a small increase in the risk for breast cancer; if consumed, alcohol intake should not exceed 2 units/d. Aflatoxin in foods causes liver cancer, although its importance in the absence of hepatitis virus infections is not clear; exposure to aflatoxin in foods.

PO151

Efficacy of Progressive Relaxation Technique and Acupressure on Pain Management and Sleep Quality Among Breast Cancer Patients

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Background/Purpose: Non-pharmacological management/complementary therapy of pain is considered neglected area of pain management for both physicians and nurses, although it is safe, noninvasive, and generally considered to be relatively free from side-effect. The aim of the current study is to identify the efficacy of progressive relaxation technique and acupressure on pain management and sleep quality among breast cancer patients

Methods: sixty patients diagnosed as metastatic breast cancer were randomly divided into two equal groups: Study group (I) were received progressive relaxation and acupressure for pain management and sleep disorders. Control group (II) were exposed to routine hospital care for pain management and sleep disorder such as pharmacological management. Tools of the study: Five tools were utilized for data collection.

Results: Mean scores for pain, sleep quality, symptom distress and anxiety improved from baseline for study group who received progressive relaxation technique and acupressure than control as well as statistically significant differences were found concerning previous mentioned items between both groups.

Conclusion: Patients exposed to relaxation sessions and acupressure experienced lower intensity of pain and high sleep quality compared to control group. So, we recommend that both techniques should be integrated as part of routine nursing care along with pharmacological interventions for the management of pain and insomnia. Future research is needed to develop and update other forms of relaxation techniques.

PO152

Effect of Antiadhesion Barrier Solution and Fibrin on Capsular Formation After Breast Reconstruction

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Background/Purpose: One of the most serious complications of breast reconstruction using silicone implants is capsular contracture. This study was performed to compare anti-adhesion barrier solutions (AABS) and fibrin in their ability to prevent fibrotic capsule formation by capsular thickness analysis and quantitative analysis of matrix metalloproteinases, tissue inhibitors of metalloproteinases, and type I collagen within the the fibrous capsule.

Methods: This study used six-week-old Sprague-Dawley rats. Eighty rats were subdivided into four following groups: AABS-treated, fibrin-treated, AABS and fibrin combined-treated, and untreated control groups. Each rat received two silicone chips under the panniculus carnosus muscle layer. The test materials were applied around the silicon chips. Four weeks later, the implantation sites were excised and analyzed.

Results: The capsular thickness was significantly decreased in all experimental groups ($p < 0.05$). The capsular thickness was greater in the fibrin-treated group than in the AABS-treated group ($p < 0.05$). The experimental groups had significantly lower expression of type I collagen and MMP-1 ($p < 0.05$). The expression of MMP-2, and TIMP-2 was not significantly different among the all group.

Conclusion: AABS is more effective in reducing capsular thickness compared with fibrin treatment in a white rat model.

PO153

Psychological Distress and Unmet Supportive Care Needs of Patients with Breast Cancer

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Background/Purpose: Few studies have investigated the psychological distress and the unmet needs among breast cancer patients and little is known about the relation between their unmet needs and psychological distress. This study aimed to identify the relation between their unmet needs and psychological distress in breast cancer patients after cancer treatment

Methods: In a cross-sectional study, 112 breast cancer patients who had been treated with a definitive surgical procedure, within 4 weeks of completion of primary treatment for breast cancer recruited from an outpatient clinic of a university hospital. They were asked to complete the 'distress thermometer (DT)' and 'Supportive Care Needs Survey-Short Form' to measure psychological distress and supportive care needs.

Results: With a cut-off of 4 on the DT, 22.3% of patients reported distress. Patients reported the most unmet needs in the health system and the information domain. Patients with DT scores ≥4 had higher needs overall and all domains than patients with DT scores <4. A higher level of psychological distress indicated higher supportive care needs.

Conclusion: This study found that one third of breast cancer patients experience distress at the end of primary treatment and the majority of breast cancer patients reported one or more unmet needs. As a higher number of unmet needs is significantly associated with psychological distress, interventions addressing this constellation of issues are needed.

PO154

10 Seconds to Understand Psychological Health of Breast Cancer Patients

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Background/Purpose: Distress is "an unpleasant experience of an emotional, psychological, social, or spiritual nature." Cancer patients' distress interfere their ability to cope with cancer treatment and beyond. The Distress Thermometer (DT) is the most widely used quick screening tool for assessing psychological distress in cancer patients. This study aims to assess level and types of distress and its association with quality of life and psychological health during breast cancer treatment continuum.

Methods: 432 patients expecting surgery were recruited for a prospective cohort study at 2 cancer hospitals in Seoul, Korea from July 2010 through July 2011. Distress level and problems were assessed using one page NCCN DT with problem list (PL) before surgery, 2-weeks, 3-, 6-, and 12-months after surgery. Quality of life, depression and anxiety was assessed using EORTC-C30 and BR23 and HADS respectively. Association between distress and quality of life was assessed using multivariate linear regression and STATA 12 was used for all the analysis.

Results: Patients expressed highest distress before surgery (5.3, SD = 2.7) and almost everyone (95%) checked at least one problem. Patients commonly reported worry, fatigue, pain, and depression across treatment continuum. Patients had distress from altered-appearance (3.4, SD = 2.9) and skin-change (1.5, SD = 2.1) at 2-weeks and 3-months after surgery. Patients were most likely to have clinical level anxiety (21.8%) and depression (50.9%) before surgery and 3-months after surgery respectively. Patients with lower distress (-2.871, SE = 0.225) had fewer problems checked (-2.131, SE = 0.130) reported better quality of life and social supports. All was statistically significant.

Conclusion: Distress level has a strong correlation with the overall number of problems and patients had different problems at each time point. One page DT with PL helps to understand patients' psychological health status and concerns that may affect patients' distress level. Routine screening of DT would help health professional to find problems patients had and appropriate intervention and support is required after DT screening at regular clinic.

PO155

Feasibility of Withholding Dexamethasone Premedication in Weekly Paclitaxel Administration and Adverse Reaction

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Background/Purpose: Premedication dexamethasone with is a crucial part in prevention of hypersensitivity reaction (HSR) associated with taxane administration. However, during weekly paclitaxel administration, patient may expose to high and prolonged dose of dexamethasone prophylaxis and may cause significant adverse effects. Our study aims to evaluate the incidence of infusion HSR in patients who received and not received dexamethasone premedication.

Methods: We retrospectively reviewed medical records of the patients with early breast cancer who received adjuvant weekly paclitaxel from January 2012 through December 2014 at the King Chulalongkorn Memorial Hospital. All patients received standard premedication protocol prior to 1st dose of paclitaxel infusion. Dexamethasone had been omitted in later cycles in some patients according to physician discretions. Baseline patient and tumor characteristics, details of premedication protocol including dose and schedule of dexamethasone, and HSR events were collected.

Results: There were 75 breast cancer patients and total 809 cycles of paclitaxel administrations. Median age of patient was 52 years and no known history of allergy or HSR to taxanes. Dexamethasone had been omitted in later cycles in total 342 cycles. Six of 75 patients who received weekly paclitaxel chemotherapy were reported grade II-III HSR (7.7%) which occurred mostly during the first six cycles (5/6, 83.3%). In total of 809 cycles, the incidence of HRS were 5/467 (1.1%) cycles with dexamethasone premedication and 3/342 (0.9%) without dexamethasone ($p = 0.54$).

Conclusion: Withholding dexamethasone premedication for weekly paclitaxel chemotherapy was feasible and did not results in higher incidence of HSR. However, an optimal dexamethasone schedule should be further investigated in a prospective manner.

PO156

Cost-Effectiveness Study on Preoperative Sentinel Lymph Node Mapping in Early Breast Cancers

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Background/Purpose: Sentinel lymph node (SLN) biopsy is currently the gold standard of treatment in early breast cancers. Preoperative identification of SLN by scintigraphy has been carried out to improve the detection of SLN. Here we analyze the cost-effectiveness of the use of scintigraphy in detection of SLN

Methods: Clinical and operative details were retrieved from a prospectively maintained database. The resources and cost data from each patient who had undergone sentinel lymph node biopsy were retrieved. Patient demographics, clinical outcomes like relapse and recurrence rate, and SLN detection rates were analyzed with multivariate analysis. *p*-value of less than 0.05 will be considered statistically significant.

Results: From January 2008 to December 2012, a total of 400 patients have undergone SLN biopsy for breast cancers. 329 had pre-operative SLN mapping with scintigraphy, while 71 patients did not due to logistic reasons. Baseline patient demographic data, relapse and recurrence rate, and SLN detection rates were comparable. However there was an additional cost for each pre-operative SLN mapping (USD$345.8).

Conclusion: Pre-operative SLN mapping does not improve the SLN detection rate, it does not affect the clinical outcomes of SLN biopsy neither. With the additional cost required to perform SLN mapping. pre-operative SLN mapping is no longer cost-effective.

PO157

Vinorelbine Monotherapy in Patient with Recurrent and Metastatic Breast Cancer

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Background/Purpose: Vinorelbine is highly active in the treatment of metastatic breast cancer, both as a single agent and in combination regimens. Furthermore, it is well tolerated, with favorable safety profile. The aim of this study was to investigate response rate, time to disease progression and the toxicity of vinorelbine monotherapy in treatment of patients with recurrent and metastatic breast cancer.

Methods: We conducted a retrospective study of 57 patients with recurrent and metastatic breast cancer pretreated with taxanes and anthracyclines at National Cancer Hospital of Viet Nam between January 2012 to December 2013 who had been treated with weekly Vinorelbine oral 80 mg/m^2 on day 1, 8 every 3 weeks. Treatment was continued until disease progression.

Results: For overall response rate of 38.6% (95% CI 33% to 49%), 4 patients (7.0%) had complete responses and 18 patients (31.6%) had partial responses. Time to disease progression was 7.3 months. A total of 456 cycles were given to 57 patients. At least one cycle of grade 3 or 4 neutropenia was seen in 6% of the patients.

Conclusion: The results indicated that vinorelbine was effective and well-tolerated. Moreover, this agent may offer the specific advantages, as fewer and shorter hospital visits, delayed use of intravenous chemotherapy, maintained social activities and therefore provided a good quality of life. However, a larger study and longer follow-up are needed to evaluate the long term outcome.

PO158

The Use of Tisseel Fibrin Sealant in Seroma Reduction After Mastectomy? A Pilot Study

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Background/Purpose: Postmastectomy seroma formation is common and associated with increased morbidity. Use of pressure garments, immobilization of the ipsilateral upper limb, quilting and use of sclerosing agents have been described to decreased seroma formation. Thus far, no method has been shown to be effective. We explore the use of fibrin sealant to reduce seroma formation through improved tissue adherence and hemostasis.

Methods: We compared the degree of seroma formation in 10 patients with 2 mL of Tisseel fibrin sealant applied to the post mastectomy wound cavity before closure with 10 patients who underwent wound closure without use of Tisseel. The amount of seroma formation (assessed by drain volume and volume of seroma fluid aspirated after drain removal) were compared between the two groups.

Results: Median time to drain removal for Tisseel group is 6.5 days; 10.5 days for control group ($p = 0.06$). Median drain volume for Tisseel group is 335.0 mL; 530.0 mL for control group ($p = 0.12$). Median aspiration volume after drain removal for Tisseel group is 52.5 mL; 89.5 mL for control group ($p = 0.12$). Median total seroma volume for Tisseel group is 507.5 mL; 770.0 mL for control group ($p = 0.05$).

Conclusion: The use of fibrin sealants like Tisseel effectively reduces seroma formation. Fibrin sealants have a good safety profile, are easy to use and do not significantly increase operative time. However increased cost may pose to be a problem. A follow-up prospective study of a larger scale is underway to analyze the cost and benefits of this technique.

PO159

Patterm and Predictors of Locoregional Failure in Locally Advanced Breast Cancer Following Neoadjuvant Chemotherapy and Modified Radical Mastectomy with or without Radiotherapy: A Philippine Tertiary Breast Center Experience

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Background/Purpose: Locally advanced breast cancer (LABC) has high risk of locoregional recurrence (LR) which impacts survival. Neoadjuvant chemotherapy (CT) in LABC downstages tumor for resection. Impact of neoadjuvant CT on LR in Filipino LABC patients is unknown. The study aimed to identify the pattern and factors associated with LR in LABC patients following neoadjuvant CT, mastectomy, with or without radiotherapy (RT).

Methods: Medical records of LABC patients who had neoadjuvant CT and modified radical mastectomy with or without adjuvant RT in the Breast Care Center, Philippine General Hospital from 2007-2010 were reviewed. Comparisons using Student's t-tests and Chi-square tests and logistic regression analysis were done with p values ≤ 0.05 considered significant.

Results: Of 63 patients, 54% had LR at 2 years with 263 days mean time to recurrence. Age, pathologic nodes (pN), percent positive pN, pStage, lymphovascular invasion (LVSI), and RT were significant LR predictors on simple logistic regression. pN (OR 1.31, $p = 0.01$) and RT (OR 0.14, $p = 0.004$) were independent predictors on multiple logistic regression. In patients without RT, no independent predictor was found.

Conclusion: LABC frequently recurred. High pN and no adjuvant RT predicted for recurrence. No variable defined low risk category to preclude adjuvant RT.

Poster Exhibition

PO160

Early Complications and Oncologic Outcome of Lipofilling in Breast Cancer Patients

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Background/Purpose: Lipofilling or autologous fat transposition has been indicated for postmastectomy and postlumpectomy breast reconstruction. Improving outcome of the breast contour is the prominent point of lipofilling in breast cancer patients underwent breast surgery. In this paper. We focused on the early complications and local recurrence after receiving this procedure.

Methods: In 18 months experience of a single institution. Ductal carcinoma *in situ* and invasive breast carcinoma patients who underwent oncologic procedure and lipofilling or Autologous fat transposition (37 single-surgeon procedures with the same fat decanting technique) for reconstructive purpose were retrospectively collected data.

Results: Total numbers were 32 patients that included invasive carcinoma (26 cases) and carcinoma *in situ* (5 cases) with 37 Lipofilling procedures. Mean volumes of fat injection was 124.09 mL (30-340 mL) and mean follow-up was 417.8 days (45-549 days) from lipofilling. Meanwhile there were five cases underwent bilateral operation. No early complications and local recurrence were detected between clinical surveillance.

Conclusion: From our experience, lipofilling in breast cancer patients can be recommended at this time. Our study along with other reports supports benefit of lipofilling in defect postsurgery for improving the breast contour.

PO161

Neoadjuvant Chemotherapy: Pathological Complete Response Does Not Predict Disease Free Survival/ Overall Survival-A Retrospective Study

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Background/Purpose: This is an audit of neoadjuvant chemotherapy (NCT) in KK Women's and Children's Hospital, Singapore over 9 years. We used retrospective data from the KKH breast cancer database for this study. The aims of the study were to determine pathological complete response (pCR) rate, to identify clinicopathologic relationship to pCR and to plot survival/recurrence curves for these patients.

Methods: Data on patients with NCT from May 2005 to December 2013 (Median follow up: 40 months) were studied. All the patients who underwent NCT (n = 137) were included.127 patients were analyzed as ten patients had missing data. pCR defined as no residual carcinoma in the breast and axilla. Statistical analysis was done by chi-square/ logistic regression. Disease free survival/overall survivals were plotted by Kaplan Meir Curves.

Results: Annual trend shows the number of patients receiving NCT is increasing. pCR rate was 23.6%. No (clinical factors, size, type, grade, lymphovascular invasion, nodal status, estrogen receptor, progesterone receptor, type of chemotherapy) variable had statistically significant association with pCR. HER2neu positivity and trastuzumab therapy showed a trend towards statistically significant benefit. No difference in Disease Free Survival (DFS)/Overall Survival (OS) seen between the patients with pCR and non pCR.

Conclusion: The patients on NCT are increasing. The pCR rate of 23.6% is comparable with international literature. Lack of correlation between pCR and DFS/OS could be due to small sample size, short term follow up, retrospective data and variable chemotherapy regimens. Longer follow up and standardization of chemotherapy regimens may show that patients with pCR go on to have better OS/DFS.

PO162

Validation Study of the Modified Injection Technique for Internal Mammary Sentinel Lymph Node Biopsy in Breast Cancer

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Background/Purpose: According to the hypothesis of internal mammary sentinel lymph node (IM-SLN) lymphatic drainage pattern, a modified radiotracer injection technique was established which could promote the visualization rate of IM-SLN significantly (from 12.5% to 72.3%). In the validation study, different tracers were injected at different sites of the breast to observe whether could reach to the same IM-SLN.

Methods: The radiotracer (99mTc-labeled sulfur colloid) was injected with the modified technique (periareolar intraparenchyma, high volume and ultrasonographic guidance), and fluorescence tracer (Indocyanine Green) was injected in the peritumoral intraparenchyma. The radioactive IM-SLN was identified by preoperative lymphoscintigraphy and/or γ probe. IM-sentinel lymph node biopsy (SLNB) was performed under the guidance of intraoperative γ probe. The fluorescence tracer was identified by the fluorescence imaging system.

Results: 159 patients were enrolled from September 2013 to December 2014. 115 patients were identified radioactive IM-SLN, the IM-SLN visualization rate was 72.3%, and the success rate of IM-SLNB was 93.6% (102/109). The radiotracer and the fluorescence tracer were identified in the same IM-SLN in 86 cases, and the concordance rate was 84.3% (86/102, Case-base, Spearman coefficient correlation 0.806, $p < 0.001$).

Conclusion: Different tracers injected in the intraparenchyma could reach to the same IM-SLN. It proved that IM-SLN receives not only the lymphatic drainage from the primary tumor area but the entire breast parenchyma, and IM-SLN detected with our modified injection technique was the "true" sentinel node in internal mammary.

PO164

Omental Flap Obtained by Laparoscopy for Breast Oncoplasty After Breast Conserving Surgery

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Background/Purpose: Technique of breast oncoplasty after breast conserving surgery using omental flap obtained laparoscopically had been developed in the past decade. Our experience with this new technique was reported.

Methods: Patients who had desires and indications for breast oncoplasty using laparoscopically obtained omental flap after breast conserving surgery were recruited. Evaluation on its oncological and cosmetic results was undertaken.

Results: Twenty five patients underwent the surgery. Twenty five patients underwent the surgery, one failed as the omentum was obtained unsuccessfully. All recovered smoothly except one patient who had colon adhesion. Follow up for mean 24 months, three fatty necrotic nodules in ometal flap without affecting the cosmesis. Two recurrent cases, which were both node positive triple negative breast cancer. The cosmetic satisfaction were 91.7% by surgeon while 95.8% by patients themselves.

Conclusion: Oncoplastic breast surgery using omental flap obtained by laparoscopy is a safe technique with less invasion and good cosmesis.

PO165

Outcomes of Triple-Negative versus Non-Triple-Negative Breast Cancers Treated with Breast Conserving Therapy in Patients Under 35 Years of Age

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Background/Purpose: Triple-negative breast cancer (TNBC), having a higher risk of both local and distant recurrence, preferentially affects young women. Conflicts remain concerning the surgical option of young patients with TNBC. This study was to compare the outcomes of TNBC and non-TNBC underwent breast conserving therapy (BCT) in women under 35 years of age.

Methods: We collected the medical records of patients younger than 35 years of age underwent BCT from 2000 to 2009 in Tianjin Medical University Cancer Institute and Hospital. Patients were divided into TNBC and non-TNBC according to their receptor status. Clinicopathological characteristics and the outcomes were compared. The independent predictors of outcome were identified by the Cox proportional hazard model.

Results: The histological grade and 5-year local recurrence rate were significantly higher in TNBC group ($p = 0.020$ and $p = 0.048$, respectively). However, no significant difference was observed in distant metastasis rate ($p = 0.731$) or OS ($p = 0.349$). Histological grade, but not TNBC, was an independent prognostic factor of local recurrence (OR = 10.686, $p = 0.019$). TNM stage (OR = 3.503, $p = 0.001$) and histological grade (OR = 5.472, $p = 0.020$) were independent factors of overall survival (OS).

Conclusion: The young female with TNBC might have a higher local recurrence rates. but the distant metastasis rate and OS were not significantly different with non-TNBC. Which indicated that BCT in young patients under 35 might have comparable outcomes for triple negative and non-triple negative breast cancers. If done appropriately, TNBC patients with young age could also be candidates for BCT.

PO166

Comparison of Outcomes After Breast Conserving Therapy with Partial and Whole Breast Irradiation in Young Women with Breast Cancer

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Background/Purpose: Partial breast irradiation (PBI) has been investigated as an alternative to whole breast irradiation (WBI). However, uncertainty persists about the use of PBI on practice for young women because young age might be associated with more aggressive disease. The purpose of this report is to review the outcomes of PBI in comparison to WBI during the same time interval.

Methods: We evaluated 426 consecutive patients with T ≤ 3cm N0-1 breast cancer who underwent breast conserving therapy (BCT) between November 2007 and December 2014. A total of 170 WBI patients received 50 Gy in 25 fractions, and 256 PBI patients received 32 Gy in 8 fractions using multicatheter brachytherapy. Patients who underwent neoadjuvant chemotherapy were not included in the analysis.

Results: Of 176 patients < 50 years, the mean age of 81 WBI patients (42.1 years) was significantly lower than that of 95 PBI patients (43.9 years, $p = 0.015$). The ipsilateral breast tumor recurrence was 2.5% and 3.1% in WBI and PBI ($p = 0.588$). There was no significant difference in the 3-year probability of disease-free survival (98.1% and 97.3%; $p = 0.986$).

Conclusion: Although this study was based on a small number of patients with a relatively short follow-up period, BCT with PBI could achieve similar clinical outcomes to that with WBI for young women with breast cancer. Further investigation with larger populations and longer follow-up is warranted to confirm that PBI is an effective alternative to WBI for those patients.

PO167

Effectiveness of Rapid Intraoperative Pathological Diagnosis for Breast Conserving Surgery

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Background/Purpose: The effectiveness of rapid intraoperative pathological diagnosis in breast-conserving surgery is unknown. It has been reported that when surgical margins are positive, additional resection or alternatively boost irradiation should be performed. However, there is no established opinion. In the present study, we investigated the effectiveness of rapid intraoperative pathological examination in breast conserving surgery.

Methods: Of the 274 patients who underwent surgery for breast cancer at our hospital between January 2007 and December 2013, 66 patients who underwent breast-conserving surgery were retrospectively examined for the relationship between the status of the resected margins and local recurrence. The resected margins was then submitted for evaluation by rapid intraoperative pathological examination.

Results: Positive margins were found in 14 patients (21%). Total mastectomy was performed in 9 patients, and additional resection in 5 patients. False negative results were found in 3.8%. There was no local recurrence observed in all patients who underwent additional resection or total mastectomy. The rate of margin positivity was significantly high in invasive lobular carcinomas, and with intraductal extension.

Conclusion: Rapid intraoperative pathological examinations will very likely yield a negative margin after resection. In the present study, we observed no patients with local recurrence. Therefore we believe that this is an effective procedure that can be expected to reduce the rate of local recurrence.

PO168

Phase II Trial of Weekly Nab-Paclitaxel and Carboplatin Treatment with or without Trastuzumab as Nonanthracycline Neoadjuvant Chemotherapy for Locally Advanced Breast Cancer

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Background/Purpose: Neoadjuvant chemotherapy (NCT) has become standard treatment for women with locally advanced breast cancer. Patients who attained a pathological complete response (pCR) have improved survival. The aim of this study was to compare the efficacy and safety of nanoparticle albumin-bound paclitaxel (nab-paclitaxel) or paclitaxel treatment combined with carboplatin.

Methods: Thirty patients were treated with weekly nab-paclitaxeland carboplatin every 21 days × 4 cycles. Ninety matched patients received weekly paclitaxel and carboplatin every 21 days × 4 cycles. Weekly trastuzumab is recommended for human epidermal growth factor receptor 2 (HER2) overexpression. Matching was conducted according to six variables: body mass index, clinical tumor stage, clinical lymph node status, estrogen receptor status, HER2 status and trastuzumab receiving rate.

Results: Two regimens showed similar clinical objective response (90.0% vs. 80.0%, $p = 0.450$). Nab-paclitaxel did not improve the pathological complete response rate in two cohorts (26.7% vs. 25.6%; $p = 0.904$). When trastuzumab was added to the containing nab-paclitaxel treatment, the pCR rate was not significantly improved (43.6% vs. 39.6%; $p = 0.769$). Nab-paclitaxel regimen caused higher grade 4 neutropenia (56.7% vs. 21.1%, $p < 0.001$).

Conclusion: Our study showed that weekly nab-paclitaxel and carboplatin with or without trastuzumab resulted in a pCR rate that was not superior to the matched cohorts. Future, larger trials are needed to validate that nab-paclitaxel treatment is beneficial for clinical tumor stage II or the triple-negative subgroup.

PO171

Factors Affecting Outcomes of Breast-Conservation Therapy in Patients with Ductal Carcinoma *In Situ* of the Breast

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Background/Purpose: Breast-conservation therapy (BCT) for patients with ductal carcinoma *in situ* (DCIS) of the breast is increasingly chosen and provides the excellent outcomes. There is little information on the demographic and clinical outcome data in Thai population. This study aimed to determine the factors affecting locoregional recurrence in a cohort of patients treated at a large tertiary care hospital.

Methods: Chart of all patients diagnosed with DCIS who underwent BCT at the Department of Surgery, Siriraj Hospital Medical School during January 2009 and June 2014 were reviewed. Patient characteristics, tumor size, tumor biology, surgical margin and adjuvant therapy were recorded. The primary endpoint was ipsilateral breast recurrence. Factors associated with locoregional recurrence were identified.

Results: Mean age of the patients was 51.47 years old (21-75 years old). No major post-treatment complication was found. A median follow-up time was 35 months (7-71 months). The ipsilateral local recurrence rate was 4.48% and an average time from initial treatment to recurrence was 23 months.

Conclusion: BCT can be the treatment of choice for appropriate patients with DCIS. Tumor grading and surgical margin are major factors affecting local recurrence.

PO172

Impact of Neoadjuvant Treatment on the Feasibility of Breast Conserving Surgery for Chinese Women

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Background/Purpose: Neo-adjuvant chemotherapy could improve the rate of Breast Conserving Surgery (BCS) for Western women. However, there is a scarcity of data if this could also be applied for Chinese women.

Methods: From January 1996 to December 2012, a total of 557 patients were treated for breast cancer in the Department of Surgery at Queen Mary Hospital and they formed the focus of this study. Their clinicopathological data and treatment outcome were reviewed.

Results: 82.0% patients had invasive ductal carcinoma before operation. A total of 95 patients had either grade I or II tumors. estrogen receptor, progesterone receptor and c-erb B2 positivity were detected in 28.0%, 21.3% and 35.0% of the patients. With respect to the choice of treatment, 85.0% of patients were proposed for mastectomy. After neo-adjuvant treatment, 67.0% patients underwent mastectomy and the remaining 23.0% patients underwent wide local excision. 8.2% patients also underwent reconstruction after mastectomy. Sentinel lymph node biopsy was performed in 11.8% patients and axillary dissection was performed in 74.9% patients.

Conclusion: Neo-adjuvant treatment could successfully convert around 20% breast cancer patients with initially proposed mastectomy to BCS in Chinese women.

PO173

Breast Cancer Patients Treated in Clinical Trials: Are They Different from Those Treated in Usual Practice?

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Background/Purpose: Different outcomes of patients treated in and out of a strict trial protocol may arise from differing treatment, patient care, behavioral changes, or the placebo effects of the consent process. It is widely believed by clinicians and researchers that patients are best treated in a trial as beneficial trial effects result in superior outcomes, but this remains a point of contention. We aimed to investigate the trial effect in breast cancer patients treated at National Cancer Center, Korea.

Methods: We identified a previous breast cancer trial conducted at our institution in which the survival outcomes were not found to be different from standard treatment, and included 110 patients from this study as the trial group. Patients who fulfilled the same inclusion criteria as the trial group, but underwent standard therapy, were taken from our database, and propensity scoring was applied to match these patients to the trial group (non-trial group).

Results: There were 110 patients in each group of trial and non-trial patients, and there were no significant differences between the groups in the baseline characteristics, after propensity score matching. However, trial patients showed better recurrence free survival (Hazard ratio [HR], 0.54; 95% confidence interval [CI], 0.31-0.95) and overall survival (HR, 0.42; 95% CI, 0.19-0.95), compared to the non-trial group.

Conclusion: Trial participation confers beneficial trial effects, resulting in superior survival outcomes. Awareness of positive trial effects may create more positive perceptions of clinical trials among cancer patients, and increase their willingness in trial participation.

PO174

Factors Associated with Non-Sentinel Lymph Node Metastases in Primary Breast Cancer Patients

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Background/Purpose: For patients with clinically node negative (cN0) but sentinel lymph node (SN)-positive, the ACOSOG Z0011 and the EORTC AMAROS trials have showed that axillary radiation therapy (ART) with or without axillary lymph node dissection (ALND) provided similar recurrence rate and overall survival. However, for patients with non-SN negative, even ART without ALND may be overtreatment without improving loco-regional recurrence rate or survival. The aim of this study was to determine the factors associated with non-SN metastases in primary breast cancer patients with SN positive.

Methods: Sixteen hundred thirty eight cN0 patients underwent SN biopsy (SNB) with surgical resection for primary invasive breast cancer from January 2010 to December 2013. From the patients, SN positive patients were included in this study. Patients who underwent neoadjuvant therapy were excluded. The SN positive patients were divided into two groups depending on the status of non-SN. We extracted these patients regarding age, histological type, estrtrogen receptor status, human epidermal growth factor receptor 2 status, tumor size, nuclear grade and Ki-67 (cut off: 30%).

Results: Of the 1,638 patients, 315 patients (19.2%) had SN positive. Eighty two of the 351 patients (26.0%) had non-SN positive. Small tumor size and low nuclear grade had significantly low incidence of non-SN positive (pT1 *vs.* pT2+3, $p < 0.001$, N1+2 *vs.* N3, $p = 0.040$). In histopathological findings, invasive lobular carcinoma had a similar trend compared to invasive ductal carcinoma ($p = 0.070$) in univariate analysis. In multivariate analysis, Invasive lobular carcinoma and tumor size were independent predictive factors of non-SN negative ($p = 0.017$, and < 0.001, respectively).

Conclusion: We demonstrated that patients with invasive lobular carcinoma or small

tumor were likely to have non-SN negative. It indicates that this population does not need ALND and have low recurrence rate. Further studies are warranted to assess whether these patients have low local recurrence rate without both of ALND and ART.

PO175

Cases of Recurrence in the Reconstructed Breast in Okayama University Hospital in Japan

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Background/Purpose: Breast reconstruction after mastectomy for breast cancer is widely prevalent and contributes to reduction of the stress for patients with loss of breast. In Okayama University hospital in Japan, Breast Cancer Treatment and Reconstruction Center founded in 2008 and have experience many case of breast reconstruction. We report cases of recurrence in the reconstructed breast among these cases.

Methods: We had 132 cases underwent breast reconstruction within 601 patients with breast surgery in our hospital from October 2007 to April 2013. The age of 132 cases were 24 to 68 years old (average age 46), pathologic stage (pStage) distribution is stage 0; 33, stage 1; 36, stage 2; 41, stage 3; 22.

Results: Seven cases (4.6%) had recurrence in the reconstructed breast (including the skin). Their pStage of local recurrence is pStage 1; 3 cases, pStage 2; 3 cases, pStage 3; 1 case. Two cases were relapsed at 7 months after reconstruction, one case was at 18 months, and four cases were more than 24 months. The methods of reconstruction were mastectomy: 5, nipple sparing mastectomy: 1, skin sparing mastectomy: 1. The methods of axillary lymph node dissection were sentinel lymph node biopsy: 5 and axillaly lymph node dissection: 2. Four cases were given neo-adjuvant chemotherapy and 3 cases were given adjuvant chemotherapy. At the first operation their resection had no cancer exposure to in all cases. One case underwent postmastectomy radiation therapy.

Conclusion: In our cases, two cases were relapsed for short time from mastectomy, they might have residual lesions. Detection of local recurrence is the examination of the patient self check-ups with physician would be important, because they cannot use mammography in the postoperative follow-up for breast after reconstruction. We need further cases and take the measures for recurrence.

PO176

Triple-Negative Breast Cancer: A Single-centre Retrospective Cohort Study of 408 Patients

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Background/Purpose: Triple-negative breast cancer (TNBC) represents a heterogeneous group of breast cancers that do not express estrogen receptor, progesterone receptor and human epidermal growth factor receptor 2 receptors. Generally, these tumors are aggressive and more common in younger women, in which an association of TNBC with mutations in the *BRCA1* gene was documented. The aim of our study was to create a representative group of patients with TNBC, which could be analyzed and the data gathered to build basic epidemiological, molecular and clinical characteristics of Czech patients with TNBC.

Methods: We retrospectively studied a consecutive cohort of 408 patients diagnosed and/or treated for TNBC at the Masaryk Memorial Cancer Institute between 2004 and 2010. Some clinical-pathologic/molecular correlations were performed to identify different subsests of TNBC and groups of patients who may potentially benefit from different modes of anticancer therapy.

Results: The median age of patients with TNBC was 56 years, range 25-88 years. A total of 9.8% of TNBC cases were diagnosed in patients under the age of 34, another 14.5 % and 15.2% of cases were in the age group of 35 to 44 years and ≥ 70 years, respectively. 'Basal-like' carcinomas accounted for 75% of TNBC. We confirmed the aggressive nature of this disease: in the follow-up period (median 77.2 months) we observed a relapse in 27.2% (111) of patients: 71% of deaths due to disease progression occured within 2 years after diagnosis of the disease. Treatment strategies include chemotherapy, in most cases (88.9%). Chemotherapy was mostly based on regimens with anthracyclines or in combination with taxanes. The most important negative prognostic factors in relation to disease specific overall survival (OS) were: higher clinical stage and

pT (both-$p < 0.0001$), pN-positive status ($p < 0.001$), absence or early withholding of chemotherapy ($p < 0.001$) and minimal disease response to neoadjuvant treatment (TRG4-TRG5) ($p = 0.005$). Beside these factors, shorter DFS was associated with high tumor proliferative activity (Ki-67, cut-off 50%, $p = 0.021$). High levels of BCL2 expression predicted poor OS in basal-like TNBC patients treated with adjuvant anthracycline-based regimens ($p = 0.033$, HR 3.04).

Conclusion: TNBC is an aggressive form of breast cancer, which may occur in patients of all ages, but more frequently in younger patients. Early detection and intensive treatment od these tumors gives a high chance of cure. BCL2 expression analysis could facilitate decision making on adjuvant treatment in TNBC patients. Better therapeutic results can be expected from targeted therapy.

PO177

Ductal Carcinoma *In Situ* in Low and Middle Income Countries (LMICs): A Marker for Management?

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Background/Purpose: To determine the clinical presentation of patients presenting with isolated ductal carcinoma *in situ* (DCIS) at a single tertiary centre in the Western Cape. To review the diagnostic techniques most commonly used and the primary surgery performed for these patients.

Methods: A retrospective chart review of patients presenting with isolated DCIS over a period from January 2005 to December 2012 was performed. Patients were identified from the oncology breast cancer database, the South African National Health Laboratory System (NHLS) histological record and the surgical operative notes. Patients with a diagnosis of DCIS were identified by these means and their medical records pooled and examined. 37 patients had surgery with surgical specimens showing isolated DCIS, 5 patients had a core biopsy or punch biopsy showing DCIS with no invasive component.

Results: 42 patients with isolated DCIS were identified. DCIS comprised less than 1% (42/3768) of all breast malignancies managed in this period. There were 41 females and 1 male. The average age was 58 years. Most patients presented with a breast lump (23/42). The diagnosis was made on core biopsy in 14 patients while 8 patients required excision of the palpable lump to make the diagnosis. 23 patients underwent a primary mastectomy, 6 patients had a wide local excision (WLE) and 6 patients had a radioguided occult lesion localization (ROLL) with therapeutic intent. Our incidence of isolated DCIS (1%) is much lower than that reported in other international series. The inappropriately high axillary clearance rate for our patients could be explained by diagnostic concerns over concurrent invasive disease.

Conclusion: Though rare, the management of DCIS in this set up highlights the challenges of diagnosing and managing breast malignancies in low and middle income countries. Practical interventions like increasing human capacity in cancer diagnostics, developing health worker training in core biopsy techniques & in the use of supportive adjuncts like ultrasound could help to improve the management of cancers.

PO178

Trastuzumab Improves Locoregional Control in HER2-Positive Breast Cancer Patients Following Adjuvant Radiotherapy

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Background/Purpose: The benefit of adjuvant trastuzumab in disease-free and overall survival for human epidermal growth factor receptor 2 positive (HER2+) breast cancer patients is well established. However, the effects of trastuzumab on locoregional control remains unclear, particularly in patients receiving adjuvant radiotherapy. In this study, we investigated the locoregional benefit of trastuzumab in patients with HER2+ breast cancer after adjuvant radiotherapy (RT).

Methods: Using a single institutional database, we identified 278 patients with stage II/III invasive HER2+ breast tumors receiving adjuvant RT between January 2008 and July 2011. We compared the locoregional outcomes of 134 patients (48.2%) that received trastuzumab to patients without trastuzumab. We also assessed the impact of hormonal receptor (HR) status on locoregional benefit of trastuzumab.

Results: At the median follow-up of 45 months, trastuzumab significantly lowered the risk of locoregional recurrence (LRR) with a 3-year LRR rate of 2.4% vs 7.5% for the cohort without trastuzumab. In the HR+/HER2+ subgroup, trastuzumab was associated with a significantly higher LRR risk (3-year LRR rate 0% vs 6.7%). For HR-/HER2+ breast tumor patients, the 3-year LRR rate was still higher for the cohort with trastuzumab (4.7% vs 8.6%). However, statistical significance was lost in this subgroup. Univariate and multivariate analyses revealed that trastuzumab treatment was the only significant predictive factor for locoregional recurrence (hazard ratio, 4.05; 95% CI, 1.07 to 15.35; $p = 0.039$).

Conclusion: Adjuvant trastuzumab in addition to radiotherapy is associated with significantly reduced LRR risk in HER2+ breast cancer and can further improve locoregional control in HR+/HER2+ tumors.

PO179

Study on the Mechanism of Lapatinib Targeted Therapy Combined with Photodynamic Therapy for the HER2 Positive Breast Cancer

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Background/Purpose: In the breast cancer patients, chest wall recurrence is common, and which is hard to cure. The photodynamic therapy was confirmed to have better curative effect. This study is to investigate whether there are synergistic effects to use 5-aminolaevulinic (5-ALA)-mediated photodynamic therapy (PDT) combined with Lapatinib targeted therapy. And to detect the inhibition effects on the growth of breast cancer cells SKBr3.

Methods: We classified four different groups; A, blank control group; B, Lapatinib group (LAP); C, PDT group and D, combined therapy group (COM). We detected cell survival rate by determining the cell optical density (OD) value with MTT method. Detected the cell apoptosis and necrosis with the flow cytometry, and used which to detect the changes in mitochondrial membrane potential. Western-blot was used to detect the expression of human epidermal growth factor receptor 2 (HER2).

Results: *In vitro* experiment, it showed the effect of photodynamic therapy and the photosensitizer were dose dependent, and combined with Lapatinib can enhance the anti-tumor effect. Group LAP and group PDT showed early apoptosis and late apoptosis. Group COM mainly showed late apoptosis and necrosis, and the 24 hr cell inhibition rate reaches as high as 69.90 ± 13.54%. It was statistically significant to compare group COM with LAP and PDT ($p < 0.05$) .The mitochondrial membrane potential of Group PDT and COM decreased significantly ($p < 0.05$). Western results showed that the expression of HER2 in SKBr3 cells decreased more obviously in group COM than LAP.

Conclusion: The effect of growth inhibition with ALA-PDT on breast cancer cells SKBr3 was significant, and combined with Lapatinib can enhance the anti-tumor effect. The photodynamic therapy mainly showed apoptosis in cellular level. And the mechanism may be associated with decreased mitochondrial membrane potential of tumor cells and down regulate the expression of HER2 protein.

PO180

Efficacy of the First-Line Endocrine Therapy for Hormonal Receptor-Positive Stage IV Breast Cancer

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Background/Purpose: Breast cancer with distant metastasis at the first presentation (stage IV disease) is often encountered in the outpatient department. A goal of metastatic disease is prolongation of survival with maintaining good quality of life. Endocrine therapy is suitable for this purpose. In our institution, endocrine therapy is the treatment of choice against hormonal receptor positive breast cancer without visceral crisis. Herein, we investigated about efficacy of endocrine therapy as the first-line treatment for stage IV disease.

Methods: The patients with stage IV disease who have started first-line endocrine therapy from June 2004 to December 2013 were reviewed retrospectively based on their clinical records.

Results: Forty patients were enrolled. The median age was 64 years (range; 44 to 88 years). Six were premenopausal and they were treated by combination of LHRH agonist and tamoxifen. Thirty-four postmenopausal patients received aromatase inhibitors. Median follow up period is 155 weeks (range; 13 to 553 weeks). The overall response rate was 75% (30/40: Clinical response; 0, Partial response; 30) and clinical benefit rate was 85% (34/40: SD > 24weeks; 4). Thirty-one patients have failed the first-line endocrine therapy and 13 patients died of the disease. Mean survival time was 379 weeks and mean time to treatment (TTF) was 68 weeks. There is no significant difference in overall survival and TTF whether the patients had visceral metastases or not.

Conclusion: First-line endocrine therapy has very excellent efficacy for hormonal receptor positive non life-threatening stage IV disease even if it had visceral metastases.

PO181

Does Tumor Burden Influence the Applicative Indications of American College of Surgeons Oncology Group (ACOSOG) Z0011 Trial Towards Chinese Women Patients?

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Background/Purpose: The ACOSOG Z0011 trial proposed that axillary lymph node dissection (ALND) could be avoided in patients with clinical T1-T2 breast cancer and 1-2 positive sentinel lymph nodes (SLNs) received breast-conserving therapy (BCT). However, 27.3% patients in ALND group had additional lymph nodes metastasis. Furthermore, the trial didn't complete random allocation before operation,and the subjective selectivity of surgeons based on tumor burden (tumor size or SLNs status) during operation would cause bias on results. We aimed to validate the relativity between tumor burden and non-SLN metastasis in a Chinese patient population, then assess Z0011 trial result application to Chinese women patients.

Methods: Patients with T1 or T2, clinically node-negative invasive breast cancer underwent ALND subsequent to SLNB and 1 or 2 positive-SLNs by routine hematoxylin and eosin staining accordingly were identified from the database of Shandong Cancer Hospital excluding those who received neoadjuvant chemotherapy, previous ipsilateral axillary surgery or mulifocality.

Results: From December 2001 to January 2015, 2,431 patients had Sentinel lymph node biopsies. 766 were histologic SLN metastasis. 628 patients met the above matched-criteria resembled Z0011 trial but the qualification of surgical procedure. 408 patients' non-SLNs were negative [non-SLNs(-), 65.0%, 408/628]. 35.0% patients (220/628) had non-SLNs metastasis [non-SLNs(+)] vs 27.3% in Z0011 ALND group. 49.0% patients (308/628) were T1 tumors vs 67.9% in Z0011 ALND group. The mean tumor size,mean positive-SLNs number and the median number of removed-SLNs had significant differences between non-SLNs(+) group and non-SLNs(-) group (2.56 vs 2.24, $p < 0.001$; 1.35 vs 1.20,

$p < 0.001$; 2 vs 3, $p = 0.002$). Additionally, statistical differences consisted in non-SLN(+) rates [0-1 cm, 21.3% (10/47); 1-2 cm, 28.0% (73/261); 2-3 cm, 41.3% (88/213); 3-5 cm, 45.8%, 49/107; 0-3 cm, 32.8% (171/521); T1, 26.9% (83/308); T2,42.8% (137/320); $p < 0.001$] and ≥ 3 non-SLN(+) rate [0-1 cm, 8.9% (4/45); 1-2 cm, 11.0% (28/255); 2-3 cm, 17.3% (35/202); 3-5 cm, 26.0% (27/104); 0-3 cm, 13.3% (67/502); T1,10.7% (32/300); T2, 20.3% (62/306); $p < 0.001$] of different tumor size level. Age, hormone-receptor status or grade didn't differ between groups. Only 18.8% (118/628) patients underwent BCT, 14.1% (31/220) in non-SLN(+) group vs 21.3% (87/408) in non-SLN(-) group. The Non-SLN(+) rate of those BCT patients was 26.3% (87/118).

Conclusion: Tumor size or SLNs status did affect the rate of Non-SLN(+), and the Non-SLN(+) burden would rise significantly with the increase of tumor size. Moreover, Z0011 trial had lower tumor burden than our data. According to the statistical results of our study, the applicative indications of Z0011 trial in Chinese women patients should be limited to T1 tumor by comparing the non-SLN(+) rates of our study with the ACOSOG Z0011 trial.

PO182

Pathologic Status of the Regional Lymph Nodes Among Patients Who Underwent Surgery for Phyllodes Tumor: 8-Year Review of Cases in a Tertiary Government Institution

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Background/Purpose: Although phyllodes tumors rarely metastasize to the axillary nodes, we have encountered cases presenting with grossly enlarged lymph nodes either preoperatively or intraoperatively necessitating surgical management of the axillary nodes. Through this study we aim to review the pathologic status of the axillary lymph nodes among cases of phyllodes tumor which underwent axillary node dissection along with surgery for the primary tumor as well as the clinicopathologic features associated with lymph node involvement to help guide the future management of the regional nodes.

Methods: This is a cross sectional study including surgical patients with phyllodes tumor .The preoperative diagnosis, biopsy ,lymph node status, characteristics of the breast tumor, intraoperative axillary node status and final histopathology were analyzed using descriptive statistics to determine the frequency of benign and malignant phyllodes tumor, the rate of misdiagnosis and the incidence of pathologically involved lymph nodes.

Results: There were 54 phyllodes tumors (69% benign and 31% malignant). The axillary nodes were palpable in 3% of benign phyllodes and 12% of malignant tumors. On final histopathology, none of the axillary nodes in benign phyllodes had metastases while all of the cases for which axillary node dissection was done in the malignant ones turned positive.

Conclusion: In this series, the incidence of axillary node metastases is only 12%. The preoperative diagnosis of phyllodes tumor was mistaken in 25% cases including 6 cases of malignant epithelial tumors. This may have implications regarding over or under treatment of the axillary nodal basin hence it is important to have a correct clinical and pathological correlation.

Antitumor Effects of Breast Cancer Vaccine Combined with Metronomic Chemotherapy in Metastatic Breast Cancer

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Background/Purpose: Metronomic chemotherapy alone or in combination with other anti-cancer therapy has been shown to inhibit the growth of breast cancer by anti-angiogenesis. This study observed the use of high-mobility group nucleosome-binding protein 1 (HMGN1) modified cancer vaccine combined with metronomic gemicitabine chemotherapy in a highly metastatic mouse model of 4T1 breast cancer and investigated the synergistic mechanism of this combination.

Methods: 4T1 cell lines were transfected with HMGN1 expression, then were loaded with UV-irradiated as cancer vaccines. Mice were vaccinated three times at weekly intervals following metronomic gemcitabine chemotherapy (twice weely) after a week. Foxp3 expression in tumor situ was detected by western blot and immunohistochemical staining. CD34 was also detected by immunohistochemical staining.

Results: HMGN1-modified cancer vaccines combination with metronomic gemicitabine chemotherapy prevented subcutaneous and orthotopic tumor development. Therapeutic vaccination was equally effective as metronomic chemotherapy. Combination of the two strategies significantly increased efficiency. Metronomic gemcitabine chemotherapy decreased microvessel density and reduced the expression of Foxp3 which was on behalf of Tregs.

Conclusion: Metronomic gemcitabine chemotherapy and HMGN1-modified tumor vaccines immunotherapy can work synergistically in the treatment of metastatic breast cancer via decreasing the number of Regulatory T cells and microvessel density.

PO184

The Role of Ki67 in Breast Cancer; Will It Change Management?

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Background/Purpose: The three standard biomarkers in breast cancer is estrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor 2 (HER2) The use of Ki-67 index, a proliferative marker, is widely practised, despite the absence of standardisation of Ki-67 pathological assessment. We aim to study the role of Ki-67 in a group of Asian women with breast cancer.

Methods: 364 women newly diagnosed with invasive breast cancer in the Subang Jaya Medical Centre from July 2013 to July 2014 were included in this study. Univariable logistic regression was used to determine the association between Ki-67 and age, ethnicity, grade, mitotic index, ER, PR, HER2, lymph node status, stage and size. All analysis was performed using SPSS Version 22.

Results: Ki-67 positivity (14% and above) was significantly associated with a younger age (< 40 years old), later stage, higher grade, ER and PR negativity, HER2 positivity, larger size, a high mitotic index and positive lymph nodes. Out of 73 Stage 1 patients who were ER positive PR positive and HER2 negative, and not Grade 3, only 4 (5.5%) were Ki-67 positive.

Conclusion: Only 5.5% of Stage 1 patients who do not have any other indication for chemotherapy may have been offered chemotherapy based on a positive Ki67. Hence information on Ki67 would have potentially changed management in an insignificant proportion of patients with Stage 1 breast cancer.

PO185

Changes in Biologic Features Between Primary and Recurrent Breast Cancers

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Background/Purpose: Recent studies have shown that the expression status of hormone receptors and human epidermal growth factor receptor 2 (HER2) in breast cancer may change during disease progression. The aim of this study was to determine and compare the estrogen receptor (ER), progesterone receptor (PR), and HER2 expressions.

Methods: Out of the patients with recurrence between 2004 and 2014, there were 34 patients from whom the lesion was resected and evaluated by immunohitochemical staining. Changes in the biological features between primary and recurrent disease based on disease free interval (DFI), site of biopsy, and adjuvant treatment were studied. Survival analyses were established.

Results: ER, PR, and HER2 discordance were found in 7 (20.6%), 10 (29.4%), and 3 (13.6%) patients respectively. Highest discordance rate was 55.5% in patients having DFI less than 2 years. Of patients without adjuvant therapy (n = 6), only 2 patients had discordance while of patients receiving adjuvant therapy (n = 28), 15 patients had discordance. There was no statistically difference in survival ratio.

Conclusion: Patients with breast cancer experience change in biological markers through the course of their disease. Changes in biological features may influence treatment decisions taken at recurrence and re-biopsy should be considered if feasible.

PO186

Effect of Neoadjuvant Chemotherapy on Hormone Receptors and HER2/neu Expression in Breast Cancer

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Background/Purpose: Estrogen receptor (ER), progesterone receptor (PR) and HER2/neu gene expression are important indicators for the treatment and prognostic prediction of breast cancer. Neoadjuvant chemotherapy (NACT) has been applied to locally advanced breast cancers and used for down staging breast-conserving surgery. Whether NACT changes the biological indicators of tumor tissues, especially ER, PR and HER2/neu expressions, is still in debates.

Methods: Both newly-diagnosed breast carcinoma sampled via core needle biopsies (CNB) and the paired surgically removed tumor tissues were obtained, including 63 pairs from patients receiving NACT (treated group) and 74 patients without NACT (control group). The obtained specimens were assayed via immunohistochemistry to determine the expression of ER, PR and HER2/neu and their change in expression, if any, after surgery.

Results: In the trial group, 8 patients (12.7%, 8/63) achieved a pathologic complete response (pCR). Of the remaining 55 patients, the changes in the expression of ER, PR and HER2/neu was found in 14.5% (8/55), 27.3% (15/55) and 21.8% (12/55) of cases respectively. The corresponding values in the control group were 8.1% (6/74), 28.4% (21/74) and 21.6% (16/74) of cases, respectively.

Conclusion: The changes in the expression between the CNB and excisional specimens were not significant, and there was also no significant group-specific changes could be identified between the trial and control group. Neoadjuvant chemotherapy had no significant effect on the status of ER, PR and HER2/neu in breast cancer tissues.

PO187

PI3K Inhibitor LY294002 Combined with RAD001, A mTOR Specificity Inhibitor, Significantly Reduced Proliferation and Induced Apoptosis of Triple Negative Breast Cancer Cell Lines MDA-MB-231 Through PI3K/Akt/mTOR Pathway *In Vitro*

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Background/Purpose: Research of targeted therapies about PI3K/Akt/mTOR pathway have became a hotspot recently, and related researches have been extended from a single-target suppression to multiple-targets combined inhibition. In this study, by using LY294002 and RAD001, the specific inhibitors of PI3K and mTOR, to observe whether the anti-tumor effects on the proliferation, cycle distribution and apoptosis of combined inhibitors were a synergistic effect, and were differences between different molecular characteristics of human breast cancer cells alone and in combination *in vitro*.

Methods: Routinely cultured MCF-7, SKBR-3 and MDA-MB-231 cells *in vitro*. Logarithmic phase cells among each cells were selected and divided into the blank control group, LY294002 group, RAD001 group and the combination group. MTT assay and flow cytometry were used to detect the cell proliferation, cell cycle distribution and cell apoptosis of different groups.

Results: LY294002 and RAD001 could significantly inhibit the proliferations of MCF-7, SKBR-3 and MDA-MB-231 cells with a dose-dependent manner respectively, and compared with other cells, MDA-MB-231 cells were more sensitive to both drugs. The anti-tumor effects were significantly increased in combination groups of different cells, and showed an additive effects. When two inhibitors were combined, the apoptosis rates of the different cells were significantly increased compared with single drug, especially in MDA-MB-231 cell. The apoptosis rates of MCF-7, SKBR-3 and MDA-MB-231 cells were 17.58%, 44.28% and 52.67% respectively, and there were significantly different between different cell lines.

Conclusion: Targeted therapy on P13K/Akt/mTOR pathway could significantly inhibit the proliferation of human breast cancer cell lines by inducing apoptosis and arresting cell cycle distribution. By using a combination of different inhibitors which were targeted on different related genes of this pathway such as PI3K and mTOR, the anti-tumor effects were more significant increased compared with monotherapy, especially in MDA-MB-231 cell line which were negative with estrogen receptor, progesterone receptor and human epidermal growth receptor-2. It was important to provide new research ideas for individualized treatment and translational medicine of breast cancer.

PO188

Prostaglandin E2 Receptor Regulates Metastasis and Stem-Cell Like Properties in Triple-Negative Breast Cancer Through SCL19A3

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Poster Exhibition

Background/Purpose: Majority of *BRCA1* mutation-associated tumors share phenotypic similarity to triple-negative breast cancer (TNBC), understanding the biology of TNBC may improve management of these patients. TNBC is associated with increased risk of metastatic disease and poor prognosis. Prostaglandin E (EP) receptors have been associated with tumor metastasis, however, the contribution on cancer stem cell compartment remains unstudied.

Methods: EP2 was predominantly expressed in human primary tumor tissues. A stable EP2-expression cell line was used to study tumorigenesis and distant metastasis in metastatic breast cancer mice model. Larger tumors and more distant metastasis were seen in MD-231-EP2 bearing mice when compared with control. Characterization of EP2 receptor on cell proliferation, flow cytometry and invasion were performed in transfected cells. Profiles of drug transporters and epithelial–mesenchymal transition (EMT) genes were compared. Tumorsphere assay was used to examine the stem-cell like properties.

Results: EP2 siRNA or antagonist (AH6809) retarded cell proliferation and invasion. Upregulation of SLC19A3 and downregulation of ZEB1 and Twist were observed by blocking EP2. There was an inverse correlation between EP2 and SLC19A3 in primary tumors. Overexpression of SLC19A3 retarded breast cancer growth and EMT phenotype. Enhanced expression of Aldehyde dehydrogenase (ALDH) (cancer stem cell marker) was seen in xenograft tumors. Twist and ALDH expression were increased in tumorspheres and the ALDH activity was reduced by blocking EP2. Twist expression was higher in breast cancer patients and was associated with ALDH expression.

Conclusion: Taken together, EP2/SLC19A3 signaling axis regulates metastasis and

stem-like cell properties in TNBC. These findings suggest that targeting EP2 receptor offers a therapeutic strategy for TNBC.

Sebaceous Carcinoma of the Breast: A Case Report

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Background/Purpose: Sebaceous carcinoma is still quite unknown regarding its morphological characteristics and biological behavior. Therefore sebaceous carcinoma of the breast is a rare malignant tumor, and only 10 cases have been reported in the world.

Methods: The present report describes a case of mammary sebaceous carcinoma in a 74-year-old Japanese woman. The lesion was firstly pointed as two small masses thorough the mammography, and the diagnosis of them were to be benign papillary lesion by needle biopsy. After 5 years from the first diagnosis, the tumors grew up to be over 3cm diameter, and the lesion was diagnosed as squamous cell carcinoma of the breast by needle biopsy. Mastectomy with regional lymph node dissection was performed. The neoplasm was identified in a mastectomy specimen.

Results: The tumor diameter was 3.6cm and located apart from the skin and the nipple in the specimen. The clear foamy cells had numerous lipid vacuoles, confirmed on immunostaining with anti-adipophilin antibody. The tumor cells were positive on immunohistochemistry for cytokeratins, some tumor cell nuclei reacted with antibodies to estrogen and progesterone receptors but failed to show overexpression of the *HER2*/*neu* protein. The MIB-1 labeling index averaged 40%.

Conclusion: The reports of sebaceous carcinoma of the breast are limited, and therefore this report will contribute to understand the clinicopathological features of sebaceous carcinoma of the breast of the breast.

Overexpression of 14-3-3θ Promotes Breast Cancer Cell Proliferation and Correlates with Human Epidermal Growth Factor Receptor 2

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Background/Purpose: 14-3-3θ has been linked with many kinds of tumor cells proliferation and apoptosis.Although some study resported that 14-3-3θ may take part in the proliferation of breast cancer cells , a direct link between human epidermal growth factor receptor 2 (HER2) and 14-3-3θ protein expression has not yet been established. In this study, we will show that 14-3-3θ may play a novel oncogenic role of breast cancer proliferation and this function may be linked with HER2 at molecular and cellular level.

Methods: We explore the role of 14-3-3θ in development of breast cancer by cell survival assay, plate colony formation assay, flow cytometry analysis, western blot, xenograft study in nude mice and Immumohistochemistry.

Results: The ability of proliferation become stronger and resist apoptosis when the breast cancer lines express more 14-3-3θ. Breast cancer cell migration reached a higher degree when the cell expressed more 14-3-3θ. The relative viability of MCF-7-14-3-3θ is higher than MCF-7-Cherry after we respectively added doxorubicin and tamoxifen for 72 hours. But after added herceptin to AU-565-14-3-3θ and AU-565-Cherry for 72 hours, we got the most significant difference. There are more p-Akt and p-mTOR in MCF-7-14-3-3θ and AU-565-14-3-3θ than control group. The data of immunohistochemistry analysis told us that the high expression of 14-3-3θ was accompanied by high expression of HER2 and Ki-67.

Conclusion: Taken all the results, they indicate that 14-3-3θ can promote breast cancer promoted proliferation and migration of breast cancer, reduce the apotosis, and this function may be associated with HER2/Akt/mTOR signal pathway. Above all, this study indicates that overexpression of 14-3-3θ in breast cancer may be a strong indicator. Therefore 14-3-3θ expression may be a candidate biomarker for breast cancer prognosis and a target for new therapies.

A Novel Peptide Targeting MDA-MB-231 Breast Cancer by Fluorescence Imaging

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Background/Purpose: This study was aimed to investigate the targeting activity of a novel peptide, named P1c to integrin αvβ3-positive MDA-MB-231 breast cancer.

Methods: Circular Dichroism (CD) spectroscopy was employed to characterize the secondary structure of P1c peptide. Molecular docking was performed to obtain the model that P1c combined with αvβ3. The FITC-P1c probe binding to MDA-MB-231 cells were analysed by flow cytometry and confocal microscopy. Cy5.5-P1c probe was evaluated in the subcutaneous MDA-MB-231 xenograft mouse model to examine its tumor targeting efficacy through *in vivo* near-infrared fluorescence (NIRF) imaging. Immunohistological staining was used to detect the expression of αvβ3 in tumor tissues.

Results: CD spectroscopy and molecular docking model exhibited that P1c possessed a random conformation, and it was tightly combined with αvβ3. Flow cytometry showed that 51.62 ± 3.22% of MDA-MB-231 cells stained positive for αvβ3. Confocal microscopy experiment demonstrated that P1c could specifically bind to MDA-MB-231 cells. For *in vivo* NIRF imaging, the subcutaneous MDA-MB-231 tumor could be clearly delineated from the surrounding background tissue after intravenous injection of Cy5.5-P1c probe, and exhibited highest tumor-to-normal tissue ratio (T/N) at 8 hours postinjection. The T/N of the P1c blocking group was significantly decreased compared to that of the non-blocking group at the 8-hour and 24-hour time point ($p < 0.05$). Immunohistological staining showed that αvβ3 was strongly expressed in MDA-MB-231 tumor tissues.

Conclusion: The P1c probe could successfully target αvβ3-positive MDA-MB-231 breast cancer cells *in vitro* and *in vivo*. It provides a new opportunity for αvβ3-positive tumor imaging and therapy.

PO192

Multimodality Imaging Evaluation of Incidental Breast Lesions Detected on Positron Emission Tomography/ Computed Tomography

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Background/Purpose: we discuss incidental breast lesions detected on Positron emission tomography-computed tomography (PET-CT), compared to ultrasonography, mammography, computed tomography (CT) and Magnetic resonance imaging (MRI) findings. To provide brief mechanism, advantage and pitfall of PET/CT. To illustrate PET/CT findings of incidental breast lesions with respect to ultrasonography, mammography, CT and MRI.

Methods: Physiologic uptake or pseudolesion.Post operative change and seroma.Benign lesions including inflammation, calcified/non calcified fibroadenoma, complex fibroadenoma, papilloma, usual ductal hyperplasia, sclerosing adenosis, ductectasia and fat necrosis.

Results: Malignancy including invasive ductal carcinoma, ductal carcinoma *in situ* which presented as mass or calcification. Internal mammary and axillary recurrence after breast cancer surgery.

Conclusion: Understand advantages and pitfalls of PET/CT will help to perform accurate diagnosis of incidental breast lesions. Thus, we emphasize that combination of other radiologic modalities including ultrasonography, mammography and MRI are necessary.

PO193

Acupuncture for Chemotherapy-Induced Peripheral Neuropathy in Breast Cancer Patients: Pilot Trial

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Background/Purpose: Some chemotherapy drugs can cause peripheral neuropathy which results in severe neuropathic pain or gait impairment. Recent studies suggest that acupuncture may be a useful treatment for chemotherapy-induced peripheral neuropathy (CIPN). The purpose of this study was to assess the feasibility and the safety of acupuncture for the treatment of peripheral neuropathy following chemotherapy in Korean breast cancer patients.

Methods: Ten breast cancer patients presenting with CIPN were enrolled in a prospective, pilot study. Acupuncture interventions were given three times a week for 4 consecutive weeks. The primary outcome measure was Neuropathic Pain Symptom Inventory (NPSI) assessed by a self-administered questionnaire, and Nerve Conduction Velocity (NCV). The secondary outcome measure was quality of life assessed by the SF-36 Questionnaire.

Results: Acupuncture significantly reduced the severity of CIPN assessed by NPSI score. 4 weeks after the last treatment the symptoms were not aggravated. According to the NCV assessment, 3 participants showed improvement of sensory neuropathy. SF-36 scores significantly increased for variables including physical functioning, role limitations due to physical health, social functioning, and general health status.

Conclusion: Acupuncture appeared to provide effective improvement of CIPN among Korean women with breast cancer, and the effects lasted for at least 1 month after the treatment. A randomized controlled prospective study with a larger sample size is required to clarify the role of acupuncture in the management of CIPN in Korean breast cancer patients.

PO194

A Case Report of 29-Year-Old Male Patient with Breast Carcinoma

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Background/Purpose: Breast carcinoma has been dominated disorder in female, whereas breast carcinoma in male is relatively rare. A breast cancer in male may be diagnosed in an older age rather than female. We present the case of a 29-year-old man with infiltrating ductal breast carcinoma; this is the report of the youngest male breast cancer we had experienced

Methods: A 29-year-old Korean man was referred to our institution complaining of progressively grown right breast tumor. Previous medical and family history did not contribute to present illness. Physical examination revealed 2.5 cm round mass in lower inner quadrant of right breast. The mass was diagnosed as invasive ductal carcinoma with fine needle aspiration biopsy. There's no metastatic evidence on Positron emission tomography-computed tomography (PET/CT).

Results: We did a modified radical mastectomy for his breast cancer and pathologic report was concluded as invasive ductal carcinoma with a 3.6 cm lesion, which was histologic grade 3 and nuclear grade 3. The axillary lymph node dissection showed four positive nodes among 24 nodes. The other reports are; Estrogen receptor/progesterone receptor (7/0), human epidermal growth factor receptor 2 (2+), Silver In Situ Hybridization (+), epidermal growth factor receptor (-), Ki67 50%.

Conclusion: A young male was diagnosed with breast cancer with diabetes and elevated estradiol, there's no specific risk genetic factors for his breast cancer.

PO195

Vesicles on the Breast Post-Mastectomy

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Background/Purpose: Lymphangioma circumscriptum is characterized by grouped vesicles formed by superficial saccular dilations from underlying lymphatic vessels that occupy the dermal papilla that are pushed upwards against the overlying epidermis. The lesions usually present at birth or arise in early childhood. However, acquired forms have been reported as rare sequelae of lymphatic damage resulting from cancer treatment, e.g. following post-mastectomy lymphedema.

Methods: We describe a patient with left breast carcinoma who underwent a left skin-sparing mastectomy with axillary lymph node clearance, and left breast reconstruction, who presented with increasing numbers of small vesicular lesions over her left axilla and reconstructed left breast over 1 year. Punch biopsy of one of the lesions was performed, which revealed the characteristic histology of lymphangioma circumscriptum.

Results: The basic pathologic process of lymphangioma circuscriptum involves the collection of lymphatic cisterns in the deep subcutaneous plane. The genesis of lymphedema following surgery or radiation therapy is presumably related to increased hydrostatic pressure within vessels proximal to lymphatic obstruction. Recurrences are common unless the entire lesion is removed or destroyed. Surgery is the treatment of choice for lymphangioma circumscriptum.

Conclusion: Lymphangioma circumscriptum can occur after radical mastectomy and axillary lymph node clearance, even in the absence of underlying lymphoedema. Treatment of lymphangioma circumscriptum post-mastectomy can be difficult, with a high recurrence rate.

PO196

Seamless Care-The Power of a Team with Community and Volunteer Services

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Background/Purpose: Breast surgery is a stressful experience for women. Disfigurement negative feeling and adjuvant uncertainty cause unfailing frustration for cancer patients. The Breast Care Services in our cluster has been providing one stop multidisciplinary team holistic service with Cancer Case Manager Care approach. To enhance coping, better support or sharing, peer group was introduced.

Methods: A biweekly Open peer group service launched at Pok Oi Hospital Breast Nurse Clinic on 20/9/2011. It was led by one CancerLink social worker and the Breast Care Nurse with 4 trained volunteers. Service introduced to all post-surgery patients who attend wound care follow up. Patient should complete a feedback questionnaire afterwards.

Results: 27 sessions conducted and 175 clients served from 20/9/2011 to 30/9/2012. Three outstanding findings: appreciating on face to face conversation, relaxing environment that feeling good and experiencing tender care. 100% clients verbalized enhanced confidence in coping with cancer and suggested program should be continued. 94% showed positive in knowing the peers, information and staff assistance.

Conclusion: Results demonstrated the importance of social support on health outcomes for people to live with cancer. Besides filling the gap for those who lack social support, it improves survivor's coping and abide by the various types of treatment. Timely peer support service was effective to alleviate worries and anxiety of post-surgery breast cancer patient and enhance their confidence towards rehabilitation.

PO197

Metastatic Breast Carcinoma to the Abdomen

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Background/Purpose: Breast cancer is a very common malignancy in woman and typical metastatic sites include lung, bone, liver and brain. Gastrointestinal metastases are reported to occur in 4-18% of breast cancer patients. The overall prognosis for this patients population is poor, most patients will die within 2-3 years of diagnosis with abdominal disease.

Methods: In December 2009, she had left total mastectomy and sentinel lymph node biopsy. The results of biopsy were confirmed invasive ductal carcinoma, first mass was invasive ductal carcinoma with ductal carcinoma *in situ* (1.8 cm × 1.6 cm), another was invasive ductal carcinoma with medullary features (1.7 cm × 1.3 cm). We report a case of metastatic invasive ductal carcinoma to the abdomen.

Results: In November 2012, she had exploratory laparotomy and we found irregular mass which was around sigmoid colon mesentery and left ovarian mass was also noted. We did segmental resection of sigmoid colon for mass remove and left salpingo-oophorectomy . Pathologist concurred about the mesenteric mass in the final diagnosis of papillary adenocarcinoma, consistent with metastatic from the breast.

Conclusion: There are no definite guidelines for treatment of abdominal metastasis of breast cancer, but medical management with systemic chemotherapy or endocrine therapy can yield better survival outcomes. Some study proved that resectable metastatic lesion is good prognostic factor as well as optimal cytoreduction.

PO198

Cardiovascular Risks Among Young Chinese Breast Cancer Patients After Adjuvant Chemotherapy

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Background/Purpose: For young Chinese breast cancer women who had received adjuvant chemotherapy, there is limited data on post-treatment cardiovascular risk.

Methods: Chinese women with breast cancer were recruited into this cross-sectional study. Eligibility criteria included breast cancer stage I-III, age ≤ 45 at diagnosis and having received adjuvant chemotherapy. Patients' background demographics including menstrual history at breast cancer diagnosis were collected. At study entry, the menopausal status based on menstrual history as well as information on body mass index (BMI) and blood pressures were collected.

Results: 280 patients were recruited; at the time of breast cancer diagnosis, 41 were ≤ 35 years, 82 were aged 36-40 and 157 were aged 41-45. Adjuvant chemotherapy regimens included anthracycline-containing (64.6%), both anthracycline- and taxane- containing (24.3%) and others (11.2%). At study entry, 34 patients were ≤ 35 years, 26 were 36-40, 76 were 41-45, 157 were 46-50 and 24 were > 50; 47.5% had become postmenopausal by age ≤ 45 years. When assessing BMI at diagnosis vs. at study entry, more patients were overweight (13.9% vs. 24.6%, $p = 0.01$) and obese (2.5%)

Conclusion: A significant proportion of young Chinese breast cancer patients became postmenopausal at ≤ 45 after adjuvant chemotherapy. Post-treatment follow-up also identified increased incidence of overweight and obese statuses among the studied population, which was associated with a higher incidence of hypertension.

PO199

Thyroid Gland Metastasis from Breast Cancer: A Case Report

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Background/Purpose: The thyroid gland is a rare site for metastatic disease to develop. The common sites of breast cancer metastasis are bone, lung, pleura and liver. Recently, we experienced a case of thyroid metastasis from breast cancer.

Methods: The 52-year-old female patient with a history of left breast cancer presented with a palpable mass on left infraauricular area. The patient had undergone a breast conserving surgery for left breast cancer (stage IIA;T2N0M0) followed by 6 cycles of cyclophosphamide, methotrexate and fluorouracil (CMF) combination chemotherapy and radiation therapy 9 years ago. Also, she had taken a tamoxifen for 5 years, but had not visited in hospital after finishing the hormonal therapy. Ultrasound of the neck revealed the two nodules on both parotid gland each other and multiple nodules on both thyroid gland.

Results: Ultrasound-guided biopsy of left thyroid nodule resulted in poorly differentiated metastatic carcinoma. The immunohistochemical staining for estrogen receptor and progesterone receptor were positive, and for thyroid transcription factor 1 was negative. Additional radiologic studies revealed the both breast nodules, which were confirmed with invasive carcinoma by core needle biopsy. Also, the distant metastases in lung, mediastinal and neck lymph nodes were detected. The patient is planned for chemotherapy.

Conclusion: The metastatic disease of thyroid is uncommon, but should be considered in patient with a history of malignancy. We report our case with literature review for thyroid metastasis from breast cancer.

PO200

Long-Term Clinical Results of Node-Negative Breast Cancer and Prognostic Factor of Regional Recurrence

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Background/Purpose: The aims of this study is to evaluated long-term clinical results of node-negative breast cancer and predicting factor of regional recurrence of node-negative breast cancer such as axillary or supraclavicular or internal mammary lymph node recurrence.

Methods: A total 586 node-negative breast cancer patients who received breast cancer surgery such as breast conserving therapy (BCT) or total mastectomy with sentinel lymph node biopsy (SLNB) from January 2003 to December 2012 were enrolled in this study. The enrolled patients were divided into two group, non-recurrent group and recurrent group. Their medical records were retrospectively reviewed including clinicopathological characteristics and Memorial Sloan Kettering Cancer Center (MSKCC) sentinel lymph node metastasis nomogram score.

Results: Mean age of study patients were 52.1 years and median follow up period was 64 months (range 0-144 months). All patients had received SLNB and confirmed node-negative breast cancer. 5-years and 10-years disease-free survival were 94.1% and 91.7%. A total 31 (5.3%) cases of relapse were detected in 586 patients. Regional recurrence in 11 (1.9%) patients, local recurrence in 8 (1.4%) patients, and systemic recurrence was 12 (2.0%) patients. Lymphovascular invasion [122 (25.3%) *vs* 6 (54.5%) ($p = 0.029$)] and MSKCC nomogram score [37.10 ± 22.25 *vs* 57.36 ± 26.84 ($p = 0.031$)] were significant higher in regional recurrent group than non-recurrent group.

Conclusion: Lymphovascular invasion and MSKCC nomogram score will be helpful in predicting the regional recurrence of node-negative breast cancer.

PO201

Adenoid Cystic Carcinoma of the Breast with Contralateral Ductal Carcinoma *In Situ* and Concurrent Lung Cancer

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Background/Purpose: Adenoid cystic carcinoma (ACC) of the breast is a very rare subtype of breast cancer with triple-negative, basal-like breast features, but presents an excellent prognosis. Although axillary lymph node and distant metastasis have been rare, but the common sites for distant mestastasis were the lung followed by the liver, the kidney, and the brain sequentially. In this report, we treated a patient with ACC of the breast with contralateral ductal carcinoma *in situ* and concurrent lung cancer. Thereby, we are reporting the extremely rare case of ACC.

Methods: A 51-year-old female presented with a painless clusters of micro-calcifications on both breasts during the regular check-up. Mammography revealed extremely dense shadows with clusters microcalcifications on left breasts. The breast ultrasonograpy showed 12 mm sized ill-defined hypoechoic mass on right breasts. A core-needle biopsy confirmed the invasive ductal carcinoma on right breast. Breast conserving surgery with sentinel node biopsy was performed on right breasts, and lumpectomy with mammography guided localization was undertaken for left ductal carcinoma *in situ* lesion.

Results: A pathological report represented the adenoid cystic carcinoma on right breast with triple-negative features which lack estrogen/progesterone, and human epidermal growth factor receptor 2 expression, and the ductal carcinoma *in situ* was confirmed on left breast. Adjuvant radiation therapy for both breasts and anti-hormone treatment such as tamoxifen are scheduled for the contralateral ductal carcinoma *in situ* lesion. During the preoperative evaluations, malignancy-suspicious nodules were detected on the lung and liver, but later they confirmed as the sclerosed hemangioma and lung primary cancer.

Conclusion: ACC of the breast is an exceedingly rare, and surgery still remains the keystone of treatment. Because of its scanty incidence, there is no definite consensus for

its adjuvant therapy so that more careful evaluations and closer follow-up would be required. Moreover, the distant mestastasis or secondary cancers associated with the primary breast cancers could be occurred. Therefore, careful systemic evaluations should be needed with any given breast cancers despite of its early stage and excellent prognosis.

PO202

Multiple Primary Cancers in Breast Cancer Patients

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Background/Purpose: According to the increase of breast cancer survival, the issue of the quality of life and disease prevalence in breast cancer survivors is receiving attention. Especially, another primary cancer in breast cancer patient and breast cancer arising in another cancer patient are standing out due to the innovative development of cancer genomics. We investigated the characteristics of breast cancer patients with another primary cancer.

Methods: From 1st January, 2000 to 30th September 2013, we retrospectively investigated 1,868 breast cancer patients who are diagnosed another primary cancer in ASAN Medical Center. According to ICD-10, we classified patients and compared the reported prevalence, by National Cancer Information Center of Korea in 2014. The clinical characteristics of breast cancer patients with another primary cancer were compared with the 17,823 breast cancer patients, who were diagnosed breast cancer in same period, in ASAN Medical Center.

Results: The mean age of 1,868 study patients was 49 (range: 14-87). The stage of breast cancer showed tendency to be higher in multiple primary cancer patients, however, it had no statistically significant. The cancer that showed the highest prevalence rate in breast cancer patients was thyroid cancer (33.1%), followed by lung (13.0%), stomach (11.1%) and liver cancer (6.9%). Except breast cancer, in the cancer prevalence in Korean women reported in 2014, thyroid cancer was the first (31.7%), followed by colorectal (10.2%), stomach (10.1%), cervical (6.3%) cancer.

Conclusion: Many studies investigated the genetic mechanisms and phenotypic results of *BRCA1/2* mutations, secondary malignancies followed by adjuvant treatment such as leukemia after chemotherapy. However, the study of multiple primary cancers in breast cancer patients is not actively proceeded due to lack of well-organized data. Especially in young breast cancer patients, multiple primary cancers should be approached with caution, because of the probability of germline mutations such as TP53 mutations, known as Li-Fraumeni syndrome.

PO203

A Case of Metastatic Malignant Melanoma with Unknown Primary Site Manifesting as Invasive Ductal Carcinoma

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Background/Purpose: Malignant melanoma commonly presents with disseminated disease in the skin and mucous membrane. Only 4-9% of all malignant melanoma is diagnosed with palpable disease. The nodal or regional metastatic malignant melanoma occasionally presents as a palpable mass. In 8-20% of metastatic malignant melanoma, primary melanoma cannot be found.

Methods: The 84-year-old woman was admitted to our clinic due to recently grown axillary mass which had existed during 2 years. She had no past and no family history of carcinoma. She had a three-vessel coronary artery disease in present illness. Physical examination revealed a 5×6 cm mass and several palpable nodes in right axilla. Ultrasonography showed suspicious breast cancer that originated from underlying accessory breast, and metastatic axillary nodes.

Results: Initial pathologic result of core biopsy was diagnosed as triple negative invasive ductal carcinoma. There was no distant metastasis in positron emission tomography-computed tomography. We recommended operation, but the patient refused because old age and risk of cardiac morbidity. Although the patient received anti-hormonal therapy for 3 months, tumor mass was more grown and had been sign of impending rupture. We performed palliative modified radical mastectomy.

Conclusion: In final pathologic result, there was no breast parenchyma in axillary mass which was proven as triple negative invasive ductal carcinoma. Moreover, this axillary mass was diagnosed as metastatic malignant melanoma. Repeat clinical examination did not found primary lesion of malignant melanoma. We report a case of metastatic malignant melanoma from unknown primary lesion presenting as invasive ductal carcinoma.

PO204

Medical Conditions of Long Term Breast Cancer Survivors

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Background/Purpose: Breast cancer survival has been increased due to awareness of screening and development of treatment. Survivors experiences persistent or late effects of cancer treatment such as lymphedema, osteoporosis, and cardiovascular diseases. Those complications affect their quality of life. In this study, we assessed medical conditions of long term breast cancer survivors to evaluate prevalence of persistent and late effects of breast cancer treatment.

Methods: Selected data from The Korea National Health and Nutrition Examination Survey (2009-2012) was used for evaluation. We identified long term breast cancer survivors (diagnosed more than 5 years ago) in the survey population. Non-cancer control group were selected with 1:4 matching of age, sex and the survey year. Medical examination and questionnaire were evaluated.

Results: Long term breast cancer survivors (n = 90) and non-cancer controls (n = 360) were included in this study. Except breast feeding history, both groups were balanced in menopausal status, history of pregnancy, area of residence, and educational status. Self-estimated health status was better in breast cancer survivors (67.91 ± 17.20) than in non-cancer controls (44.84 ± 21.47) but it was not statistically significant. No difference was found in incidence of cardiovascular diseases. Smoking, alcohol intake, and intensity of physical activity did not show differences. Incidence of osteopenia and osteoporosis measured by bone marrow density examination was not significantly different between survivors and controls ($p = 0.121$). Mean vitamin D levels were deficient (18.35 ± 7.37 vs 17.53 ± 6.71) in both groups, and there were no difference in hemoglobin level, fasting glucose, and lipid profiles.

Conclusion: No significant difference was found in health status between long term

breast cancer survivors and non-cancer population based on health survey and examination. Specified questionnaire and medical record review is required for evaluation of late effects in breast cancer survivors.

PO205

Fibroadenoma Arising from Accessory Breast Tissue

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Background/Purpose: Accessory breast has received little attention in its screening, although it is common occurring in 2-6% women. It develops the same pathological changes as the normally located breast tissue such as inflammation, fibroadenoma, phyllodes tumor, and carcinoma.

Methods: A thousand patients who have been treated with an excision of accessory breast tissue from September 2012 to August 2014 at the Damsoyu Hospital were analyzed for pathological tumorous lesions retrospectively.

Results: Eleven patients had accessory breast tissues with fibroadenoma (1.1%). There were no any other tumorous conditions except fibroadenoma. Unmarried patients were 8 (72.7%), and married patients were 3 (27.3%). The age of the patients ranges from 24 to 43 years. The major clinical manifestations were cyclic pain and cosmetic problem. The size of tumors ranges from 4 mm to 36 mm. 8 patients were diagnosed to fibroadenoma arising from accessory breast tissue on preoperative breast ultrasound examination. 3 patients were diagnosed to fibroadenoma arising from accessory breast tissue by pathological reports after operation.

Conclusion: In conclusion, breast surgeons should keep in mind that accessory breast tissues can develop any tumorous conditions as normally located breast tissue and when tumors or nodules are found along the mammary line, the presence of accessory breast tissue should be considered during the investigation.

PO206

The Clinical Experiences in a Thousand Patients with Gynecomastia

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Background/Purpose: 5-10% adult men have gynecomastia. In most men, gynecomastia is asymptomatic, but in some cases they may periodically cause physiologic and pathologic changes because they are influenced by estrogen hormone. In most cases, pain and abnormal appearance are the indications of surgical operation.

Methods: A thousand patients who have been treated with gynecomastia from January 2013 to October 2014 at the Damsoyu Hospital were analyzed for clinical factors retrospectively. Subcutaneous mastectomy and liposuction were performed on all cases by two surgeons (Dr. Hwang and Dr. Lee). All patients with gynecomastia were classified according to Simon's classifications (1973).

Results: True gynecomastia was found in 566 patients (56.6%), pseudogynecomatia in 180 patients (18%), and mixed type of gynecomastia in 254 patients (25.4%). Out of a thousand patients, 36 patients were having unilateral gynecomastia. The most frequent age group in gynecomastia was twenties (63%). According to Simon's classification, Type I was in 376 patients (37.6%), Type IIa in 374 patients (37.4%), Type IIb in 214 patients (21.4%) and Type III in 36 patients (3.6%). Their mammary tissues averaged 79g and liposuction averaged 615 mL. Mean operation time was 58 minutes. The incision line varied depending upon the type, and postoperative drains were not applied to any cases. In our study, 96.4% of patients enjoyed cosmetically satisfying outcomes.

Conclusion: It appears that the surgical excision with liposuction is the most effective against gynecomastia.

PO207

Lost in Transition Impact of Living Environment on Surveillance Behaviors and Psychological Health during Survivorship

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Background/Purpose: Once treatment is over, patients often experience abandoned feelings as they are away from health professionals and hospitals. During survivorship living environment such as transportation, finance, access to information, and social services might affect patients' surveillance behavior and mental health. This study aims to evaluate living environment of breast cancer survivors and it impact on surveillance behaviors and psychological health.

Methods: From August to October, 2013, a cross-sectional survey was conducted with breast cancer survivors at two cancer hospitals in Seoul, Korea. Patients were eligible for this study if they were at least 1 year survivors, no sign of recurrence, completed active treatment, and under regular surveillance. Living environment (LE) was assessed WHO-QOL BREF. Anxiety and depression using Hospital Anxiety and Depression Scale (HADS), fear of cancer recurrence, and surveillance behaviors was also assessed. Uni- and multi-variable analysis was performed to find association between living environment and behavior and psychological health using STATA 13.

Results: Total 842 breast cancer survivors participated in the study. Survivors reported better LE (BE) were more likely to live metropolitan ($p < 0.01$), had college education ($p < 0.01$), and had higher income ($p < 0.01$) compared to the survivors reported poorer LE (PE). While both groups were willing to have active surveillance exams ($p = 0.846$), PE were less likely to received surveillance exams ($p = 0.03$) than BE. PE were more likely to be disturbed when they were waiting for surveillance exam and worried more about the cost of the exam than BE. In multivariable analysis, PE had significantly higher fear of recurrence ($p < 0.01$) and report depression compared to BE ($p < 0.01$).

Conclusion: Survivors living in a poor environment experience more difficulties with surveillance resulting in higher anxiety, fear of recurrence, and depression. Appropriate supports and resources such as transportation, finances, and social services are necessary for assuring survivors' long term quality of life.

PO208

Borderline Phyllodes Tumor in the Male Breast

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Background/Purpose: Phyllodes tumors of the breast are rare neoplasms, composing less than 1% of all breast tumors and only 2-3% of fibroepithelial neoplasms. Phyllodes tumor of the male breast is an extremely rare disease presented by only few reports in the literature. It is referred to hormonal disturbances and/or gynecomastia like male breast cancer, however, its pathobiology is regarded as a difference from that of breast cancer. The aim of our report was to describe borderline phyllodes tumor with gynecomastia in the male breast.

Methods: A 39-years-old man visited our hospital for a palpable mass on left breast first noticed 20 days ago. Mammography revealed 1 cm sized partly obscured oval high density mass on left breast subareolar area with skin thickening and retraction, but no abnormal calcification. On ultrasonography (US), 0.9 cm sized spiculated irregular hypoechoic mass with edema, but no posterior feature or vascularity. The lesion was diagnosed as BIRADS category 4c, so US-guided core needle biopsy and excision were performed.

Results: Microscopic examination of the core biopsy specimen revealed chronic and active inflammation with infiltration of lymphocytes, histiocytes, neutrophils and a few multinucleated giant cells. Neither mass nor nodular lesions are noted. The excised left breast consisted of a 3.0 × 2.5 cm sized gray-whitish, multinodular mass with tense and elastic consistency. Histologic sections revealed a phyllodes tumor with generally well-circumscribed border, moderate stromal cellularity, minimal stromal cell atypia and absent stromal overgrowth. However, foci of permeative margins and increased mitotic activity (up to 9/10 HPF) were found, taken together, the pathologic diagnosis as a borderline phyllodes tumor was made (Figure 2a to e). Additionally, gynecomastia was noted with abortive lobule formations in the background breast parenchyma.

PO208

Conclusion: Phyllodes tumor of the male breast is an extremely rare entity with only few reports available in the literature. We present a rare case of borderline phyllodes tumor with gynecomastia in the male breast.

PO209

Evaluation of Breast Edema in Early Breast Cancer Patients After Breast Conserving Surgery: A Pilot Study

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Background/Purpose: Breast edema (BE) after breast conserving surgery (BCS) is common and it could cause poor cosmetic prognosis, discomfort or pain. Especially in early breast cancer patients underwent BCS not including axillary lymph node dissection, BE is one of the important complications that lower the quality of life. However, there is a problem with diagnosis, treatment and prediction of BE owing to the absence of evaluation standard. Authors tried to develop a standardized severity scale for evaluation of edema.

Methods: This is a pilot study for a observational study including eligible 28 patients underwent lumpectomy with sentinel lymph node biopsy due to carcinoma *in situ* or invasive breast cancer. BE is assessed via physical exam with a scoring system, measurement of breast volume using the fomula published by Quoi et al. and elastography on 6 months after surgery. Clinicopathologic characteristics and operative details including location of wound and total volume of drained seroma are also recorded.

Results: The volume of the operated breast increased in 71.4% of patients, was significantly larger than that of the nonoperated breast ($p = 0.022$). The difference between the operated and nonoperated breast was 28.00 ± 58.78 cc and it was significantly correlated with the BE score by physical exam ($r = 0.588$, $p = 0.002$), but not with the elasticity ratio of the operated breast. Also there was a positive correlation between the BE score and the period after completion of radiation therapy ($r = 0.445$, $p = 0.043$).

Conclusion: Physical exam with a simple scoring system reflected the objective severity of BE based on complicated calculations of the breast volume. It could be an useful tool in clinical field and helpful to diagnosis and treatment of BE. Further study with more patients is necessary to validate this method.

PO210

Care Pathway for Cancer Patients to Improve Survivorship in Korea (cCISK): Adding the Numbers

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Background/Purpose: The survival rate of cancer patients has exceeded 60%. Although cancer survivors may die of other diseases except cancer, the health management system including chronic disease prevention-management for cancer survivors has not been established in the diverse aspects. Therefore, services according to the care pathway of cancer patients need to be provided through the support system based on the platform concept able to be used for patient's need in various ways.

Methods: We analyzed National cancer Registration Data collected in 2007 to 2012 in order to establish a service provision model. The survivor group after diagnosed with breast cancer was classified into: first, patients under active treatment with surgery and chemotherapy; second, survivors with relatively less side effects and no sign of a recurrence; third, cancer survivors under palliative treatment after a recurrence. The survivor group was categorized into five stages, such as 'Diagnosis and Treatment', 'Supportive care', 'Monitoring', 'Progressive Illness' and 'End-of-life care', the scale of breast cancer survivors was estimated.

Results: The result of estimation of breast cancer survivors through a care pathway by survival stage is shown below. There were 16,600 cases of the incidence of cancer in 2012 in the Diagnosis and Treatment. Among cases of the incidence of cancer in the previous year, the number of one-year survivors was 18,100 and they were included in the Supportive care. In the Monitoring, 111,700 survivors maintaining a healthy life were included. Total 4,000 survivors were checked to identify an ongoing disease and

included in the Progress illness. In the End-of-life care, 2,000 end-stage cancer patients requiring hospice care were included.

Conclusion: We establish a care pathway by survival stage in order to fulfill prevention and health management services post-treatment management steps.

PO211

The Impact of Intraductal Papilloma on Newly Developed Lesion at Vacuum Assisted Breast Biopsy Site

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Background/Purpose: Recently FDA approved use of vacuum assisted breast biopsy (VABB) instrument for therapeutic purpose of benign lesions. But physicians sometimes experienced the tumor regrow that previous VABB site or adjacent tissue. We wanted to evaluate the factors that impact on remained or regrowth tumor at post biopsy site or adjacent tissue. Especially our study focused on intraductal papilloma influence in tumor regrowth.

Methods: From January 2000 to December 2014, we could analyze 1,050 cases because of follow up period of the patients was 19 months. The patient age at initial diagnosis, the age of menarche, status of marriage, the number of babies, presence or absence of feeding Hx. status of menopause, presence or absence of family history were obtained from medical records. Tumor size, pathologic diagnosis, presence or absence of calcification were obtained from pathology reports.

Results: In our study, mean age is 43 years old and about 23.4% (n = 246) cases has belongs to intraductal papilloma. And tumor recurrence rate was 10.4%. The number of tumor that had more than 10 mm tumor size was 33 cases. Intraductal papillomas were not significantly associated with tumor regrowth at post VABB site. Additionally tumor with more than 10 mm size, tumor located in lower inner quadrant in breast, and menopause status also were significantly associated with tumor regrowth at post VABB site.

Conclusion: intraductal papilloma were not significantly associated with tumor regrowth at post VABB site.

PO212

Nipple Adenoma in Young Woman

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Background/Purpose: Nipple adenoma, also called florid papillomatosis, papillary adenoma or erosive adenomatosis, is a rare benign proliferative lesion originating from the lactiferous ducts of the nipple. Nipple adenoma include various manifestations such as nipple erosion, nipple crusting, nipple discharge and nodular formation, but most patients are asymptomatic. Nipple adenoma occurs mostly in middle-aged woman. Nipple adenoma needs to be distinguished from Paget disease, intraductal papilloma of the nipple, and breast cancer.

Methods: A 34-years old woman, with the complain of small palpable mass and bloody discharge in the left nipple, visited our department. Breast magnetic resonance imaging (MRI) demonstrated a nodular enhancement in left nipple with persistent kinetic pattern.

Results: We performed a tumor resection with preservation of the nipple. Operation finding was as follow: 1.2 cm sized cauliflower shaped whitish colored mass on left nipple. The histological finding was adenoma of the nipple.

Conclusion: Nipple adenoma is a rare, but present benign process. Physical examination and diagnostic studies are important part of diagnostic workup; however, surgical treatment and pathologic evaluation are the only approach for definitive diagnosis to rule out a potential malignancy.

PO213

Immediate Free TRAM Breast Reconstruction Following the Removal of a Giant Phyllodes Tumor

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Background/Purpose: Phyllodes tumors (PT) account for less than 1% of breast tumors in women, and giant PTs are defined as a lesion measuring 10 cm or more in diameter. These tumors are unpredictable and fast growing with a high local recurrence rate, making this disease challenging to treat. Previous literature focused on surgical resection, and breast reconstruction following a mastectomy in patients with PT is rarely addressed. We report a case of a recurrent malignant PT treated with a nipple-sparing mastectomy followed by immediate free TRAM breast reconstruction.

Methods: The patient is a 47-year-old premenopausal female with a history of left breast PT who presented for management of a left breast lump. She was initially diagnosed in 2009 with 5.0 cm-diameter borderline PT that was treated with wide excision, although it is unclear how widely the margins were excised at the time. She had no clinical follow-up after initial operation and re-visited in 2014 due to a painful and swollen left breast with bleeding.

Results: Breast MRI demonstrated a large, heterogeneous, mixed, cystic and solid enhancing, well encapsulated mass measuring 17 × 14 × 14 cm in the left breast. There was no extension of the mass into the chest wall. Axillary lymph nodes were not detected in MRI. Core biopsy was performed and demonstrated stromal expansion with increased cellularity, and mitotic figures suggestive of recurrent PT. The patient underwent a total mastectomy of the left breast with immediate free TRAM breast reconstruction. The weight of resected breast was 1,250 grams, left deep inferior epigastric perforator (DIEP) flap was used and left lateral vessels were used as recipient vessels.

Conclusion: Specimen histopathology demonstrated a 16.5-cm-diameter borderline PT of the left breast with direct involvement of skin. The mitotic count was 9/10 HPF, stromal cellularity and atypia were moderate. All margins has negative resection margin. PT is a rare breast tumor that presents challenges with both surgical resection and immediate reconstruction. Because this disease is rare, identifying a large cohort is of-

ten difficult. Furthermore, PT is associated with high recurrence rates and, thus, long-term follow-up is necessary to determine the success of a specific surgical technique and reconstruction.

PO214

Incidence of Vitamin D Deficiency During Breast Cancer Treatment

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Background/Purpose: Vitamin D levels has been considered to be inversely related to breast cancer development, recurrence risk, and mortality. Mean vitamin D levels in Korean population is lower than western countries due to higher incidence of lactose intolerance and lower exposure to sunlight. The purpose of this study was to assess incidence of vitamin D deficiency at diagnosis with comparison of general population and during breast cancer treatment.

Methods: Breast cancer patients seen at a single tertiary cancer center were enrolled (n = 361). Serum 25-hydroxyvitamin D (25(OH)D) was measured at the time of surgery and after completion of adjuvant chemotherapy or after one year during endocrine therapy. Non-cancer controls were selected from Korean National Health and Nutrition Examination Surveys 2011 to 2013, with 1:1 matching of age and body mass index (n = 361). Statistical analyses used chi-square test, Fisher's exact test, t-test, and ANOVA.

Results: A notable decrease in 25(OH)D concentration was observed (17.7 ng/mL *vs.* 14.1 ng/mL, $p = 0.0002$) after chemotherapy but was not related to chemotherapy regimens, while the endocrine treatment group was not at the time of one year after diagnosis. There was seasonal variation of serum vitamin D levels measured before treatment. Significant lower 25(OH)D levels measured at winter season (from October to March, $p = 0.0056$). The 25(OH)D levels were deficient (< 20 ng/mL) in 253 patients (70.1%), insufficient (20-29 ng/mL) in 63 patients (17.5%), and sufficient (30-150 ng/mL) in 45 patients (12.5%). There was no difference ($p = 0.763$) of serum 25(OH)D level between breast cancer patients (mean 15.4 ng/mL) and non-cancer controls (15.6 ng/mL).

Conclusion: A decrease of serum vitamin D level was observed after chemotherapy

in breast cancer patients. Most of the breast cancer patients showed deficient or insufficient serum vitamin D concentration. Consideration should be given to the supplement of vitamin D to those patients.

PO215

Oncological Safety of Immediate Breast Reconstruction in a Matched Case-Control Study

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Background/Purpose: Immediate breast reconstruction is continuously increasing not only in numbers but also with expanding indications. Many studies have reported similar or even more excellent survival compared to conventional mastectomy. But due to lack of randomized trials or matched case-control studies, the oncological safety of mastectomy followed by immediate reconstruction is still debatable. The purpose of this study is to compare the locoregional, disease free survival rate of reconstruction group to that of control-matched mastectomy group. We will analyze especially in skin or nipple sparing mastectomy group and advanced breast cancer.

Methods: All patients who underwent immediate breast reconstruction between 2002 and 2010 at Seoul National University Hospital, Korea were retrospectively reviewed. We compared the immediate breast reconstruction group with 1:2 matched control group who underwent conventional mastectomy. Matching control variables included age (<35, ≥ 35 and <50, ≥ 50), tumor size (≤ 2 cm, 2 cm), axillary lymph node metastasis, estrogen receptor (ER) status and type of primary treatment (surgery or neoadjuvant chemotherapy).

Results: 190 patients received immediate breast reconstruction (study group) and 363 patients received conventional mastectomy without reconstruction (control group). Matching variables including T stage ($p=0.818$), N stage ($p=0.849$) and ER ($p=0.847$) status has shown no significant difference between study and control group. Locoregional recurrence survival (LRFS) rate, disease-free survival (DFS) rate and overall survival rate all did not differ significantly between the study and control group (log rank test $p=0.392$, $p=0.724$, $p=0.914$, respectively). LRFS was 5.8% in the study group and 5.0% in the control group, similar to previous reports. Subgroup analysis was done for advanced breast cancer and skin-sparing or nipple areolar com-

plex-sparing mastectomy, showing no difference in LRFS and DFS.

Conclusion: Immediate breast reconstruction has no negative impact on patient survival, even when expanding indications and skin preservation are applied.

PO216

Breast Cancer After Kidney and Liver Transplantation: A Report from ASAN Medical Center

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Background/Purpose: improvements in immunosuppression and operation have resulted in long life expectancy of transplantation. This study was to evaluate the nature of post transplant breast cancer (PTBC) compared with breast cancer in general population, and to suggest optimal treatment strategies

Methods: Using information from three ASAN Medical Center databases between 1989 and 2014, including ASAN Medical Center breast cancer database, Kidney transplantation database and liver transplantation database, two cohort composed of PTBC cohort and normal breast cancer control cohort. Survival were compared the patients who received breast cancer operation before 2008.

Results: After median 58.3 month after liver transplantation, 10 patients were diagnosed as breast cancer and 23 patients after median 108.3 month kidney transplantation ($p<0.001$). Mean age of breast cancer were 53.2 (± 8.5) in liver transplantation patients and 44.2 (± 4.8) in kidney transplantation patients. Asymptomatic screening was the detection method of 33.4% of PTBC cohort but 21.0% of control cohort ($p<0.001$). 21.3% (10 patients) in PTBC cohort were stage 0 breast cancer compared with 9.4% (1,002 patients) in control cohort ($p<0.001$), 90% patients were lymph node negative tumor compared with 62.9% in control group ($p<0.001$). Estrogen receptor, Progesterone receptor, human epidermal growth factor receptor 2 status were not difference between cohorts. On multivariate analysis, immunosuppressant was not a poor prognostic factor for breast cancer patients (HR 1.319, 95% CI 0.329-5.287).

Conclusion: Post transplantation breast cancer patients have early breast cancer and prognosis was comparable compared with other breast cancer patients. Early breast cancer is due to screening in post transplantation breast cancer patients. Immunosuppressants does not adversely affect breast cancer.

PO217

ASSURE (Automated SMS Surgical Reminders): Developing an Application to Improve Follow-Up Rates of Breast Cancer Patients

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Background/Purpose: To improve outcomes in management of breast cancer patients, good follow up rate is essential. This study aims to create a program to improve follow up rates of breast cancer patients. There has been strong evidence showing that Short message service (SMS) has been effective in improving follow-up rates of patients. The purpose of this study is to develop an application called "ASSURE" which will provide SMS reminder messages for patients with Breast cancer and to use the ASSURE application in providing reminder messages for patients with Breast cancer.

Methods: The study was conducted in the Philippine General Hospital Breast Care Center. The study was conducted in two phases. Phase 1. Tool development phase. Investigator and Programmer of National Telehealth Center, University of the Philippines collaborated to create a windows based application that can automatically send text reminders. Phase 2. Tool Application phase.

Results: Pilot study employed a randomized controlled trial design. Study participants fulfilled a pre-set inclusion and exclusion criteria. A total of 20 participants was enrolled. Study duration was 3 months. A window based application automatically sending text reminders was developed by the investigator and programmer. Pilot testing on Breast cancer patients showed improved awareness and attendance to follow up and better patient satisfaction.

Conclusion: An application called "ASSURE" was developed and improved follow up rates and patient satisfaction of breast cancer patients.

PO218

Health-Seeking and Health Care Availment Behaviors of Women with Breast Complaints in a Developing Country

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Background/Purpose: Despite various screening programs and numerous awareness campaigns that have been attempted for early detection of breast cancer, patients still present in later stages. This study is aimed at understanding and identifying the health-seeking and health care availment behaviors of Filipino women with breast complaints and identify the factors causing the delay.

Methods: This is a quantitative and qualitative cross sectional study of Filipino women with breast complaints seen during the period of January 1, 2012 to June 30, 2012 in two major government hospitals using a Survey Questionnaire. Causes of delay due to structural, organizational, psychological and Socio-cultural factors were analyzed. Summary and descriptive statistics were used.

Results: A total of 178 patients were included in this study. Patients were mostly aged 30-50 years old and married. Most were high school graduates and held blue collar jobs. Less than half had knowledge of breast cancer; the initial consult preferred was a specialist or hospital; and there was low availment of government health centers. Patients with breast complaints had a median delay of 12 months. Factors associated with delay were low awareness, lack of finances, nobody to take care of the household and fear of surgery.

Conclusion: Programs for early detection of breast cancer must understand and address health-seeking behavior of patients. This stufy shows significant delay in consultation was multifactorial.

PO219

Hereditary Breast Cancer in the Philippines: Results of Establishing a Genetic Counselling Clinic in the Philippine General Hospital

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Background/Purpose: The establishment of Asian Hereditary Breast Cancer Consortium made aware that some Asian countries, notably South Korea have well-established hereditary breast cancer screening programs which have led to identification of many founder mutations that have facilitated more simplified array-based testing. Low resource countries belonging to ABRCA on the other hand, were stimulated to develop genetic counselling programs.

Methods: 1) Establishing a Philippine Hereditary Breast and Ovarian Study Group, 2) Establishing a genetic counseling clinic to screen for patients that are high risk for hereditary breast and ovarian cancer. This is a descriptive study. A genetic counseling clinic was set in place at the Breast Care Center at the Philippine General Hospital along with a screening protocol and screening tool (self-administered questionnaire) to select patients that are potentially at high risk for hereditary breast cancer.

Results: The screening tool was administered to 93 breast cancer patients selected for their young age at the time of diagnosis (50 year old and below) out of 10, 173 patients. Out of the 93 selected patients 92 were female and 1 was male. 52% (49/93) were 41-50 years of age at the time of diagnosis, 20% (19/93) of which had first -degree relatives who had cancer, while 37% (35/93) has a relative who had cancer. Among those who had first -degree relatives with cancer, 42% (8/19) were known to have breast cancer, 10% (2/19) have ovarian cancer and 10% (2/19) have cervical cancer.

Conclusion: Genetic counseling is now offered as a regular service in our breast clinic. Our future goal is to develop thru linkages with our Asian counterparts to make available genetic testing to Filipinos who are at risk of Hereditary breast and ovarian cancer.

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