CoBrCa

5th World Congress
on Controversies in
Breast Cancer
When is Less More?

hosted by

www.cobrca.org

CoBrCa on Controversies in Breast Cancer
When is Less More?

Congress Program

September 4-6, 2019 • San Francisco, CA, USA

www.cobrca.org
### Timetable

#### Wednesday, September 4, 2019

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<tr>
<th>Time</th>
<th>Hall A</th>
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<tbody>
<tr>
<td>12:30-15:00</td>
<td>Pre-Congress Industry Symposium</td>
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<td>15:30-15:45</td>
<td>Congress Opening</td>
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<tr>
<td>15:45-17:30</td>
<td>Session 1: Neoadjuvant therapy</td>
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<td>17:30-19:00</td>
<td>Session 2: Barriers to progress</td>
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<td>19:00</td>
<td>Networking Reception</td>
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#### Thursday, September 5, 2019

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<th>Time</th>
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<tr>
<td>06:45-08:00</td>
<td>Industry Breakfast Symposium</td>
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<td>08:00-09:30</td>
<td>Session 3: Genetics</td>
<td>Session 5: Imaging/Screening</td>
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<td>09:30-10:30</td>
<td>Session 4: Endocrine therapy side effects</td>
<td>Coffee break and poster viewing</td>
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<td>10:30-11:00</td>
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<td>11:00-12:30</td>
<td>Session 6: HER2 positive breast cancer</td>
<td>Session 7: DCIS</td>
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<td>12:30-14:00</td>
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<td>12:45-13:45</td>
<td>Industry Lunch Symposium</td>
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<td>14:00-15:30</td>
<td>Session 8: Imaging in systemic disease</td>
<td>Session 9: Free papers: Oncoplastic/Imaging</td>
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<tr>
<td>16:00-17:30</td>
<td>Session 10: Issues in locoregional management</td>
<td>Session 11: Free papers: Medical Oncology</td>
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<td>17:30-18:30</td>
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#### Friday, September 6, 2019

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<td>08:00-09:30</td>
<td>Session 12: Adjuvant endocrine therapy</td>
<td>Session 13: Imaging as locoregional staging</td>
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<td>09:30-10:30</td>
<td>Session 14: Triple negative breast cancer</td>
<td>Session 15: Management of impalpable lesions</td>
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<td>11:00-12:30</td>
<td>Session 16: Issues in advanced disease</td>
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<td>12:45-13:45</td>
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<td>13:45-15:15</td>
<td>Session 17: Reconstruction</td>
<td>Session 18: Metastatic Breast Cancer</td>
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<td>15:15-16:15</td>
<td>Session 19: Vision for breast cancer 2025</td>
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<td>16:15-16:30</td>
<td>Congress closing and award presentation</td>
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Dear Friends and Colleagues,

We are pleased to welcome you to the 5th World Congress on Controversies in Breast Cancer (CoBrCa): When is Less More? hosted by the University of California, San Francisco (UCSF).

The 5th CoBrCa Congress continues to explore and address controversial issues in breast cancer management. We are pleased to have assembled a stellar international and national faculty and thank all of those who have agreed to participate and those who have submitted abstracts.

We would like to thank the supporters, without whose backing this congress could not take place, as well as all of you who have travelled from across the country or the world to attend the congress.

We look forward to your participation in the sessions and trust that it is an informative and enjoyable experience.

Enjoy your time in the exciting city of San Francisco.

Sincerely,
CoBrCa Congress Chairpersons
General Information

Congress Venue
Hyatt Regency San Francisco
5 Embarcadero Center
San Francisco, CA 94111
USA

Language
The official language of the Congress is English.

Registration Desk
The registration desk will be open during the following hours:

- **Wednesday, September 4, 2019**: 12:00 – 19:30
- **Thursday, September 5, 2019**: 06:30 – 18:30
- **Friday, September 6, 2019**: 06:30 – 16:30

Name badge
All participants are kindly requested to wear their name badges throughout the Congress in order to be admitted to the lecture halls and scheduled activities.

Certificate of attendance (non CME/CPD)
Certificates of attendance will be available for all participants and may be collected at the Registration Desk on Friday, September 6, 2019.

Exhibition
The exhibition will be open during sessions hours. Lunch and coffee breaks will be held in the exhibition area.

Clothing
Business casual for all occasions.

Smoking policy
This is a non-smoking event.

Refreshments
A Networking Reception will be held in the exhibition area on Wednesday, September 4, 2019 at 19:00.
Boxed lunch will be served in the exhibition area during the lunch breaks on Thursday, September 5 and Friday, September 6, 2019.
Coffee will be served during the coffee breaks throughout the congress.

Speakers’ Preview Room
Invited speakers and oral presenters are invited to visit the Speaker’s Preview Room to upload their presentations.

Poster Display
Please check the Scientific Program for the poster board number on which you should display your poster/s.
Posters should be mounted between 07:30-08:30 on Thursday, September 5, 2019 and removed by the end of sessions on Friday, September 6, 2019.

Poster Session
We would like to invite you to the official poster session which will take place on Friday, September 5, 2019 from 17:30 to 18:30 in the Poster Area.
Refreshments will be served during the session.
Photography
It is forbidden to take photographs, film or make recordings during the scientific program (sessions and posters).

Safety and Security
Please do not leave any bags or suitcases unattended at any time, whether inside or outside session halls.

Liability
The Congress Secretariat and Organizers cannot accept liability for personal accidents or loss or damage to private property of participants either during or directly arising from the 5th World Congress on Controversies in Breast Cancer. Participants should make their own arrangements with respect to health and travel insurance.

Social Media
Follow CoBrCa social media pages for the latest updates, key date reminders, and discussions with colleagues and experts from around the world.

@Cobrcacongress
Controversies in Breast Cancer (CoBrCa)
@CoBrCaCongress/#CoBrCa

Congress Organizer

www.congressmed.com

ACCME Accreditation
This activity has been planned and implemented in accordance with the accreditation requirements and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the Joint Providership of UCSF and The University of Texas MD Anderson Cancer Center and The Royal Melbourne Hospital. UCSF is accredited by the ACCME to provide continuing medical education for physicians.

UCSF designates this live activity for a maximum of 16.25 AMA PRA Category 1 Credits™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

For the purpose of recertification, the American Nurses Credentialing Center accepts AMA PRA Category 1 Credit™ issued by organizations accredited by the ACCME.

AAPA accepts category 1 credit from AOACCME, Prescribed credit from AAFP, and AMA PRA Category 1 Credit™.
Faculty List

Amit Agrawal, Dr, MBBS, MS, FRCS Ed, DM, FRCS
Michael David Alvarado, MD
Donald A. Berry, PhD
Alexander D. Borowsky, MD
Judy C. Boughey, MD
Thomas Arthur Buchholz, MD
Julia Camps-Herrero, MD
Abigail Caudle, MD, MS
Mariana Chavez MacGregor, MD
Stephen Chia, MD, FRCPc
Jo Chien, MD
Hiram S. Cody III, MD
Deborah E. Collyar
Javier Cortes, MD, PhD
Angela DeMichele, MD, MSCE
Richard De Boer, MBBS, FRACP
Laura J. Esserman, MD, MBA
Robert R. Flavell, MD, PhD
Steven Goodman, MD, MHS, PhD
Heather I. Greenwood, MD
Sara A. Hurvitz, MD
Nola Hylton, PhD
Debra M. Ikeda, MD
Kevin Kalinsky MD, MS
Christiane K. Kuhl, MD
Allison W. Kurian, MD, MSc
Ava Kwong, MBBS FRCS
Antonio Llombart, MD, PhD
Gregory Bruce Mann, MBBS, PhD, FRACS
Ritse M. Mann, MD, PhD
Ingrid Mayer, MD, MSCI
Michelle E. Melisko, MD
Tanya W. Moseley, MD
Stacy L. Moulder, MD, MSCI
Rita A. Mukhtar, MD
Dean Ornish, MD
Catherine Park, MD
Mark D. Pegram, MD
Jane Perlmutter, PhD, MBA
Donna B. Pinto, BA Journalism
Merisa Louise Piper, MD
Elissa R. Price, MD
Michael W. Rabow, MD
Alistair Ring, MA FRCP MD
Allison K. Rose, MBBS M MED FRANZCR
Hope S. Rugo, MD
Mark Schaverien, MD
Richard J. Schwab, MD
Harpreet Singh, MD
Alastair M. Thompson, ALCM, BSc(Hons), MBChB, MD, FRCS Ed
Laura van ‘t Veer, PhD
Jinsong Wu, Prof.
The following faculty speakers, moderators, and planning committee members have disclosed they have no financial interest/arrangement or affiliation with any commercial companies which produce or market products or services relating to their presentation(s) or commercial support for this continuing medical education activity:

- Michael David Alvarado, MD
- Alexander D. Borowsky, MD
- Judy C. Boughey, MD
- Abigail Caudle, MD MS
- Jo Chien, MD
- Hiram S. Cody III, MD
- Deborah E. Collyar
- Laura J. Esserman, MD, MBA
- Robert R. Flavell, MD, PhD
- Steven Goodman, MD, MHS, PhD
- Heather I. Greenwood, MD
- Nola Hylton, PhD
- Debra M. Ikeda, MD
- Christiane K. Kuhl, MD
- Ava Kwong, MBBS FRCS
- Antonio Llombart-Cussac, MD, PhD
- Gregory Bruce Mann, MBBS, PhD, FRACS
- Rita A. Mukhtar, MD
- Catherine Park, MD
- Jane Perlmutter, PhD, MBA
- Donna B. Pinto, BA Journalism
- Merisa Louise Piper, MD
- Elissa R. Price, MD
- Michael W. Rabow, MD
- Mark Schaverien, MD
- Harpreet Singh, MD
- Jinsong Wu, Prof.

The following faculty speakers have disclosed a financial interest/arrangement or affiliation with a commercial company which produce or market products or services relating to their presentation(s) or commercial support for this continuing medical education activity. All conflicts of interest have been resolved in accordance with the ACCME Standards for Commercial Support:

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<th>Company/Institution</th>
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<td>Alastair M. Thompson, ALCM, BSc(Hons), MBChB, MD, FRCSed</td>
<td>Pfizer</td>
<td>Honorarium Recipient</td>
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<td>Laura Johanna van’t Veer, PhD</td>
<td>Agendia NV</td>
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US Federal and California State Law
Regarding Linguistic Access and Services for Limited English Proficient Persons

I. Purpose.
This document is intended to satisfy the requirements set forth in California Business and Professions code 2190.1. California law requires physicians to obtain training in cultural and linguistic competency as part of their continuing medical education program. This document and the attachments are intended to provide physicians with an overview of federal and state laws regarding linguistic access and services for limited English proficient ("LEP") persons. Other federal and state laws not reviewed below also may govern the manner in which physicians and healthcare providers render services for disabled, hearing impaired or other protected categories.

The Federal Civil Rights Act of 1964, as amended, and HHS regulations require recipients of federal financial assistance ("Recipients") to take reasonable steps to ensure that LEP persons have meaningful access to federally funded programs and services. Failure to provide LEP individuals with access to federally funded programs and services may constitute national origin discrimination, which may be remedied by federal agency enforcement action. Recipients may include physicians, hospitals, universities and academic medical centers who receive grants, training, equipment, surplus property and other assistance from the federal government.

HHS recently issued revised guidance documents for Recipients to ensure that they understand their obligations to provide language assistance services to LEP persons. A copy of HHS’s summary document entitled "Guidance for Federal Financial Assistance Recipients Regarding Title VI and the Prohibition Against National Origin Discrimination Affecting Limited English Proficient Persons – Summary" is available at HHS’s website at: http://www.hhs.gov/ocr/lep/.

As noted above, Recipients generally must provide meaningful access to their programs and services for LEP persons. The rule, however, is a flexible one and HHS recognizes that "reasonable steps" may differ depending on the Recipient’s size and scope of services. HHS advised that Recipients, in designing an LEP program, should conduct an individualized assessment balancing four factors, including: (i) the number or proportion of LEP persons eligible to be served or likely to be encountered by the Recipient; (ii) the frequency with which LEP individuals come into contact with the Recipient's program; (iii) the nature and importance of the program, activity or service provided by the Recipient to its beneficiaries; and (iv) the resources available to the Recipient and the costs of interpreting and translation services.

Based on the Recipient’s analysis, the Recipient should then design an LEP plan based on five recommended steps, including: (i) identifying LEP individuals who may need assistance; (ii) identifying language assistance measures; (iii) training staff; (iv) providing notice to LEP persons; and (v) monitoring and updating the LEP plan.

A Recipient’s LEP plan likely will include translating vital documents and providing either on-site interpreters or telephone interpreter services, or using shared interpreting services with other Recipients. Recipients may take other reasonable steps depending on the emergent or non-emergent needs of the LEP individual, such as hiring bilingual staff who are competent in the skills required for medical translation, hiring staff interpreters, or contracting with outside public or private agencies that provide interpreter services. HHS’s guidance provides detailed examples of the mix of services that a Recipient should consider and implement. HHS’s guidance also establishes a "safe harbor" that Recipients may elect to follow when determining whether vital documents must be translated into other languages. Compliance with the safe harbor will be strong evidence that the Recipient has satisfied its written translation obligations.

In addition to reviewing HHS guidance documents, Recipients may contact HHS’s Office for Civil Rights for technical assistance in establishing a reasonable LEP plan.

The California legislature enacted the California’s Dymally-Alatorre Bilingual Services Act (Govt. Code 7290 et seq.) in order to ensure that California residents would appropriately receive services from public agencies regardless of the person’s English language skills. California Government Code section 7291 recites this legislative intent as follows:

“The Legislature hereby finds and declares that the effective maintenance and development of a free and democratic society depends on the right and ability of its citizens and residents to communicate with their government and the right and ability of the government to communicate with them.

The Legislature further finds and declares that substantial numbers of persons who live, work and pay taxes in this state are unable, either because they do not speak or write English at all, or because their primary language is other than English, effectively to communicate with their government. The Legislature further finds and declares that state and local agency employees frequently are unable to communicate with persons requiring their services because of this language barrier. As a consequence, substantial numbers of persons presently are being denied rights and benefits to which they would otherwise be entitled.

It is the intention of the Legislature in enacting this chapter to provide for effective communication between all levels of government in this state and the people of this state who are precluded from utilizing public services because of language barriers.”

The Act generally requires state and local public agencies to provide interpreter and written document translation services in a manner that will ensure that LEP individuals have access to important government services. Agencies may employ bilingual staff, and translate documents into additional languages representing the clientele served by the agency. Public agencies also must conduct a needs assessment survey every two years documenting the items listed in Government Code section 7299.4, and develop an implementation plan every year that documents compliance with the Act. You may access a copy of this law at the following url: http://www.sbp.ca.gov/bilingual/dymallyact.htm.

-12-
Scientific Program
Wednesday, September 4, 2019

15:30-15:45  **Congress Opening**  
Laura Esserman, USA  
Bruce Mann, Australia

15:45-17:30  **Session 1: Neoadjuvant therapy**  
Chairpersons: Angela DeMichele, USA  
Alastair Thompson, USA

15:45-16:30  **DEBATE:** That NACT has little role for ER+ HER2- breast cancer  
15:45  Yes: Ingrid A. Mayer, USA  
16:00  No: Hope S. Rugo, USA  
16:15  Discussion

16:30-16:45  I SPY the future: Using the neoadjuvant model to optimize outcome  
Laura Esserman, USA

16:45-17:30  **DEBATE:** A path CR allows de-escalation of further therapies  
16:45  Yes: Javier Cortes, Spain  
17:00  No: Mark D. Pegram, USA  
17:15  Discussion

17:30-19:00  **Session 2:** Barriers to progress  
Chairpersons: Bruce Mann, Australia  
Richard de Boer, Australia

17:30-17:50  Why data does often not change opinion  
Steven Goodman, USA

17:50-18:20  **DEBATE:** That RCTs are the only way to change practice  
17:50  Yes: Alistair Ring, UK  
18:00  No: Donald Berry, USA  
18:10  Discussion

18:20-18:40  How and why the FDA cares about real world evidence  
Harpreet Singh, USA

18:40-19:00  Discussion

19:00  Networking Reception
Thursday, September 5, 2019

08:00-09:30  
**Session 3: Genetics**  
**Chairpersons:** Laura Esserman, USA  
Jane Perlmutter, USA  

08:00-08:35  
**DEBATE:** That most patients with breast cancer should be panel tested  
08:00  
Yes: Laura van ‘t Veer, USA  
08:10  
No: Allison W. Kurian, USA  
08:20  
Discussion

08:35-09:10  
**DEBATE:** That all gene carriers with early breast cancer should have a bilateral mastectomy  
08:35  
Yes: Rita Mukhtar, USA  
08:45  
No: Ava Kwong, Hong Kong  
08:55  
Discussion

09:10-09:30  
Interplay of lifestyle and genetics in breast cancer  
Dean Ornish, USA

09:30-10:30  
**Session 4: Endocrine therapy side effects**  
**Chairpersons:** Deborah Collyar, USA  
Allison W. Kurian, USA  

09:30-10:00  
**DEBATE:** That topical estrogens are an acceptable treatment in patients with HR+ve early breast cancer  
09:30  
Yes: Michelle Melisko, USA  
09:40  
No: Alistair Ring, UK  
09:50  
Discussion

10:00-10:30  
**DEBATE:** How to best manage endocrine therapy symptoms: Pharma or Sweat  
10:00  
Pharma: Michelle Melisko, USA  
10:10  
Sweat: Sara A. Hurvitz, USA  
10:20  
Discussion

10:30-11:00  
Coffee break and poster viewing
09:30-10:30  **Session 5:**  
*Imaging/Screening*  

**Chairpersons:**  
Bruce Mann, Australia  
Debra Ikeda, USA  

**09:30-09:45**  
MRI screening in women without hereditary risk  
Ritse Mann, The Netherlands  

**09:45-09:55**  
The implications of a move to MRI screening  
Allison Rose, Australia  

**09:55-10:15**  
**DEBATE:** That women with low risk for breast cancer should only be screened every 3 years  

- **09:55**  
  Yes: Martin Eklund, Sweden  
- **10:05**  
  No: Heather I. Greenwood, USA  

**10:15-10:30**  
Panel discussion:  
Martin Eklund, Sweden  
Ritse Mann, The Netherlands  
Allison Rose, Australia  
Heather I. Greenwood, USA  

**10:30-11:00**  
Coffee break and poster viewing  

**11:00-12:30**  
**Session 6:**  
*HER2 positive breast cancer*  

**Chairpersons:**  
Stacy Moulder, USA  
Kevin Kalinsky, USA  

**11:00-11:35**  
**DEBATE:** That all high-risk adjuvant HER-2 patients should receive dual antibody therapy  

- **11:00**  
  Yes: Mark D. Pegram, USA  
- **11:10**  
  No: Antonio Llombart, Spain  
- **11:20**  
  Discussion  

**11:35-12:10**  
**DEBATE:** That shorter durations of anti HER2 therapy are now warranted in selected patients  

- **11:35**  
  Yes: Sara A. Hurvitz, USA  
- **11:45**  
  No: Javier Cortes, Spain  
- **12:55**  
  Discussion  

**12:10-12:30**  
De-escalating therapy in HER2 positive disease  
Jo Chien, USA  

12:30-14:00  
Coffee break and poster viewing
11:00-12:30  Session 7:  
DCIS  

Chairpersons:  
Hiram S. Cody III, USA  
Donna Pinto, USA  

11:00-11:35  DEBATE: That most DCIS should not be a target for screening  
11:00  Yes: Laura Esserman, USA  
11:10  No: Bruce Mann, Australia  
11:20  Discussion  

11:35-12:10  DEBATE: Most patients with DCIS should not have radiotherapy after Breast Conserving Surgery  
11:35  Yes: Alastair Thompson, USA  
11:45  No: Thomas A. Buchholz, USA  
11:55  Discussion  

12:10-12:30  Role of genomic assays in DCIS  
Rita Mukhtar, USA  

12:30-14:00  Lunch break and poster viewing  

14:00-15:30  Session 8:  
Imaging in systemic disease  

Chairpersons:  
Angela DeMichele, USA  
Nola M. Hylton, USA  

14:00-14:55  Imaging as a biomarker  
14:00  Can we predict outcomes using imaging characteristics?  
Ritse Mann, The Netherlands  
14:20  Lessons from I SPY  
Elissa Price, USA  
14:40  Discussion  

14:55-15:30  DEBATE: That PET CT alone should be the diagnostic tool of choice for metastatic workup for stage 2/3 patients  
14:55  Yes: Robert Flavell, USA  
15:05  No: Richard de Boer, Australia  
15:15  Discussion
When is Less More?

14:00-15:30  Session 9: Free papers: Oncoplastic/Imaging*

Chairpersons:  
Mark V. Schaverien, USA  
Julia Camps-Herrero, Spain  
Stuart McIntosh, UK

14:00-14:10  Making sure no tumor is left behind: Micro-elastography proves an accurate technique to assess tumor margins
Christobel M. Saunders, Australia

14:10-14:20  Temporal trends in the management of women diagnosed with DCIS of the breast in Australia and New Zealand
Rachel Farber, Australia

14:20-14:30  Reduction of margin positivity by Enhanced Intraoperative Breast Specimen Assessment (EISA) to a similar degree as routine Cavity Shave Margins (CSM)
Sami Shoucair, USA

14:30-14:40  Dosimetric planning technique comparison of Aeroform™ tissue expanders versus saline tissue expanders in patients ungoing post-mastectomy radiation therapy
Jennie Gilliman, Australia

14:40-14:50  Prepectoral reconstruction with Braxon® ADM mesh
Ahmed Shalaby, UK

14:50-15:00  A simple intervention for long-term relief of chronic post mastectomy pain
Holly Keane, Australia

15:00-15:10  Salvage of the previously un-salvageable peri-prosthetic breast infection after breast reconstruction
Farid Meybodi, Australia

15:10-15:20  Subjective versus objective evaluation of aesthetic outcome after breast surgery
Negin Sedaghat, Australia

15:20-15:30  Outcomes following single-stage pre-pectoral breast reconstruction using implant and acellular dermal matrix: A single-centre experience of 500 reconstructions
Rajiv Dave, UK

15:30-16:00  Coffee break and poster viewing

16:00-17:30  Session 10: Issues in locoregional management

Chairpersons:  
Michael Alvarado, USA  
Jiong Wu, China

16:00-16:35  DEBATE: Despite ACOSOG Z11 and AMAROS, there is still a role for axillary surgery in patients with a positive sentinel node
Yes: Abigail Caudle, USA  
No: Hiram S. Cody III, USA  
16:20  Discussion

16:35-17:00  DEBATE: That regional nodal radiation should be routine for patients with axillary metastasis
Yes: Thomas A. Buchholz, USA  
No: Catherine Park, USA  
16:55  Discussion

17:10-17:30  Management of chronic lymphedema: Are we there yet?
Mark V. Schaverien, USA
16:00-17:30 Session 11: Free Papers: Medical Oncology*

Chairpersons: Javier Cortes, Spain
Richard Schwab, USA
Jo Chien, USA

16:00-16:10 Pathological characteristics and treatment outcome of Inflammatory Breast Cancer (IBC) in Egypt: A multicenter retrospective case series
Aliaa Shamardal, Egypt

16:10-16:20 Efficacy of low dose methotrexate treatment for granulomatous mastitis
Jeffrey Sugandi, USA

16:20-16:30 Utilisation and short-term outcomes of neoadjuvant systemic therapy in breast cancer: A national prospective multi-centre cohort study
Stuart McIntosh, UK

16:30-16:40 The influence of neoadjuvant chemotherapy on the plan for breast-conserving surgery in early or locally advanced breast cancer
Adeline Rankin, UK

16:40-16:50 Electronic data capture in clinical trials: State of play and improvements for the future
Marie Osdoit, France

16:50-17:00 Tumor microenvironment of metastasis (TMEM): A new biomarker and treatment paradigm
Jesus Anampa Mesias, USA

17:00-17:10 Development of a multi-ethnic polygenic risk score for use in a trial of breast cancer screening
Mandy Che, USA

17:10-17:20 The use of 18F-FDG PET/CT as an initial staging procedure for stage II-III breast cancer: A multicenter value analysis
Colby Hyland, USA

17:20-17:30 Disease free survival in node positive Invasive Lobular Carcinoma with or without axillary dissection
Mary Kathryn Abel, USA

*Sessions 9 and 11 are non-CME sessions

17:30-18:30 Poster Session

Refreshments will be served
Friday, September 6, 2019

08:00-09:30  Session 12:  
Adjuvant endocrine therapy  
Chairpersons:  
Michelle Melisko, USA  
Jane Perlmutter, USA  

08:00-08:45  DEBATE: That side effects of dual endocrine therapy outweigh the benefits for most young women  
Yes: Richard De Boer, Australia  
No: Ingrid A. Mayer, USA  
Discussion  

08:45-09:30  DEBATE: That ten years of adjuvant endocrine therapy is overtreatment for most patients  
Yes: Mariana Chavez MacGregor, USA  
No: Richard Schwab, USA  
Discussion  

08:00-09:30  Session 13:  
Imaging as locoregional staging  
Chairpersons:  
Alastair Thompson, USA  
Allison Rose, Australia  

08:00-08:35  DEBATE: That axillary ultrasound is an essential part of early breast cancer workup  
Yes: Debra M. Ikeda, USA  
No: Hiram S. Cody III, USA  
Discussion  

08:35-09:15  DEBATE: That contrast imaging should be part of the workup of early breast cancer  
Yes: Christiane Kuhl, Germany  
No: Michael Alvarado, USA  
Discussion  

09:15-09:30  Intraoperative imaging  
Julia Camps-Herrero, Spain  

09:30-10:30  Session 14:  
Triple negative breast cancer  
Chairpersons:  
Antonio Llombart, Spain  
Mariana Chavez MacGregor, USA  

09:30-10:10  DEBATE: That immunotherapy will become standard of care for TN MBC  
Yes: Javier Cortes, Spain  
No: Kevin Kalinsky, USA  
Discussion  

10:10-10:30  New strategies in early TNBC  
Stacy Moulder, USA  

10:30-11:00  Coffee break and poster viewing  

09:30-10:30  Session 15:  
Management of impalpable lesions  
Chairpersons:  
Judy C. Boughey, USA  
Amit Agrawal, UK  

09:30-09:40  Why we need to change  
Bruce Mann, Australia  

09:40-09:50  The case for Magtrace  
Michael Alvarado, USA  

10:40-10:50  Discussion  

11:00-11:30  Coffee break and poster viewing  

11:30-12:30  Lunch break  

14:00-17:00  Poster presentations  

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<th>Time</th>
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| 09:50-10:00 | The case for ICG  
*Ava Kwong, Hong Kong* |
| 10:00-10:10 | The case for Seeds  
*Abigail S. Caudle, USA* |
| 10:10-10:20 | The case for radar localization (Savi Scout)  
*Tanya Moseley, USA* |
| 10:20-10:30 | Discussion |
| 10:30-11:00 | Coffee break and poster viewing |
| 11:00-12:30 | Session 16: Issues in advanced disease  
*Hall A* |
|           | Chairpersons:  
*Ingrid A. Mayer, USA*  
*Deborah Collyar, USA* |
| 11:00-11:35 | DEBATE: After treatment response of de novo metastatic breast cancer, how should the primary lesion be managed?  
11:00  
*Wait and watch: Richard Schwab, USA*  
11:10  
*Same as for early stage disease: Judy C. Boughey, USA*  
11:20  
*Discussion* |
| 11:35-11:55 | Oligometastatic disease should be treated with curative intent  
*Catherine Park, USA* |
| 11:55-12:30 | DEBATE: That the ASCO guidelines for palliative care should be internationally applied  
11:55  
*Yes: Michael W. Rabow, USA*  
12:05  
*No: Stephen Chia, Canada*  
12:15  
*Discussion* |
| 12:30-13:45 | Lunch break and poster viewing |
| 13:45-15:15 | Session 17: Reconstruction  
*Hall A* |
|           | Chairpersons:  
*Thomas A. Buchholz, USA*  
*Donna Pinto, USA* |
| 13:45-14:20 | DEBATE: That one surgeon is better than two  
13:45  
*Yes: Amit Agrawal, UK*  
13:55  
*No: Mark V. Schaverien, USA*  
14:05  
*Discussion* |
| 14:20-14:40 | Pre-pectoral implants: Does anyone still need a sub muscular implant?  
*Merisa Piper, USA* |
| 14:40-15:15 | DEBATE: That patients requiring postmastectomy radiotherapy should not undergo immediate reconstruction  
14:40  
*Yes: Alastair Thompson, USA*  
14:50  
*No: Jiong Wu, China*  
15:00  
*Discussion* |
13:45-15:15  Session 18: Metastatic Breast Cancer

Chairpersons:  
Mark Pegram, USA  
Alistair Ring, UK

13:45-14:20  DEBATE: CDK 4/6 inhibitors should be first line therapy for all patients with newly diagnosed HR+ MBC
13:45  Yes: Stephen Chia, Canada
13:55  No: Mariana Chavez MacGregor, USA
14:05  Discussion

14:20-14:40  What is the approach for patients progressing on CDK 4/6 inhibitors?
Angela DeMichele, USA

14:40-15:15  DEBATE: ctDNA is now the best method to monitor response in patients with metastatic breast cancer
14:40  Yes: Kevin Kalinsky, USA
14:50  No: Antonio Llombart, Spain
15:00  Discussion

15:15-16:15  Session 19: Vision for breast cancer 2025

Chairpersons:  
Bruce Mann, Australia  
Alastair Thompson, USA

15:15-15:25  Consumers’ perspective
Jane Perlmutter, USA

15:25-15:35  Early detection
Christiane Kuhl, Germany

15:35-15:45  Pathology
Alexander D. Borowsky, USA

15:45-15:55  Locoregional treatment
Judy C. Boughey, USA

15:55-16:05  Systemic therapy
Angela DeMichele, USA

16:05-16:15  Supportive care
Michael W. Rabow, USA

16:15-16:30  Congress closing and award presentation

Chairpersons:  
Bruce Mann, Australia  
Alastair Thompson, USA
About Current Oncology

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- Open Access publication
- Distributed in print gratis to the Canadian oncology community
- Published six times per year

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When is Less More?

Medical and Scientific Publishers

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Maurizio Pinamonti, Fabrizio Zanconati (Trieste)

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Posters

Thursday, September 5 – Friday, September 6, 2019

Breast cancer genetics

P01 Contribution of germline mutations in lysosomal storage disease-related genes contributes to breast cancer development
Han-Byoel Lee, South Korea

P02 Multifocality in BRCA-associated breast cancer: A cross-sectional analysis
Stuart Mcintosh, UK

Breast cancer screening

P03 Women informed to screen depending on measures of risk (WISDOM): A personalized breast cancer screening in a population based study
Irene Acerbi, USA

P04 Has the transition to digital mammography in breast cancer screening resulted in real benefits?
Rachel Farber, Australia

P05 Barriers and lessons learned after implementing coverage with evidence progression with private payers in a national, precision medicine breast screening trial
Yash Huilgol, USA

Breast imaging

P06 Correlation of breast background parenchymal enhancement on MRI with morphophysiological parameters of breast and breast lesions
Zehra Hilal Adibelli, Turkey

P07 Pure fibrocystic change diagnosed at MRI-guided vacuum-assisted breast biopsy: Imaging features and follow-up outcomes
Shu-Tian Chen, USA

P08 A multi-center open-label parallel phase-2 clinical trial to evaluate the efficacy and safety of LuminoMark™ for localization in patients with non-palpable breast lesions
Seung Ki Kim, South Korea

P09 Factors associated with MRI detection of occult lesions in newly diagnosed breast cancer
Julie Lang, USA

P10 3D automatic density analysis device might be better for accurate breast density in Japanese women with breast cancer
Misaki Matsuyanagi, Japan

P11 Magnetic resonance imaging features of pure sclerosing adenosis in the breast undergoing vacuum assisted breast core biopsy
Satoko Okamoto, Japan

P12 Radial sclerosing lesions of the breast. A single-institution experience and literature review
Nikolaos Salemis, Greece
When is Less More?

When is Less More?

CoBrCa

Terumasa Sawada, Japan

Utility of contralateral breast ultrasound in diagnosing synchronous breast cancer in newly diagnosed cancer patients

Ying Ching Tan, Singapore

Breast reconstruction

Outcomes and complications of immediate and delayed breast reconstruction

Marwa Badawi, UK

What should be used for lower pole coverage in immediate two-stage expander/implant breast reconstruction? A feasibility study

Negin Sedaghat, Australia

DCIS

Patient-centered initiatives to enhance recruitment to the COMET study

Donna Pinto, USA

Endocrine resistance

Response rate by geographic region in patients with hormone receptor-positive, human epidermal growth factor receptor-2–negative advanced breast cancer from the SOLAR-1 trial

Ingrid Mayer, USA

Her2 positive breast cancer

Randomized, double-blind, phase 3 study of pembrolizumab vs placebo combined with neoadjuvant chemotherapy and adjuvant endocrine therapy for high-risk, early-stage ER+/HER2– breast cancer

Javier Cortes, Spain

Fluorescence in situ hybridization analysis of HER2 3+ breast cancer patients with neoadjuvant chemotherapy using pertuzumab and trastuzumab

Choi Jin Hyuk, South Korea

Locoregional therapy

A case of metaplastic breast carcinoma presenting as a bleeding breast mass

Ma Corazon Cabanilla-Manuntag, Philippines

Factors associated with false negative rate of sentinel lymph node biopsy in breast cancer patients

Joyce Hazel Chua, Philippines

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Abstracts
which are treated with breast conservation can be managed using regional therapeutic strategies. In light of these findings, four independent high-quality, large-scale randomized trials with matched sets of patients treated with breast conservation (n=10,922) and postmastectomy radiation (n=18,060) (4,5) demonstrated that radiation of the axilla and supraclavicular fossa achieved excellent tumor control and was less morbid compared to a completion axillary dissection (2). While these trials did not assess the benefits of whether more conservative radiation treatment volumes (3-9) selected patients with lymph node positive breast cancer, others conducted single arm (no radiation) prospective trials to define low risk cohorts. These trials demonstrated a statistically higher local failure rate compared to the radiation arm. However, the overall rate of recurrence was approximately 1% per year, suggesting that this was acceptable for some patients (2). Similarly, the 0011 trial suggested that many patients with positive sentinel lymph nodes may not benefit from radiation treatments to the level III axillary, supraclavicular, or internal mammary lymph nodes. For appropriately selected patients, radiation can eradicate disease within these lymphatics: level I, II, and the internal mammary lymph nodes. For appropriately selected patients, radiation plays an important role in helping to achieve these favorable results in addition to improving overall survival after 5 years without distant metastases, and improving survival. Which subsets of patients with ductal carcinoma in situ (DCIS) have been one of the most comprehensively studied topics in medicine, and the role of radiation plays in helping to achieve these favorable results safely avoid a completion axillary dissection (1). The role of radiation in helping to achieve these favorable results is controversial. In addition, continued improvements in radiation techniques and biology. In addition, continued improvements in radiation techniques and biology, and the internal mammary lymph nodes. For appropriately selected patients, radiation can eradicate disease within these lymphatics: level I, II, and the internal mammary lymph nodes. For appropriately selected patients, radiation plays an important role in helping to achieve these favorable results in addition to improving overall survival after 5 years without distant metastases, and improving survival. Which subsets of patients with ductal carcinoma in situ (DCIS) have been one of the most comprehensively studied topics in medicine, and the role of radiation plays in helping to achieve these favorable results safely avoid a completion axillary dissection (1). The role of radiation in helping to achieve these favorable results is controversial. In addition, continued improvements in radiation techniques and biology.
Radiotherapy plays an important role in the management of breast cancer lymphatics: level I-II axilla, the supraclavicular fossa, and the internal mammary lymph nodes. For appropriately selected patients, radiotherapy can eradicate disease within lymph nodes and avoid regional recurrences, minimizing the risk of distant metastases and improve survival. Which subsets of breast cancer patients require comprehensive treatment of all of these regions is controversial. In addition, how to optimally combine surgical and radiotherapy lymphatic treatments remains an important therapeutic decision. Data from the American College of Surgeons Oncology Group Z-0011 trial suggested that many patients with positive sentinel lymph node(s) who are treated with breast conservation can safely avoid a completion axillary dissection (1). The role of radiation played in helping to achieve these favorable results could not be specifically assessed in this study. The AMAROS trial investigated a similar cohort of patients and demonstrated that radiation of the axilla and supraclavicular fossa achieved excellent tumor control and was less morbid than a completion axillary dissection (2). While these trials led to a new standard of doing less axillary treatments for selected patients with lymph node positive breast cancer, they did not assess the benefits of whether more comprehensive radiation approaches benefited compared to more conservative radiation treatment volumes. In contrast, two large radiation oncology studies (MA.20 and EORTC22922-10925) evaluated whether more extensive lymphatic treatment benefited patients with higher-risk lymph node-negative, or lower risk lymph node-positive disease. A meta-analysis of these two studies suggested that the addition of radiation treatment to the level III axillary, supraclavicular and upper internal mammary lymph nodes improved overall survival, disease free survival and distant metastasis free survival (3). The overall survival advantage was low, approximately 1-2% overall, but was statistically significant in the meta-analysis. Most patients in both of these studies have stage I-II breast cancer. Based on the MA.20 and EORTC studies, some advocate that all patients with positive lymph nodes should receive comprehensive regional lymph node radiation. However, data from MD Anderson and Memorial Sloan Kettering studies suggested that favorable cohorts of patients with 1-3 positive lymph nodes may not benefit from regional lymph node radiation (as a component of postmastectomy radiation) (4,5). In contrast, a National Cancer Database study that evaluated regional lymph node radiation in a matched set of patients treated with breast conservation (n=10,922), found no difference in overall survival after 5 years with the additional radiation (6). It is clear that patients with 1-3 positive lymph nodes represent a heterogeneous group, both with respect to tumor burden and biology. In addition, continued improvements in systemic therapies can also affect the potential benefits of local-regional therapeutic strategies. In light of these important questions, new clinical trials focusing on the value of regional treatments for patients with biologically favorable stage II breast cancer patients are currently ongoing.

References:

ROLE OF RADIATION FOR PATIENTS WITH DUCTAL CARCINOMA IN SITU

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The benefits of radiotherapy for patients with ductal carcinoma in situ (DCIS) has been one of the most comprehensively studied topics in medicine. Four independent high quality, prospective trials randomized patients with DCIS treated with a breast conserving surgery to whole breast radiation versus no radiation. In aggregate, over 3000 patients were randomized on these trials. The results of these 4 trials were remarkably consistent with each trial demonstrating a statistical reduction in ipsilateral recurrences of DCIS and a statistical reduction in ipsilateral invasive breast cancer recurrence. The proportional benefit for both of these endpoints was approximately the same, around a 50% proportional reduction in the recurrence. There was no survival benefit noted in either the individual trials or a meta-analysis that aggregated the data from all 4 of these studies (1). These data led efforts to define lower risk subgroups of patients with DCIS, on the basis of size, grade and margins. For example, a more recent randomized trial of radiation vs observation limited enrollment to DCIS patients with the following favorable features: size less than 2.5 cm, non-high grade, and negative margins of at least 3mm. Unfortunately, this trial again found that the observation arm had a statistically higher local failure rate compared to the radiation arm. However, the overall rate of recurrence without radiation was approximately 1% per year, suggesting that this may be an acceptable risk for some patients (2). Similarly, others conducted single arm (no radiation) prospective studies to define low risk cohorts. These trials demonstrated that patients with low-intermediate grade, small volume disease with negative margins had an approximate 14-16% risk of an ipsilateral event at 10 years (3-4). The risk of events for patients with high grade disease was much higher, 25% at 10 years (3). While clinical features proved to risk stratify, many patients and providers continued to feel that risks exceeding 10% at 10 years in the low risk cohorts was still too high and the benefits of radiation therefore would be still clinically relevant. To address this, more recent studies have incorporated more novel biomarkers to aid in the identification of low risk groups. Two such studies have led to approved assays being introduced into the marketplace. The Genomic Health DCIS score is able to segregate patients into low, intermittent and high risk groups. On its own it did not identify a group with a less than 10% risk at 10 years but when it was combined with clinical parameters it was able to do so. Specifically, for patients over 50 years of age with tumor sizes less than or equal to 1 cm whose DCIS had a low risk bioassay score, the 10 year risk of recurrence was 7.2% (5). Similarly, at Prelude RT test, which also incorporates biological and clinical features, identified a low risk cohort with a 10 year ipsilateral recurrence risk of only 4% without radiation (6). In summary, radiation plays an important role in the management of DCIS. For the majority of patients, this...
treatment helps to minimize the risk of subsequent recurrence and potential need for additional treatments of cancer. Newer molecular approaches combined with clinical features, help to risk stratify an individual’s risk of recurrence and thereby better predict the absolute benefit of radiation treatment.

References:


I SPY THE FUTURE: USING THE NEOADJUVANT MODEL TO OPTIMIZE OUTCOME

Laura Esserman, MD, MBA, USA

I-SPY2 is an adaptive platform trial of neoadjuvant therapy for high-risk, early stage breast cancer, designed to accelerate the process of finding the right drugs for the right patients at the right time. An adaptive design is defined as one that “allows modifications to the trial and/or statistical procedures of the trial after its initiation without undermining its validity and integrity”. The goal is to make clinical trials more flexible, efficient and fast. Clinical drug development in oncology typically begins in the metastatic setting -- phase 1 (safety and dose finding), 2 (signal generating), and 3 (efficacy) trials conducted in people with advanced disease -- before evaluating them for early cancers. Moreover, it is traditional to test only one drug at a time. This approach is slow and extremely expensive – it can take 15-18 years for a drug to move from a phase 1 study to routine clinical use. For example, the biologic trastuzumab, which represents one of the most important advances breast cancer treatment in years, took 18 years of clinical development before approval for early breast cancer. The FDA is extremely interested in new and more efficient approaches to trial design and has encouraged the use of adaptive designs. (Woodcock & LaVange, 2017)

I SPY 2 description

Using a multi-agent, adaptive platform design, the I-SPY trial has evolved into a model for translational research and innovation in clinical trial design. An important goal of the study is to re-engineering of the drug development process. Once safety data has been established, the focus for testing and development of promising agents should be shifted to the early stage, high-risk cancer setting, within a framework for rapid evaluation of which agents and/or combinations of agents will be effective for each tumor subtype. This can be accomplished by selecting patients with high risk for early recurrence, and changing the order of therapy, starting with systemic therapy followed by definitive surgical resection, where the impact of therapy can be assessed. Importantly, the impact of improving response in the early stage setting does not just extend survival, it can actually save lives. Thus moving the focus of drug development to the early stage setting has the potential for shortening the time to market of highly effective agents. A key element of this approach is the use of an early endpoint. Over the last 20 years, we and others have worked to establish complete pathologic response or ‘pCR’ (Yee et al., 2018) and (residual cancer burden) (Symmans et al., 2007) as an early indicator of treatment response and long-term outcome. Another critical advance is the use of biomarker and imaging guidance, and the ability to identify the category of patients at risk for early recurrence for inclusion in the study. Together, these permit the evaluation of multiple drugs in parallel within the same trial, instead of creating a new trial for every drug tested. Drugs enter and leave the trial by protocol amendment, saving significant time compared to writing and reviewing a new protocol for each drug. The fourth is the use of new tools for real time data capture. A longitudinal Bayesian adaptive statistical model is used to predict if an agent “graduates,” meaning it has reached a threshold of >85% predicted probability of success in a subsequent 1:1 randomized neoadjuvant therapy trial of 300 patients. The purpose of the graduation threshold is to identify those agents with a large signal so we can focus on those combinations most likely to improve outcomes for patients. Finally, the trial is collaborative by design, and has included the FDA, pharmaceutical and biotechnology companies, academic centers, and patients at the table, from the inception. The trial design leverages a pre-competitive framework, to align incentives, and drive efficiency. (Barker et al., 2009; Esserman et al., 2012; Woodcock, 2010). Several agents have graduated since I-SPY opened in 2010. One of the most striking results was the near tripling of pCR with the immunotherapeutic pembrolizumab when added to standard-of-care taxol, a result that was recently confirmed in a follow-on phase 3 trial (Nanda et al., 2017). To date, 18 drugs and combinations have entered into the trial over the last decade, with many more in the pipeline (Park et al., 2016; Rugo et al., 2016). There are currently 20 major academic sites in the network, with 4 more, including community cancer center networks, slated to enter in 2020. Over twenty companies participate. When the trial started, it was the first trial to bring multiple pharma companies into the same trial. One of the objectives of the I-SPY 2 platform was to serve as a precompetitive consortium for the industry, helping to rapidly identify agents by class that are most likely to cure patients and to help the industry as a whole make better choices. Learning what is not likely to work, quickly, with a small number of patients is just as important as learning which are likely to work.

Future of adaptive trials in the neoadjuvant setting

Early endpoints are increasingly being accepted by both regulators and clinicians because they provide prognostic information that matters to patients (Prowell & Pazdur, 2012). The impact of achieving a pCR is clinically important, and trials and care have evolved to adapt care based on response to therapy. Similar to how T cell counts became the standard of efficacy for treatment of HIV, breast cancer patients and their oncologists know that their outcome is
better if they can achieve a complete response prior to surgery.

This has led to a change in clinical practice in early breast cancer, where pCR is increasingly becoming the goal of neoadjuvant treatment. Once early endpoints like pCR are accepted clinically, clinicians and patients simply do not accept a poor outcome, but rather look for additional or different therapies to achieve pCR and improve their chance of a good outcome. The implication for clinical trials is enormous, as current designs generally lack the flexibility to alter treatment regimens depending upon an individual patient’s response.

Through a program project grant (PO1CA210961) and the support of the Quantum Leap Healthcare Collaborative (trial sponsor), we are designing the next generation of I-SPY2 with the explicit 5-year goal of getting 90% of patients to a pCR. “I-SPY2.2” will establish a new paradigm for clinical trials by encouraging the escalation/de-escalation of treatment depending upon an individual’s response. I-SPY2.2 will leverage the Bayesian adaptive, biomarker-driven approach of the current I-SPY2, combined with the ‘Sequential Multiple Assignment Randomized Trial’ or ‘SMART’ trial model that facilitates multiple randomizations within the same trial. In this hybrid model, patients who fail to respond to the therapy for which they have been initially randomized may be subsequently randomized to a second, (and in some cases, third) biologically targeted therapy as a ‘second chance’ to achieve pCR. As therapies continue to improve, we will have the chance to test targeted and potentially less toxic agents, knowing that if a patient does not respond, they will move on to the agent most likely to work for their specific disease subtype. Those with persistent disease despite 2 regimens of therapy may have the chance to be rescued by an agent specifically targeted at emerging resistance. A further innovation will feature an additional, confirmatory arm that serves as a seamless transition from phase II to phase III development – a “Regulatory Evidence Generation” arm – designed to establish a more efficient means of gathering the evidence required for regulatory approval of an agent/combination. As I-SPY2.2 prepares for its transition in 2020, a number of supporting innovations in statistics and data acquisition and management are currently underway. I-SPY2, in its past and looking towards its future, highlights the opportunity of pragmatic solutions to adapt to learning and change in the field of drug development, and to enable rapid learning, even as new therapies emerge and standard of care evolve. It is critical that we design trials that are patient centered and that can succeed and lead the way in an ever changing environment.

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THAT PET CT ALONE SHOULD BE THE DIAGNOSTIC TOOL OF CHOICE FOR METASTATIC WORKUP FOR STAGE 2/3 PATIENTS – YES
Robert Flavell, MD, PhD, USA

The use of diagnostic imaging in stage 2/3 patients varies considerably based on provider preference, and evidence based guidelines including those from the NCCN provide multiple options to choose from. Options for imaging include breast MRI for local assessment of disease, and a multitude of choices for whole body staging, including diagnostic CT, bone scan, and PET/CT. In principle, the advantage of performing whole body imaging is to reveal occult distant metastases, as well as possibly refining locoregional staging. While options in this setting include diagnostic CT, bone scan, and FDG PET/CT, we would like to propose that PET/CT is a superior choice in this diagnostic setting. It offers similar radiation dose, and helps to reduce false positives and false negative studies when compared against CT and bone scan. In many cases, differences in staging as detected by PET/CT may cause changes in patient management, more commonly in stage III when compared against stage II patients, with ranges from 13-16%, depending on the study. One challenge
in the routine use of PET/CT in this setting is increased cost of the study. However, we have recently found that the false positive findings on standard imaging such as bone scan and CT incur an additional cost. When the costs associated with false positive findings are factored in, we found a significant decrease in cost when using PET/CT guided management, when compared against CT and bone scan alone. When all of these considerations are taken together, we would like to propose that PET/CT should be the diagnostic tool of choice for metastatic workup of patients with stage 2 or 3 breast cancer.

DEBATE: HOW TO BEST MANAGE ENDOCRINE THERAPY SYMPTOMS: PHARMA OR SWEAT? – PHARMA
Sara A. Hurvitz, MD, USA

The use of endocrine therapy has undoubtedly led to statistically significant and clinically meaningful long-term improvements in breast cancer recurrence rates as well as overall survival. These benefits cannot be overstated as we now understand that a person’s risk of distant recurrence or death from hormone receptor positive breast cancer lasts decades, if not a lifetime. Treating systemically with anti-death from hormone receptor positive breast cancer lasts decades, if not a lifetime. Treating systemically with anti-

SYMPTOMS: PHARMA OR SWEAT?

DEBATE: HOW TO BEST MANAGE ENDOCRINE THERAPY SYMPTOMS: PHARMA OR SWEAT?

When trastuzumab was approved in the adjuvant setting, almost 13 years ago, its indication was limited to those with lymph node positive disease. Since then, the standard use of trastuzumab has vastly expanded such that the NCCN guidelines now recommend considering its use even in node negative disease with tumors less than 5 mm. This change in practice is undeniably due to mounting long-term evidence from large randomized trials indicating that treatment with trastuzumab plus chemotherapy in HER2-driven breast cancer has altered the natural history of this disease from one with the poorest prognosis to one with the best. Thus, it is only natural to be reticent to reduce the use of this life-saving agent without convincing evidence that less therapy is as effective as the standard approach. This compulsion to give more rather than less therapy for HER2-positive disease is evidenced by the recent approvals of two new adjuvant therapies—neratinib and pertuzumab—based on phase III trials that showed only marginal improvements in disease-free survival benefits, primarily in patients without nodal involvement, yet significant increases in toxicity. In response to this escalation in therapy—which is seen by some as both unnecessary and potentially dangerous—there has been a counter-movement gaining steam in the past several years that is calling on clinicians and scientists to make strides toward reducing the overtreatment of patients. The drive to de-escalate therapy is supported by a need to reduce not only toxicity but the financial consequences to the individual and society in an age where healthcare costs can be massive. As such, five trials with a non-inferiority endpoint have been conducted and reported that have compared 12-months of adjuvant trastuzumab to either 9-weeks (Short-HER and SOLD) or 6-months (HORG, PHARE and PERSEPHONE). Non-inferiority was not demonstrated in the first four of these studies, leading many to conclude that 12-months should remain the standard. However, this year, results of the largest of these studies, PERSEPHONE were published, demonstrating that 6-months of therapy is non-inferior to 12-months. So, how are these data to be reconciled with the opposite conclusions from the other four studies? In this presentation, the PERSEPHONE data will be explained in the context of the four similarly designed non-inferiority studies that did not meet their endpoint and an evidence-based argument in favor of reducing length of adjuvant trastuzumab in select patient populations will be presented.

DEBATE: THAT SHORTER DURATIONS OF ANTI HER2 THERAPY ARE NOW WARRANTED IN SELECTED PATIENTS - YES
Sara A. Hurvitz, MD, USA

When trastuzumab was approved in the adjuvant setting, almost 13 years ago, its indication was limited to those with lymph node positive disease. Since then, the standard use of trastuzumab has vastly expanded such that the NCCN guidelines now recommend considering its use even in node negative disease with tumors less than 5 mm. This change in practice is undeniably due to mounting long-term evidence from large randomized trials indicating that treatment with trastuzumab plus chemotherapy in HER2-driven breast cancer has altered the natural history of this disease from one with the poorest prognosis to one with the best. Thus, it is only natural to be reticent to reduce the use of this life-saving agent without convincing evidence that less therapy is as effective as the standard approach. This compulsion to give more rather than less therapy for HER2-positive disease is evidenced by the recent approvals of two new adjuvant therapies—neratinib and pertuzumab—based on phase III trials that showed only marginal improvements in disease-free survival benefits, primarily in patients without nodal involvement, yet significant increases in toxicity. In response to this escalation in therapy—which is seen by some as both unnecessary and potentially dangerous—there has been a counter-movement gaining steam in the past several years that is calling on clinicians and scientists to make strides toward reducing the overtreatment of patients. The drive to de-escalate therapy is supported by a need to reduce not only toxicity but the financial consequences to the individual and society in an age where healthcare costs can be massive. As such, five trials with a non-inferiority endpoint have been conducted and reported that have compared 12-months of adjuvant trastuzumab to either 9-weeks (Short-HER and SOLD) or 6-months (HORG, PHARE and PERSEPHONE). Non-inferiority was not demonstrated in the first four of these studies, leading many to conclude that 12-months should remain the standard. However, this year, results of the largest of these studies, PERSEPHONE were published, demonstrating that 6-months of therapy is non-inferior to 12-months. So, how are these data to be reconciled with the opposite conclusions from the other four studies? In this presentation, the PERSEPHONE data will be explained in the context of the four similarly designed non-inferiority studies that did not meet their endpoint and an evidence-based argument in favor of reducing length of adjuvant trastuzumab in select patient populations will be presented.

DEBATE: THAT AUXILLARY ULTRASOUND IS AN ESSENTIAL PART OF EARLY BREAST CANCER WORKUP – YES
Debra M. Ikeda, M.D., FACR, FSBI, FSMR
Stanford University School of Medicine, Stanford, California, USA

Given that women eligible for the ACOSOG Z0031 trial undergoing sentinel lymph node biopsy (SLNB) with 1-2 sentinel nodes (SN) showing macrometastases had non-inferior results in loco-regional disease free and overall survival compared to axillary lymph node dissection (ALND) at 6.3 and 10 year follow up (Giuliano 2010, 2017), demonstrating that the axilla can be staged with SLNB in early breast cancer, why scan the axilla for staging in early breast cancer? First there are known limitations of clinical
examination to detect positive lymph nodes. Second, ultrasound may be used for SLNB patient selection using ACOSOG Z0011 criteria by excluding women with 3 or more suspicious axillary lymph nodes, matted nodes or gross extra nodal disease. US and US-guided needle biopsy (UNB) was shown to have 79.6% sensitivity, 98.3% specificity and PPV of 97.1% shown by a 2011 meta-analysis of preoperative US plus UNB (Houssami 2011). Wellington et al (2018) showed that, based on predictive modeling, routine axillary ultrasound does not increase the rate of ALND. As suggested by Pesek et al (2018) and NCNN V 2.2019, a specific group of women with early breast cancer who might benefit from axillary US are those with low risk of recurrence (with negative US or with suspicious lymph nodes negative on US-biopsy) who might be potentially spared SLNB, particularly if radiation therapy is undertaken. Unrelated to scientific data, USA market forces and patient expectations drive immediate same day biopsy of suspicious breast masses directly after imaging discovery, most often without clinical axillary examination. Because there is no information on tumor genetics, hormonal status or Ki67 prior to UNB to indicate tumor predisposition for metastases, the axilla is often scanned for the presence and number of suspicious lymph nodes for BI-RADS 4C and 5 breast lesions. Later, UNB tumor pathology and axillary US imaging informs the breast cancer team on decision to perform pre-operative UNB as needed to plan potential chemotherapy, surgery type, radiation therapy and reconstruction. Further, axillary US results inform preliminary discussions with the patient about what to expect for their treatment and management. Last, axillary ultrasound showing no suspicious axillary lymph nodes is may be of significance in the future to avoid SLNB altogether, depending on trial data comparing SLNB vs observation alone when axillary US is negative; examples are the SOUND Trial (Gentilini 2012, 2015) and the Dutch BOOG trial (Van Roozendael, 2017).

CTDNA IS NOW THE BEST METHOD TO MONITOR RESPONSE IN PATIENTS WITH METASTATIC BREAST CANCER- YES
Kevin Kalinsky, MD, MS, USA

In patients with metastatic breast cancer (MBC), monitoring for therapeutic response with circulating tumor DNA (ctDNA) holds significant promise. In a proof-of-concept trial, ctDNA demonstrated a greater dynamic range, as well correlation with tumor burden changes, compared to other blood measures, such CA15-3 and circulating tumor cells (Dawson et al, NEJM 2013). The reliability and depth of analysis achieved with ctDNA continues to advance. Studies with ctDNA in MBC have varied from focusing on specific mutations, while others have sequenced panels of cancer-associated genes. In triple negative MBC, having a ctDNA tumor fraction > 10% has been associated with worse survival (Stover et al, JCO 2018). In addition to quantifying ctDNA levels, ctDNA can be used for genomic profiling. For example, in the BEECH study in hormone receptor + (HR+) MBC, the median progression free survival (PFS) was significantly improved in patients with suppressed ctDNA at 4 weeks vs. those without low levels of ctDNA in the validation cohort (median difference: ~ 5 months, Hazard ratio: HR 0.20) (Hrebien et al, Annals of Oncology 2019). Similar results were observed with capivasertib in patients with AKT1 E17K mutations who achieved and had persistent decreases in ctDNA into cycle 2 (PFS: median difference: ~2.5 months, HR: 0.18) (Hyman et al, JCO 2017). In addition, prospective-retrospective analyses have demonstrated the differential impact of ESR1 mutations, with the presence of an ESR1 mutation by ctDNA predicting improved PFS with fulvestrant compared to aromatase inhibition (median difference: ~ 2.5 months: HR: ~52) (Fribbons et al, JCO 2016). Given that the ESR1 mutation rates are higher in ctDNA than those reported in tumor tissue, ctDNA has clinical utility in selection of the anti-estrogen partner in HR+ MBC (Chandarlapaty et al, JAMA Oncology 2016). CTDNA can offer important information in the development of acquired mutations. In Paloma-3, fulvestrant +/- palbociclib, the rate of hotspot PIK3CA mutations significantly increased after fulvestrant use (O’Leary et al, Cancer Discovery 2018). In SOLAR-1, a similar PFS was observed in patients with PIK3CA mutations by ctDNA with the addition of the PI3K inhibitor alpelisib to fulvestrant as those identified in tumor tissue (Juric D et al, SABCS 2018). With the clinical approval of the alpelisib, ctDNA can be utilized as a non-invasive means for determination of potential benefit of this targeted therapy. For these reasons, it is anticipated that the clinical utility for ctDNA will continue to increase in patients with MBC.

IMMUNOTHERAPY WILL BECOME STANDARD OF CARE FOR TRIPLE NEGATIVE BREAST CANCER – NO
Kevin Kalinsky, MD, MS, USA

Checkpoint inhibition is approved in patients with newly diagnosed PD-L1 positive metastatic triple negative breast cancer. We have learned that the earlier that checkpoint inhibition is incorporated into clinically use in metastatic disease, the higher the likelihood that patients will benefit from checkpoint inhibition. In IMPASSION 130, ~40% of patients had PD-L1 positive tumors by the Ventana SP142 assay (Schmid et al, NEJM 2018). Thus, the current clinical indication for checkpoint inhibition is for a narrow cohort of patients, as the patients with PD-L1 negative tumors did not have a treatment benefit with the addition of atezolizumab to chemotherapy. In IMPASSION 130, various other markers, including CD8 positivity, stromal tumor infiltrating immune cells, and BRCA mutation status, did not provide additional prediction of clinical benefit beyond PD-L1 positivity (Emens et al, SABCS 2018). In the updated IMPASSION 130 analysis, the median improvement of progression free survival was 2.5 months (Hazard Ratio: HR 0.62) (Schmid et al, ASCO meeting 2019). While there was an overall survival difference of ~ 9.5 months (HR: 0.71), this was not formally tested due to the pre-specified hierarchical analysis plan. These data show that there is a select group of patients who appear to have clinically significant benefit from checkpoint inhibition, with durable responses. As with any other treatment, the potential risks with immunotherapy, including rare but serious adverse events, need to be balanced with potential benefits. In addition, IMPASSION 130 excluded patients who relapsed within 12 months of completion of operable chemotherapy, arguably a chemo-refractory population at greatest need for novel systemic treatment options. We are awaiting the results of other randomized checkpoint inhibitor trials, such as KEYNOTE-355. In addition, other immunotherapeutic strategies beyond checkpoint inhibition are being investigated. However, it would be an overstatement to say that immunotherapy is standard for all patients with triple negative breast cancer.
DEBATE: THAT ALL GENE CARRIERS WITH EARLY BREAST CANCER SHOULD HAVE A BILATERAL MASTECTOMY - NO
Ava Kwong
The University of Hong Kong, Hong Kong

The last twenty years have seen a complete change in society's attitude to the strategy of risk reduction of breast cancer in high-risk individuals by means of proactive mastectomy. Once termed 'prophylactic mastectomy', risk reducing mastectomy (RRM) was considered two decades ago not only extreme, but in some quarters almost unethical. RRM is now commonly undertaken in specialist breast units for women at high individual breast cancer risk, by virtue of an inherited breast cancer related gene mutation or from calculated high statistical risk from family history data, and the efficacy of RRM in reducing subsequent incident diagnoses of breast cancer has been published from a number of centres. RRM is offered routinely in conjunction with total breast reconstruction, using the whole range of reconstructive surgical techniques. The public announcement by the actor Angelina Jolie in 2013 that she had inherited and harboured a BRCA1 gene mutation, and was undergoing RRM and breast reconstruction to lower her intrinsic breast cancer risk, had a significant effect on public attitudes and perception. Whilst there are other means of lowering breast cancer risk by means of selective oestrogen receptor modulators, such as tamoxifen and raloxifene, their lowering effect on risk of breast cancer remains substantially less than that afforded by surgical removal of 'at risk' breast tissue. The progressive development and increasing sophistication of techniques of breast reconstructive surgery has paralleled the trend for more RRM surgery, and the substantial majority of women who opt for bilateral mastectomies, RRM and choose immediate breast reconstruction. Bilateral mastectomies however comes with a cost. The pros and cons of risk reduction surgery will be debated.

APPLICATION OF INDOCYANINE GREEN (ICG) FLUORESCENCE IN SENTINEL LYMPH NODE BIOPSY FOR BREAST CANCER PATIENTS
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Sentinel lymph node (SLN) biopsy performed by the conventional dual-tracer method comprising of radioisotope and blue dye has known pitfalls. Radioisotope carries radioactive hazard and requires availability and support from nuclear medicine; while patent blue dye has problems of skin staining, and rare but potential complications of severe allergic reaction and skin necrosis. The use of indocyanine green (ICG) has been shown to have a low side effect profile and been widely applied in various surgical procedures, such as perfusion assessment and cholangiography. Lately, feasibility of fluorescence detection of SLN with ICG in breast cancer has been demonstrated and will be illustrated in the current presentation. Our centre has been using ICG fluorescence for identification of SLN since 2016. ICG fluorescence allows transcutaneous imaging of lymphatic vessels, thus it is a feasible tracer for SLN biopsy with additional benefits of real-time mapping and avoidance of radioactivity. Pre-operatively, ICG was injected in the periareolar area. Fluorescence was detected by a near-infrared camera. Two systems for ICG fluorescence detection were available: SPY Elite Fluorescence Imaging System or SPY Portable Handheld Imager (SPY-PHI) (Striker), or ICG Fluorescence Imaging System (Karl Storz). All patients also received (99m) Tc-labelled sulphur radiocolloid for SLN scintigraphy 1 day before operation and blue dye injection pre-operatively, as in conventional method. Completion of SLN biopsy was confirmed with low nodal basin count by gamma probe and absence of ICG fluorescence in axilla after the procedure. Since 2016, 126 patients received SLN biopsy guided by ICG fluorescence in our centre. The SLN detection rate by radio-isotope was 93%, by patent blue-dye was 92% and by ICG was 92%. Metastatic lymph nodes were diagnosed in 22 patients. Twenty of them could be detected by all three tracer agents while 2 were detected by blue dye and ICG only.

ICG fluorescence has been becoming a standard SLNB localization method and replacing blue dye injection in our centre.

CAN WE PREDICT OUTCOME USING IMAGING CHARACTERISTICS?
Ritse Mann, The Netherlands

While reports of mammograms, ultrasound and MRI examinations of women with breast cancer can look strikingly similar, the underlying pathology is often quite different. If you look a bit more closely to the images it is evident that one “irregular speculated mass” is quite different from another. These differences reflect the type of breast cancer that is present. It is common knowledge that there are several different molecular subtypes of breast cancer, that can be classified by their receptor expression. Still, imaging is not clearly separating these categories. This is partly due to overlapping imaging features, but also to the fact that, while there are indeed different types of breast cancer, there are many more than just the 4 (or 5 if you separate the luminal B cancers in a Her 2 negative and a Her 2 positive group) defined in the St. Gallen consensus. Moreover, these cancers grow in an environment that is specific to the individual patient, which may affect their appearance. Consequently, imaging shows a breast cancer phenotype that can be correlated to the classic molecular subtypes, but cannot and does not completely match. Still, the more aggressive cancers are in general those with a round to oval shape, relative sharp borders and a high fluid content. As a result these tend to resemble benign lesions on ultrasound and MRI, albeit enhancement patterns are usually highly characteristic. In addition the presence of peri-focal and diffuse edema may point in the direction of an inflammatory response. Slow growing cancers on the other hand, are heavily spiculated due to the desmoplastic reaction of the surrounding tissue, and very dense due to the large fibrotic component and the low water content. Also enhancement may not be as suspicious as in the more aggressive subtypes, whereas edema is generally absent. It should therefore not be surprising that imaging characteristics are highly predictive of therapy response and have strong prognostic value, which may be complementary to tissue based evaluations. However, standardization is currently lacking, and quantification is cumbersome. For optimal integration of imaging findings with histopathological and genetic assessment these issues should be overcome. Still imaging provides key insights in cancer heterogeneity that may improve therapy and eventually outcome.
MRI SCREENING IN WOMEN WITHOUT HEREDITARY RISK
Ritse Mann, The Netherlands

Breast MRI has been extensively trialed in women with a hereditary risk for the development of breast cancer, as well as in those at increased risk due to family history. This has led to recommendations to screen women with a lifetime risk of more than 20% for the development of breast cancer with annual mammography and MRI. Still in large parts of the world, this recommendation is not followed. MRI screening is restricted to women at hereditary risk, mainly those with BRCA 1 or 2 mutations and small selected populations at increased risk due to other causes, such as chest irradiation during puberty. In all populations that breast MRI is tested in, its sensitivity is roughly double that of mammography. Specificity is only slightly lower, with overall identical positive predictive values for biopsy that range between 15 and 40%. This has resulted in a paradigm shift. For women screened with breast MRI, all other imaging techniques should be regarded as supplemental, with only a minor contribution to cancer detection. Mammography still has some value (roughly 5%), but also increases false positive findings. Supplemental ultrasound is pointless, and should be avoided. In women with a positive family history, the first randomized controlled trial ever on breast MRI shows that breast MRI detects not only more cancer, but more importantly, detects cancer when they are smaller (12 vs 18 mm) and have not yet spread to the lymphatic system (node positivity 17 vs 63%). In recent years, extensive evaluations have been performed in women with a personal history of breast cancer. These women are at relative risk of about 2 to 3 compared with the general female population, which is quite similar to those with a family history, but no hereditary risk. Results show unequivocally that sensitivity of mammography compared to MRI is 50% at best, and likely lower. Specificity of MRI is excellent, which should make this the follow-up modality of choice if any. Current research in women without risk factors, but with very dense breasts seems to echo these findings. Sensitivity is much higher, whereas detected cancers are of lower stage and are less often node positive. MRI screening also largely reduces the frequency of interval cancers in women screened. These findings herald a screening shift towards screening breast MRI for a much larger population than it is currently offered to. This will be a major step that will not only transform breast cancer screening, but also breast cancer treatment, as earlier detection enables much less aggressive therapy.

DEBATE: THAT ALL HIGH-RISK ADJUVANT HER-2 PATIENTS SHOULD RECEIVE DUAL ANTIBODY THERAPY
Mark D. Pegram, USA

Whether or not to continue pertuzumab (in combination with trastuzumab) in the post-neoadjuvant setting in patients who achieve a pathologic complete response (pCR) is controversial. The following arguments have been made to continue pertuzumab post-operatively for the balance of one year, given that there are no randomized trial results yet available to answer this question. 1) Clinicians do not withhold adjuvant trastuzumab from patients who achieve a pCR following chemotherapy plus trastuzumab alone. Indeed, we have data from the randomized NOAH trial from which we may estimate the outcome for patients who achieve a pCR on chemotherapy plus trastuzumab. The 5-year event free survival (EFS) in the pCR population was just a modest 87%, and we know now that there is a substantial increase in risk of recurrence in HER2+, trastuzumab-treated early breast cancer between years 5-10 – the Joint Analysis, BCRG06, and HERA all now indicate ≥25% risk of relapse by year 10. In fact in NOAH, the hazard for EFS (trastuzumab vs. not) was 0.92 (95% CI 0.61-1.49) suggesting the non-pCR patients area the ones who do not derive benefit from post-operative trastuzumab for up to one year. 2) What little data we have on time-to-event outcomes for patients who achieved a pCR in the NEOSPHERE and TRYPHAENA studies are not reassuring to support a de-escalation strategy post-operatively (5-year %DFS in the pCR subgroup for NEOSPHERE “<85%, and 3 year DFS in TRYPHAENA is 87-90% which will only decrease with time). 3) The use of adjuvant pertuzumab is indicated for HER2+ early breast cancers with “high risk” (not otherwise specified by the FDA), including in particular those with lymph node+ disease and some with ER+ disease. Therefore, inasmuch as the clinical indications for use of neoadjuvant therapy in the first place are essentially all “high risk” features, it would not make clinical sense to withhold an FDA-approved adjuvant therapy from such patients. 4) And finally, the concept of de-escalation of pertuzumab for patients with pCR breaks down in patients with extreme risk. For example, some patients with high risk disease (advanced HER2+ breast cancer) will achieve a pCR (23% in our series of patients with mean tumor size of 9.2cm). Stage III patients tend to have high number of positive lymph nodes as well. For such patients at high risk of relapse based on stage considerations alone, would it be wise to withhold a treatment which has been shown to be associated with an improvement in median OS in advanced breast cancer of 16 months? The answer is clearly...no.

DEBATE: A PATH CR ALLOWS DE-ESCALATION OF FURTHER THERAPIES
Mark D. Pegram, USA

Which patients with HER2+ early breast cancer should be treated with adjuvant pertuzumab? Pertuzumab increases the rate of pathological complete response in the preoperative context and increases overall survival among patients with metastatic disease when it is added to trastuzumab and chemotherapy for the treatment of HER2+ breast cancer. In the phase III, randomized, registrational, placebo-controlled APHINITY trial (N=4,804 patients), pertuzumab significantly improved the rates of invasive-disease–free survival among patients with HER2-positive, operable breast cancer when it was added to trastuzumab and chemotherapy (hazard ratio, 0.81; 95% confidence interval [CI], 0.66 to 1.00; P=0.045). However, in the intent-to-treat population, this translated to an absolute difference of disease recurrence of 171 patients (7.1%) in the pertuzumab group, vs. 210 patients (8.7%) in the placebo group. Such a small absolute difference in outcome, while statistically significant, and in support of the scientific hypothesis that adjuvant pertuzumab is associated with favorable impact in long-term time-to-event analysis, borders on clinical relevance. What accounts for such a minute difference in outcomes for a drug with such profound effects on pCR rates and OS in the metastatic setting. The answer lies in the patient population under study in the APHINITY trial. The clinico-pathologic and demographic characteristics of patients enrolled in APHINITY were astonishingly favorable: 36% lymph node-negative, 64% hormone receptor positive, and about 40% with tumor size < 2cm. In fact, the sample size of APHINITY had to be increased (by protocol amendment) by
1,000 patients and the number of node-negative patients had to be capped in order to achieve the necessary statistical power to test the study hypothesis. Accordingly, the outcome in the control arm was an astonishing 93.2% iDFS at 3 years. It is simply not possible to achieve an absolute double-digit improvement in iDFS with a control arm of 93.2%. This simple fact explains the modest delta between iDFS outcomes in the ITT population. Are there subgroups of interest with higher risk that merit treatment with adjuvant pertuzumab? The answer is yes. In the 64% of patients with positive lymph nodes, the results were more pronounced – at 4 years, the projected iDFS is 89.9% versus 86.7% for the control group, an absolute difference of 3.2%, which rivals that of benefit of taxanes in the adjuvant setting (19.2% vs. 22% recurrence risk at 5 years – 2.9% difference [N=33,084], Early Breast Cancer Trialists’ Collaborative Group, Lancet 2012). In subset analysis of APHINITY, other risk factors for prediction of benefit from adjuvant pertuzumab are counterintuitive. Indeed, contrary to popular believe, steroid receptor status made no significant difference in 3-year iDFS hazard ratio (HR 0.86 vs. 0.76/ER+ vs. neg, interaction p=0.543). Similarly, postmenopausal status and small tumor size (<2cm) had more favorable HRs with addition of pertuzumab compared to placebo. Consequently, the FDA, preferring to define label indications based on intent-to-treat principles, have (rightly) allowed physicians (and their patients) some latitude and discretion in defining “high risk” for patient selection for adjuvant pertuzumab.

PREPECTORAL IMPLANTS: DOES ANYONE STILL NEED A SUBMUSCULAR IMPLANT? 
Merisa Piper, USA

Over the past five years, there has been a growing interest in prepectoral, also known as muscle sparing, implant-based breast reconstruction. One benefit of this reconstruction is that the final implant position is above the pectoralis muscle, thus maintaining the reconstruction to the normal breast anatomical plane. Acellular dermal matrix or mesh is often used to cover the anterior surface to both secure the implant and provide an additional layer of support. Another benefit is that the prepectoral technique avoids the morbidity associated with pectoralis muscle dissection, thus leading to decreased pain and avoidance of animation deformity. However, long-term data is lacking and limited to case series. This technique is highly dependent on the quality of the mastectomy flaps, and fewer patients are candidates compared with the traditional submuscular reconstruction. Nonetheless, many reconstructive surgeons are offering this approach to their patients and patients actively seek surgeons who perform this method of reconstruction. In this presentation, we will further explore prepectoral breast reconstruction, its risks, benefits, and indications, and how it matches up to submuscular reconstruction.

THAT RCTS ARE THE ONLY WAY TO CHANGE PRACTICE: YES. 
Alistair Ring, UK

It is essential that patients are offered the best possible treatment for their breast cancer: with the best chances of a successful outcome and the risks of toxicity clearly understood. The options for treatment of breast cancer are also rapidly evolving, and in parallel the costs of cancer care are escalating. In the US $90 billion are spent annually on cancer related healthcare, with costs contributed to by private insurers, Medicare and a significant contribution from patients’ out-of-pocket expenses. It is therefore essential that new cancer therapies are subjected to sufficient scrutiny to ensure they represent the best therapy possible for each individual patient, and that the costs are justified by robust evidence. Historically large randomised control trials have long been regarded the gold standard approach to evaluating new therapeutic approaches. However over recent years there has been increasing interest in whether earlier phase trials (often phase 2 trials), which may not be randomised, may expedite approval of new agents and access for patients to novel therapies. This talk will discuss the case that earlier phase and unrandomised studies are by their nature exploratory and, whilst hypothesis generating, are not sufficient grounds on which to change standard of practice. The limitations of phase 2 trials will be discussed and key practical examples will be given as to where results from earlier phase trials have not been borne out in later randomised studies. The conclusion of this presentation is to hope that the audience will agree with the proposal that RCTs are the only appropriate basis by which to change clinical practice.

THAT TOPICAL OESTROGENS ARE AN ACCEPTABLE TREATMENT IN PATIENTS WITH HORMONE RECEPTOR POSITIVE EARLY BREAST CANCER. NO. 
Alistair Ring, UK

Over recent years many countries have seen significant increases in the number of women being treated for early breast cancer and surviving in the longer term. This emphasises the importance of addressing long term survivorship issues, including the gynaecological complications of anti-cancer therapy. Vaginal atrophy and vaginal dryness are particular issues in post-menopausal women who are receiving aromatase inhibitors and pre-menopausal women receiving aromatase inhibitors combined with ovarian function suppression. In women without a history of breast cancer topical vaginal oestrogens are often considered and can be an effective way to ameliorate the symptoms associated with vaginal atrophy. However there is increasing evidence that topical oestrogens can be absorbed systemically. There is therefore a theoretical risk that this absorption may counteract the beneficial effects of aromatase inhibitor therapy in women with a prior history of early breast cancer in the adjuvant setting. These data will be reviewed in this presentation. Furthermore a variety of alternative strategies to manage the gynaecological symptoms associated with aromatase inhibitor therapy will be discussed. These will include lubricants and moisturisers, lidocaïne, CO2 laser and the possibility of endocrine therapy switching. At the conclusion of this presentation it is hoped that the audience will have an understanding of the potential risks associated with vaginal estrogens in breast cancer survivors and also an appreciation of the range of other effective and safe strategies for managing these symptoms.

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The outcomes of the DENSE screening trial have significant implications for screening programs worldwide and provide real opportunity to provide a tailored approach to at least one group in the population at large. Resources in every country will differ but many of the issues in implementation will be common to all. In Australia, breast cancer screening is provided through a nationally co-ordinated mammographic screening program, BreastScreen Australia, using FFDM. It is funded by federal and state governments. The service is free to all women over the age of 40 with relatively poor compliance at approximately 60% of the eligible women attending. It is run separately from mainstream radiology. There is no requirement to report breast density, so in the first instance automated breast density software would need to be acquired and applied to the population for at least one screening round. In Australia, BIRADS D density accounts for approximately 12% of the currently screened population. In the state of Victoria this would mean accommodating approximately 31,000 women per year in an MR screening program. Australia has relatively few MR scanners – 15 per million population compared with 37.6/106 USA, 34.4/106 in Germany, 10/106 in Canada. In Australia, access is already very limited and mostly unfunded. If scans were restricted to 10 centres in Victoria to maintain a balance of accessibility and expertise, this would mean scanning approximately 60/week/scanner (50 weeks of the year). Even with abbreviated protocols, 2 coils, and teams of radiographers and nurses, it would require 2-2.5 days scanning time in each of the centres and another 0.5 days for MR intervention (from an estimated recall rate of 9% in the first round). Clearly, we would need more scanners and perhaps need to consider and trial the use of contrast enhanced mammography as an alternative modality, even as an interim measure. Shortage of specialised breast radiologists and MR radiographers is problematic. Australia has 1 radiologist/12,600 population, compared with US 1/10,000 (considered adequate), UK 1/20,000 very short and relatively few subspecialists. In the long term the MR screen reading may be completed by AI, but in the short to medium term radiologists will be required. We need a PR campaign to attract radiologists to the subspecialty. Training and credentialing the workforce to this required level of expertise in the time frame is also challenging. There are pros and cons about the organisation of an MR screening program and the choice of bureaucracy to co-ordinate the activity. Because of the capital investment, frequent changes in technology, and deskilling of staff which has occurred in a separate unimodality workforce such as BreastScreen Australia, it is probably best maintained in mainstream radiology rather than in completely separate screening facilities. However, BreastScreen Australia manages the front and back end co-ordination well (invitations, results, appointments, communications, recruitment and data maintenance). At a minimum, there would need to be much closer integration of the current national mammographic screening program with mainstream radiology, so that women with BIRADS D breasts could be seamlessly transferred to an MR screening regimen. The change will require significant resources and careful planning to maximise the outcomes for women in an efficient and cost-effective manner. We should grasp the nettle and start the dialogue now!

MANAGEMENT OF CHRONIC LYMPHEDEMA: ARE WE THERE YET?
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Lymphedema is a common, chronic and debilitating condition. It affects approximately 10 million people in the US, with over 200,000 new cases diagnosed each year, mainly resulting from lymphadenectomy for the treatment of cancer, in particular breast cancer [1]. The risk is increased by adjuvant radiotherapy, especially regional nodal irradiation [2], total mastectomy, higher body mass index, and taxane-based chemotherapy regimens [3,4]. Although our understanding of the pathophysiology of the condition is incomplete and a cure remains elusive, a growing body of evidence supports the effectiveness of modern surgical techniques in ameliorating the long-term disability and functional impairment inflicted by lymphedema on the lives of those affected and reducing the risk of future episodes of cellulitis [5-9]. These procedures can be broadly categorized as physiological or debulking. Physiological procedures, including lymphovenous bypass (LVB) and vascularized lymph node transplant (VLNT) procedures, aim to restore lymphatic fluid drainage within the affected area [10-12]. The operations are effective at decreasing the symptoms of lymphedema, reducing the risk of future infections, and decreasing the amount of time spend daily for lymphedema care; selected patients may be able to discontinue their compression garments. The lymphovenous bypass procedure involves identification of obstructed lymphatic vessels and targeted bypass of these into neighboring venules. The VLNT procedure involves microvascular anastomosis of lymphatic vessels into an extremity. In patients undergoing postmastectomy breast reconstruction this may be performed by transferring a deep inferior epigastric artery perforator flap with a chimeric groin lymph node flap [13]. For patients that have undergone breast-conserving surgery or for whom a free abdominal flap is contraindicated, many other vascularized lymph node transplant options are available; these include flaps harvested from within the axillary, inguinal, or cervical lymph node basins, or from within the abdominal cavity with the opportunity for laparoscopic harvest [14,15]. Once established, the chronic lymphedema phenotype is characterized by hypertrophy of fibroadipose soft tissue deposition that can only be removed directly. Traditional excisional surgeries that result in unacceptable scarring and morbidity have been replaced except in the most severe cases by minimally invasive suction-assisted lpectomy (SAL) [16] which restores function and appearance and reduces the risk of future infections [17]. SAL debulking provides only minimal physiological improvement of the lymphatic system and therefore patients need to wear compression garments lifelong to prevent recurrence. The techniques, algorithms, and outcomes of surgical procedures to treat lymphedema are reviewed.

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PATIENTS REQUIRING POSTMASTECTOMY RADIOTHERAPY COULD UNDERGO IMMEDIATE RECONSTRUCTION
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Immediate breast reconstruction significantly improves the quality of life for breast cancer patients. According to real world data, immediate breast reconstruction rate has been increasing rapidly during the last two decades. Along with the popularity of implant-based breast reconstruction (IBBR), post-mastectomy radiation therapy (PMRT) after immediate breast reconstruction has raised concerns that patient may get worse cosmetic outcomes compared to delayed breast reconstruction. For patients requiring adjuvant radiotherapy, immediate breast reconstruction is not contraindicated. Even PMRT itself is controversial in patients with only 1-3 lymph node metastasis. Besides, advances in breast reconstruction technology allow this group of patients to undergo immediate breast reconstruction. Autologous tissue flaps and autologous flap combined with prostheses are well tolerated for radiotherapy. After skin sparing mastectomy (SSM)/ nipple sparing mastectomy (NSM), direct to implant (DTI) has been widely accepted in clinical practice especially combined with mesh. According to reports in the literature, the overall complications of postoperative radiotherapy for breast reconstruction are within acceptable limits. For patients are not clear for PMRT or not, expander-implant based reconstruction or autologous reconstruction could be considered to reach a better cosmetic outcome. Furthermore, the application of beam intensity modulated radiotherapy technology and image guided radiotherapy technology could ensure safety and cosmetic results. Additionally, we should also pay attention to the psychological benefits that could be gained when immediate breast reconstruction was applied that has been demonstrated in several patient-reported outcome (PRO) studies.

ORAL ABSTRACTS

DISEASE FREE SURVIVAL IN NODE POSITIVE INVASIVE LOBULAR CARCINOMA WITH OR WITHOUT AXILLARY DISSECTION
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Background: Randomized trials have shown that for many breast cancer patients with 1-3 positive axillary nodes, undergoing axillary dissection does not impact recurrence rates. However, whether omission of axillary dissection is safe for those with invasive lobular carcinoma (ILC), a more diffuse tumor type, has not been well studied. We sought to determine the impact of axillary dissection on recurrence in patients with ILC, particularly in the setting of 1-3 positive nodes. Methods: We performed a cross-sectional analysis of an ILC database at our institution. We used t-tests, chi-squared tests, and Kaplan Meier survival estimates to evaluate the relationship between axillary surgery and disease free survival (DFS). We defined DFS as the absence of local or distant recurrence. Results: We identified 700 patients with ILC and excluded those with de novo stage 4 disease (n=12), neoadjuvant therapy (n=154), and < 6 months of follow-up time (n=52), leaving 482 cases. Of these, 240 (50%) underwent breast conservation surgery (BCS) and 242 (50%) underwent mastectomy. Radiation was received by 79% of the BCS group and 18.6% of the mastectomy group. For patients with BCS, 199 (83%) were node negative, 28 (12%) had 1-3 positive nodes, and 13 (5%) had ≥ 4 positive nodes. Axillary dissection was performed in 17% of node negative patients, 46% of those with 1-3 positive nodes, and 92% of patients with ≥ 4 positive nodes. For the mastectomy cohort, 148 (61%) were node negative, 65 (27%) had 1-3 positive nodes, and 29 (12%) had ≥ 4 positive nodes. Axillary dissection was performed in 18% of node negative patients, 57% of patients with 1-3 positive nodes, and 97% of those with ≥ 4 positive nodes. Among patients with 1-3 positive nodes, there was no difference in 5 year DFS between those
who did or did not undergo axillary dissection (86.6% 5 year DFS [95% CI 66.5-95.1] versus 84.8% [95% CI 69.2-92.9]). Similar results were seen in the BCS group and mastectomy group when analyzed separately. Conclusion: These findings support the safety of omitting axillary dissection in patients with ILC and I-3 positive nodes, regardless of whether they receive BCS or mastectomy. Further studies of axillary management in this tumor type are warranted.

DEVELOPMENT OF A MULTI-ETHNIC POLYGENIC RISK SCORE FOR BREAST CANCER SCREENING Sarah Theiner¹, Sarah D. Sawyer¹, Paigee Kendall¹, Alexandria S. Perry¹, Denise Wolf³, Donglei Hu¹, Irene Acrébi¹, Yiwey Shieh¹, Scott Huntsman¹, Bo Pan¹, Jeffery A. Tice¹, David A. Pearce², Thomas Cink³, Laura Esserman⁴, Elad Ziv⁵, Laura van ‘t Veer⁶, Mandy Che²
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Problem statement: The WISDOM trial is comparing risk-based screening for breast cancer with annual mammography, and part of the risk assessment in the trial includes polygenic risk score (PRS). This score, calculated by adding the individual breast cancer risk association for each common genetic variant (SNP), has been shown to improve risk prediction when incorporated into breast cancer risk models. In order to take into account race/ethnicity in the risk assessment, we developed an approach to apply the PRS across race/ethnicity to more accurately stratify risk.

Methods: We constructed two different PRS models one based on 168 SNPs and the other on 313 SNPs originally discovered in European populations and added Asian, Hispanic and African ancestry SNPs for each of the different ancestral populations. We test this approach using datasets from several case-control studies in multiple racial/ethnic populations and compared discrimination of the models using area under the receiver operating characteristic curve (AUROC). Furthermore, we apply the PRS in a sample of ~3000 multi-racial/ethnic women, sampled by Gail score to be at elevated (Gail 1.67) and average (Gail1.67) risk, to quantify the likely impact on identifying women recommended for risk-reducing strategies. Results: A PRS based on 313 SNPs has higher discrimination compared to one base on 168 SNPs in a multi-racial/ethnic population with AUROCS of 0.65 and 0.64, respectively. By incorporating PRS into Gail, 20% of average-risk women transitioned to a risk above 1.67% and thus would be eligible for breast cancer risk-reducing counseling and therapy. Conversely, the addition of PRS indicated that 38% of elevated risk patients would no longer be recommended risk-reducing counseling.

Conclusion: We constructed a PRS model that can be applied to a multi-racial/ethnic population and found that a PRS based on 313 SNPs in addition to racial/ethnic-specific SNPs has higher discrimination. The addition of SNP based PRS to Gail model significantly changes clinical care recommendations due to reclassification of women as average and elevated risk.

OUTCOMES FOLLOWING SINGLE-STAGE PRE-PECTORAL BREAST RECONSTRUCTION USING IMPLANT AND ACELLULAR DERMAL MATRIX: A SINGLE-CENTRE EXPERIENCE OF 500 RECONSTRUCTIONS Rajiv Dave, Aleksander Vucicevic, James Harvey, Richard Johnson, Cliona Kirwan, Lyndsey Highton, John Murphy
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Problem Statement: Over the past few years, pre-pectoral breast reconstruction using an acellular dermal matrix (ADM) and implant has become a popular option for selected patients. There is no randomised data to demonstrate outcomes, and our collective knowledge of the safety of this technique is reliant on large cohort studies. Methods: We analysed our prospective database of pre-pectoral implant based breast reconstructions. Over 500 reconstructions have been performed in over 6 years, and is, to our knowledge the largest single-centre study of its kind. Patient demographics, clinical outcomes, complications and revision procedures were studied. Results: The mean age of the cohort was 44.4 years, and the majority of reconstructions were performed using a one stage direct to implant technique for skin reduction (47.3%) and malignancy (25.4%). The ADMs used were primarily Strattice™ (70.8%), ARTIA™ (9.9%) and a combination of the two (15.8%). Further revision aesthetic procedures following the initial reconstruction were performed in 18.5% of reconstructions, usually lipomodelling (8.4%). Minor complications (seroma, delayed wound healing, pain, stitch abscess) were seen in 11.2% of procedures and major complications (skin/nipple necrosis/major wound problem) were seen in 5.9% of procedures. Implant loss was seen in 3.3% of procedures. On univariable analysis, surgery for malignancy, concurrent axillary surgery, neoadjuvant chemotherapy, adjuvant radiotherapy, wise-pattern incision (compared to IMF and peri-areolar/ellipse), smoking, mastectomy weight 500g and BMI 30Kg/m² were all predictive for complications. The use of an inferior dermal flap (following a skin reduction procedure) was not associated with higher complications. In the multinominal regression model, smoking and mastectomy weight all independently and significantly impacted on the development of a minor/major complication, but only smoking was independently predictive of a major complication. Implant loss was significantly predicted by concurrent axillary surgery and adjuvant radiotherapy, neither of which were independently predictive on the multinominal regression model. Conclusions: We demonstrate safety of the pre-pectoral implant and ADM reconstruction technique, but careful patient selection is advised, as this technique is not immune to the effects of the usual high-risk factors. We identify use of a wise pattern skin reduction to be associated with higher risk of complications.

TEMPORAL TRENDS IN THE MANAGEMENT OF WOMEN DIAGNOSED WITH DCIS OF THE BREAST IN AUSTRALIA AND NEW ZEALAND

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Problem statement: Since the introduction of mammography, a greater extent of Ductal Carcinoma In Situ of the breast (DCIS) has been diagnosed. From a pathological
and molecular view, DCIS cells have many similar characteristics of invasive cancer cells. Therefore, DCIS has been presumed to be a precursor of invasive breast cancers. However, treating these lesions does not seem to decrease the amount of invasive breast cancers. This has brought into question the potential of overdiagnosis as well as overtreatment. Women who have a diagnosis of DCIS only (a DCIS that does not progress to invasive cancer) may be receiving unnecessary aggressive treatments. The aim of our study is to describe current trends in the management of DCIS in Australian and New Zealand women. Methods: Using the BreastSurgANZ Quality Audit database, we conducted a descriptive study of the trends of management of women diagnosed with DCIS in Australia and New Zealand between the years of 2007-2016. In our study we looked at the surgical treatments, the adjuvant therapies, as well as the axillary surgeries conducted on women who only have a DCIS diagnosis. Results: There were 17883 women diagnosed with DCIS only in Australia and New Zealand from 2007-2016. We found that the treatment patterns for women diagnosed with DCIS were persistent over years, where no major changes in the management was observed. The most common type of surgery performed was breast-conserving surgery (66%), followed by mastectomy (37%). Sentinel node biopsy was conducted among 36%. Conclusions: We concluded that the practices performed on women diagnosed with DCIS in Australia and New Zealand between the years of 2007-2016, appear stable over time. However, further investigation is needed into exploring how well these treatment patterns are in accordance with current practice guidelines. In addition, we need to look at the results of the ongoing prospective studies, i.e. LORD, LORIS and COMET, investigating active surveillance for low-grade DCIS to understand if some of these women could be treated less aggressively. The outcomes of the treatment of DCIS with surgery are very good, however the need of this for all types of DCIS is uncertain.

DOISMETRIC PLANNING TECHNIQUE COMPARISON OF AEROFORM™ TISSUE EXPANDERS VERSUS SALINE TISSUE EXPANDERS IN PATIENTS UNDERGOING POST-MASTECTOMY RADIATION THERAPY

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Problem Statement: Post-mastectomy radiation therapy (PMRT) is an important part of breast cancer treatment in women with node-positive disease. Saline tissue expanders have traditionally been the method of choice; however, air expander systems are becoming increasingly popular with patients. The aim of the study was to validate the dose prescribed by the clinician with the dose calculated by the Pinnacle v9.10 (Philips, USA) treatment planning system (TPS) when different tissue expanders are in situ. Methods: A retrospective dosimetry analysis was completed on 20 breast patients, 10 with Aerof orm™ (AirXpander®, Palo Alto, California) expanders and 10 with saline expanders in situ. All patients had a CT simulation on the Optima CT 580 RT (GE Healthcare) scanner using the metal artefact reduction (MAR) scan protocol. Patients were retrospectively planned with a prescribed dose of 5000 centi-gray (cGy) in 25 treatments, using the Pinnacle TPS. All patients were dual planned using a three-dimensional (3D) conformal radiation therapy (CRT) wedged pair technique and a hybrid intensity modulated radiation therapy (IMRT) technique. 5mm-10mm bolus was applied over the whole chest wall to all air expander patients. Bolus application was at the radiation oncologists discretion for saline expander patients. Specific overrides were applied to critical structures in pinnacle to improve accuracy of the dose calculation for all patients. Results: All 20 patients achieved dose goals in both planning techniques without exceeding doses to organs at risk. There was no correlation seen between the air volume calculated within in the Aerof orm™ implants and the total monitor units required to achieve dose goals. Similarly, there was no link between planning target volume (PTV) size and monitor units to achieve dose in both saline and air expanders. Conclusion: The 3D CRT wedged pair technique used for the air expander patients eliminated dose uncertainties associated with the IMRT comparison plans completed for this cohort of patients. The reverse result was seen in the saline expander patient cohort where the IMRT technique produced superior dose distributions. Although we acknowledge this is a small cohort patient study, the data concluded that while homogeneity varied between the expanders, clinically relevant doses remained equivalent.

THE USE OF 18F-FDG PET/CT AS AN INITIAL STAGING PROCEDURE FOR STAGE II-III BREAST CANCER: A MULTICENTER VALUE ANALYSIS

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Problem Statement: Metastatic staging imaging is not recommended for asymptomatic stage I-II breast cancer patients, but is warranted in stage II-III patients with high-risk biological subtypes. Chest/Abdomen/Pelvis CT and bone scan is considered standard (STD), although PET/CT is a more patient-centered alternative. NCCN guidelines endorse STD, but not PET/CT, for stage III patients. Methods: Data were available for 799 high-risk clinical stage II-III patients who initiated screening for the I-SPY2 trial at four large academic institutions. Records were reviewed for 564 who completed screening. Costs were determined from the payer perspective using the national 2018 Medicare Physician Fee Schedule and representative reimbursements to UCSF. Incremental cost effectiveness ratio (ICER) measured the cost of using PET/CT per percent of patients who avoided a false positive (FP). Results: The de novo metastatic disease rate was 4.6%. Imaging varied among the four sites (p = 0.0001). FP rate was higher with STD (22.1%) vs. PET/CT (11.1%) (p = 0.05). Mean time between incidental finding on baseline imaging to FP determination was 10.8 days. Mean time from diagnosis to neoadjuvant chemotherapy initiation was 44.3 days (STD) vs. 37.5 days (PET/CT) (p = 0.05). Mean cost/patient was $1132 (STD) vs. $1477 (PET/CT) using the Medicare Physician Fee Schedule with an ICER of $31 per percent patient who avoided a FP. Using representative reimbursements to UCSF, mean cost/patient was $1236 (STD) vs. $1073 (PET/CT) for Medicare, and $3083 (STD) vs. $1656 (PET/CT) for Anthem Blue Cross, with ICERs of $-159 and $-130, respectively. Conclusion: There is considerable metastatic staging practice variation. PET/CT added value by decreasing FP two-fold. The
potential for having metastatic disease is terrifying to patients. Reducing FP risk by half, which also helps decrease time needed for assessment of incidental findings and may allow for earlier treatment start, adds great value. ICRs suggest PET/CT may be cost effective, and at one institution, PET/CT is cost saving. Our data establish the value of PET/CT in this high-risk clinical stage II-III trial population and highlight the need for alignment between hospital pricing strategies and payer coverage policies in order to deliver high value care.

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

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Problem statement: Post-mastectomy pain syndrome (PMPS) is a common and often debilitating condition. One likely etiology is neuroma formation after injury to the cutaneous branches of the T4 and T5 intercostal nerves during breast surgery. We aimed to assess the rate of long-term resolution of post-mastectomy pain after trigger point injections to relieve neuropathic pain. Methods: Prospective single arm cohort study of women undergoing breast surgery at a single institution presenting with clinical symptoms consistent with PMPS. The syndrome is defined by chest wall pain unresponsive to standard pain medications and the presence of exquisite point tenderness along the infra-mammary fold at the site of egress of the T4 and T5 cutaneous intercostal nerve branches that reproduces the patient’s spontaneous pain. Each trigger point identified on physical exam was used to direct a perineural injection, consisting of a 2mL mixture of equal parts 0.5% bupivacaine with 4mg/mL dexamethasone. Results: A total of 91 trigger points were treated in 52 patients. Mean follow-up time is 43.9 months. The overall treatment success rate was 91.2% (83 of 91 trigger points) which was defined as long-term pain resolution with no further treatment. Among those with long-term resolution of pain, 60 trigger points (72.3%) required only a single injection. Patients with relief were evaluated to determine which characteristics may increase likelihood of relief with TPI. These features included, number of surgeries prior to initial injection, history complications resulting from their prior breast operation(s), period of time with pain (in months), age at first injection, and the number of times each trigger point was injected. Higher number of surgeries prior to injection, having a surgical complication and having a major surgical complication were all statistically significant on unadjusted bivariate analysis. Conclusion: Perineural infiltration with a combination of bupivacaine and dexamethasone is a safe, simple, and effective treatment for post-mastectomy pain syndrome that presents with a trigger point along the inframammary fold. Surgeons performing breast surgery should inquire about the presence of symptoms consistent with PMPS in the immediate post-operative period and understand the importance of early intervention in treating neuropathic pain.

UTILISATION AND SHORT-TERM OUTCOMES OF NEOADOJUVANT SYSTEMIC THERAPY IN BREAST CANCER: A NATIONAL PROSPECTIVE MULTI-CENTRE COHORT STUDY

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Problem statement: Neoadjuvant systemic therapy (NST) has potential advantages in treating breast cancer, including downstaging disease to minimise surgery, and assessing tumour sensitivity to treatment. There is considerable variation in NST use; it is unclear whether pathological response rates reflect those reported in clinical trials, and whether downstaging impacts on surgical decision-making. The NeST study aimed to investigate patterns of care in the UK, through a national prospective multicentre cohort study. Methods: Women undergoing NST as primary breast cancer treatment from 1/12/17-30/11/28 were included. Anonymised data was collected and uploaded to REDCap. Results: 1166 patients received NST, 41% had HER2+ disease, 28% TNBC and 31% ER+/HER2- disease. Indications for neoadjuvant treatment were: Downstaging (mastectomy to breast conservation) 37%, Facilitate dual anti-HER2 therapy 33%, Inoperable disease 19%, Improved cosmesis (reduced excision volume) 17%, Facilitate BRCA testing 9%, Inflammatory breast cancer 6%. Without NST, the surgical plan was mastectomy in 5% of patients, and breast conserving surgery in 34%, with 3% of patients classed as inoperable. 87% of patients received chemotherapy and 13% endocrine therapy. For ER+ disease, the commonest reasons for prescribing chemotherapy were high grade disease/pre-menopausal status. 21% of patients with TNBC were treated with platinum-containing regimens. 54% of HER2+ tumours were treated with dual anti-HER2 therapies/chemotherapy, with 10% receiving chemotherapy/single agent trastuzumab only. Surgical data was available for 765 patients, with a mastectomy rate of 48% and a reconstruction rate of 15%. Pathological response data was available in 672 patients, with a pCR rate of 29%. pCR rate according to molecular subtype was 37% for HER2+ disease, 35% for TNBC and 7% for ER+/HER2- disease... Conclusions: This prospective national audit suggests that surgical downstaging remains a key indication for NST, reflected in a reduction in mastectomy rates compared with original surgical plans. Additional indications for NST are emerging, according to disease biology. Widespread use of dual anti-HER2 targeted therapies is seen, with increasing use of platinum-containing regimens for TNBC. Significant numbers of patients with ER+/HER2- disease are treated with NST;
known low pCR rates in this context are confirmed. Low rates of neoadjuvant endocrine therapy use are reported. Data collection is ongoing; updated data will be presented in September 2019.

TUMOR MICROENVIRONMENT OF METASTASIS (TMEM): A NEW BIOMARKER AND TREATMENT PARADIGM

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Metastasis is the primary cause of death in breast cancer, the most frequently diagnosed cancer and the leading cause of cancer death among women. The Condellis laboratory has previously shown TMEM serve as the doorway to metastasis (Harny et al. Cancer Discovery 2015, PMID: 26269515). TMEM are microanatomic structures that serve as conduits for invasive tumor cells to intravasate and metastasize in animal models and human breast cancer. TMEM may be identified using a triple immunostain using digital pathology, and TMEM score has been shown in 2 independent cohorts to prognostic in early-stage breast cancer (EBCS), and provide complementary prognostic information to the 21-gene Recurrence Score and IHC4 (a proxy for RS) (Rohan et al, JNCI 2014, PMID: 24895374; Sparano et al, NPJ Breast Cancer 2017, PMID: 29138761). It has also been shown that cytotoxic chemotherapy, including paclitaxel, eribulin, and other cytotoxic agents promote the formation of TMEM structures and metastasis in animal models and human breast cancer. TMEM may be discovered in an unrecognized mechanism of resistance to therapy (Karagiannis et al. Science Translational Med 2017, PMID: 28679654). We are currently evaluating novel strategies to block TMEM function by performing a phase-I-II trial of paclitaxel or eribulin in combination with rebastinib, an oral TIE2 inhibitor that blocks intravasation at TMEM sites (Harny et al. Mol Cancer Ther 2017, PMID: 28838996). Preliminary data in 20 patients treated with rebastinib and paclitaxel or eribulin has identified a recommended phase II rebastinib dose (100 mg PO BID), clinical activity of the combination, and pharmacodynamic evidence of TMEM blockade. This work provides a foundation for additional studies evaluating TMEM score as a prognostic biomarker, and therapeutically targeting TMEM function in early and advanced stage breast cancer.

SALVAGE OF THE PREVIOUSLY UN-SALVAGEABLE PERI-PROSTHETIC BREAST INFECTION AFTER BREAST RECONSTRUCTION

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Problem statement: Severe infections of implant-based breast reconstruction are complicated to treat. Peri-prosthetic breast infections that are resistant to usual therapy of antibiotics +/- aspiration are generally associated with low successful salvage rates. Methods: This study is a prospective review of the outcomes of a treatment protocol utilising negative pressure wound therapy with instillation (NPWTi) to salvage peri-prosthetic breast infections after breast reconstruction. This treatment protocol has previously been described, with early experience suggesting good outcomes. Results: The treatment protocol was utilised in 22 consecutive cases of severe peri-prosthetic breast infection from 2013-2019. Peri-prosthetic infection occurred during the direct to implant reconstruction (n=9), first-stage expander/implant (n=11) and following the second stage (n=2). Cultures of fluid/tissue grew Pseudomonas aeruginosa, Escherichia coli, Serratia Marcescens, Staphylococcus haemoiyticus, Staphylococcus aureus and Klebsiella oxytoca. Based on the type of micro-organisms, different solutions including normal saline, Prontosan and 1% acetic acid were used for instillation of the breast pocket. 21 cases were successfully salvaged without compromise of the cosmetic outcome at mean follow up of 14.6 months. The median length of stay and time to achieve negative culture were 4 (7-18) days and 3 (0-14) days respectively. Conclusion: Continued experience with this treatment protocol demonstrates that salvaging infected breast prostheses utilising NPWTi is associated with a high success rate.

ELECTRONIC DATA CAPTURE IN CLINICAL TRIALS: STATE OF PLAY AND IMPROVEMENTS FOR THE FUTURE

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Problem Statement: Paper-based data collection in trials has been largely replaced because it is expensive, time consuming, and error-prone. While electronic data collection and electronic medical records (EMR) have eliminated data storage, current systems still involve inefficient data extraction and re-entry. Transforming the data extraction process for trials necessitates changing data capture at the source—during clinical care. The optimal solution is to create tools that enable structured data capture using checklists to generate a single source-of-truth for diagnosis, treatment, side effects, quality of life, and follow-up. We present a checklist solution to improve capture of staging data in the clinic, and assess whether this system could improve both care and research. Methods: We evaluated the accuracy of recorded breast cancer clinical stage in patients enrolled in a prospective neoadjuvant chemotherapy trial (I-SPY2 TRIAL). To facilitate data capture, we built a prototype staging tool as part of the “OneSource” solution (a standards-based open source tool to capture critical data at the point-of-care) designed to integrate with the EMR and clinical case report forms. It is designed to be prepopulated with initial staging data but requires verification and updating for additional staging studies. Results: Clinical stage was submitted with the eligibility form prior to completing diagnostic staging studies. Some patients received additional staging procedures, including PET, CT, axillary ultrasound, biopsy and clip placement. However, much of this data was not captured at randomization, leading to potential understaging in 20%. This does not impact the study’s primary endpoint, but accurate baseline data would facilitate future analyses. To improve collection, review, and adjudication of staging, the checklist was created and prepopulated with clinical staging data. We will present how surgeons can review, verify, and add additional staging data and whether they would employ such a tool during clinical care. Conclusion: Data in trials may have errors that are best addressed by rethinking its collection methodology. The optimal solution is to have an intuitive, efficient tool at the point of care, eliminating
THE INFLUENCE OF NEOADJUVANT CHEMOTHERAPY ON THE PLAN FOR BREAST-CONSERVING SURGERY IN EARLY OR LOCALLY ADVANCED BREAST CANCER

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Problem statement: In 2018 the National Institute of Clinical Excellence (NICE) released guidance recommending that patients with oestrogen-receptor-negative (ER-negative), ER-positive and human-epidermal-growth-factor-negative (HER2-negative) breast cancer be offered neoadjuvant chemotherapy (NACT) to reduce tumour size which may facilitate breast conserving surgery (BCS) instead of mastectomy. The aim of this study is to assess whether NACT influences the surgical plan with respect to performing BCS.

Methods: A cross-sectional cohort study was performed in a high-volume breast cancer unit, treating 650 new patients each year. The multidisciplinary team (MDT) database was screened over a 12-month period for patients receiving NACT. Baseline data collected included demographics, tumour characteristics, staging, NACT, and tumour response. The primary outcome measure was change in surgical plan following NACT. Statistical analysis performed. Results: Between August 2013 to July 2014 out of 2,854 patients discussed in the MDT, 72 patients (2.5%) were eligible and included. All patients were female, with median age 53.5 years. Diagnoses included cancer of no special type (n=58; 80.6%), lobular (n=8; 11.1%) and tubular carcinoma (n=3; 1.4%). There were 51 (70.8%) ER-positive, 16 (22.2%) HER2-positive and 14 (19.4%) triple-negative tumours. The axilla was involved in 47 cases (65.3%). The tumour grade was 1, 2, and 3, in 1 (1.4%), 21 (29.2%), and 50 (64.9%) cases respectively. The NACT course was completed in 69 cases (95.8%). Response to NACT was determined by clinical or radiological assessment; in 4 cases (5.6%) there was no response. BCS was the pre-NACT plan in 17 cases (23.6%). After NACT, the plan was revised from mastectomy to BCS in 5 cases (6.9%) and BCS to mastectomy in 5 cases (6.9%); in one case due to patient preference. There was no significant change in plan with respect to BCS after NACT (p=0.774).

Conclusion: In this cross-sectional study, there was no evidence of a significant change in plan with regards to BCS after NACT. Multiple factors other than the size of the tumour after NACT seem to influence the surgical decision. Extension of the study time period may be required to definitively assess the influence of NACT on the surgical plans in this institution.

MAKING SURE NO TUMOR IS LEFT BEHIND: MICRO-ELASTOGRAPHY PROVES AN ACCURATE TECHNIQUE TO ASSESS TUMOR MARGINS

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Problem statement: Inadequate margins in breast-conserving surgery (BCS) are associated with increased likelihood of local breast cancer recurrence. Currently, approximately 20% of BCS patients require repeat surgery due to inadequate margins at the initial operation. There is a need for an accurate, intraoperative margin assessment tool to assist surgeons in reducing this re-excision rate. Methods: This study determined the diagnostic accuracy of quantitative micro-elastography (QME), an optical coherence tomography (OCT)-based elastography technique that produces images of tissue micro-scale elasticity, for detecting tumor within 1 mm of BCS specimens margins. Simultaneous OCT and QME were performed on margins of freshly excised specimens from 83 BCS patients and on dissected specimens from 7 mastectomy patients. The resulting three-dimensional images (45 x 45 x 1 mm) were co-registered with post-operative histology to determine tissue types present in each scan. Data from 12 BCS and 7 mastectomies served to build a set of images for training seven readers. 154 sub-images (10 x 10 x 1 mm) termed regions of interest (ROI) from the remaining 71 BCS patients were included in the blinded reader study. Figure 1 shows ROIs containing malignant tissue designated “impalpable” pre-operatively and requiring hookwire guidance for lesion excision. Changes in mechanical properties on a micro-scale are detectable by QME.

Figure 1. Images of ductal carcinoma in situ (DCIS) and mucinous carcinoma. OCT, QME, and H&E histology of (A) DCIS 0.15 mm from the margin and (B) invasive mucinous carcinoma present on the margin. Colorbars: OCT 0 to 40 dB; Elasticity 3.63 to 363 kPa.

Results: Of the 154 study ROIs, 24 (15.6%) had cancer within 1 mm of the surface. Most ROIs were made up of a mix of tissue types, including adipose, stroma, and parenchymal tissues. Based on the average of all seven readers, the sensitivity and specificity for detecting cancer within 1 mm of the margin using OCT images were 69.0% and 79.0%, respectively versus 92.9% and 96.4%, using elasticity images. Conclusion: These results demonstrate high accuracy of QME for detecting tumor within 1 mm of the margin and the potential for this technique to improve outcomes in BCS.
SUBJECTIVE VERSUS OBJECTIVE EVALUATION OF AESTHETIC OUTCOME AFTER BREAST SURGERY
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Problem Statement: A gold standard method of evaluation of aesthetic outcomes from breast surgery utilising a validated, objective measure remains elusive. Obtaining an objective value such as Root Mean Square (RMS) from Breast 3D photography (3DP) may quantify breast morphology. This study compares RMS from Breast 3DP with current methods of assessing aesthetic outcome. Methods: Aesthetic assessment was completed in women presenting to the Westmead Breast Cancer Institute undergoing breast surgery. The assessments included physical examination, review of two-dimensional photographs, Breast 3DP, and the Breast Cancer Conservative Treatment cosmetic results (BCCT.core) software using two-dimensional photographs. These assessments were compared to each other utilising Pearson’s correlation coefficient. Results: A total of 49 women were included. The majority of cases had breast conservation surgery or breast reconstruction (n=36, 74%). For the assessment of overall breast symmetry, RMS from Breast 3DP demonstrated positive correlation with all other methods of assessment (review of two-dimensional photographs: r=0.65, p<0.01; BCCT.core: r=0.67, p<0.01). The strongest correlation was observed between Breast 3DP and physical examination (r=0.73, p<0.01). Conclusion: As breasts are three dimensional structures, all its parameters may not be assessable with methods based on two-dimensional photographs. Breast 3DP has much potential for objective assessment of breast symmetry and overall aesthetic result, however further studies are needed to confirm if it can be recognized as a new gold standard for objective assessment of aesthetic outcomes.

PREPECTORAL RECONSTRUCTION WITH BRAXON® ADM MESH
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Problem statement: There is an increasing trend of skin sparing mastectomies with implant-based breast reconstruction for therapeutic treatment of breast cancer patients and for risk-reducing surgery in high-risk patients. Conventionally, a subpectoral implant placement with partial detachment of the pectoralis major muscle is recommended. However, this can be associated with partial muscle injury, resulting in impaired function, breast animation deformity (dancing breast), and postoperative pain1. The subcutaneous positioning of the breast implant using Braxon mesh serves avoids detaching the pectoralis major1. This study aims to evaluate the cosmetic outcome and patient satisfaction in implant based breast reconstruction using Braxon mesh.

Methods: This is a prospective case series for patients who had skin/nipple sparing mastectomy with immediate or delayed reconstruction using Braxon mesh with either implant or tissue expander. All data were collected from data base and theatre diary at North Tees and Hartlepool Foundation Trust, between the period February 2016 and June 2018. BREAST-Q® V2 reconstruction module questionnaire was the method used for evaluation of satisfaction, with response of 80%. Results: 60 patients were included in this study, out of which 10% had bilateral reconstructions in the same setting (except 1 patient who had 2 stage surgery). Mean patients’ age was 55 ±10 years. Post-operative complication requiring re-admission occurred in 15.2%, with 4.5% implant loss. Patients’ post-operative psychological well-being score mean was 76%, and a mean score of 81% for satisfaction with their breasts. 78% were very satisfied about how their implants feel and mean score of chest physical well-being was 85%. Conclusion: Adding Braxon wrap to implant based reconstruction contribute in eliminating implant animation and complication, with increase in patient reported satisfaction and better self-evaluation of reconstruction cosmetic outcome.


PATHOLOGICAL CHARACTERISTICS AND TREATMENT OUTCOME OF INFLAMMATORY BREAST CANCER (IBC) IN EGYPT: A MULTICENTER RETROSPECTIVE CASE SERIES
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Problem statement: Inflammatory Breast Cancer (IBC) is an aggressive locally advanced breast cancer. It is defined as a clinico-pathological entity characterized by diffuse erythema and edema involving one-third or more of the breast skin. In comparison to breast cancer cases worldwide, Egyptian patients are usually diagnosed at younger age (45 years). Studies also suggest a higher incidence of IBC among Egyptians (10-15%) compared to worldwide incidence rates (1-5%). This study aims to determine the characteristics of IBC in Egypt and evaluate survival and factors affecting it.

Methods: A retrospective case series of IBC patients, presenting to three specialized breast cancer units in 4 years (2012-2015), with mean follow-up of 25±11 months. Selected units were: Arab Breast Center in Cairo, Oncology Center Mansura University and Fakous Cancer Center in rural Delta area. Protocol based multidisciplinary management were implemented, patients received neoadjuvant chemotherapy followed by surgery and radiotherapy, hormonal and/or targeted therapy according to their molecular type. Patients’ data were collected from medical records and analyzed. Pearson Correlation analysis of survival was done, Kaplan-Meier analysis was performed using SPSS® V23. The significance level was set at P ≤ 0.05. Results: 48 patients were diagnosed with primary IBC, incidence of IBC was 9.8% of total breast cancer cases presented to the units during the study timeframe. Mean age at diagnosis was 49±11 years and 8.3%of patient presented with gestational IBC. Also 70.8% were pathological grade II and 29.2%were grade-III. Complete
clinical response to neoadjuvant treatment was observed in 6.3% of patients, partial response was found in 87.5%. Median survival was 87.5%. Significant correlation was found between tumor grade and overall survival (r=0.498, p=0.002) and between Nottingham prognostic index (NPI) and time to recurrence (r=0.415, p=0.021). Kaplan-Meier survival curve (figure1) showed a statistically significant (CI:95%) survival benefit for patients diagnosed with pathological grade-II (44-49 months) compared to patients diagnosed with grade III (17-25 months). Conclusions: Our cohort of patients confirms that IBC presents in younger age and with a higher incidence in Egyptian patients. NPI was a significant indicator of time to recurrence of IBC. Advanced tumor pathological grade was associated with decrease of patients’ survival.

REDUCTION OF MARGIN POSITIVITY BY ENHANCED INTRAOPERATIVE BREAST SPECIMEN ASSESSMENT (EISA) TO A SIMILAR DEGREE AS ROUTINE CAVITY SHAVE MARGINS (CSM)
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Problem Statement: 20-40% of patients have positive margins after partial mastectomy requiring re-operation. No standardized protocols have been established regarding intraoperative specimen assessment. This study presents our experience with margin positivity, generating a hypothesis and study design for evaluating the benefit of enhanced intraoperative breast specimen assessment in reducing margin positivity and reoperation rates. Methods: A retrospective review of a prospectively maintained database from 2014 to 2016 was performed. Data were collected including preoperative imaging studies, use of preoperative needle localization, intraoperative ultrasound, digital specimen radiography (Faxitron), and gross consultation. Data were analyzed to calculate margin positivity and reoperation rates. Results: 213 patients with DCIS (49 patients) or invasive carcinoma (156 patients) undergoing partial mastectomy were identified. Gross consultation, ultrasound, and Faxitron were used for specimen assessment. Positive margins were identified by: gross consultation 60 patients (28.2%), Faxitron 34 (15.5%), surgeon discretion 32 (15%) and ultrasound 10 (4.6%). Pathology results showed an average margin positivity of 14%. We propose a prospective cohort non-inferiority study comparing margin positivity between 2 groups: “shave margin” undergoing circumferential tissue excision and “intraoperative assessment” undergoing a defined intraoperative assessment tool protocol. Sample size was calculated at 244 subjects (112 in each group) with a power of 80%. Conclusion: Our experience suggests that EISA compares favorably to CSM in reducing margin positivity which may reduce the amount of tissue removed. A prospective trial comparing EISA to CSM after developing standard protocols for specimen management is proposed.

EFFICACY OF LOW DOSE METHOTREXATE TREATMENT FOR GRANULOMATOUS MASTITIS
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Problem statement: Granulomatous mastitis (GM) is a rare, benign, chronic inflammatory disease of the breast that usually affects women of childbearing age. Diagnosis can be challenging due to confusion with infectious etiology. The most common symptoms are palpable breast mass associated with overlying erythema, induration, pain or drainage. Imaging is non-specific and histopathology is needed for confirmative diagnosis. The etiology is unclear, but an autoimmune reaction is favored and it has been linked to contraceptive use, history of pregnancy and breastfeeding. Given the limited knowledge, treatment of this benign, yet locally aggressive disease remains controversial. Observation alone, antibiotics, surgical excision, systemic or local steroids, and immunosuppressive agents have all been described. There is no consensus on treatment and only limited data in the literature. Surgical debridements can be associated with morbidity, therefore medical management such as low dose methotrexate is a good option. Methods: A chart review of patients with histological confirmation of GM between January 2011 and December 2017 was performed to identify response to methotrexate treatment. Fourteen adult female patients, age range 22-57, were diagnosed with GM. The majority of patients are of Hispanic and Native American ethnicity. Treatment protocol included methotrexate administered at 2.5-10 mg orally once weekly together with daily folic acid. Liver function tests and full blood counts were
POSTER ABSTRACTS

P01 CONTRIBUTION OF GERMLINE MUTATIONS IN LYSOSONAL STORAGE DISEASE-RELATED GENES CONTRIBUTES TO BREAST CANCER DEVELOPMENT

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2Division of Hematology and Medical Oncology, Department of Internal Medicine, Seoul National University Hospital, Seoul, South Korea

Problem statement: Lysosomal storage diseases (LSD) are caused by inborn errors of metabolism. It has been suggested that lysosomal dysfunction contributes to carcinogenesis and carriers of potentially pathogenic variants (PPVs) of LSD-related genes are at increased risk of cancer. We aimed to elucidate the oncogenic contribution of germline mutations in LSD genes to patients at high risk for hereditary breast cancer (BC). Methods: 153 patients with high risk of hereditary BC (multiple primary cancer, age 40, family history of BC ≥3, bilateral BC) who showed no pathogenic germline mutation on 64-enzyme hereditary cancer panel were analyzed. DNA extracted from blood samples of these patients underwent targeted sequencing for 42 LSD-related genes. Germline variants classified as PPVs were analyzed according to risk category. Results: PPVs were detected in 19.0% (29/153) of samples sequenced. Compared to the PPV rate of 13.5% in the normal population from the 1000 Genome Project, it showed an odds ratio (OR) of 3.55 (p-value 0.0001). Samples from patients with multiple primary tumours showed a PPV rate of 20.9% and an OR of 4.02 (p-value 0.0001). Samples with a family history of BC ≥3 had a PPV rate of 17.4% and an OR of 3.20 (p-value = 0.0478). Samples from patients with age 40, ≤35, and ≤25 showed PPV rates of 15.6%, 17.7%, and 22.2%, respectively. Conclusion: High risk patients who do not possess germline mutations in commonly known hereditary cancer-related genes carry higher rate of PPVs in LSD-related genes compared to the normal population, especially in patients with multiple primary cancer and 3 or more family history of breast cancer. Carriers of these PPVs are more likely to develop hormone receptor-positive / HER2-negative breast cancers. Further large scale studies are warranted to discriminate patients who could benefit from sequencing of LSD-related genes.

P02 MULTIFOCALITY IN BRCA-ASSOCIATED BREAST CANCER: A CROSS-SECTIONAL ANALYSIS

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Problem statement: Multifocality has a reported incidence of around 10% in sporadic breast cancer. We hypothesised that multifocal disease may be more common in patients with breast cancer who harbour a pathogenic mutation in the BRCA1 or BRCA2 breast cancer risk predisposition genes. BRCA1/2 are involved in DNA damage repair; therefore, pathogenic mutations in these genes may result in a DNA repair pathway deficiency. This may cause genomic instability, with consequent widespread field changes within breast tissue, potentially resulting in the development of multifocal cancer. However, previous studies have not specifically addressed the incidence of multifocality in BRCA mutation carriers, which may have implications for clinicians treating patients with BRCA-associated breast cancer. This study set out to investigate the prevalence of multifocality in BRCA-associated breast cancer in Northern Ireland (NI).

Methods: Using the BRCA database held within Belfast City Hospital, women with a known pathogenic BRCA1/2 mutation and BRCA-associated breast cancer diagnosed between 1998–2018 in NI were identified. Clinical and pathological data was retrospectively collected. Differences in tumour characteristics were explored using Chi-squared test. Results: 211 women with BRCA-associated breast cancer were included, 57% BRCA1 and 43% BRCA2 mutations. Mean age at diagnosis was 45 years. Overall prevalence of multifocality was 25% but prevalence amongst BRCA2 carriers was over double that of BRCA1 carriers, summarised in Table 1. Women affected by BRCA1 or BRCA2 breast cancer risk predisposition genes.

<table>
<thead>
<tr>
<th>Tumour multifocality</th>
<th>BRCA status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unifocal</td>
<td>78 (86.7)</td>
</tr>
<tr>
<td>Multifocal</td>
<td>40 (33.1)</td>
</tr>
</tbody>
</table>

Conclusion: Results suggest a significantly higher than anticipated prevalence of multifocality amongst BRCA carriers diagnosed with breast cancer. Further validation and prospective studies are necessary to accurately assess the risk of multifocality in BRCA-associated breast cancer, and to elucidate the underlying molecular mechanisms driving this.

Table 1:

BRCA status
BRCA1 n (%) | BRCA2 n (%)
--- | ---
Multifocal | 40 (33.1) | 12 (13.3)
Unifocal | 78 (86.7) | 81 (66.9)
WOMEN INFORMED TO SCREEN DEPENDING ON MEASURES OF RISK (WISDOM): A PERSONALIZED BREAST CANCER SCREENING IN A POPULATION BASED STUDY
Irene Acerbi1, Mandy Che1, Yiwei Shei1, Lisa Madlinski2, Jeffrey Tice1, Elad Ziv1, Martin Eklund1, Amie Blanco3, Barry Tong1, Deborah Goodman4, Lamees Nassereddine4, Nancy Anderson1, Heather Harvey4, Hannah Park4, Antonia Petruese4, Skye Stewart4, Janet Wernisch5, Larissa Risty6, Barbara Koenig1, Leah Sabacan7, Yash Hullgol8, Patricia Choy8, Stephanie Flores9, Celia Kaplan10, Robert Hatt11, Barbara Parker2, Neil Wengert4, Vivian Lee4, Diane Heditsian11, Susie Brain11, Allison Stover Fiscalan1, Alexander Borowsky9, Hoda Anton-Culver3, Arash Naeimi6, Andrea Kaster2, Melinda Tailley4, Sharon Hunt1, Laura van ’t Veer12, Andrea LaCroix12, Wisdom Study and Athena Breast Health Network

Investigators and Advocates Partners1, Laura Esserman7,8
1Athena Breast Health Network & WISDOM Study, University of California, San Francisco, San Francisco, USA, 2Athena Breast Health Network & WISDOM Study, University of California, San Diego, San Diego, USA, 3Athena Breast Health Network & WISDOM Study, University of California, Irvine, Irvine, USA, 4Athena Breast Health Network & WISDOM Study, University of California, Los Angeles, Los Angeles, USA, 5Athena Breast Health Network & WISDOM Study, University of California, Davis, Davis, USA, 6Athena Breast Health Network & WISDOM Study, Sanford Health, Sioux Falls, USA, 7Athena Breast Health Network & WISDOM Study, Karolinska Institutet, Stockholm, Sweden

Problem Statement: Current breast screening guidelines create confusion among women and providers, have a high healthcare cost, low specificity, and have high rates of morbidity. The goal of WISDOM is to determine if personalized screening, compared to annual screening, is as safe, less morbid, enables prevention, and is preferred by women. The novelty of WISDOM personalized screening is the integration of validated genetic and clinical risk factors (age, family history, breast biopsy results, ethnicity, mammographic density) into a single risk assessment. WISDOM is a preference-tolerant, pragmatic study.
Methods: Women aged 40-74 years who never had breast cancer or DCIS, can join the study online at wisdomstudy.org. Participants can elect randomization or select a study arm. 5-year risk of developing breast cancer is calculated according to the Breast Cancer Screening and Cancer Risk Calculator (BCSC-PRS). For participants in the personalized arm the risk assessment includes a Polygenic Risk Score (BCSC-PRS) from a panel of over 100 single nucleotide polymorphisms (SNPs), and mutations (BRCA1, BRCA2, TP53, PTEN, STK11, CDH1, ATM, PALB2, and CHEK2), known to increase breast cancer risk. 5-year risk level thresholds are used to stratify for low-, moderate- and high risk. Risk stratification determines screening recommendation. Results: As of June 2019, the WISDOM study is open to all eligible women in California, North Dakota, South Dakota, Minnesota, Iowa, New Jersey, and Illinois. 30,309 eligible women have registered and 21,280 women have consented to participate in the study. The median age was 56 years. 82% were White, 1% African-American, and 6% Asian. 9% self-reported as Hispanic. We are partnering with health insurers and self-insured companies using coverage with evidence progression. To strengthen generalizability, we are expanding to other states and we are recruiting both English and Spanish speakers. WISDOM enrollment will continue in 2020. Conclusions: Our findings demonstrate that incorporating genetic variants into a validated model is feasible and impacts risk classification compared to a model without genetic risk factors. Results at 5 years will reveal if this classification improves healthcare value by reducing screen volumes and costs without jeopardizing outcomes. ClinicalTrials.gov, NCT02620852.

HAS THE TRANSITION TO DIGITAL MAMMOGRAPHY IN BREAST CANCER SCREENING RESULTED IN REAL BENEFITS?
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Problem statement: Most breast screening programmes worldwide have replaced Screen-Film mammography (SFM) with Full-field Digital Mammography (FFDM). While FFDM provides significant technical and practical advantages over SFM in the provision of population screening programs, whether this move has had beneficial effects on health outcomes remains unclear. An increase in screen-detection rates is only beneficial if the additional cancers detected would have otherwise presented at a later stage and caused morbidity and premature mortality. An indirect measure of this is an observed decrease in interval cancer rates.
Methods/Results: This study compares health outcomes before, during and after the transition from SFM to FFDM in women in NSW, Australia. We linked data to capture women’s journeys from screened/unscreened to cancer diagnosis/no cancer diagnosis to treatment/no treatment and to dead/alive. For the period 1988 to 2016, women screened by Breastscreen NSW and/or choosing to opt for breast cancer in NSW Cancer Registry records’ were linked with NSW Admitted Patient Data, and NSW Mortality Data. We use interrupted time series regression to evaluate the effectiveness of the transition to digital mammography over time and a segmented regression to analyse the effect of change in technology in mammography screening on each outcome. We will present the results of our evaluation on whether the transition from SFM to FFDM was associated with changes in screen-detected cancer rates, interval rates, positive predictive values, recall rates and false positive recall rates. We will evaluate changes in breast cancer tumour characteristics for screen-detected and interval cancers (stage at diagnosis, size, histological type, node status, grade), and differences in breast cancer treatment and breast cancer mortality rates. We will conduct analyses stratified by age, breast density, and initial and subsequent screening examinations. Conclusion: This research will evaluate incremental benefits and harms of changes in breast cancer screening programs that can be translated to health policy recommendations as well as the information provided to women invited to screen. The innovative approach of estimating benefits and harms using rates of screen-detected cancers and interval cancers will allow for more timely and rigorous evaluation of changes in screening technologies and practice.
When is Less More?

CoBrCa

Health, San Francisco, USA, 1, , Quantum Leap Healthcare Collaborative, San Francisco, USA

Problem Statement: An important opportunity for supporting research is to design value-based policies that more efficiently use or repurpose the resources already spent on care to improve healthcare delivery. Methods: The Women Informed to Screen Depending On Measures of risk (WISDOM) Study is a Patient Centered Outcomes Research Institute (PCORI) and Breast Cancer Research Foundation (BCRF) funded national trial that serves as a case study. The study uses a coverage with evidence progression (CEP) payment model with private payers. The WISDOM Study has pioneered a collaborative implementation process to generate evidence for how to optimize breast cancer screening and improve healthcare value. Results: The WISDOM Study faced five overarching challenges when adopting and expanding nationwide using the CEP payment model: convincing payers of the value of study endpoints; scalable and cost-effective implementation; restricting eligibility of CEP-covered participants; strategic alignment of goals among payers and investigators; and, engagement with healthy participants. There are five key lessons that should inform future studies. First, to get payers to adopt CEP, investigators must make a case for generating higher healthcare value and provide an ability for insurers to participate in an active learning system. Second, CEP-based trials must develop efficient, scalable study services and billing processes to be cost-effective. Third, CEP is mostly feasible for fully insured plan members, so there need to be different approaches for self-insured plans that normally do not covered study services. Fourth, CEP trials must collaborate with senior leaders to align strategic goals of the payers and investigators to expand the study. The WISDOM Study recruited among healthy participants who may not have a strong interest in participating in research; therefore, the fifth lesson is that CEP-based trials must be ready to engage participants through other community and employer partnerships. Conclusion: If investigators, stakeholders, and payers want to promote value-based care, there must be systems in place tostandardize and incentivize the adoption of CEP for pragmatic studies. The WISDOM Study implementation of the CEP process identifies key barriers, and provides some lessons learned for use in future study planning and policymaking.

P06

CORRELATION OF BREAST BACKGROUND PARENCHYMAL ENHANCEMENT ON MRI WITH MORPHOPHYSIOLOGICAL PARAMETERS OF BREAST AND BREAST LESIONS

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Problem statement: Our aim is to assess the relationship among background parenchymal enhancement (BPE) and density (BPD) on MRI with benign and malignant breast lesions, malignant lesions subtypes according to hormone receptor status (ER, PR, and HER2), benign lesions subtypes, patient age, menopausal status and breast volume. Methods: This study was carried out on patients who underwent breast MRI scan between May 2015 and February 2017. We studied among 899 patients. Results: The mean age of all patients was 47.1±11.90. 246 (27.4%) patients showed type 1, 286 (31.8%) patients showed type 2, 237 (26.4%) patients showed type 3 and 130 (14.5%) patients showed type 4 enhancement. 246 patients had histopathological results, of whom 140 patients were malignant, while 116 were benign. In malignant cases, BPE and BPD were statistically significantly lower compared to benign cases (p = 0.002 and p = 0.001 respectively). Fatty breasts were seen in 58.6% of malignant and 36.2% of benign cases. There was no statistically significant difference between breast volumes of benign and malignant cases (p = 0.143). No statistically significant difference was found between the molecular subtypes of malignant patients in terms of BPE, BPD, menopausal status and breast volume (p = 0.739, 0.426, 0.344, 0.933, respectively). This was also true for patients in pre-, peri- and post-menopausal periods (p = 0.885, 0.380; p = 0.553, 0.873; p = 0.128, 0.787 respectively). There was no statistically significant difference in BPE and BPD according to PR and ER status between groups of malignant lesions in pre-, peri- and post-menopausal periods (p = 0.05; p=0.05). There was no significant difference in BPE, BPD, menopausal status and breast volume in patients with benign lesions compared to histopathological subgroups (p = 0.05). The OR calculations were given in table 1. Conclusion: Our study showed that there is a correlation between BPE and BPD, although there was no correlation between BPE and malignant lesions or molecular subtypes. Patients with benign lesions were found to have a higher BPD and BPE. It can be concluded by this study that high BPE and high BPD are not risk factors for the development of malignancy.

Table 1: Odds ratio of the variables related to the malignancy in breast lesions

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR (95% CI)</th>
<th>P-value</th>
<th>Adj OR (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.093 (1.008, 1.18)</td>
<td>0.042</td>
<td>1.093 (1.008, 1.18)</td>
<td>0.042</td>
</tr>
<tr>
<td>BPE (low vs high)</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>BPD (low vs high)</td>
<td>1.084 (1.073, 1.096)</td>
<td>0.224</td>
<td>1.084 (1.073, 1.096)</td>
<td>0.224</td>
</tr>
<tr>
<td>Menopausal status</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Breast volume</td>
<td>0.864 (0.78, 0.946)</td>
<td>0.001</td>
<td>0.864 (0.78, 0.946)</td>
<td>0.001</td>
</tr>
</tbody>
</table>
P07
PURE FIBROCYSTIC CHANGE DIAGNOSED AT MRI-GUIDED VACUUM-ASSISTED BREAST BIOPSY: IMAGING FEATURES AND FOLLOW-UP OUTCOMES
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Problem statement: To identify MRI characteristics of pure fibrocystic change having no other associated pathologies on MRI-guided Vacuum Assisted Breast Biopsy (VABB), describe findings on follow-up and evaluate outcomes after VABB.

Methods: We retrospectively reviewed 598 lesions undergoing 9-gauge MRI-guided VABB from January 2015 to April 2018, identifying 49 pure FCC lesions in 43 women for inclusion. Patient and lesion characteristics, MRI lesion morphologies and kinetic features prompting biopsy, VABB pathology, subsequent surgery or follow up MRIs were reviewed.

Results: The mean patient age was 51.7 years old (range 30 - 75 years). MRI morphology features of pure FCC included non-mass enhancement (NME)(30/49, 61%), mass(17/49, 35%), and focus (2/49, 4%). The NME size mean was 3.1 cm (range 1.1 - 11 cm), and mass mean size was 0.8 cm (range 0.5 -1.5). The distributions of the 30 NME lesions included 7 focal (23%), 9 linear (30%), 4 regional (13%), and 10 segmental (34%). NME internal enhancement was clumped in 19 (64%), heterogeneous in 7(23%) and homogeneous in 4(13%). Of the 17 mass lesions, 13(76%) had irregular margins, and 4(24%) were circumscribed. Initial and delayed kinetic data were available in 15 and 16 lesions for 19 mass/focal lesions, respectively. The initial phase was fast 14/15(93%), and medium 1/15(7%). The delayed phase showed washout 10/16(63%), plateau 4/16(25%), or persistent 2/16(12%) kinetics. 13 lesions in 11 (25.6%) patients received subsequent surgical procedures. All 13 FCC lesions were confirmed in the surgical specimens by MRI markers, without high-risk or cancer upgrades. 20 (46.5%) patients, not receiving surgical resection of the FCC after biopsy, underwent follow up MRI. The average time interval between VABB and MRI follow-up was 18.0 months (range 11-41 months, median 17) showing that 13(59%) lesions resolved or regressed, 8(36%) lesions were stable, and 1(5%) lesion grew, no cancers were found on follow-up at the site of MRI biopsy for fibrocystic changes.

Conclusion: Our study shows MR imaging features for pure FCC may mimic internal enhancement regardless kinetic curves, and irregular mass with fast/washout kinetics. After VABB of pure FCC, a 12-month follow-up MRI may be reasonable.

P08
A MULTI-CENTER OPEN-LABEL PARALLEL PHASE-2 CLINICAL TRIAL TO EVALUATE THE EFFICACY AND SAFETY OF LUMINOMARK™ FOR LOCALIZATION IN PATIENTS WITH NON-PALPABLE BREAST LESIONS
Isaac Kim1, Hee Jun Choi2, Jai Min Ryu2, Se Kyung Lee2, Jong Han Yu2, Jeong Eon Lee1, Seok Jin Nam1, Seung Ah Lee1, Seung Ki Kim1, Hyuk Jai Shin1, Seok Won Kim2
1Department of Surgery, Bundang CHA Medical Center, Bundang, South Korea, 2Division of Breast and Endocrine Surgery, Samsung Medical Center, Gangnam-gu, South Korea, 3Department of Surgery, Myongji Hospital, Ilsan, South Korea

Problem statement: With increasing screening for breast cancer, non-palpable breast lesions are detected more frequently. A preoperative localization is very important for a minimal but accurate excision of non-palpable lesions.

Methods: In this prospective, randomized clinical trial, we included 50 female patients with non-palpable breast lesions who then underwent surgery. After exclusion, 44 patients were sequentially assigned to the control, test1, or test2 group by 1:1:1 ratio. A localization was done through ultra sound(US) guidance. For localization, 0.3 to 1.0ml Charcotrace™(activated charcoal, 40mg/ml) was injected in the control group. Then 0.1ml LuminoMark™ was injected in test1 and 0.2ml was injected in test2 group. The primary variable for effectiveness was the completeness of resection, which was defined as the value of the largest length of the excised specimen divided by the greatest length on pre-OP US. Secondary variables were the success rate of marking on the breast lesion, marking on the excised specimen, the pathological completeness and the value of the largest length of the pathological lesion divided by the greatest length of the excised specimen and the pigmentation on the skin.

Results: According to the pathology, fibroadenoma accounted for the largest share(38.6%,17/44) and malignancy accounted for 11.4%(5/44). There was no AE in any of the groups. There was no significant difference in the pathological completeness, marking rate on breast lesion, or excised specimens. However, the completeness of resection was lower in test group than control group. The average was 3.7,2.2 and 2.1 in the control, test1 and test2 group, respectively. There was no significant difference(p=0.037 between control and test1, p=0.026 between control and test2, p=0.744 between test 1 and 2). This value closer to 1 meant resection as much as the size on pre OP US. And skin pigmentation was only in the control group(64.8%).

Conclusion: This is a multicenter phase-2 clinical trial to evaluate the efficacy and safety of LuminoMark™ for localization compared to Charcotrace™. According to our results, LuminoMark™ was not inferior to Charcotrace™ for localization in patients with non-palpable breast lesions. In addition, it has a cosmetic advantage. These results encourage us to continue using and developing this technique.

Disclosure of interest: The authors have declared that they have no competing interests
P09
FACTORS ASSOCIATED WITH MRI DETECTION OF OCCULT LESIONS IN NEWLY DIAGNOSED BREAST CANCER
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1Department of Surgery, Division of Breast and Soft Tissue Surgery, Norris Comprehensive Cancer Center, University of Southern California, Los Angeles, USA, 2Department of Surgery, Tumor Service, LAC+USC (LA County) Medical Center, Los Angeles, USA, 3Department of Surgery, Catholic University of Daegu School of Medicine, Daegu, South Korea, 4Department of Breast Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, USA, 5Department of Preventive Medicine, University of Southern California, Los Angeles, USA, 6Department of Radiology, Division of Oncology Women’s Imaging, Norris Comprehensive Cancer Center, University of Southern California, Los Angeles, USA.

Problem statement: The appropriate use of preoperative magnetic resonance imaging (MRI) for newly diagnosed breast cancer remains a topic of debate. We aimed to determine factors associated with the detection of occult multicentric, multifocal, and contralateral malignant lesions not detected by ultrasound or mammography and only seen by MRI. Methods: We performed a retrospective analysis of consecutive patients who underwent preoperative MRI without neoadjuvant systemic therapy for breast cancer. All newly diagnosed patients underwent preoperative breast MRI according to our service policy during this timeframe for our two academic institutions with a shared medical faculty. MRI was performed with a 1.5 Tesla field scanner with a dedicated breast coil in the prone position and read by the same radiologist for both of our institutions. Demographic, radiographic and pathologic variables were assessed for each patient with respect to the findings of multifocality, multicentricity, and the presence of contralateral lesions based on mammogram, breast ultrasound, and MRI. We analyzed the association of factors with these findings on breast MRI by univariate and multivariate analysis. Results: Of 857 consecutive patients undergoing breast MRI, 770 patients were identified who met inclusion criteria. The mean size of the lesions was 0.48 cm (range 0.15 to 2.00 cm). Multifocality was found in 78 (10.1%) of the cases. The most common findings on mammography were benign round calcifications. 10/12 of the cases were associated with contralateral lesions detected by ultrasound only. When available, we reviewed mammograms and ultrasound findings and the MRI findings were correlated. Conclusion: MRI was the most likely modality to detect occult lesions not visible on ultrasound or mammography. The dense breast images gained from MRI were assessed for the presence of biopsy proven multicentric and multifocal cancers on MRI. Larger lesion size and mammographic density were associated with the detection of multicentric lesions. The presence of invasive lobular carcinoma and progesterone receptor (PR)-positivity were associated with contralateral cancers. Conclusions: Our study analyzed clinical and pathologic factors associated with multicentric, multifocal, and contralateral lesions seen only on MRI to aid clinicians in patient selection for preoperative MRI. In this study, African-American race, heterogeneously or extremely dense mammographic density, the presence of invasive lobular carcinoma, and PR-positivity were associated with additional biopsy proven cancers based on breast MRI. These factors should be taken into account to assess the clinical utility of preoperative breast MRI.

P10
3D AUTOMATIC DENSITY ANALYSIS DEVICE MIGHT BE BETTER FOR ACCURATE BREAST DENSITY IN JAPANESE WOMEN WITH BREAST CANCER
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Problem statement: In generally, about 80% of Japanese women are reported as a dense breast and is associated with the increase of the false negative (masked abnormalities) of mammography screening. Women with dense breasts are recommended to receive the additional examination. Therefore, the precise measurement of breast density is a very important. But conventional visual estimate of the breast density have reported subjective, and then poorly reproducible. Recently 3D automatic density analysis device such as Volpara software was marketed around the world that has measured the breast density with accurate and reproducibility. We compared the false negative (masking) rates of mammography by visual estimate and Volpara software retrospectively. Methods: The 532 primary breast cancer cases in 2017-2018 have conducted to measure the breast density by visual estimate and Volpara. Breast density was categorized to four types by BI-RADS: a. fatty, b. scattered, c. heterogeneously dense, d. extremely dense. Absolute dense volume was 0-4.7%, a. 4.8-7.9%, b. 8.0-15.0%. c. 15.1; d by volpara. The dense breast was defined as integrated c and d in Volpara. We defined the abnormal findings as to asses category 3 to 5 by using BI-RADS and the Japanese radiological society mammography guidelines. Results: The correlation rate of the breast density was very low (cohen’s kappa coefficient k=0.181) between visual estimate and Volpara. Although the ratio of dense breast in the breast cancer case was decided 77.1% by visual estimate, it was decided 87.6% by Volpara. We have a tendency to evaluate the much more patients as a lower breast density compared to by using Volpara. By visual estimate, the masking rates of the abnormalities on mammography were 9.0% in Non-dense breasts, and 28.3% in dense breasts. Whereas, by Volpara, the masking rates of the abnormalities were 4.5% in Non-dense breasts, and 26.6% in dense breasts. Conclusion: The overwhelming rates by Volpara were lower than by visual estimate in the both breast density. We should recommend to receive the other examination for dense breast women. In this study, we investigated primary breast cancer cases, but we need to use Volpara at mammography screening in future study.

P11
MAGNETIC RESONANCE IMAGING FEATURES OF PURE SCLEROSING ADENOSIS IN THE BREAST UNDERGOING VACUUM ASSISTED BREAST CORE BIOPSY
Satoko Okamoto1, Shu Tian Chen1, James Covelli2, Bruce Daniel3, Wendy DeMartini4, Debra Ikeda4
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Problem statement: Sclerosing adenosis (SA) is a benign proliferative disease, associated with calcifications and/or architectural distortion. Prior investigations describe SA mammographic and ultrasound appearances, but few report MRI features. We evaluated the frequency, MRI morphologic and kinetic features, and imaging follow up of pure SA on
MRI-guided vacuum-assisted breast biopsy (VABB). METHODS: We retrospectively reviewed 598 lesions undergoing 9-gauge MRI-guided VABB at our institution from January 2015 to April 2018, to identify patients with SA. We reviewed patient characteristics, breast MRI BI-RADS descriptors/kinetics, mammography density and results on imaging follow-up. When available, we reviewed mammographic features of the area around the MRI biopsy. RESULTS: Of 598 lesions undergoing VABB, 51 (8.5%) lesions showed SA. Of the 51 lesions, 3 (5.9%) were associated with DCIS, 8 (15.7%) high-risk lesions (4 atypical lobular hyperplasia, 3 papilloma, 1 radial scar), 28 (54.9%) associated with other benign pathologies most common usually ductal hyperplasia (7/40, 17.5%), proliferative fibrocystic change (6/40, 15%) and were excluded. There were 12 pure SA which comprise this study. The patients’ age ranged from 36-70 years old (mean 53.6 years old). The SA appeared as masses (7/12, 58.3%), non-mass enhancement (NME) (3/12, 25.0%) or foci 2 (2/12, 16.7%). Mass sizes ranged from 0.5-0.9 cm (mean, 0.66 cm), and were most commonly irregular both in shape (4/7, 57.1%) and margin (5/7, 71.4%). The 3 NME sizes ranged from 2.1-7 cm (mean, 5.2 cm). With 2 regional distributions and 1 linear enhancement. Kinetics were most commonly rapid initial (8/12, 66.7%) with delayed wash-out (6/12, 50%). 10/12 patients had mammograms before the biopsy showing BI-RADS C/D dense breast tissue and dense tissue around the marker in all patients except 1. 3 pure SA had histopathological microcalcifications and 2 mammograms showed benign round calcifications. 10/12 (83.3%) had follow-up imaging 6 MRI, 2 mammograms, 2 mammogram/ultrasound at an average time follow-up of 19 months, with no appearance of malignancy. CONCLUSION: The MR imaging characteristics of pure SA was most commonly a small irregular mass lesion with initial rapid and delayed washout kinetics.

P12 RADIAL SCLEROSING LESIONS OF THE BREAST. A SINGLE-INSTITUTION EXPERIENCE AND LITERATURE REVIEW

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Problem statement: Radial sclerosing lesions (RSL) of the breast which include radial scars and complex sclerosing lesions are benign histopathological entities of unknown histogenesis that have been reported to 0.03%–0.09% of all core needle biopsies. RSLs may pose a diagnostic dilemma as their imaging characteristics may mimic breast carcinoma. Material and methods: We retrospectively reviewed the medical records of patients who were diagnosed with RSLs of the breast, over a 4-year period. RSL that was incidentally detected during breast surgery for unrelated indications, were not included in the study. Results: From January 2015 to April 2019, 20 pathologically proven cases of RSLs of the breast were identified in 17 patients. The mean age of the patients was 55.1 years (range 34 to 81 years). The mean size of the lesions was 1.29 cm (range 0.2 to 4cm). In 9 (53%) of the cases, the size of RSL was larger than 1cm. Multiple RSL was found in 3 (17.6%) of the cases. The most common mammographic findings included a spiculated mass and architectural distortion (65%) whereas the most common ultrasonographic finding was that of a hypoechoic mass with irregular margins (76.5%). Eighty-two percent of the cases were classified as suspicious for malignancy (BI-RADS 4). A core needle biopsy was performed in cases larger than 1 cm. All cases underwent surgical excision. Five (20%) cases were upstaged to high-risk lesions, one (5%) case was upstaged to invasive carcinoma, and one case (5%) to Ductal carcinoma in situ. Conclusions: RSLs have been associated with a reported 2-3 fold increased relative risk of breast cancer development and associated risk of concurrent cancer in 3-40% of the cases following excision. Several risk factors have been reported to be associated with cancer upstaging including postmenopausal status, radiographic size of RSL larger than 1cm and presence of atypical hyperplasia. Recently published data show a 5-19% rate of associated malignancy suggesting that a non-operative approach could be considered in carefully selected cases. Larger well-designed studies are however needed. Complete surgical excision of RSLs remains the recommended treatment in most cases.

P13 UNIQUE CHARACTERISTICS OF THE BREAST DENSITY (CANCER, BENIGN DISEASE, SCREENING) IN JAPANESE WOMEN ARE CLARIFIED USING VOLPARA™

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Problem Statement: The dense breast images gained from mammography (MG) is thought to have a high risk of breast cancer compared to other women with non-dense breast tissue. In addition, abnormal findings are more likely to be masked on mammograms (false-negative) in women with dense breast tissue. We have conducted to ensure the breast density of the previously statement by using Volpara volumetric density analysis. (Methods) The breast density of 3207 cases (breast cancer 763 cases, screening 1676 cases, benign disease 768 cases) were measured by Volpara software in Showa University Hospital. The feature of Volpara is known as a fully automated computer algorithm and images are processed in a high-throughput manner, producing an objective measurement of breast density each time. Output images were classified to the four categories: a (fatty), b (scattered), c (heterogeneously dense), d (extremely dense) defined by BI-RADS. We have retrospectively studied breast density with our experienced cases respectively in our institute by Volpara. (Results) According to the polygonal line graph (Figure) of high breast density rates, cancer cases showed a higher position compared to the screening cases. We recognized that the density of the benign disease has also revealed the higher ratio of dense breast than screening cases. Moreover, when we checked clinicopathological characteristics of the breast cancer cases, the ratio which we couldn’t identify the abnormal findings (masking rates) was higher with dense breast than non-dense breast. The over-looking rates of abnormalities due to high breast density were approximately 24%, and most of those pathological characteristics were ≤T1, ≤20% of Ki67 and ER (+). (Conclusion) The results of this study were interesting for us that highly breast density rates were not only the breast cancer cases but also the benign disease than screening cases. Furthermore, the over-looking factors in the dense breasts were affected by the tumor size,
positive of Estrogen receptor and low index rate of Ki67. We’d like to show the availability of Volpara software and to present the future perspectives.

P14
UTILITY OF CONTRALATERAL BREAST ULTRASOUND IN DIAGNOSING SYNCHRONOUS BREAST CANCER IN NEWLY DIAGNOSED CANCER PATIENTS
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Problem statement: Breast cancer is the leading cause of death in females in Singapore. Women with an index breast cancer are also 2 to 6 times more likely to develop a contralateral breast cancer (CBC). The incidence of a synchronous contralateral breast cancer ranges from 5-15%. Bilateral mammograms have traditionally been used to screen breast cancer in females above the age of 50 and has been shown to reduce the rate of mortality. However, the accuracy of mammograms have been subject to controversy. With advancements in technology, ultrasound (US) has emerged as a useful adjunct to screening mammograms in the detection of breast cancer. Methods: This study aims to investigate the usefulness of screening ultrasounds in detecting mammographically occult breast cancers in the contralateral breast. In an 8-year period from 2008 to 2016, 560 patients had a biopsy proven breast cancer after a screening mammogram was conducted in the National Cancer Centre Singapore. Retrospective data collection was then conducted to identify patients who were subsequently diagnosed with contralateral breast cancer as well. Results: 368 US scans were performed (331 US screens, 37 diagnostic). 62.3% of patients had contralateral breast ultrasounds conducted. 35 patients (6.3%) were diagnosed with contralateral breast cancer. The overall CBC detection rate for MMG was 3.0% (17/560) while the overall CBC detection rate for US was 8.2% (30/368). 4.9% (16/327) of patients with normal MMGs had CBCs detected on screening ultrasounds. A higher proportion of these patients (86.7%) with false negative mammograms had dense breasts. In addition, US found additional contralateral auxiliary metastatic lymph nodes, all related to ipsilateral locally advanced breast cancer (LABCs). This will upstage disease to distant metastases and significantly change management.

P15
OUTCOMES AND COMPLICATIONS OF IMMEDIATE AND DELAYED BREAST RECONSTRUCTION
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Problem statement: With numerous advances in the field of plastic surgery, breast reconstruction is available today to almost any woman undergoing surgery for breast irradiation. Several methods can be used for restoration of the breast either at the same time as breast cancer surgery (immediate reconstruction) or months or even years later, at the patient’s discretion (delayed reconstruction). Methods: This is a retrospective study where patients’ data were collected from breast unit at North Tees and Hartlepool foundation trust between 2015-2017. The scope of this study was focused on patients who received breast reconstruction, they were grouped into (immediate, delayed, implant based and autologous reconstruction). The primary outcome was looking into re-admission for unplanned complication. Complication were classified according to Clavien-Dindo score. Results: This study included 171 patients of them had bilateral reconstruction, implant loss, return to theatre and unplanned re-admissions were compared to ABS and BAPRAS guidelines. Unilateral reconstructions were further divided to 130 immediate (76%) and 38 delayed procedures (23.3%). 14 patients (8.2%) had prophylactic mastectomies. 49 (28.6%) patients had reconstruction using LD flap among these 80% had additional prosthetic implants to obtain matching volume. Implant support was used in 109 patients, 25 dermal slings, 64 ADM meshes, 10 patients had combination of ADM and DS, and 10 patients had Tiloop. 15.3% of the patients needed to return to theatre for debridement and washout. Implant loss rate was 4.91%. In immediate reconstructions and 1.1% implant loss in delayed reconstruction. 21% had unplanned hospital re-admissions. 3.5% were re-admitted for unplanned complications in delayed reconstruction group while in immediate reconstruction that number was 21%.

Conclusion: Immediate breast reconstruction is the preferred method of reconstruction. However, delayed reconstruction was associated with lower complication rates in compared to immediate reconstruction. Overall the results from this study are comparable to NMBRA and best practice guidelines. References: 1 Tran NV, Evans GRD, Kroll SS, Baldwin BJ, Miller MJ, Reece GP, Robb GL: Postoperative adjuvant irradiation: effects on transverse rectus abdominis muscle flap breast reconstruction. Plast Reconstr Surg 2000, 106:313-317. Abbreviations: ADM: Acellular dermal matrix, LD flap: Latissimus Dorsi Flap, DS: Dermal Sling.
Problem Statement: A common criticism of two-stage implant-based breast reconstruction is the lack of lower pole projection compared to single-stage, direct to implant reconstruction. While the use of different methods to provide lower pole coverage is well established in single-stage reconstruction, the best method for coverage in two-stage reconstruction remains unclear. Methods: Two-stage implant-based breast reconstructions over a nine month period were assessed. Three-dimensional photography was performed to assess breast volume for every case before and after each individual expansion and at the completion of the expansion process. The different methods used to achieve lower pole coverage were compared with respect to upper and lower pole breast volume distribution. Results: There were 24 two-stage implant-based breast reconstructions in 20 patients. Lower pole coverage was achieved using a lipodermal flap in 12 cases (50%), biologic mesh in 5 cases (21%), serratus anterior advancement flap in 3 cases (13%) and synthetic mesh in 4 cases (17%). Volume distribution immediately after each expansion was not significantly different between groups. Mean final lower pole expansion was significantly higher with lipodermal flap and biologic mesh compared to serratus anterior advancement flap and synthetic mesh (47±10% versus 36±8%; p=0.05). Conclusion: In comparison to study suggests that better lower pole expansion was achieved using lipodermal flap or biologic mesh compared to total muscle coverage and synthetic mesh. Further studies such as clinical trials are needed to evaluate this more definitively.

Problem Statement: In patients (pts) with hormone receptor-positive (HR+), human epidermal growth factor receptor-2-negative (HER2−) advanced breast cancer (ABC), approximately 40% have PIK3CA-mutated tumors, resulting in phosphatidylinositol 3-kinase (PI3K) pathway hyperactivation and endocrine therapy resistance. SOLAR-1 is a phase 3, randomized, double-blind study in 262 men and postmenopausal women with HR+, HER2− ABC who progressed on or after aromatase inhibitor treatment. Pts were treated with alpelisib (ALP), an oral selective PI3Kα inhibitor, or placebo (PBO), + fulvestrant (FUL). Here we report results by major region from SOLAR-1. Methods: Pts (N=572) received ALP 300 mg or PBO once daily + FUL 500 mg every 28 days × Cycle 1, Day 15. Median PFS (mPFS) was estimated by Kaplan-Meier analysis. Results: Data for Japan will be presented separately and were excluded. Results: Pts (PIK3CA-mutant (mut) cohort) were enrolled in Europe (EU; n=173), North America (NA; n=43), Asia (n=34), and Latin America (LA; n=31). Pts in the ALP arm (vs PBO) in EU had mPFS of 11.0 mo (vs 3.6 mo; HR=0.56; 95% CI, 0.39-0.81) and overall response rate (ORR) of 27.9% (vs 11.5%); in NA, mPFS...
was 15.2 mo (vs 3.6 mo; HR=0.41; 95% CI, 0.19-0.91), ORR 21.1% (vs 16.7%); in Asia, mPFS was 14.5 mo (vs 9.0 mo; HR=0.55; 95% CI, 0.20-1.51), ORR 46.7% (vs 10.5%); in LA, mPFS was 9.4 mo (vs 12.9 mo; HR=1.43; 95% CI, 0.54-3.79), ORR 21.4% (vs 17.6%). Among all pts (mut and non-mut) in the ALP arm, median ALP exposure in EU, NA, Asia, LA, and overall was 5.5, 5.5, 7.6, 6.0, and 5.5 mo, respectively. Median average daily dose for ALP ranged from 260.2-298.1 mg/d. Most common all-grade adverse events were hyperglycemia in EU (13% vs 12%), anemia in EU (8% vs 7%), diarrhea in EU, NA, LA (61%, 66%, 53%); and decreased appetite (58%) in Asia. Conclusions: In SOLAR-1, PFS in the PIK3CA-mut cohort was generally improved in the overall population and across regions in the ALP vs PRO arm; however, low PFS events and pt numbers in some regions may limit conclusions. Disclosures of Interest: Authors of research articles should disclose any financial arrangement they may have with a company whose product is pertinent to the submitted manuscript or with a company making a competing product.

P19
RANDOMIZED, DOUBLE-BLIND, PHASE 3 STUDY OF PEMBROLIZUMAB (vs PLACEO) COMBINED WITH NEOADJUVANT CHEMOTHERAPY AND ADJUVANT ENDOCRINE THERAPY FOR HIGH-RISK, EARLY-STAGE ER+/HER2 – BREAST CANCER
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Problem statement: A high-risk subgroup of ERs/HER2– breast cancer (BC) is characterized by high-grade tumors, decreased sensitivity to endocrine therapy (ET), higher responsiveness to chemotherapy (CT), and worse prognosis. Prior studies suggest that increased pathological complete response (pCR) rates after neoadjuvant CT may have a substantial impact on patients for high-risk, early-stage HR+/HER2– BC. KEYNOTE-756 (ClinicalTrials.gov, NCT03725059) is a global, randomized, double-blind, phase 3 study of pembrolizumab (vs placebo) + CT as neoadjuvant treatment followed by pembrolizumab (vs placebo) + ET as adjuvant treatment for patients with high-risk, early-stage ER+/HER2– BC. METHODS: Stratification of patients with T1c-2 C1N1-2 (tumor size ≥2 cm) or T3-4 C0-2 grade 3, invasive, ducal ER+/HER2– BC by lymph node involvement (positive vs negative), tumor PD-L1 status (positive [≥50%] vs negative [≤50%]), ER positivity (ER+ ≥10% vs ER– 10%), and anthracycline dosing schedule (every 3 weeks [Q2W] vs Q1W), will be followed by 1:1 randomization to neoadjuvant treatment with pembrolizumab 200 mg Q3W or placebo combined with paclitaxel (80 mg/m2 Q1W) for 4 cycles, followed by doxorubicin (60 mg/m2) or epirubicin (100 mg/m2), each with cyclophosphamide (600 mg/m2) Q3/W for 4 cycles. After definitive surgery (± radiation therapy, as indicated), patients will receive adjuvant pembrolizumab (200 mg Q3W) or placebo for 9 more administrations combined with ET, which can be given for ≤10 years. Crossover is not permitted between treatment cohorts when transitioning from neoadjuvant to adjuvant treatment. Cophymary endpoints are pCR rate (ypT0/Tis ypN0) and event-free survival (EFS). Secondary endpoints include ypT0/Tis and ypT0 ypN0 pCR rates in all patients and all 3 pCR definitions in those with PD-L1+ tumors, EFS in patients with PD-L1+ tumors, overall survival, safety, and health-related quality of life. Enrollment is currently ongoing. Author disclosures: These authors report financial relationships for themselves or family member: JC (Roche, Novartis, Eisa, Celgene, Pfizer, AstraZeneca, Cellstessa Biotech, Biothera, Merus, Seattle Genetics); FC (Amgen, Astellas/Medivation, AstraZeneca, Celgene, Daiichi-Sankyo, Eisai, GE Oncology, Genentech, GlaxoSmithKline, Macrogenics, Merck Sharp & Dohme, Merus BV, Mylan, Mundipharma, Novartis, Pfizer, Pierre-Fabre, Roche, Sanofi, Seattle Genetics, Teva); AB (Merck, Pfizer, Radius, Immunomedics, Novartis); FA (AstraZeneca, Novartis, Pfizer, Lilly, Roche); DWC (Merck, Pfizer, Novartis, AstraZeneca); HM (Merck, Spectrum Pharma, Syndax, OBI Pharma, Caliterra Biosciences, Roche, Genentech, Lilly, Peregrine Pharma, TapImmune, Amgen, Puma Biotechnology, Immunomedics, Pfizer); MT (Merck, Genentech, Immunomedics, Celgene, Aduro, Pfizer, G1 Therapeutics); SI (Novartis, Bristol Meyers Squibb, Merck, Roche-Genentech, Puma Biotechnology, Pfizer, Seattle Genetics); PS (Pfizer, Boehringer, Bayer, Puma, Eisai, Celgene, Genentech/Roche); NH (MSD, Roche); CD (Amgen, MSD, Pfizer, Teva, Novartis, Sividon Diagnostics); CI (MSD); LJM, KMH, and VK are employees of Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA, and may hold stock/options in Merck & Co., Inc., Kenilworth, NJ, USA. Funding source: Funding for this study was provided by Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA. Medical writing and editorial assistance were provided by Rajni Parthasarathy, PhD, and Diane Neer, ELS, MedThink SciCom. This assistance was funded by Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

P20
FLUORESCENCE IN SILU HYBRIDIZATION ANALYSIS OF HER2 3+ BREAST CANCER PATIENTS WITH NEOADJUVANT CHEMOTHERAPY USING PERTUZUMAB AND TRASTUZUMAB
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Problem statement: HER2 is amplified approximately 20% of breast cancers and HER2 receptor targeting therapy is associated with a significant improvements in disease-free and overall survival. In NeoSphere and TYPHAENA clinical trials, the pathologic complete remission (pCR) rate was significantly increased when combined with pertuzumab and trastuzumab treatment. Although the efficacy and safety of anti-HER2 dual blockade therapy has been reported, the markers that predict the response are still unclear. This study aimed to investigate the relationship between the HER2 and centromere17 (CEP17) ratio and the pCR to neoadjuvant...
therapy based on trastuzumab and pertuzumab. **Methods:** Twenty HER2 3+ breast cancer patients who had received neoadjuvant docetaxel, carboplatin, trastuzumab and pertuzumab (TCHP) therapy were included in this study. HER2/CEP17 ratio was measured by fluorescence in situ hybridization analysis. The relationship between HER2/CEP17 ratio and tumor pCR status (ypT0 ypN0) was investigated. **Results:** The Median age was 47.5 years (range: 36-62). 30% of the patients were hormone receptor (HR) positive and 70% of the patients were HR negative. The pCR rate in the breast and axilla was 70%. The patients who experienced a pCR had a median HER2/CEP17 ratio of 7.07 (range: 3.16-10.40) in comparison with median ratio of 4.89 (range: 1.06-6.15) if they did not (p=0.019). **Conclusion:** pCR was highly correlated with HER2/CEP17 ratio in the neoadjuvant setting with anti-HER2 dual blockade. This suggests that the HER2/CEP17 ratio can be used as a predictive marker to predict pCR in neoadjuvant trastuzumab and pertuzumab therapy.

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**P22**

**FACTORS ASSOCIATED WITH FALSE NEGATIVE RATE OF SENTINEL LYMPH NODE BIOPSY IN BREAST CANCER PATIENTS**

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**Problem Statement:** Sentinel lymph node (SLN) biopsy is the routine surgical procedure for axillary nodal staging. The reported false negative rate varies widely up to 33%. Contraindications to SLNB are still debated. Weighing the benefits of doing a minimally invasive procedure versus risk of understaging has important implications for adjuvant therapy, and the possibility of persistent axillary nodal disease. **Methods:** Data was obtained from clinical records of Chinese General Hospital from January 2005 to December 2016. Patients underwent SLN biopsy using methylene blue dye followed by completion axillary lymph node (ALN) dissection. SLN and non-SLN were then submitted to pathology for H&E staining. Clinical factors, tumor and SLN characteristics, were included. **Results:** 558 patients underwent SLN biopsy with completion ALN dissection. There were 178 (31.9%) cases of true positive (TP) SLN biopsy, 331 (59.3%) cases of true negative (TN) and 45 (8.1%) cases of false negative (FN) SLN biopsy, with an overall FN rate of 20.18%. Age, gender, tumor palpability, lymph node palpability, laterality, location, clinical stage, menopause, tumor size, histopathology, lymphovascular invasion, Nottingham grade and hormonal status did not demonstrate any statistical significance. Univariate analysis showed statistical significance in FN rates in patients who underwent neoadjuvant chemotherapy (14.77%). **Conclusion:** Significant factors predictive of FN rate were identified. Similar to other studies, identification of multiple SLN and increased number of positive non-SLN resulted to improved FN rate. Other factors that may have contributed to the high FN rate in this study but were not included are the surgeon’s experience, use of IHC stains, biopsy technique and type of dye used. Injection of radioactive colloid in combination with blue dye improves the ability to identify multiple sentinel nodes compared with the use of blue dye alone. In this study, blue dye alone was used which may also account for the high FN rate.

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**P21**

**A CASE OF METAPLASTIC BREAST CARCINOMA PRESENTING AS A BLEEDING BREAST MASS**

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A 44/F came to the ER for massive bleeding from an ulcerated right breast mass. She was treated with mastectomy for local control of the tumor however the tumor progressed rapidly to the axillary lymph nodes and recurred aggressively. When the histopathologic diagnosis of metaplastic breast carcinoma was finally available, the lesion was already locally advanced and it had already metastasized to the lung. Despite the difficulty, there has been an increase in the diagnosis of metaplastic breast carcinoma (MBC). The focus now is to detect it early and institute appropriate management to improve the known survival rates. While the role of surgery remains central, radiotherapy has been shown to prolong overall survival and chemotherapy may give some benefit according to newer studies. **Problem statement:** There is still difficulty in diagnosing metaplastic breast carcinoma because of resources and low degree of suspicion. **Methods:** This is a retrospective analysis in the diagnosis and management of a case of metaplastic breast carcinoma. **Results:** Using immunohistopathology, metaplastic breast carcinoma was identified and possible management options in literature were explored. **Conclusion:** Despite the difficulty, there has been an increase in the diagnosis of metaplastic breast carcinoma (MBC). The focus now is to detect it early and institute appropriate management to improve the known survival rates. While the role of surgery remains central, radiotherapy has been shown to prolong overall survival and chemotherapy may give some benefit according to newer studies.

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**P23**

**CAN WE AVOID AXILLARY LYMPH NODE DISSECTION (ALND) IN PATIENTS WITH 1-2 POSITIVE SENTINEL/LOW AXILLARY LYMPH NODES (SLN/LAS+) IN THE INDIAN SETTING?**

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PROBLEM STATEMENT: The ACOSOG Z0011 study, heralded as a “practice changing” trial, suggested women with T1-2 breast cancer (EBC) with 1-2 SLN+, undergoing breast conservation therapy, need not be offered further Axillary Lymph Node Dissection (ALND). However, whether these results are applicable to all women in the Indian setting, remains debatable. METHODS: All women at our center with cNO undergo Low Axillary Sampling (LAS), ALND is performed only if LAS positive. We analyzed data from 2013-2015 to detect the percentage of additional LN positive(LN+) in ALND in women with LAS+ and compared it ACOZOG Z11 trial. Additionally we evaluated the risk of non LAS positive LN using the MD Anderson Normogram (NM) in our cohort.

RESULTS: Of the 963 cNO with EBC who underwent LAS, 317 (33%)were LN+ on pathology, Among these, 266 (83.9%) patients had 1-2 LN+, 26(8.2%)patients had 3 LN+and 25 (7.9%)had 4 LN+. In ACOZOG Z-11, 1-2 SLN+ was 40% in ALND and in 27.3%, there were additional LN+ in ALND, whereas in our cohort 36.6% had additional LN+ on ALND. The NM also predicted more than 10% risk of additional LN+ in axilla in 37.7% of our cohort. Demographic features in the ACOSOG Z11 are different from those in our study, with a median pT1.7 cm in ACOSOG Z-11, as against 2.8 cm in our cohort. LN positivity is an all macro-metastasis in our study compared to 45% micro-metastasis in ACOZOG Z11. Grade 3 tumors accounted for 28-30% of their population while it comprised 65.3% of our cohort. CONCLUSION: In our data, 31.6% of women with EBC with 1-2LN+ in LAS had additional LN+ on ALND. The actual percentage may even be higher if we include multiple sections from LN as was done in the ACOSOG Z11. Keeping in mind the above, it may not be appropriate to apply the results of the ACOSOGZ11 trial directly to our general population. Possibly, only a select subset of patients who match the trial population of the ACOSOG Z11 could be offered observation of the axilla in spite of1-2 nodes positive and validated NM can be used to identify high risk patients.

P24 BREAST CARCINOMA WITH MEDULLARY FEATURES.
A CLINICOPATHOLOGIC STUDY

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Problem statement: Breast carcinoma with medullary features (BCMF) has been described by WHO as a separate overlapping group of breast tumors consisting of medullary carcinoma (typical medullary carcinoma and invasive carcinoma no special type (NST) with medullary features in 11 (55%) patients. The proportions of ER and PR positivity were 30% and 25% respectively. Her 2 overexpression was seen in 6 (30%) of the cases and neuroendocrine differentiation was observed in 1 (5%) of the cases. Triple negative tumors were detected in 13 (65%) cases. All but one (95%) cases were classified as Grade III tumors. Metastatic axillary lymphadenopathy was detected in 11 (55%) patients. Fifteen (75%) patients received adjuvant chemotherapy, 14 (70%) patients received adjuvant radiotherapy and 6 (30%) patients received hormonal therapy. The median follow-up was 90.5 months (range 2-171 months). The 5-year overall survival was 85%. Conclusions: BCMF is a rare histological subtype of breast cancer. Despite its poor and aggressive pathological characteristics, BCMF is associated with a more favorable clinical course compared to invasive ductal carcinomas. The treatment approach is considered similar to that for invasive ductal carcinoma and includes mastectomy or breast conserving surgery along with chemotherapy or radiation depending on the histopathological characteristics and stage of the tumor.

medullary carcinoma was detected in 3 (15%) patients, atypical medullary carcinoma in 6 (30%) and invasive carcinoma no special type (NST) with medullary features in 11 (55%) patients. The proportions of ER and PR positivity were 30% and 25% respectively. Her 2 overexpression was seen in 6 (30%) of the cases and neuroendocrine differentiation was observed in 1 (5%) of the cases. Triple negative tumors were detected in 13 (65%) cases. All but one (95%) cases were classified as Grade III tumors. Metastatic axillary lymphadenopathy was detected in 11 (55%) patients. Fifteen (75%) patients received adjuvant chemotherapy, 14 (70%) patients received adjuvant radiotherapy and 6 (30%) patients received hormonal therapy. The median follow-up was 90.5 months (range 2-171 months). The 5-year overall survival was 85%. Conclusions: BCMF is a rare histological subtype of breast cancer. Despite its poor and aggressive pathological characteristics, BCMF is associated with a more favorable clinical course compared to invasive ductal carcinomas. The treatment approach is considered similar to that for invasive ductal carcinoma and includes mastectomy or breast conserving surgery along with chemotherapy or radiation depending on the histopathological characteristics and stage of the tumor.

P25 ADENOID CYSTIC CARCINOMA OF THE BREAST

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Problem statement: Adenoid cystic carcinoma of the breast is a very rare tumor comprising less than 0.1% of all breast cancers. It was first described by Geschickter and Copeland in 1945. The aim of this study is to present the clinical and pathological characteristics of 2 cases of adenoid cystic carcinoma of the breast who treated at our institution, along with a review of the relevant literature. Material and methods: The medical records of 2 patients who were diagnosed with adenoid cystic carcinoma of the breast, over a 2 year period were retrospectively reviewed. Clinical, mammographic, sonographic and pathological findings were analyzed. A review of the literature was also carried out. Results: From May 2017 to April 2019, two pathologically proven cases of adenoid cystic carcinoma of the breast were identified. Both patients presented with a palpable left breast mass. The first patient, aged 57 years old, underwent mastectomy and the second patient, aged 70 years old, underwent breast-conserving surgery. The histopathological examination revealed a coexisting Grade III breast carcinoma with medullary features in the first patient and negative sentinel nodes in both patients. On immunohistochemical analysis, both cases were triplenegative. Adjuvant chemotherapy was administered to the first patient and adjuvant radiotherapy to the second. Both patients do well without any sign of recurrence 24 and 12 months after surgery respectively. Conclusions: Adenoid cystic carcinoma of the breast is a very rare malignancy that usually runs an indolent clinical course despite its triple-negative status. The incidence of axillary node involvement is low. Due to the rarity of these tumors, there is currently no consensus on the optimal treatment approach. Surgical excision is the mainstay of treatment. Further research is needed to assess the extent of axillary surgery and the role of adjuvant therapy.
Problem statement: Treatment for elderly breast cancer patients has not been established. In our country, the proportion of breast cancer aged 80 years and over was only 2.8% in 1975, after that increased to 8.2% in 2014. Surgery is recommended for elderly people with breast cancer according to the guidelines. Although there is no consensus for patients over 80 years old. Methods: Of the 630 patients who underwent surgery for breast cancer from 2007 to 2018. 54 primary breast cancer patients aged 80 and over (80 to 93 years old) were included. Clinicopathological factors (main complaint, stage, co-morbidity, tumor size, surgery, drug therapy, radiotherapy, ER, PgR, HER2, ADL change) were examined. Results: The chief complaints were 39 cases (72%) with mass palpability, 9 cases (17%) with abnormalities such as medical checkup, and 6 cases (11%) with other cases such as PET/CT in the case of other diseases. The surgery was performed in 21 patients with partial mastectomy, 13 patients with total mastectomy (without reconstruction). There were 37 sentinel lymph node biopsies and 12 axillary lymph node dissections (including 5 sentinel node positive cases). The stages are 0: 5(3.3%), I: 28(51%), II: 20 (37%), III: 1 (1.9%). Histopathologically, estrogen receptor (ER) positive 45 cases (83%), progesterone receptor (PgR) positive 35 cases (67%) and HER2 positive 20 cases (38%). Hormonal therapy was given to 26 patients. There were 4 patients who received chemotherapy. Radiation therapy was given to eight patients. Conclusion: Older people often can’t perform standard treatment because of co-morbidities. Therefore, radical surgical treatment may be important. There is no stipulation regarding the upper limit of the age of the patient. Early detection for breast cancer is important even in the elderly people, but the ADL and PS are often difficult to receive due to the decrease in PS. It is necessary to consider the correspondence in individual cases, because the elderly people over 80 years old and the super elderly people over 90 years old are inferior in physical function by aging. Aromatase inhibitors are effective if they are hormone sensitive.

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Does Metastatic Inflammatory Breast Cancer Have a Worse Prognosis After Surgery?

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Problem statement: Inflammatory breast cancer (IBC) is a rare and aggressive form of breast cancer with poor prognosis and is often resistant to chemotherapy with risk of early recurrence and systemic spread of disease. The indication of local control for metastatic inflammatory breast cancer (MIBC) is controversial. We hypothesized that the local control is of clinical value, even for MIBC. Methods: This retrospective analysis consisted of 52 patients, comprising 37 patients with Nonmetastatic IBC (NMIBC) and 15 patients with MIBC who received similar multidisciplinary treatment between 2005 and 2017 at our hospital. Clinical and pathological factors, overall survival (OS) and recurrences were compared. Results: Among 11,610 operated cases from 2005 to 2017 excluding Stage IV, 37 cases (0.3%) had IBC. During the period, 15 cases of MIBC underwent operation. The median age of all was 55 years old. The subtypes were hormone receptor (HR)/HER2+ in 27(51.9%), HR+/HER2+ in 3(5.8%), HR-/HER2+ in 13(25%), triple negative in 9(17.3%). All cases had received neoadjuvant chemotherapy, neoadjuvant endocrine therapy for 4 cases, and anti-HER2 therapy for 11 cases. The pCR for primary lesion was achieved in 9 cases, of which 2 cases had MIBC. None of the 4 cases with NMIBC achieved pCR had recurrence. Two MIBC cases achieved pCR showed cCR in distant metastatic sites and neither of the 2 cases had new lesion at observation period. With a median follow-up of 72.5 months, the 5-year postoperative cancer-specific survival rate was 100% in pCR cases, even with MIBC. Among patients with NMIBC, 15 had distant recurrence and 1 had isolated locoregional recurrence, who did not have an adjuvant radiotherapy. The 5-year postoperative OS was 56.9% in all. There was no difference in OS between patients with NMIBC and MIBC (median OS: 59 months in NMIBC vs 60.5 months in MIBC). Ten of 15 cases in the MIBC group died. Conclusion: Although IBC is considered a unique biologic subtype and having poor outcomes, our study suggested that long-term survival was achieved in some cases especially those with pCR, even among patients with MIBC, indicating that multidisciplinary approach could improve the outcome.

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How Patient Advocates and Researchers Work Together in Precision* to Identify Low-Risk Ductal Carcinoma in Situ (DCIS) that May Not Need Aggressive Treatment

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Problem Statement: Ductal carcinoma in situ (DCIS) now accounts for 15-25% of all ‘breast cancers’ in over 60,000 women annually worldwide. Most receive invasive breast cancer (IBC) treatments, with questionable benefit and many complications, including financial burdens. Studies show most DCIS never becomes IBC, even if left untreated. PRECISION, an international consortium of clinicians, scientists and patient advocates, studies the biology of DCIS to distinguish low-risk from high-risk DCIS to build confidence in Active Surveillance (AS) as an option for low-risk DCIS. Patient advocates are fully integrated into PRECISION and 3 national clinical trials: LORID (NL), LORIS (UK) and COMET (US) studying whether or not AS is equivalent to surgery for low-risk DCIS. PRECISION uses samples from each trial and other cohorts. Methods: The Patient Advocate Involvement Panel (PAIP) includes women from each country: NL, UK, and US. PAIP helps shape ongoing projects into a cohesive team, while encouraging new projects to improve clinical practice. We: Foster teams for better outcomes for women with DCIS; Help design informational tools for clinicians and patients; Share international differences in services, culture, and expectations. Measure patient involvement impact. PAIP
participates in Steering Group, Work Packages, and internal and external communications, including: conferences, reviews, website and newsletter content, interviews, publications, and social media campaigns. Results: PAIP has helped: a) develop PRECISION and trial information; b) offer patient-oriented ideas/collaborations; c) resolve international contract barriers; d) identify additional cohorts; e) suggest recruitment improvements; f) give feedback on surveys; g) co-author publications; h) build relationships with postdocs; and i) engage the public and clinicians on DCIS dilemmas in each country. Additional PAIP plans: reduce pathology DCIS grade discordance within and between countries (a critical issue for women diagnosed with DCIS). Conclusions: We need to better understand DCIS subtypes, accurately stratify risks for IBC, harmonize communication, and improve pathology standards. PAIP works closely with PRECISION researchers and communicates evidence about risk factors for women who may or may not need treatment for DCIS. *PRECISION is sponsored by a Cancer Research UK and improve pathology standards. PAIP works closely with PRECISION researchers and communicates evidence about risk factors for women who may or may not need treatment for DCIS. *PRECISION is sponsored by a Cancer Research UK Grand Challenge Award, which is also funded by the Dutch Cancer Society.

P29
SOMATIC MUTATION IN BREAST CANCER THROUGH NEXT GENERATION SEQUENCING: A SINGLE INSTITUTION EXPERIENCE
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Problem statement: The next generation sequencing (NGS) technology has the advantages of high speed, high throughput and high accuracy. Because of these advantages, it is used in various cancer fields. Several gene pannels have been applied to breast cancer to assess risk and determine treatment direction accordingly. The purpose of this study was to improve the prognosis and future treatment of patients with breast cancer by applying NGS. Methods: From January 2018 to December 2018, we studied patients who underwent surgery at Kosin University Gospel Hospital. The study patients were from stage 1 to stage 3 of breast cancer. Patients who were not able to undergo surgery or who had more than stage 4 patients were excluded. This study included patients who underwent Neo-systemic therapy(NST). NGS was performed postoperatively. And in patients who underwent NST, NGS proceeded to pre-chemotherapy specimens. Results: The expression of somatic mutation was different for each type of breast cancer. Most of them have been observed to have more than two mutations. Overall, TP53, PIK3CA, and ERBB2 showed high expression frequencies. Figure1 shows the frequency of mutation incidence frequent in each type of patient. Conclusion: Various types of somatic mutations are also expressed in breast cancer, and they are different according to each type. These various manifestations may be associated with the prognosis of breast cancer. Further studies are needed to determine for them.

P30
A RANDOMIZED CONTROLLED TRIAL TO COMPARE THE EFFICACY OF HYPERBARIC OXYGEN ALONG WITH NEOADJUVANT CHEMOTHERAPY WITH NEOADJUVANT CHEMOTHERAPY ALONE FOR CARCINOMA BREAST
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Problem Statement: Carcinoma breast continues to be a major cause of mortality and morbidity worldwide. Incidence of breast cancer has particularly risen in young females in 3rd and 4th decade. In large, aggressive cancers, neoadjuvant chemotherapy can reduce tumour bulk and breast-conserving surgeries may be done, albeit with a significant risk of recurrence. With a novel neoadjuvant regimen, it may be possible to downsize tumour to achieve cosmetically better results and allow conservative surgery with a better prognosis. Methods: A randomized prospective study was conducted on thirty patients of breast cancer from stage IIB onwards and were randomly allocated into two groups. Group A included breast cancer patients who underwent neoadjuvant chemotherapy (comprising cyclophosphamide, 5-fluorouracil and epirubicin) along with hyperbaric oxygen therapy (HBOT) given thrice during each chemotherapy cycle (before, during and after chemotherapy). Group B comprised breast cancer patients who received only neoadjuvant chemotherapy as described. Clinical and ultrasonographic assessment were done for tumour size and volume. Repeat staging was also performed post-therapy. All patients thereafter underwent modified radical mastectomy (MRM) and histopathological specimens assessed for tumour-free margins. Data was compared using Student t test and Mann-Whitney test with p-value of Results: Patients given neoadjuvant chemotherapy with HBOT (group A) showed a significant decrease in the percentage reduction of volume as compared to patients treated with neoadjuvant chemotherapy alone (group B) (p = 0.05). There was also a significant reduction in the largest diameter in Group A. There was down-staging of tumour observed in all stages in group A whereas down-staging was mostly observed in advanced stages (Stage IIIa and IIB) in Group B. Conclusions: Neoadjuvant chemotherapy along with hyperbaric oxygen can significantly downstage advanced breast cancers pre-operatively, allowing breast-conserving surgery to be done with tumour-free margins. Over long term, the modalities used are also expected to reduce the recurrence rates of these cancers on follow-up. There is a promising scope of larger studies using hyperbaric oxygen to reproduce similar findings and determine better patient selectivity using on molecular and hormone status of these tumours.
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A CALL TO CHANGE WORLD GUIDELINES: MEDICAL THERAPY 1st
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Problem Statement: To give the patient the benefit of up to date knowledge and treatment. Before the introduction of systemic medical therapy in 1970, local treatment alone made no impact on survival. Tumour Biology is currently the determining guide in Breast Cancer management. Methods: In daily practice, all newly presenting patients were considered having potential systemic disease and treated medically before surgery, the goal being to treat the disease locally and systemically. Today we recognize the crucial relevance of Tumour markers for individualizing treatments - now mandatory before a medical decision is taken. Pathology report-guided treatment shrunk possible micro-metastases, regional and breast tumour. Medical Rx is not a question of simply saving the Breast – it is to treat the disease. Results: We gained experience from treating this disease – all can be treated medically first. We accepted the concept of treating with more specific available therapies before any invasive surgery. Patients are happier to see as well the efficacy of given Rx and better tolerate the toxicity of Rx. Offered opportunity for 2nd look residual tumour biology. Conclusion: The Modern treatment – Enough experience to adopt the modern route. First, Medical Systemic Therapy (according to tumour characteristics), Followed by Surgery (to identify resistant clones which further help in improving management). Medical Rx given First – The present + the future. The disease is a systemic disease – deal with it at diagnosis. We believe that this management approach is the way to go. This technique gives a wonderful opportunity to continuously assess response during treatment – a marker of in-vivo systemic response and monitor of in-vivo information. The future will be Medical therapy only. The aim is to just Rx the disease according to its own identity – not the unknown stage – Benefiting all – physically and psychologically.

P32
RISK OF IPSILATERAL BREAST TUMOR RECURRENT IN BREAST CONSERVING SURGERY AFTER NEOADJUVANT THERAPY
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Problem statement: Local recurrence is the most important problem for patients who underwent breast conserving surgery after neoadjuvant chemotherapy (NAC). In this study, we analyzed the risk of local recurrence in these patients. Methods: From 2011 to 2015, we identified patients treated with NAC and breast conserving therapy (BCT) for all stages of breast cancer. Chi-square test, Fisher’s exact test and logistic regression analysis were performed to determine the relationship between the various factors and local recurrence. We used the Kaplan-Meier curve analysis to determine if there was a difference in local recurrence free survival according to margin status. Results: A total of 294 patients were included. The median age was 45 years [range 25-69] and median follow-up for all patients was 13.5 months. Local recurrence was noted in 24 (8.2%) patients. Pathologic complete response (pCR) was achieved in 23 (7.8%) patients, and all of these patients had no local recurrence. Margin status was positive in 10 (3.4%) patients. There was a slight decrease in the risk of local recurrence associated with estrogen receptor (ER) positivity (HR = 0.634, p = 0.292) and an increase in human epidermal growth factor receptor 2 (HER 2) positivity (HR = 2.2, p = 0.128). There was no difference in local recurrence free survival for margin status. No statistically significant risk factors were identified in this study. Conclusions: The results of this study suggested that there was no difference in local recurrence between the various factors such as age, pathologic T stage, pathologic N stage, histology, hormone receptors, HER 2 receptor, axillary surgery and margin status in the patients treated with NAC and BCT. Further study is needed with a larger number of patients over a longer period to identify the risk factors for local recurrence.

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RADIOLOGIC COMPLETE RESPONSE AFTER NEOADJUVANT CHEMOTHERAPY IN ADVANCED BREAST CANCER CAN PREDICT SURVIVAL OUTCOME, BUT NOT PATHOLOGIC COMPLETE RESPONSE
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Problem statement: Advances in neoadjuvant chemotherapy(NAC) reduced the extent of breast and axillary surgery, but still have yielded favorable oncologic outcome. Predicting pathologic complete response (pCR) and planning the surgery after NAC is commonly done with the help of radiologic imaging. We investigated the radiologic complete response (rCR) of axillary nodes and breast in correlation with pathologic complete response and survival outcome. Method: We retrospectively reviewed 1042 breast cancer patients in a single institution from January 2008 to December 2016, who had completed chemotherapy preoperatively. The clinical response to treatment was evaluated by MRI and ultrasonography, in case of discordance between the two modalities, the results of the MRI was taken. Radiologic and pathologic complete responses were compared using Cohen’s Kappa statistic, and disease-free survival (DFS) rates of each group were calculated. Result: The axillary rCR and pCR rates following NAC were 27.1%(283/1042) and 52.0% (542/1042). In the breast, rCR and pCR rates were 16.4% (171/1042) and 28.2% (294/1042). Axillary rCR corresponded to axillary pCR by 88.0% (+positive predictive value), with Cohen’s kappa value of 0.384, interpreted as ‘fair’, but sensitivity to detect axillary pCR was only 45.9%. Similarly, breast rCR corresponded to breast pCR by 78.4%, with Cohen’s kappa value of 0.465, meaning ‘moderate’, but sensitivity was 45.6%. Patients achieving breast rCR presented significantly higher 5-year DFS rates than patients without rCR (89.8% vs 67.9%, HR: 0.29; p=0.001) This is comparable to 5-year DFS of patients with breast pCR (88.1% vs.64.8%, HR: 0.25; p=0.001). Conclusion: Radiologic complete response may not accurately correlate with pathologic complete response but may predict the disease-free survival of patients treated with neoadjuvant chemotherapy.
PERIAEOLAR ROUND BLOCK TECHNIQUE OF BREAST CONSERVING SURGERY: A SINGLE INSTITUTION EXPERIENCE
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Problem statement: Round block technique is a volume displacement technique to reshape breast after breast-conserving surgery (BCS) especially with tumor in the superior or lateral side of nipple-areola-complex (NAC). Generally, when the tumor is located inferior or medial side of the NAC, flap surgery or tennis racket method have been required. The purpose of this study is to evaluate the usefulness of round block technique for at all location of tumor. Methods: A total of 73 patients were identified. Round block technique after BCS at Kosin University hospital from February 2018 to April 2019. Preoperative markings varied based on tumor size and location. After the wide excision from general surgery, the remnant glandular tissue was lifted off from pectoralis muscle for approximation. After that we dissected skin from glandular tissue extensively to release dimpling and de-epithelialized between two circles. The measured results were assessed for 1-13months follow up. Results: The median weight of resected tumor was 29g (range 5-74g) by electronic scale. The tumor was located on superolateral (53%) most, inferolateral (30%), superomedial (10%), inferomedial (7%). Median nipple-tumor distance was 5.6cm, maximally 10cm (range 1-10cm) Conclusion: Round block technique is a method that can produce good cosmetic results after BCS regardless of position or direction in patients who do not want flap surgery.

ELEVATED LEVELS OF SERUM TUMOR MAKER P53 IS A PROGNOSTIC PARAMETER AND A MONITORING BIOMAKER FOR PATIENTS WHO HAD UNDERTaken SURGICAL RESECTION IN BREAST CANCER
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Problem statement: Elevated levels of p53 antibody is expected as an indicator of early diagnosis and a parameter of recurrence in breast cancer. Preoperative high level of p53 antibody in breast cancer patients tend to associate with worse prognosis. This study investigated the prognostic value of preoperative serum p53 levels, and the significance as a biomarker to evaluate a recurrence after surgical resections in breast cancer. Methods: Preoperative serum p53 levels were measured in total of 259 breast cancer patients, who had undergone either a total mastectomy or a partial mastectomy, through 2010 to 2015 in our facility. Patients with elevated levels of p53 (29 patients) and normal levels of p53 (230 patients) were compared to analyze the association of a marker level with the prognosis and the indication to diagnose recurrence in breast cancer. Results: High p53 mutation was identified in 29 (11%) patients. The size of tumor, staging, and pathology did not associate with the level of p53. Patients with high p53 correlated to the high score of nuclear grade (NG2,3) and the high percentage of Ki-67 (> 14%), which leading to the worse prognosis. Triple negative breast cancer was the major molecular subtype in the group of high p53 comparing with the group of low p53. Survival analysis using the Kaplan-Meier method was performed to examine DFS and OS of high serum level of p53 patients. Patients with high level of p53 were significantly showed worse DFS than a normal group. Serum level of p53 was also reflected to the recurrence and metastasis of postoperative breast cancer. Some patients with the group of high p53, who got increase p53 level as emerging the local recurrence and metastasis even though they had gotten the normal levels of p53 after surgical resections. It showed that the increasing of the level of p53 was reflected to the recurrence and metastasis of tumors after surgical resections in breast cancer. Conclusions: This study suggests that preoperative level of p53 can be an independent prognostic parameter and a monitoring biomarker for breast cancer.
evaluate whether risk-based screening will improve uptake of chemoprevention in the WISDOM Study population.

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COMPARISON OF ESTRO AND RTOG CONTOURING GUIDELINES FOR TARGET VOLUME DELINEATION IN EARLY STAGE BREAST CANCERS
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Problem Statement: Adjunct radiotherapy (RT), including regional lymph node (RLN) irradiation is an important treatment in early stage breast cancer patients after breast-conserving surgery. The Radiation Therapy Oncology Group (RTOG) and European Society for Radiotherapy and Oncology (ESTRO) have published contouring guidelines to aid Radiation Oncologists (ROs). Our primary aim was to quantitatively compare target volumes delineated by ROs specializing in breast cancer, to assess if either guideline has superior contouring reproducibility. Methods: Three ROs contoured breast clinical target volumes (CTVs), axillary lymph node levels 1–3, supraclavicular and internal mammary nodal (CTVn_1MN) volumes for 8 post-operative (4 right-sided and 4 left-sided) patients, providing 24 sets of observations. The inter-observer variability in contouring was measured by the Generalized Dice Similarity Coefficient (DSC), with a value of 1.0 indicating complete overlap and 0.0 indicating no overlap. The DSC was also used to assess the differences between volumes based on ESTRO and RTOG guidelines, delineated by the same RO. Results: Within each guideline, the breast CTV contours showed the highest level of agreement between the ROs. This was also the only volume to show significant difference in the DSC mean value, with 0.92 [standard deviation 0.04] for ESTRO guidelines compared with 0.90 (0.03) for the RTOG guidelines (p=0.031). The mean DSC for CTVn_1MN was 0.63 (0.10) for ESTRO and 0.62 (0.20) for RTOG guidelines, showing the least level of agreement for both guidelines. Within the axillary nodal volumes, level 1 showed the greatest agreement among the ROs for both ESTRO and RTOG guidelines with a mean DSC of 0.810.08) & 0.820.06) respectively. The range of mean DSC values for ESTRO and RTOG guidelines was 0.66-0.92 and 0.62-0.90 respectively and when comparing volumes produced using ESTRO to those using the RTOG guidelines the range of mean DSCs was 0.52-0.94.

Conclusion: Only the breast CTV volume suggested greater RO consistency with the ESTRO guidelines, although the discrepancy was small and unlikely to be of clinical significance. All other volumes showed no significant difference between ESTRO and RTOG guidelines. Overall, neither guideline showed greater reproducibility between ROs.

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A DOSIMETRIC COMPARISON OF TANGENT FIF, VMAT AND HYBRID-VMAT FOR CHEST WALL RADIATION THERAPY WITH AEROFORM TISSUE
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Purpose/Objective(s): AeroForm tissue expander (AirXpanders, Inc) for breast reconstruction post mastectomy presents dose inhomogeneity around the high density stainless steel material and low density CO2 using tangent beam. Three planning strategies: Tangent with field-in-field (FIF), volumetric modulated arc therapy (VMAT) and hybrid of tangent with VMAT can reduce the dose inhomogeneity. This study will compare the dosimetric parameters of the three planning techniques. Materials/Methods: A double mastectomy patient with AeroForm tissue expanders underwent left chest wall radiation therapy. A tangent FIF plan, a VMAT plan and a hybrid (tangent/VMAT) plan were created using Pinnacle treatment planning system (Phillips Medical System 16.2). The radiation prescription is 50 Gy for 25 fractions. Planning target contour PTV eval is the breast PTV exclude 3mm skin and exclude the AeroForm canister plus approximate 2cm of surrounding CO2. Plan 1: Tangent FIF plan was created using total 8 segments. Three segments for medial beam, the open segment weighted 91%. Five segments for lateral beam, the open segment weighted 82%. Plan 2: Two arc VMAT plan was optimized using “allow jaw motion” option in Pinnacle. Each arc has 183 degree rotation angle with 3 degree gantry spacing for each control point. Gantry rotation for arc 1 is counter clockwise from 127° to 304°, gantry rotation for arc 2 is clockwise from 306° to 129°. Plan 3: The Hybrid-VMAT plan combines a 6.75% weighted open tangent beam and a 22.5% weighted VMAT plan optimized using fixed jaw size the same as the open tangent beam. The medial arc in the Hybrid-VMAT plan has 33 degree clockwise rotation gantry angle from 303° to 336°. The lateral arc in the Hybrid-VMAT plan has 30 degree counter clockwise rotation gantry angle from 130° to 100°. Results: All three planning methods achieve coverage for PTV eval: V47.5 Gy (95% Rx) ≥ 95%, as well as meet the OARs dose criteria according to RTOG 1304. The differences for the three plans are the dose inhomogeneity and the maximum dose (hot spot). The tangent FIF plan is the least homogeneous plan which just meet the acceptable criteria with 1cc PT Veval receives 55.84 Gy (111.7% Rx) and max dose of 57.06 Gy (114.1% Rx); The VMAT plan improves the dose inhomogeneity with 1cc PT Veval receives 54.4 Gy (108.8% Rx) and max dose of 55.24 Gy (110.5% Rx); The Hybrid-VMAT plan achieves the ideal dose homogeneity with 1cc PT Veval receives 54.07 Gy (108.1% Rx) and max dose of 54.97 Gy (109.9%). Conclusions: Although the dose homogeneity for VMAT plan and for the Hybrid-VMAT plan are superior to tangent FIF plan, the accuracy of the execution for the VMAT plan and for the Hybrid-VMAT plan demands higher precision in contouring accuracy for high density material and precise density override for the treatment planning. The tangent FIF plan allows relatively large tolerance in contouring accuracy and density override.

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A PRACTICAL FORMULA TO GUIDE PARTIAL INFLATION OF CONTRALATERAL TISSUE EXPANDERS FOR OPTIMAL POST-MASTECTOMY RADIATION
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Problem: A challenge for radiation treatment of breast patients with tissue expanders post-mastectomy is the fully expanded contralateral (CL) breast, which may traditional tangent beams. However if the CL tissue expander is only partially inflated there may be beam clearance to treat the ipsilateral chest wall and nodes. To avoid sending the patient back to the surgeon to deflate post simulation, we present an empirical formula for partial inflation of the CL expander at the surgeon’s office without CT. Methods: Twelve breast cancer patients with tissue expanders were CT simulated. Three out of the twelve patients required deflating the contralateral expander after initial simulation, two of which needed IMN node radiation coverage.

With supine patient measure (cm): 1) Widest separation at the middle transverse cut of breast (2cm posterior of the lateral breast edge), D; 2) Vertical height of h; 3) Sternal height (middle), H; 4) Distance between sternum and contralateral breast apex, A. 5) Apex M CL breast

For optimum tangent beam angle, the maximum apex height, M of contralateral breast should be less than M0−3 with IMN irradiation or less than M0−2 without IMN irradiation, while

\[ M_0 = H + 2A \times (H-h)/D \]

Therefore, M-M0=3 0 provides adequate beam angle clearance for IMN; while M-M0=2 0 may need deflation of the contralateral expander. M-M0=2 0 provides adequate beam angle clearance for planning without IMN; while M-M0=2 0 may need deflation of the contralateral expander. Results: The formula was tested with 12 cases. The initial plan for Case #1 exceeded the contralateral breast dose limit. Initial plans for Case #2 and #3 exceeded the ipsilateral lung dose limit. After partially deflating the CL expander, the plans then met all the RTOG 1304 criteria. Cases 4-12 met the RTOG 1304 criteria at first simulation. Conclusion: The formula presented can efficiently guide the surgeon in estimating the extent of inflation for contralateral tissue expanders when the patient requires subsequent radiation, and/or help radiation teams estimate the beam clearance at the initial consultation prior to CT to streamline the patient process.

JUSDisclosure: C Tan and M Svatos consult for AirXpanders

PRELIMINARY RESULTS OF HYPOFRACTIONATED POST-MASTECTOMY RADIOTHERAPY (PMRT-HF): DOSEIMETRY, LOCO-REGIONAL CONTROL AND TOXICITY
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AIMS: Post-mastectomy radiation therapy (PMRT) with conventional fractionation is typically delivered in 5 to 6 weeks. Data supporting hypofractionated PMRT is limited. This study aims to determine whether a short course of hypofractionated schedule in 5-16 fractions is safe and effective. METHODS AND MATERIALS: Eligible patients with stage IA to IB primary breast cancer received hypofractionated PMRT with fixed beam IMRT or VMAT technique to the chest wall (CW) with or without loco-regional lymph node. Prescription dose was 40.5 Gy in 15 and 42.5Gy in 16 fractions daily, with an optional simultaneous integrated boost (SIB) of 3.2 Gy/fraction to 48Gy. The primary endpoint was loco-regional recurrence free survival (LRFS); secondary endpoints were acute and late skin toxicity, overall survival (OS) and disease free survival (DFS). RESULTS: Between 2012 and 2018, 83 patients with a median age of 51 years were retrospectively analysed. All patients received adjuvant hypofractionated PMRT: 90.3% with 40.5Gy/15 frs /2.7Gy per fraction and 9.5% with 42.5Gy/16 frs /2.66Gy. SIB with 3.2Gy/fr was adopted in only 5 cases. Bolus 5 mm was used in 33 patients (40%). CVT- PTV volumes included CW in 8 patients (9,5%) and CW + regional LN in 75 patients (90,5%). At a median follow-up of 34 months, 2 patients developed loco-regional recurrence (locally, 1 in the scar and one in-field regional lymph node). 10 patients developed distant metastatic disease, including the 2 patients with loco-regional relapses. LRFS and distant metastasis free survival were 98.6% (95% CI 0.89 – 1.00) and 89.0% (95% CI 0.89 – 1.00), respectively. The hypofractionated regimen was well tolerated with 24.1% (20/83) G2 and 3.6% (3/83) acute skin toxicity. So far no cases of G3 late skin toxicity have been observed. The 3-year actuarial OS and DFS were 94.3% (95% CI 0.88 – 1.00) and 89.0 (95% CI 0.88 – 0.90), respectively. CONCLUSIONS: Hypofractionated PMRT is well tolerated. Median follow-up in is still insufficient to assess long-term loco-regional control and late toxicity. Our experience suggests local control rates and toxicity outcomes aligned with those already reported in literature with longer follow-up.

CASE CONTROL STUDY; SEROMA CONTROL USING AXILLARY EXCLUSION TECHNIQUE
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Problem statement: Seroma is the commonest early complication after axillary lymph node dissection (ALND) in management of breast cancer, with a reported incidence of 60%. Adverse effects of increased morbidity, re-admission and antibiotic usage are associated with the development of infection within the seroma. Various techniques have been studied in an attempt to minimize incidence of seroma and post mastectomy drainage volumes. This study aims to...
evaluate Axillary exclusion technique in comparison to conventional technique. Methods: In this prospective case control study, we evaluated 40 female patients presenting to Cairo University Hospitals during the period between 1/2016-10/2016. All patients underwent modified radical mastectomy, axillary exclusion closure technique was used in cases and conventional closure technique in controls. Axillary exclusion technique involves suturing the superior mastectomy skin flap down to the free edge of the pectoralis major muscle and the lateral chest wall, with interrupted sutures placing between pectoralis major and minor to reliably exclude the axillary fossa from the remainder of axillary cavity. Total drain outputs were recorded and compared the results in the two groups. Results: Patients’ demographic characteristics as well as size of tumor and number of involved lymph nodes were comparable among cases and controls. Mean total drain output for cases is 80±7.1 ml ranging from 30-120 ml significantly compared to a mean total drainage of 128±10.9 ml ranging from 40-270 ml among controls, a reduction of 62.5%, P<0.001 (figure1). Conclusion: Axillary exclusion technique has resulted in significant reduction of drainage volumes and fewer seroma following mastectomy and axillary clearance. References1-Woodworth, Philip A., et al. “Seroma formation after breast cancer surgery: incidence and predicting factors/discussions.” The American surgeon 66.5 (2000): 444. 2-Chand, Natalie, Anna MG Aertszen, and Gavin T. Royle. “Axillary “Exclusion”—A Successful Technique for Reducing Seroma Formation after Mastectomy and Axillary Dissection.” Advances in Breast Cancer Research 2.01 (2013): 1. Figure1 Mean amount of seroma collected in axilla drains in different days post operatively

P43 TARGETING SEMAPHORIN 3C IN TRIPLE NEGATIVE BREAST CANCER INDUCES APOPTOSIS AND CHEMO-SENSITIVITY
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Problem Statement: Therapeutic regime for treatment of triple negative breast cancer has always been challenging due to its hormone receptor negative and epidermal growth factor receptor 2 (HER2) negative characteristics. On the other hand, there has been increased interest in studying the role of semaphorins especially semaphorin 3C (Sem3C) which has been implicated in several human malignancies through the activation of its receptors: neuropilins and plexins. The objectives of this study are to understand the role of Sem3C in the progression of triple negative breast cancer (TNBC). Methods: The Sem3C expressions in a panel of breast cancer cell lines were studied, and the effects of Sem3C antisense oligonucleotide (ASO) on Sem3C expression, and Akt- and Src-signaling pathways in BT-549 and MDA-MB-468 cells were assessed by quantitative reverse transcription-PCR, and Western blotting, respectively. The effects of Sem3C ASO on BT-549 and MDA-MB-468 cell growth and chemosensitization to anticancer agents were assessed in vitro and in vivo. Results: Triple-negative breast cancer cell lines expressed Sem3C mRNA and protein. The expressions of Sem3C mRNA and protein in BT-549 and MDA-MB-468 cells were significantly suppressed by Sem3C ASO treatment in a dose-dependent manner. Also, Sem3C ASO treatment reduced the phosphorylation levels of Akt and Src kinases, increased cellular apoptosis, and decreased cell growth in breast cancer. In addition, Sem3C ASO treatment augmented the cytotoxic effects of docetaxel and paclitaxel in vitro. Systemic administration of Sem3C ASO in athymic mice significantly delayed MDA-MB-468 tumor progression and enhanced paclitaxel chemosensitivity. Conclusion: There is a positive correlation between SEMA3C expression and pro-survival signaling pathways such Src and Akt which are generally activated in triple negative breast cancer and made the tumor more sensitive to chemotherapy which leads to a reduction in tumor volume size as compared to administration of chemotherapy alone. Therefore, this study helped in laying a foundation for targeting SEMA3C through small molecules or biologics in combination therapy for this subtype of breast cancer.
P44
RADIATION STIMULATES THE INVASIVENESS AND LUNG METASTASIS DEVELOPMENT IN A MOUSE MODEL OF TRIPLE-NEGATIVE BREAST CANCER
Benoit Paquette
Department of Nuclear Medicine and Radiobiology, Université de Sherbrooke, Sherbrooke, Canada

Problem statement: In 30% of patients with triple-negative breast cancer (TNBC, estrogen, progesterone, and HER2-negative receptors), a recurrence occurs within the first 3 years after treatment, and cure is unlikely. In all patients, radiotherapy increases the level of several inflammatory cytokines, some of which are known to promote cancer cell invasion. Using a mouse model of TNBC, we have determined if radiation-stimulated metastasis development was associated with inflammatory cytokines, and if the protease MT1-MMP could serve as a predictive marker for the development metastasis post-irradiation. MT1-MMP is a protease that promotes the cancer cell invasion by cleaving extracellular matrix proteins. Methods: Wild-type or MT1-MMP knockdown D2A1 cells of TNBC cancer were implanted in a mammary gland of Balb/c mice. Eight days later, the tumor was irradiated daily with four fractions of 6 Gy. Inflammatory cytokines were quantified in plasma before, mid-way and after tumor irradiation. Effects of tumor irradiation and expression of MT1-MMP on cancer cell invasion, number of circulating tumor cells and lung metastasis development were determined. Results: Tumor irradiation significantly increased the plasma level of IL-1β which was associated with a larger number of circulating tumor cells (3.5-fold) and lung metastases (2.3-fold). Ability of IL-1β to stimulate the invasiveness of D2A1 cells was confirmed in vitro. Down regulation of MT1-MMP prevented the increase of circulating tumor cells and lung metastases. Conclusions: This study suggests that MT1-MMP is needed to observe the radiation-stimulated metastasis development and that this effect of radiotherapy could be prevented with an anti-IL-1β treatment.
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Methods: Wild-type or MT1-MMP knockdown D2A1 cells of TNBC cancer were implanted in a mammary gland of Balb/c mice. Eight days later, the tumor was irradiated daily with four fractions of 6 Gy. Inflammatory cytokines were quantified in plasma before, mid-way, and after tumor irradiation. Effects of tumor irradiation and expression of MT1-MMP on cancer cell invasion, number of circulating tumor cells, and lung metastasis development were determined.

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Conclusions: This study suggests that MT1-MMP is needed to observe the radiation-stimulated metastasis development and that this effect of radiotherapy could be prevented with an anti-IL-1β treatment.

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Wednesday, September 4, 2019

12:30-15:00 Pre-Congress Industry Symposium: Margin detection Supported by OncoRes Medical

Seacliff Room

Lunch will be served prior to the session at 12:30

Aim: This mini-symposium, sponsored by an Australian biomedical start-up OncoRes Medical, aims to explore when, how and why getting a clear margin in breast conserving surgery matters, and what technical advances can help us achieve this.

13:00-13:20 Margins and the Surgeon
Jasmine Wong, USA

13:20-13:35 Margins and the Pathologist
Poonam Vohra, USA

13:35-13:50 Margins and the Radiologist
Julia Camps-Herrero, Spain

13:50-14:05 Overview of margin technology
Brendan Kennedy, Australia

14:05-14:20 OncoRes – concept, results and trial
Christobel Saunders, Australia

14:20-15:00 Moderated discussion
Alastair Thompson, USA and Panel

Thursday, September 5, 2019

06:45-08:00 Morning Industry Symposium: New surgical techniques for removing and staging breast cancer Supported by Endomag

Hall B

Breakfast will be served prior to the session

Chairperson: Bruce Mann, Australia

Lesion localization and Targeted Axillary Dissection with Magseed: The MD Anderson experience
Abigail Caudle, USA

Magnetic SLNB and the new technique of Delayed Sentinel Node Biopsy
Michael Alvarado, USA
Friday, September 6, 2019

06:45-08:00  Morning Industry Symposium:
Identifying the right patients for chemotherapy in ER+ HER2- breast cancer
Supported by Genomic Health

*Breakfast will be served prior to the session*

**Chairperson:**  Christy A. Russell, USA

07:00-07:30  Treatment decision-making for young patients in light of new evidence from TAILORx
Tiffany Traina, USA

07:30-08:00  Should all women with breast cancer and positive lymph nodes receive chemotherapy?
Christy A. Russell, USA

12:45-13:45  Industry Lunch Symposium:
HER2-positive early breast cancer: Determining adjuvant treatment following neoadjuvant therapy
Supported by Genentech

HER2-positive early breast cancer: Determining adjuvant treatment following neoadjuvant therapy
Francis Arena, USA
Current Women's Health Reviews

Volume 15, Issue 1, 2019 | ISSN: 1573-4848 (Print) | eISSN: 1875-6581 (Online)

Aims & Scope:
Current Women's Health Reviews publishes original research papers, frontier reviews/mini-reviews, drug clinical trial studies and guest edited thematic issues written by leaders in the field covering a range of current topics on obstetrics and gynecology. The journal’s aim is to publish the highest quality articles dedicated to research in the field. The journal is essential reading for all clinicians and researchers in the fields of obstetrics and gynecology.

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Current Cancer Therapy Reviews

Volume 15, Issue 1, 2019 | ISSN: 1573-4848 (Print) | eISSN: 1875-6581 (Online)

Aims & Scope:
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