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# SECTION 1

# **Handbook**



## WELCOME

On behalf of the Executive Committee, I welcome you to the Sixth Scientific Meeting of the Australasian Society for Breast Disease.

This multidisciplinary Scientific Meeting is designed to help health care professionals advance their knowledge of the latest techniques of investigation and management of breast cancer. The program includes sessions on breast cancer in younger women, metastatic disease, gene signature reporting, and complex and controversial issues in prevention, detection, diagnosis and treatment of breast cancer. A range of optional workshops are also included. The Meeting also provides an excellent opportunity for professional and social interaction between delegates from the various disciplines.

I wish to thank our sponsors AstraZeneca Oncology, Roche Products, Pfizer Australia and Novartis Oncology, as well as all the exhibitors for their tremendous support. It would not be possible to hold this Scientific Meeting without their support. Please take the time to meet with the representatives of the participating companies.

If you are not a member of ASBD, we would like you to consider joining. Membership application forms are available from the Meeting Office.

To help us in our future planning, we would greatly appreciate it if you took the time to complete the brief questionnaire provided in your satchel. Please drop the completed questionnaire into the box placed in the Meeting Office.

I believe that this will be a great Meeting and hope that you will enjoy all aspects of it.



**Jennet Harvey**  
President

## AUSTRALASIAN SOCIETY FOR BREAST DISEASE EXECUTIVE COMMITTEE

A/Prof Jennet Harvey	Pathologist, President
Dr Marie-Frances Burke	Radiation Oncologist, Secretary/Treasurer
Dr Geoffrey Beadle (co-opted)	Medical Oncologist
Dr Natacha Borecky	Radiologist
Dr Daniel de Viana (co-opted)	Surgeon
Dr Nehmat Houssami	Breast Physician
Dr Michael Izard (co-opted)	Radiation Oncologist
Mr James Kollias	Surgeon
Dr Warwick Lee	Radiologist
Dr Lynne Mann	Surgeon
Dr Wendy Raymond	Pathologist
A/Prof Mary Rickard (co-opted)	Radiologist
Prof Robin Stuart-Harris	Medical Oncologist
Ms Solei Gibbs	Executive Officer

## Previous Executive Committee Members

A/Prof Michael Bilous	Pathologist
A/Prof John Boayges	Radiation Oncologist
Dr Colin Furnival	Surgeon
Prof Michael Green	Medical Oncologist
Dr Cherrell Hirst	Breast Physician
Ms Elspeth Humphries (co-opted)	BCNA Representative)
Dr Jack Jellins	Scientist
Ms Veronica Macaulay-Cross (co-opted)	BCNA Representative
Mr William McLeay	Surgeon
Ms Lyn Moore (co-opted)	BCNA Representative
Dr Margaret Pooley	Surgeon

## CONTACT DETAILS

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Email: [info@asbd.org.au](mailto:info@asbd.org.au)  
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## Platinum Sponsor



### Platinum Sponsor of the Sixth Scientific Meeting of the ASBD

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AstraZeneca is one of the largest and most successful pharmaceutical companies, providing healthcare solutions across six therapeutic areas. We produce oncology, cardiovascular, neuroscience, gastrointestinal, infection, and respiratory medicines. In Australia AstraZeneca employs more than 1,000 people.

At any time, AstraZeneca participates in more than 40 clinical trials in over 200 centres around Australia. In 2006, more than \$10 million was invested in Australian clinical research. AstraZeneca has a history of investing in research. In 1993 a Natural Product Discovery partnership was formed with Griffith University, involving an investment of more than \$100 million.

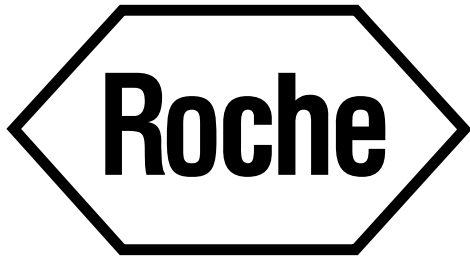
AstraZeneca exports pharmaceutical products from the Sydney plant to more than 30 countries with export sales exceeding \$175 million in 2006.

AstraZeneca, makers of Nolvadex (tamoxifen), Zoladex (goserelin), Arimidex (anastrozole) and Faslodex (fulvestrant), is continuing its tradition of research excellence and innovation with a range of novel targeted products such as anti-proliferative, anti-angiogenic, vascular targeting and anti-invasive agents. AstraZeneca is also harnessing rational drug design technologies to develop new compounds that offer advantages over current cytotoxic and hormonal treatment options. AstraZeneca currently has over 20 different anti-cancer projects in research and development.

AstraZeneca is proud to be supporting the 2007 Meeting of the Australasian Society for Breast Disease.

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- The annual HOTT scientific meeting
- The Australian Blood Cancer Registry
- Surviving Cancer in Rural and Regional Australia (Satellite Symposium telecast to 58 towns throughout the country)

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### Venue

Surfers Paradise Marriott Resort & Spa  
158 Ferny Avenue  
Surfers Paradise Qld 4217  
Australia

Tel: (07) 5592 9800 (from overseas: +61 7 5592 9800)  
Fax: (07) 5592 9888 (from overseas: +61 7 5592 9888)

### Meeting Office

The Meeting Office is located in the Boardroom on level 2 and it will be open during the following times:

Thursday 27 September 2007	1300-1900 hours
Friday 28 September 2007	0730-1730 hours
Saturday 29 September 2007	0730-1500 hours

### Speakers' Audiovisual Testing Room

The Speakers' Audiovisual Testing will be available during the following times:

Thursday 27 September 2007	1500-1900 hours
Friday 28 September 2007	0730-1600 hours
Saturday 29 September 2007	0730-1300 hours

### Namebadges

Please wear your namebadge at all times. It is your admission pass to sessions and morning and afternoon teas. If you misplace your namebadge, please contact the Meeting Office.

### Tickets

Attendance at workshops and social functions is by ticket only. Tickets are enclosed in your registration envelope with your namebadge, according to your attendance indication on the registration form. If you misplace any tickets or do not have tickets to the activities you wish to attend, please contact the Meeting Office.

### Special Diets

If you have made a special dietary request, please identify yourself to serving staff at functions.

### Messages

A message board is located near the Meeting Office. Please advise potential callers to contact the Surfers Paradise Marriott Resort & Spa (see details above) and ask for the Australasian Society for Breast Disease Meeting Office. Please check the board for messages as personal delivery of messages cannot be guaranteed.

### Dress

Smart casual attire is appropriate for Meeting sessions. A jacket may be needed for air conditioned Meeting rooms. Dress for Meeting dinner is cocktail wear.

### Lunches

Lunches will be served in the Garden Terrace room and the Trade Exhibition area. Lunch service is by ticket only. Please ensure you have the correct tickets. Additional tickets are available at \$35 per person.

### Welcome Drinks

Thursday 27 September 2007, 1800-1900 hours

Meet your fellow delegates for a relaxed drink by the pool area or, in case of the weather not being favourable, in the Garden Terrace room. Included for fulltime delegates and registered partners. Additional tickets cost \$35 per person.

### Networking Drinks

*Sponsored by AstraZeneca Oncology*

Friday 28 September 2007, 1715-1845 hours

Following the last session for the day, join your colleagues and trade representatives for drinks in the Trade Exhibition area. Included for fulltime and Friday delegates and registered partners only. No additional tickets.

### Meeting Dinner

*Sponsored by AstraZeneca Oncology*

Saturday 29 September 2007, 1930-2300 hours

The Meeting finale will be the 'Springtime Butterfly Ball', providing for a final opportunity for interaction with your colleagues. The evening will start with pre dinner drinks in the Garden Terrace, followed by a fine dinner, drinks and music in the Marriott Ballroom. Wearing the butterfly or bumble bee is compulsory for admission to the festivities! Included for full time delegates and registered partners. Additional tickets at \$110 per person are available from the Meeting Office.

## ANNUAL GENERAL MEETING

The Annual General Meeting of the Australasian Society for Breast Disease will be held in the Verandah Room at 0730 hours on Saturday 29 September 2007. Breakfast will be served during the Meeting. Please reconfirm you attendance / nonattendance upon registration. Admission is free to members only.

## OPTIONAL SOCIAL ACTIVITIES

For information about and bookings for leisure activities such as golf, fishing and cruises, please contact the Tour Desk at the Marriott during your stay.

## CONSUMER FORUM

Breast Cancer Network Australia (BCNA) will host a Forum for Consumers on Saturday 29 September 2007, from 1030 hours in the Hinterland Rooms. Speakers will include Raelene Boyle, Olympian, BCNA Board member and breast cancer survivor, Julie Hassard from BCNA, Dr Nicole McCarthy, Medical Oncologist, and Amanda Berra from BCNA.

## BREAST PHYSICIANS

The Annual General Meeting of the Australasian Society of Breast Physicians will be held at 1700 hrs on Saturday 29 September 2007, in Terrace Room 1.

### Clinical A/Professor Michael Bilous

MA, MB ChB, FRCPA

Michael Bilous studied Medicine at Cambridge and Birmingham Universities. Following Pathology training in the UK, New Zealand and Australia, he was appointed Staff Specialist Pathologist at the Institute of Clinical Pathology and Medical Research (ICPMR), Westmead Hospital, Sydney. He is currently Director of Tissue Pathology at that institution.

Professor Bilous has had a long-standing interest in breast pathology and is a member of federal and state committees concerned with best practice in breast pathology. He was directly involved in organising the pathology components of the national mammographic screening and assessment program for BreastScreen Australia, and is RCPA representative on the NSW Accreditation and Quality Improvement Committee of BreastScreen NSW. He has chaired Australian Cancer Network Working Parties responsible for publication of *Pathology Reporting of Breast Cancer – A Guide for Pathologists, Radiologists, Oncologists and Surgeons*, the 3rd edition of which is in preparation, again under his chairmanship.

Professor Bilous is a member of the International HER2 Testing Advisory Board, Chairman of the Australian HER2 Testing Advisory Board and a member of the Editorial Board of *The Breast*. He has authored over 65 publications, the majority concerned with breast pathology.

### A/Professor Stefano Ciatto MD, PhD

Stefano Ciatto is Associate Professor of Radiology at the Florence University and Head of the Department of Diagnostic Imaging at the Centro per lo Studio e la Prevenzione Oncologica (centre for the study and prevention of cancer), Florence. His areas of interest include breast cancer imaging and image-guided intervention, and cancer screening (breast, cervix, colorectal and prostate cancer). He has over 400 peer-reviewed publications, of which more than 200 relate to breast cancer, and has presented more than 600 papers at national and international congresses. His current breast research interests include underestimation of malignancy with core biopsy, evaluation of digital mammography in screening practice, and clinical quality assurance in breast screening including review of interval cancers. His past research in breast diagnosis has included: accuracy of mammography and ultrasound, fine needle cytology, accuracy of double and CAD reading in screening, breast density and BI-RADS categorisation.

Professor Ciatto established the European Group for Breast Cancer Screening, and is a member of the National Task Force for Breast Cancer and the European Society of Mastology. He is an Editorial Board member for *The Breast*, the *Journal of Medical Screening*, and the *International Journal of Biological Markers*.

### Professor David Joseph MBBS, FRANZCR, MRACMA

David Joseph has extensive experience in national and international clinical trials. He is the Co-Chair of the International TARGIT Study, which is a randomised trial of conventional versus intraoperative radiotherapy for low risk breast cancer after conservation treatment. He is the Australian Chair of the RADAR Trial looking at hormone therapy Biophosphonates and dose escalation (3DCRT, IMRT, HDR brachytherapy) for prostate cancer. He is the Founder of The Western Australian Tissue Network and involved in ongoing research with the National Translational Cancer Research Network, University of Oxford, UK.

Professor Joseph was a founding member of TROG and organised for TROG participation at Geelong and Western Australia. Both sites have been major accruals to TROG studies. He is also on the SAC of AGITG, ANZBCTG, and has organised Fellowships in Oncology for Clinicians, Therapists and Physicists.

Professor Joseph's major interest is in translational research involving molecular biology and tissue microarrays and he has presented and published on this area numerous times. He also has an interest in and has published and presented on translational research in physics in relation to RT. He is a Supervisor of PhDs in Molecular Biology, physics and technical aspects of radiation therapy treatment.

### Professor Mark Pegram MD

Mark Pegram has just been appointed Sylvester Professor of Medicine at the University of Miami Miller School of Medicine and is Director for Translational Research, Braman Breast Cancer Institute, Sylvester Comprehensive Cancer Center, Miami, Florida. Until recently, he was Professor of Medicine in the Division of Hematology/Oncology at the UCLA School of Medicine, and Director of the Women's Cancer Program at the UCLA/Jonsson Comprehensive Cancer Center. Professor Pegram took his medical training at the University of North Carolina, Chapel Hill and attended medical internship and residency at the University of Texas Southwestern Medical School in Dallas (Parkland Memorial Hospital), before moving to UCLA for fellowship training in Hematology/Oncology. He conducted his research fellowship in Dr Dennis Slamon's laboratory at UCLA before joining the UCLA faculty in 1993. Professor Pegram has a number of honors and awards to his credit including the Revlon/UCLA Fellowship, the UCLA Clinical Cancer Research Career Development Award, and the Basic Science Award from the Society of Gynecologic Oncology. His expertise is in the development of targeted therapeutics in solid tumor oncology. He has grant support for his work in the area of targeting growth factor receptors and angiogenesis in breast cancer. Professor Pegram has numerous publications to his credit including authorships or co-authorships in the *New England Journal of Medicine*, *Cancer Research*, *Journal of the National Cancer Institute*, *Journal of Clinical Oncology*, *Proceedings of the National Academy of Sciences*, *Biochemistry*, *Oncogene*, *Journal of Organic Chemistry*, *Clinical Cancer Research*, *Biochemical Pharmacology*, *Cancer Gene Therapy*, and *Breast Cancer Research and Treatment*.

### Mr Richard Rainsbury MBBS, BSc, MS, FRCS

Dick Rainsbury is Director of the Breast Unit at the Royal Hampshire County Hospital in Winchester, past Tutor of Breast Disease at The Royal College of Surgeons of England and now Director of Education at The Royal College of Surgeons of England. He has been a strong advocate of the model of the 'oncoplastic' breast surgeon, as a new type of specialist providing a comprehensive breast and reconstructive service in the context of a modern Health Service.

Mr Rainsbury's main interests include the changing configuration of breast surgery, the development of new hybrid skills in oncoplastic procedures, and increasing the recruitment into the new specialty of breast surgery. He was Founder Chairman of the Interface Breast Training Group of the British Association of Surgical Oncology and the British Association of Plastic Surgeons. This group negotiated an agreement with the Department of Health to finance and develop a new cross-specialty training scheme for nine senior trainees. These posts are in major oncoplastic breast units and have supported 36 fellows, many of whom are now consultant oncoplastic breast surgeons. Mr Rainsbury is also Chairman of the National Breast Reconstruction Audit.

## Dr Rosemary Balleine MBBS (Hons), PhD, FRCPA

Rosemary Balleine is a medical and PhD graduate of the University of Sydney who trained as a Pathologist at Westmead Hospital. She is currently a Cancer Institute NSW Fellow and research group leader in the Translational Oncology section of Cancer Services, Sydney West Area Health Service. In her current role, Dr Balleine is involved in a range of clinically orientated research projects. She is also one of the Chief Investigators involved in the establishment of a Breast Cancer Tumour Bank.

## Dr Geoffrey Beadle MBBS, FRACP, FRANZCR

Geoffrey Beadle is a graduate of the University of Queensland and trained in medical oncology and radiation oncology at the Peter McCallum Cancer Institute in Melbourne. He subsequently worked at the Joint Centre for Radiation Therapy, Harvard Medical School, Boston as a Radiation Oncologist. After returning to Brisbane, Dr Beadle worked at the Queensland Radium Institute as a Radiation Oncologist before moving to the Wesley Medical Centre where he currently practices as a Medical Oncologist. He is a visiting Medical Oncologist at the Royal Brisbane and Women's Hospital and currently holds a part-time appointment at the Queensland Institute of Medical Research as Head of the Translational Research Laboratory. Dr Beadle's research interests include long term outcomes of women with breast cancer and molecular markers to predict breast cancer outcomes.

## Dr Meagan Brennan BMed, FRACGP, DFM, FASBP

Meagan Brennan is Director of Breast Assessment at the NSW Breast Cancer Institute and Clinical Senior Lecturer at the University of Sydney. She is a Breast Physician with Fellowships in general practice and breast medicine. Her interests include the management of benign breast disease, the provision of continuous and holistic care to women through the phases of breast cancer diagnosis, treatment and follow-up and the multidisciplinary management of women at high genetic risk of breast and ovarian cancer.

## Dr Marie-Frances Burke MBBS, FRACR

Marie Burke graduated in medicine from the University of Queensland in 1982. Since 1989, she has been a Fellow of the Royal Australasian College of Radiologists, having done her training in radiation oncology at the Queensland Radium Institute, in Brisbane. She is currently in practice as a Radiation Oncologist at the Wesley Cancer Care Centre, Brisbane. Dr Burke's major interests are in breast and gynaecologic cancers. She is the current Secretary / Treasurer for the Australasian Society of Breast Disease.

## Dr Bill Cockburn MBBS, FRACS

Bill Cockburn is a Plastic Surgeon who trained in Brisbane, Melbourne and in the United Kingdom. He has been the Secretary and then President of the Queensland Society of Plastic Surgeons, on the State Committee of The College of Surgeons, and Councillor and then immediate past President of the Australian Society of Plastic Surgeons. Dr Cockburn practices general plastic surgery with particular interests in skin cancer, breast surgery, head and neck surgery and microsurgery.

## Professor Afaf Girgis FRACGP, DFM, FASBP

Afaf Girgis is the Director of the Centre for Health Research and Psycho-oncology (ChERP) of the Cancer Council NSW and the University of Newcastle. As a conjoint Professor in Faculty of Health at the University of Newcastle, she teaches communication skills. Her key achievements include developing consensus guidelines on 'breaking bad news', which have been adopted by medical schools in Australia and overseas into their interactional skills teaching program, and leading national communication skills training programs for senior clinicians. She has also developed and updated a number of communication skills packages for the National Breast Cancer Centre and facilitated workshops for the American Society of Clinical Oncology. Her interest in this area includes research into the effectiveness of consultation-skills training programs on improving patients' quality of life, preventing patients' psychological morbidity and reducing the risk of burnout amongst doctors.

## A/Professor Jennet Harvey MBBS, FRCPA

Jennet Harvey is Associate Professor at The University of Western Australia and Head of Pathology. She is a consultant Pathologist working at the PathWest Laboratory Medicine WA, with a particular interest in breast pathology. In addition to currently serving on the WA State Committee of the Royal College of Pathologists of Australasia, she is a member of a number of University and Faculty committees and the Board of Basic Surgical Training of the Royal Australian College of Surgeons. Professor Harvey is a Councillor, Australian Council on Smoking and Health and the current President of the Australasian Society for Breast Disease.

## Dr Nehmat Houssami

MBBS (Hons), MPH, M Ed, FAFPHM (RACP), FASBP, PhD

Nehmat Houssami is a Breast Physician and a Public Health Physician and has worked in breast services for the past 18 years. She has experience in clinical and clinical epidemiology research in breast diagnosis, imaging and screening. Dr Houssami works as a Breast Physician at the Australian Breast Centre (Sydney) and the Royal Hospital for Women (Randwick), and is Senior Lecturer with the Screening & Test Evaluation Program, School of Public Health (Sydney University). She is a research advisor and affiliate with the NSW Breast Cancer Institute and a research associate with Centro per lo Studio e la Prevenzione Oncologica (Florence). Dr Houssami has over 60 publications in the peer-reviewed literature, and currently leads several international research collaborations. She is Specialty Editor for 'Imaging, Screening & Early Diagnosis' with *The Breast*.

## Clinical A/Professor Judy Kirk MBBS, FRACP

Judy Kirk gained her medical degree at Sydney University in 1980. She originally trained in paediatric oncology, obtaining her Fellowship of the Royal Australasian College of Physicians in 1987. From 1991, Professor Kirk spent three years working in the field of cancer genetics at the Fred Hutchinson Cancer Research Center, Seattle, USA. In 1995, she was appointed as a staff specialist in Cancer Genetics at Westmead Hospital. She is now the Director of the Familial Cancer Service, a service that provides genetic counselling and testing for families with a strong family history of cancer. Professor Kirk participates in local and national research regarding the familial aspects of cancer. She was a founding member of kConFab and serves on the Executive.

### **Mr James Kollias** MBBS, FRACS, MD

James Kollias is a specialist breast surgeon at the Royal Adelaide Hospital, St Andrews Breast Clinic and BreastScreen South Australia. He is the current Chairman of the Royal Australian College of Surgeons (RACS) Breast Section and the Clinical Director of the RACS National Breast Cancer Audit. Mr Kollias' special interests include breast training and oncoplastic breast surgery. He has published over 50 scientific manuscripts in scientific refereed journals and book chapters.

### **Dr Warwick Lee** MBBS, BSc(Med), FRANZCR, DDU

Warwick Lee is a radiologist in private practice in Bowral, NSW and a Visiting Radiologist with BreastScreen – NSW. He has been involved with breast cancer screening since 1988 when he was part of the pilot mammography screening programme, The Central Sydney Area Health Service Breast X-ray Programme. He was part of the Breast Radiology Training Program of the RANZCR and Breast Screen NSW, is currently an image reviewer for the RANZCR Mammography Quality Assurance Program, is on the Committee of the Breast Imaging Reference Group of the RANZCR and on the Editorial Committee for the NBCC's *Clinical Update – Breast Cancer*. Dr Lee is a past President of the Australasian Society for Breast Disease.

### **Dr Lynne Mann** MBBS, FRACS

Lynne Mann is a Staff Specialist General Surgeon, with a major interest in breast surgery, with the Sydney West Area Health Service. She works at Auburn Hospital and the NSW Breast Cancer Institute at Westmead Hospital. Dr Mann is a member of the Breast Section of the Royal Australasian College of Surgeons, and a member of the NSW Breast Cancer Trials Group. She has been on the Australasian Society for Breast Disease Executive Committee since 2003.

### **Dr Nicole McCarthy** MBBS, MHSc, FRACP

Nicole McCarthy is a graduate of the University of Queensland and is currently a Senior Lecturer at the University of Queensland, a Staff Specialist in Medical Oncology at the Royal Brisbane and Women's Hospital (RBWH), and a Visiting Medical Officer at The Wesley Hospital. After completing her training in medical oncology, Dr McCarthy joined the National Cancer Institute in Bethesda, Maryland, where she completed a Masters in Health Sciences in Clinical Research and pursued research interests in new drugs and immunological treatments for breast cancer. She was subsequently a recipient of the Breast Cancer Research Trust Fellowship Grant in Auckland, New Zealand and was a founding member of the Breast Cancer Advocacy Coalition before returning to Brisbane. Dr McCarthy manages the Breast Cancer Clinical Trials program at the RBWH and is on various committees, including the Chair of the Systemic Subcommittee of the ANZ Breast Cancer Trials Group.

### **Miss Katrina Read** MBBS, FRACS

Katrina Read is a general Surgeon. She graduated in medicine from the Melbourne University in 1989 and obtained her Fellowship in Surgery in 1998. Miss Read specialises in breast and skin oncology at the Royal Women's Hospital and private practice in Melbourne.

### **Professor David Roder** DDSc, MPH, AM

David Roder heads the Research and Information Science Unit at The Cancer Council South Australia and is attached as a consultant to Cancer Australia, the Cancer Institute NSW and the National Breast Cancer Centre. He has a Professorial position at Flinders University. He directed the SA Epidemiology Branch between 1980 and 2001, which included the development of population and hospital cancer registries. He was made a Member of the Order of Australia in 2000 for contributions to cancer registration and epidemiology. Professor Roder has authored approximately 150 peer-reviewed journal publications and many technical reports. He has been a member of the State Accreditation Committee of BreastScreen SA and since the mid-1990s, the National Quality Management Committee of BreastScreen Australia.

### **Professor Robin Stuart-Harris** MD, FRCP, FRACP

Robin Stuart-Harris trained in medical oncology and palliative care at the Royal Marsden Hospital, London, United Kingdom, but migrated to Australia in 1987. In 1998, he took up the appointment of Senior Staff Specialist in Medical Oncology at the Canberra Hospital. In 2004, he was appointed as Director of the Capital Region Cancer Service. Professor Stuart-Harris has particular interests in the management of both early and advanced breast cancer and the psychosocial aspects of cancer.

### **Dr Nicholas Wilcken** PhD, FRACP

Nicholas Wilcken is senior Staff Specialist in Medical Oncology at Westmead and Nepean Hospitals, and Senior Lecturer, University of Sydney. He did his oncology training at Royal Prince Alfred Hospital, Sydney, followed by a PhD at the Garvan Institute in Sydney, studying the cell cycle regulation of breast cancer cells. He has also been involved in clinical epidemiology projects (mainly systematic reviews) and guideline development for the National Breast Cancer Centre of Australia. He is currently co-ordinating editor for the Cochrane Collaboration Breast Cancer Group and Director of Research at the NSW Breast Cancer Institute.

## **PRESENTERS – PROFFERED PAPERS**

### **Dr Peter Bird** MBBS, FRACS

Head of Surgery, AIC Kijabe Hospital, Kenya

### **Ms Elisabeth Black** RN, DipAppSc (Nurs), BN (Midwifery), PGDipNursSc (Breast Care)

Clinical Nurse Consultant, Specialist Breast Care Nurse, NSW Breast Cancer Institute, Westmead, NSW

### **Dr Meagan Brennan** BMed, FRACGP, DFM, FASBP

Breast Physician, North Shore Breast and Surgical Oncology Centre, North Sydney, Western Clinical School, The University of Sydney, NSW

### **Dr Charles Douglas** BMed, BMedSci, FRACS

Breast Cancer and Melanoma Surgeon, The Breast Centre, Gateshead, Lecturer in Clinical Ethics and Health Law, University of Newcastle, NSW

### **Dr Andrew Spillane** FRACS, MD

Oncological Surgeon, North Shore Breast and Surgical Oncology Centre, The Sydney Cancer Centre and Mater Hospital, The University of Sydney, NSW

# POSTER PRESENTATION

The Poster Presentation will be located outside the main Meeting session room for the duration of the Meeting.

## VENUES

### Thursday 27 September 2007

- |               |  |
|---------------|--|
| 1300-1900 hrs | Registration<br>Venue: outside Boardroom   |
| 1500-1900     | Speakers' audiovisual testing<br>Venue: Ballroom   |
| 1530-1730     | Workshop:<br>Eliciting and responding to emotional cues<br>Venue: Terrace Room 2                                     |
| 1600-1730     | Workshop:<br>Borderline core biopsy: Imaging, core needle and excision histology findings<br>Venue: Hinterland Rooms |
| 1800-1900     | Welcome drinks<br>Venue: Pool side   |
| 1830-2030     | Workshop:<br>Eliciting and responding to emotional cues<br>Venue: Terrace Room 2                                     |
| 1900-2030     | Workshop: Combined oncoplastic breast surgery and radiation oncology<br>Venue: Hinterland Rooms                      |

### Friday 28 September 2007

- |               |  |
|---------------|--|
| 0730-1730 hrs | Registration<br>Venue: Boardroom                       |
| 0730-1600     | Speakers' audiovisual testing<br>Venue: Terrace Room 2 |
| 1715 - 1845   | Networking Drinks                                      |

### Saturday 29 September 2007

- |           |   |
|-----------|---|
| 0730-1500 | Registration<br>Venue: Boardroom  |
| 0730-0845 | Australasian Society for Breast Disease Annual General Meeting<br>Venue: Verandah Room    |
| 0730-1300 | Speakers' audiovisual testing<br>Venue: Terrace Room 2                                    |
| 1700-1800 | Australasian Society of Breast Physicians Annual General Meeting<br>Venue: Terrace Room 1 |
| 1930-2300 | Meeting dinner<br>Venue: Garden Terrace / Ballroom  |

The venue for all scientific program plenary sessions is the Marriott Ballroom

**Thursday 27 September 2007**

1300 – 1900 Registration

1800 – 1900 Welcome Drinks

**WORKSHOPS**

1530 – 1730 **Eliciting and responding to emotional cues in cancer patients**

Afaf Girgis, Katrina Read

A National Breast Cancer Centre communication skills workshop.

*Sponsored by National Breast Cancer Centre*

1600 – 1730 **Borderline core biopsy: Imaging, core needle and excision histology findings (includes case studies)**

Stefano Ciatto, Michael Bilous, Nehmat Houssami

1830 – 2030 **Eliciting and responding to emotional cues in cancer patients**

Afaf Girgis, Katrina Read

A National Breast Cancer Centre communication skills workshop.

*Sponsored by National Breast Cancer Centre*

1900 – 2030 **Combined oncoplastic breast surgery and radiation oncology: Case scenarios and tidbits**

Richard Rainsbury, James Kollias, David Joseph

*Sponsored by Roche Products*

**Friday 28 September 2007**

0730 – 0900 Registration

0900 – 1030 **SESSION 1 – BREAST CANCER IN YOUNGER WOMEN I**

*Sponsored by AstraZeneca Oncology*

Chair: Jennet Harvey

**Opening Remarks, Welcome** Jennet Harvey

**Age and the prognosis of breast cancer** Nicholas Wilcken

**Keynote Address: Is breast cancer different in younger women?** Michael Bilous

**Keynote Address: Imaging in younger women** Stefano Ciatto

**Discussion** Faculty

1030 – 1100 Morning Break

1100 – 1230 **SESSION 2: BREAST CANCER IN YOUNGER WOMEN II**

*Sponsored by Pfizer Australia*

Chair: Geoffrey Beadle

**Oncoplastic breast surgery** Richard Rainsbury

**Endocrine therapy for early breast cancer in younger women** Nicole McCarthy

**Management of pregnancy-related breast cancer** Geoffrey Beadle

**Discussion** Faculty

**Ablation of fibroadenoma** Meagan Brennan

1230 – 1330 Lunch

1330 – 1515 **SESSION 3: PROFFERED PAPERS**

Chair: Nehmat Houssami

**Intra-operative ultrasound-guided hook-wire localisation for impalpable breast lesions** Meagan Brennan

**A multidisciplinary risk management clinic for women at high genetic risk of breast and ovarian cancer - Experience and evaluation** Meagan Brennan

**Hormone receptor status in East African breast cancer patients - A different disease?** Peter Bird

**Minimal access breast surgery - A single breast incision for breast conservation surgery and sentinel lymph node biopsy**

Andrew Spillane

**The breast care nurse practicum - A multidisciplinary approach to breast care nurse education and support**

Elisabeth Black

**Intraoperative ultrasound for determining clear histological margins during breast conservation therapy** Charles Douglas

**Preoperative ultrasound of axillary lymph nodes in patients with breast cancer** Charles Douglas

1515 – 1545 Afternoon Break

1545 – 1715 **SESSION 4: METASTATIC DISEASE**

*Sponsored by Novartis Oncology*

Chair: Marie-Frances Burke

**Radiotherapy for breast cancer - Palliation** David Joseph

**Chemotherapy for metastatic breast cancer: Single agents or combinations?** Robin Stuart-Harris

**Phase II Combined Biological Therapy Targeting the HER2 Proto-Oncogene and the Vascular Endothelial Growth Factor (VEGF) Using Trastuzumab (T) and Bevacizumab (B) as First Line Treatment of HER2-Amplified Breast Cancer**

Mark Pegram

**Discussion** Faculty

1715 – 1845 Networking Drinks *Sponsored by AstraZeneca Oncology*

**Saturday 29 September 2007**

0730 – 0845 Breakfast – ASBD Annual General Meeting

0900 – 1030 **SESSION 5: PROGNOSIS AND PREDICTION IN BREAST CANCER**

*Sponsored by Roche Products*

Chair: Robin Stuart-Harris

**Keynote address: Estimating prognosis** Mark Pegram

**Will breast cancer genetic profiles replace formal pathology reporting?** Michael Bilous

**Assessing the genetic risk** Judy Kirk

**Predictive indicators in breast cancer pathology** Rosemary Balleine

**Discussion** Faculty

1030 – 1100 Morning Break

1100 – 1245 **SESSION 6: NEW APPROACHES IN DIAGNOSIS AND MANAGEMENT OF BREAST DISEASE**

Chair: Lynne Mann

**Keynote address: Partial breast radiation** David Joseph

**Keynote address: The evolution of a 21st century breast surgeon** Richard Rainsbury

**Digital mammography: Evidence and clinical applications and other 'new' technology in breast imaging** Stefano Ciatto

**Novel paradigms in drug development in breast cancer** Mark Pegram

**Discussion** Faculty

1245 – 1345 Lunch

1345 – 1500 **SESSION 7: PREVENTION, DETECTION AND DIAGNOSIS: COMPLEX AND CONTROVERSIAL ISSUES**

Chair: Warwick Lee

**Beyond randomised trials: Is there evidence of the effectiveness of breast screening in Australia?** David Roder

**False negative assessment in women recalled for suspicious screening mammography** Stefano Ciatto

**The problem of the "Borderline" (B3) core needle biopsy result** Michael Bilous

**Is prevention of breast cancer a reality?** Nicholas Wilcken

**Discussion** Faculty

1500 – 1530 Afternoon Break

1530 – 1700 **SESSION 8: CONTROVERSIES IN TREATMENT APPROACHES**

Chair: James Kollias

**Immediate breast reconstruction** Richard Rainsbury

**Reconstructive surgery** Bill Cockburn

**Post mastectomy radiotherapy** David Joseph

**Discussion** Faculty

**Presentations: Best Proffered Paper and Best Poster**

**Closing comments** Jennet Harvey

1700 – 1800 Annual General Meeting of the Australasian Society of Breast Physicians

1930 – 2300 Meeting Dinner *Sponsored by AstraZeneca Oncology*

SECTION 11  
**Abstracts**



# WORKSHOP

Sponsored by National Breast Cancer Centre

## Eliciting and responding to emotional cues in cancer patients

National Breast Cancer Centre Communication Skills Workshops

### Afaf Girgis

Centre for Health Research & Psycho-oncology, University of Newcastle, and The Cancer Council NSW, Australia

### Ms Katrina Read

Breast Surgeon, Melbourne, Victoria, Australia

Psychological distress is common in cancer patients and is often unrecognised or untreated. Consultations with anxious, angry or depressed cancer patients can be challenging and good communication is an effective tool to benefit both the patient and health professional. Patients can provide verbal and non verbal information or cues about their emotional or psychological state. Appropriately eliciting and responding to these cues is part of effective care and communication skills for health professionals<sup>1</sup>.

The *Eliciting and responding to emotional cues*<sup>1</sup> workshops will provide an overview of current evidence and recommendations for consulting and communicating with anxious, angry or depressed cancer patients.

Effective communication between health professionals and cancer patients can significantly benefit the patient and their family, including improvements in psychosocial adjustment, decision-making, treatment compliance and satisfaction with care. Effective communication has been shown to improve patient satisfaction with care and improves understanding of their problems, investigations and treatment options. Communication skills training has been shown to be effective in improving the wellbeing of health professionals through alleviating stress and reducing burnout<sup>2</sup>.

Communication skills training supports the implementation of the recommendations provided in the *Clinical practice guidelines for the psychosocial care of adults with cancer*<sup>2</sup>. The *Eliciting and responding to emotional cues*<sup>1</sup> workshops will provide practical techniques including active listening, using open questions and emotional words, and responding appropriately to a patient's emotional cues. Participants will receive a workshop pack with evidence based information and resources from the National Breast Cancer Centre's Communication Skills Training Initiative<sup>3</sup>.

Further information about the National Breast Cancer Centre's Communication Skills Training Initiative<sup>3</sup> can be found at the NBCC's dedicated communication skills website: <http://www.nbcc.org.au/bestpractice/commskills/>

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3. National Breast Cancer Centre. Communication Skills Training Initiative – better communication, better care, 2007. Website: <http://www.nbcc.org.au/bestpractice/commskills/>

## WORKSHOP

### Borderline core biopsy: Imaging, core needle and excision histology findings (includes case studies)

**Stefano Ciatto<sup>1</sup>, Michael Bilous<sup>2</sup>, Nehmat Houssami<sup>3</sup>**

*1. CSPO – Istituto per la Prevenzione Oncologica, Florence, Italy*

*2. Institute of Clinical Pathology and Medical Research (ICPMR), Westmead Hospital, Sydney, NSW, Australia*

*3. CSPO – Istituto per la Prevenzione Oncologica, Florence, Italy  
The University of Sydney, NSW, Australia*

## Combined oncoplastic breast surgery and radiation oncology: Case scenarios and tidbits

**Richard Rainsbury<sup>1</sup>, James Kollias<sup>2</sup>, David Joseph<sup>3</sup>**

*1. Oncoplastic Breast Unit, Royal Hampshire County Hospital, Winchester, United Kingdom*

*2. Royal Adelaide Hospital, St Andrews Breast Clinic and BreastScreen South Australia*

*3. Radiation Oncology, Sir Charles Gairdner Hospital, Perth, WA, Australia*

Radiotherapy is recommended in most cases of breast conserving surgery for DCIS and invasive breast cancer and for cases of “high-risk” breast cancer after mastectomy. A number of clinical trials are currently addressing issues of postmastectomy radiotherapy for moderate risk breast cancer, radiotherapy dosing schedules in case of DCIS and partial breast irradiation in early breast cancer.

Immediate breast reconstruction using tissue expanders or autogenous tissue methods is offered to many women with early breast cancer. The cosmetic impact of postmastectomy flap irradiation is not often appreciated by surgeons performing these procedures and should be discussed with women whose cancers are likely to require such therapy.

A staged approach to mastectomy to obtain definitive histopathology before deliberating on immediate breast reconstruction is an option that could be considered in cases where postmastectomy radiotherapy is being considered.

The recent introduction of oncoplastic techniques has lead to a need to reappraise the impact of breast irradiation on local recurrence rates and cosmesis. Issues of breast conserving therapy in BRCA1 / BRCA2 mutation carriers, radiotherapy after therapeutic mammoplasty and skin-sparing mastectomy are unresolved and require careful consideration. There is a paucity of high-level evidence for treatment results in such cases. Recommendations about treatment can be made after extrapolation of results from historical studies using more traditional surgical methods.

This workshop aims to present several case studies illustrating the clinical dilemmas faced by radiation oncologists and surgeons in cases undergoing oncoplastic surgical procedures and total breast reconstruction. Audience participation will be encouraged.

# SESSION 1: BREAST CANCER IN YOUNGER WOMEN 1

*Sponsored by AstraZeneca Oncology*

## Age and the prognosis of breast cancer

Nicholas Wilcken

*Westmead and Nepean Hospitals, NSW, Australia*

Young age (perhaps defined as <35 years) has long been associated with an adverse prognosis in early breast cancer. It has consistently been shown that younger women have larger, higher grade tumours that are less likely to be hormone receptor positive, and thus a worse outcome might be expected. Whether young age itself confers an adverse prognosis remains an issue of some debate. Large datasets suggest that this is the case, but that the adverse prognosis is mainly seen in those young women who did not receive adjuvant chemotherapy<sup>1</sup>.

Consistent with this, data from randomised trials suggest that the younger the age, the better the response to chemotherapy, and also that chemotherapy benefits are seen more in women with ER negative rather than ER positive tumours, further helping younger women<sup>2,3</sup>.

There are also data pooled from randomised trials that examine the fate of young women treated with adjuvant chemotherapy but with no additional endocrine therapy for those with ER positive tumours<sup>4</sup>. These data show very clearly (and counter-intuitively) that it is the young women with ER positive disease who have the worse prognosis.

Putting all this together, it is clear that young women with breast cancer do have an adverse prognosis, probably even when factors such as tumour stage, grade and receptor status are taken into account. However, this adverse prognosis is largely (but perhaps not completely) mitigated by the appropriate use of adjuvant chemotherapy and endocrine therapy. It is also likely that appropriate therapies targeting the HER2 receptor will further reduce the disadvantage of youth.

### References

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4. *Lancet* 2000; 355: 1869-74

## Keynote address: Is breast cancer different in younger women?

Michael Bilous

*Institute of Clinical Pathology and Medical Research (ICPMR), Westmead Hospital, Sydney, NSW, Australia*

There is a common perception among many of those involved in the diagnosis and treatment of young women with breast cancer that their disease will follow a poor clinical course. This perception may be enhanced by the publicity surrounding high profile young patients who have had aggressive disease as well as by personal experience. The questions to be answered are whether the perception is correct and if so why is breast cancer worse in young women? Is the prognosis related to age *per se* or to other pathology features of the cancer?

There is persuasive evidence that breast cancer in young women has a poorer prognosis when compared with older women. The Experts' Consensus of the 1998 St Gallen Conference concluded that age <35 was a poor prognostic factor. The evidence for this statement is derived from a number of studies which, however, show variation in the definition of "young" and also in the choice of a comparative age group. The latter is important as there is evidence for example of very good survival in the 40-44 age group and poorer survival in the over 70 age group. There is the added complication that breast cancer in the very young (childhood and adolescence) is most often of the secretory type which has a very good prognosis. Given that breast cancer is rare in women under 35 years (<2% of all breast cancer patients) many studies are of relatively small numbers of patients. However, in most series of under 35 year old women with breast cancer there is a decrease in metastasis-free survival and overall survival. In addition, there is an increase in the risk of local recurrence and a higher rate of distant metastasis when compared to older women. A detailed analysis of the pathology features of breast cancer in young women gives a partial explanation for this poor prognosis. One study by Colleoni et al (2002) reflects the findings of many groups. When compared to women aged 35-50 described as "less young", women aged <35 "young" had a higher rate of grade 3, ER and PR negative cancers, a higher rate of lymphovascular invasion and a higher proliferation rate as assessed by Ki-67 immunohistochemistry. There was no difference in tumour size, stage at presentation, lymph node status or HER2 overexpression between the two age groups. The large majority of studies have shown a similar preponderance of poor pathology factors in women <35. Differences of opinion arise however concerning whether age 35 and younger is a significant poor prognostic factor when these pathology features are excluded. These differences may relate in part to the population group with which they are compared but there remains some evidence that age remains a significant predictor of time to recurrence, time to distant failure and overall mortality from breast cancer after the exclusion of pathology factors.

As many as 15-30% of breast cancers in young women may be the result of BRCA1 and BRCA2 germline mutations. These tumours are more often associated with high grade, lack of ER and PR and an increased proliferation rate. An unspecified number are probably the result of gene polymorphisms, and a very small number arise in women who have had radiation therapy for another malignancy such as Hodgkin's disease. The cause of the majority however remains unknown. An increased incidence of high grade ductal carcinoma in situ has been noted in association with cancers in young women and this together with the "triple negative" status of the invasive tumours suggests a specific pathway in common with similar appearing grade 3 cancers seen in older age groups, and lacking a recognized precursor lesion such as atypical ductal hyperplasia or lobular neoplasia.

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## Keynote address: Imaging in younger women

Stefano Ciatto

CSPO – Istituto per la Prevenzione Oncologica, Florence, Italy

### Clinical diagnosis in women <40 years of age

Breast cancer (BC) is rare <40 years of age (4.8 % of all cancers, 4 times less frequent than at age 40-49, 10 times less frequent than at age 50-59), which partly explains why no population based screening option is under discussion at this age. Benign lesions which may cause symptoms and create problems of differential diagnosis with cancer are much more frequent at younger age. This is known by clinicians which may cause bias towards a more optimistic attitude, and possibly using a less aggressive diagnostic approach. This, in addition to the limitation of imaging in young women, may contribute to a tendency to have a lower index of suspicion for non-specific or borderline clinical findings, potentially reducing sensitivity.

BC is reported to be more aggressive in younger women, but prognosis is not clearly related to age when adjusted for stage. Stage at diagnosis is often reported to be more advanced in younger women, but this not our experience when screen detected cancers are excluded<sup>1</sup>. Similarly, histological type is not different according to age. Also morphology at imaging (M and/or US) is generally similar, with a slight prevalence of masses over microcalcifications in younger as compared to older women, although one might expect masses to be more easily masked by dense breast<sup>1</sup>.

Clinical studies comparing diagnostic tests accuracy at different ages are often affected by selection biases. Many guidelines and policies arbitrarily select an age (such as 35 or 40) to recommend M or US as initial or preferred imaging investigation in symptomatic women, but this is not strictly based on evidence. In addition, it should be kept in mind that, while younger women (<40) are mostly self referring for symptoms, over the age of 40, even in clinical series, the proportion of asymptomatic women having imaging for 'screening' (i.e. attending via a diagnostic clinic but seeking screening) might be substantial, and not easy to be clearly identified and excluded from evaluation. Evidence from pooled analysis of clinical studies suggests US to be more sensitive than mammography in younger women up to a certain age (which varies between studies). One study (based on a large series from Florence) was designed to establish the "cross-over" age (the age range for which one test may be more sensitive than the other, and the 'cross-over' is the age at which the sensitivity of both tests is equal) – this showed that US is more accurate than M up till age 48 years<sup>2</sup> (cross-over age = 48 years). After the age of 48 years mammography is more sensitive than US. A recent study on 1,000 clinically evident breast cancers<sup>3</sup> confirms a higher sensitivity of US as compared to mammography up to age 49 (so almost the same cross-over age), and shows that for younger women triple diagnosis employing US as the imaging method of choice allow for the best achievable results, with no additional benefit of including mammography (for the purpose of diagnosis). Overall, there is no evidence that combined multimodal imaging diagnosis in symptomatic younger women is less sensitive compared to older women (especially if needle biopsy is included as part of triple assessment in line with standard practice).

### Screening of women aged <40 years with hereditary-familial risk

This is a special and unique subset of the population, harbouring a minority of all BC (approximately 5%) but with very high individual risk, 5-8 folds higher than the general population. This makes screening for early diagnosis a reasonable option. BC is expected at a younger age than the affected relative, that is at an average age where the radiological density of the breast limits the efficacy of mammography screening – even where it is integrated with US screening accuracy is still limited. The higher sensitivity of breast MRI compared to mammography has suggested the use of MRI as a periodic screening test in this group.

In fact, a higher sensitivity of MRI as compared to mammography +/- US is well proven<sup>4,5</sup>. On the down-side, MRI has poor specificity, false positives being reported in the range of 15%. Considering the possible negative psychological impact of a false positive report in these subjects, one should ensure that MRI is only used where false positives are immediately ruled out with MRI guided biopsy (if mammography and US second look is negative), but MRI guided biopsy is not currently available in most settings. Watchful waiting and/or US second look are used, as an alternative, but their reliability and reassuring impact are still unclear. It is important to also keep in mind that there is no scientific evidence that MRI screening of young high risk women confers benefit (i.e. no evidence that MRI screening reduces mortality)<sup>5</sup>, nor any evidence that it is cost-effective.

These women have a substantial risk of dying of breast cancer (5-8 folds more than 4% currently observed in the general population). Based on what we know on screening efficacy in 40-49ers, and presuming the impact of screening 'standard risk' populations translates to these younger women, expecting a 20% reduction in mortality by screening (even with MRI) may be quite optimistic. On the other hand we know that any surveillance regimen, due to expected diagnostic aggressiveness and to screening test limited

specificity, will lead to a high cost in terms of recall rate, invasive assessments, unnecessary benign surgical biopsy, and possibly a high psychological cost. Chemoprevention (e.g. Tamoxifen) might be an alternative to screening some women, or might be combined with it. We cannot ignore that for the time being bilateral prophylactic mastectomy is the only highly effective option we have to control BC death (and incidence) in these subjects<sup>6</sup>. This alternative, associated with high personal cost but also a very high (otherwise unachievable) benefit, should be carefully explained to the woman seeking prevention, to be sufficiently informed to allow a really conscious decision. Imbalance in proposing possible options, from surveillance to prophylactic bilateral mastectomy, would be clearly unethical.

### Screening of women aged 40–49 years

Mammography screening of women aged 50–69 years is currently recommended in most developed countries in the world, and population-based service screening is ongoing in the European Union and in other countries. The current policy on screening women aged 40–49 years is much more debated. This mainly depends on the fact that the evidence on screening efficacy is more uncertain. Classic trials were not specifically designed to demonstrate screening efficacy for 40–49s, were lacking statistical power, and gave conflicting results. Several meta-analyses were carried out, most showing a 10–15% borderline significant mortality reduction. This is further complicated by the fact that trials investigated the effect of screening in invited vs. not invited (rather than in screened vs. not screened) and in women at age 40–49 “at entry”, with at least 60% of screen detected cancers being diagnosed after age 50. Also, it should be noted that interval cancer rates are relatively high (in service screening) in this age-group. Lower efficacy of screening in 40–49 year olds has also been attributed to ‘older’ technology used in the classic screening trials (done in the late 1960’s to early 1980’s) which might be less sensitive than modern mammography, and inadequate (two year) interval adopted in the trials. Nevertheless the UK “age trial” adopting “modern” yearly mammography of women in their forties has confirmed a 17% borderline significant (0.83, 95% CI = 0.66–1.04) mortality reduction

Due to the uncertainty of the cost-effectiveness of screening at age 40–49, population based (active invitation, government-funded) screening is not recommended as a current population health policy in the European Union, and individual decision whether to be screened or not is encouraged, after proper information on screening pros and cons. Correct information is very important, as it has been shown that women tend to exaggerate screening benefits, overestimating its impact on mortality by several folds. Inadequate information might lead to unrealistic expectations of prevention by screening, induce false reassurance, and cause underestimation of subjective symptoms.

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## SESSION 2: BREAST CANCER IN YOUNGER WOMEN II

*Sponsored by Pfizer Australia*

### Oncoplastic breast surgery

**Dick Rainsbury**

*Oncoplastic Breast Unit, Royal Hampshire County Hospital, Winchester, United Kingdom*

#### Introduction

Until lately, the surgical management of breast cancer has centred around two options – breast-conserving surgery or mastectomy. Recently, techniques combining resection with reconstruction in one procedure are leading to the emergence of oncoplastic breast-conserving reconstruction (BCR) as a third alternative. The rise in popularity of these techniques indicates that their future impact on surgical management of breast cancer will be of a similar order of magnitude as the introduction of radical mastectomy and breast-conserving surgery (BCS). Oncoplastic BCR techniques address the ‘clash of interests’ between achieving a thorough local excision whilst minimising the risk of local deformity. The wider the local resection and margin of clearance achieved, the smaller the risk of incomplete excision and subsequent local recurrence. For the first time, the direct impact of local recurrence on long term survival has recently been confirmed,<sup>1</sup> highlighting the need for thorough local excision.

The extent of local excision increases the risks of local deformity, an unacceptable cosmetic outcome and psychological distress.<sup>2,3</sup> Loss of breast volume is the key factor leading to cosmetic deformity, particularly when resecting tumours in the central, medial and inferior locations.<sup>4</sup> BCR procedures extend the role of BCS to a group of patients who would otherwise require mastectomy to achieve tumour clearance. These procedures combine the best principles of resection to achieve clear margins with the best principles of reconstruction to optimise the cosmetic outcomes. They also require the simultaneous deployment of general surgical oncological skills and plastic surgical reconstructive skills.

The emergence of oncoplastic surgeons with a range of oncological and reconstructive skills is increasing the availability and use of these procedures in clinical practice.<sup>5</sup>

#### Indications

The most frequent indication for BCR arises when the patient with operable breast cancer requests BCS, but the surgeon is unsure whether adequate excision can be achieved without causing major breast deformity. The likelihood of unacceptable deformity escalates when > 20% of the breast excised.<sup>4</sup> BCR is used most commonly to extend the role of BCS when resecting 20-50% of breast volume,<sup>5</sup> and new assessment tools enabling objective assessment of volume loss following BCS are being evaluated.<sup>4</sup> BCR is proving a useful alternative to total mastectomy and immediate reconstruction in patients requiring post-mastectomy radiotherapy by virtue of nodal status or other histopathological features.<sup>6</sup>

#### Potential benefits

BCR offers a ‘win-win’ option for an increasing number of patients. These techniques enable very extensive local excision with resulting oncological benefits,<sup>7</sup> while the patient avoids extensive surgery, and the higher complication and morbidity rates associated with total mastectomy and immediate reconstruction. Early evidence suggests good local control,<sup>8</sup> fewer complications, reduced sensory loss and less disability, when compared with skin-sparing mastectomy and immediate reconstruction.<sup>9</sup>

#### Choice of technique

BCR encompasses two fundamentally different techniques. Firstly, volume displacement (VD) or reshaping techniques, which transpose local breast parenchymal flaps into the resection defect. Secondly, volume replacement (VR) techniques, which transpose autologous tissue from an extra-mammary site. VD techniques are most suitable for patients with medium to large, ptotic breasts, for whom volume loss may have physical benefits. Contralateral breast reduction is usually required to achieve symmetry. Conversely, VR techniques are most suitable for patients with small or medium sized breasts who wish to avoid volume loss and contralateral surgery to achieve symmetry. VD techniques adapt conventional reduction mammoplasty procedures to facilitate tumour resection within the wide margin of tissue normally discarded during the cosmetic procedure. Adaptation of a range of reduction mammoplasty approaches have been described.<sup>10</sup>

The majority of VR procedures described use either latissimus dorsi or adipose tissue flaps.<sup>11,12</sup> This approach can be used for immediate and delayed reconstruction as well as for correction of volume loss after previous BCS. BCR can be performed as a one-stage procedure with intraoperative margin analysis, or as a two-stage procedure with paraffin section margin analysis prior to reconstruction.

## Outcomes

For VD, 11 retrospective studies involving 433 patients have reported local recurrence rates of 0-7% and cosmetic failure rates of 0-18% at a median follow up of 21-54 months. For VR, 7 studies involving 189 patients have reported local recurrence rates of 0-5% and cosmetic failure rates of 0-9% with a median follow up of 24-53 months. Complications experienced following BCR include fat necrosis, haematoma, positive margins, infection, local recurrence and flap loss, experience at some time by 68%, 55%, 47%, 41%, 16% and 10% of respondents to a recent UK survey, respectively.<sup>5</sup>

## Conclusion

BCR techniques offer greater choice to women with breast cancer and are extending the role of BCS without cosmetic or oncological penalties. Greater use of these techniques awaits assessment of their clinical utility and the wider availability of oncoplastic skills.

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## Endocrine therapy for early breast cancer in younger women

Nicole McCarthy

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Breast cancer in women of a young age has been reported to pursue a more aggressive clinical course and is associated with a more unfavourable prognosis compared with the disease in older women. Endocrine therapy is an essential component of effective adjuvant therapy with the "optimal" treatment in the premenopausal woman remaining elusive. The Early Breast Cancer Trialists' Collaborative Group reports the oldest form of hormonal treatment, ovarian ablation, offered an unequivocal survival benefit compared with no therapy for women under the age of 50 years<sup>1</sup>. In addition, the ovarian suppressive or ablative effects of chemotherapy in young women have been recognised which raised the possibility that the benefits of chemotherapy might be mediated in part by the indirect effects on the ovary leading to oestrogen deprivation. This observation led to a generation of clinical trials comparing ovarian ablation (OA) with surgery or radiation therapy or ovarian suppression (OS) using luteinising hormone-releasing hormone (LHRH) agonists with chemotherapy or in addition to chemotherapy. Unfortunately, the short fall of these trials was the failure to incorporate tamoxifen because of the belief it was not effective in premenopausal women. This was proven to be incorrect in 1995.

Direct comparisons of OA/OS with chemotherapy using mainly cyclophosphamide, methotrexate and fluorouracil-based regimens show similar survival benefits<sup>2</sup>. The addition of OA/OS to chemotherapy has shown a small survival benefit in women 40 years of age or younger with no additional benefit seen in women over 40 years<sup>2</sup>. This younger age group are less likely to become menopausal as a result of chemotherapy and achieving chemotherapy-induced amenorrhoea at 12 months has been shown to be associated with a superior relapse-free and overall survival. The question regarding the role of LHRH agonists in the younger woman with hormone receptor positive early breast cancer who remains premenopausal following chemotherapy will become increasingly important given the newer and more effective chemotherapy regimens are often associated with a lower chance of inducing premature menopause. Unfortunately, no trials have assessed the role of an LHRH agonist versus chemotherapy with tamoxifen in both arms.

The role of the aromatase inhibitors (AI) in premenopausal women is unknown. These agents have been used in women with chemotherapy-induced amenorrhoea and have resulted in subsequent recovery of ovarian function. In this setting, tamoxifen should be considered or an LHRH agonist must be given in combination with the AI.

Several key international trials are looking to answer some of the questions regarding optimal hormonal therapy in premenopausal women with hormone receptor positive breast cancer that remain elusive. The Suppression of Ovarian Function Trial (SOFT) compares 5 years of tamoxifen, OA/OS plus tamoxifen and OA/OS plus exemestane in premenopausal women who have not had chemotherapy or who continue to have premenopausal levels of oestradiol after chemotherapy. The TEXT (Tamoxifen and Exemestane) Trial compares LHRH agonist plus tamoxifen versus LHRH agonist plus exemestane.

The implications of the potential benefits of amenorrhoea have significance for young women, particularly those concerned about fertility and for some this may impact on treatment choices. The return of menstrual cycling is unfortunately an imperfect surrogate for ovarian functioning and fertility. Other physical and psychological consequences of hormonal therapies are also very important such as hot flushes, genitourinary problems, psychosexual difficulties and accelerated bone loss. Screening and prevention of such problems among premenopausal survivors may improve health outcomes.

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# Management of pregnancy-related breast cancer

Geoffrey Beadle

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The relationship of pregnancy and breast cancer is problematic in clinical practice but offers potentially important molecular insights into breast cancer risk and behaviour. Key issues extend beyond the management of breast cancer during pregnancy and include the feasibility and advisability of pregnancy after a diagnosis of breast cancer, and the impact of pregnancy on a subsequent diagnosis of breast cancer.

Approximately 6% of Australian women with breast cancer are 39 years or younger at the time of diagnosis and preservation of fertility is an important, and sometimes unrecognised, concern for these women. As the evidence to support the use of adjuvant chemotherapy increases, more young women are now being offered treatment that can suppress ovarian function. This is a particularly important issue since the overwhelming majority of good prognosis subsets are exposed to the risk of suppression of ovarian function during the first year after diagnosis increases with older pre-menopausal age and the use of cyclophosphamide-based chemotherapy and tamoxifen<sup>1</sup>. Recovery of menstruation is also inversely related to age<sup>2</sup>. The use of alkylating agents such as cyclophosphamide are particularly gonadotoxic but the addition of anthracyclines appears to add little to this risk of infertility. The emergence of taxanes as an important class of drugs in adjuvant chemotherapy regimens has created further uncertainty about increased infertility since amenorrhoea appears to be slightly more likely in regimens containing this class of drugs.

Efforts to protect against chemotherapy-induced ovarian damage remain controversial. The use of LH RH analogues to suppress ovarian function are intuitively attractive but the protective effect remains uncertain<sup>3</sup>. Assisted reproductive technologies include embryo cryo-preservation and the more controversial ovarian tissue cryo-preservation. Ovarian hyperstimulation is successful in retrieving oocytes but there are concerns about the resulting surge of estrogen levels and the delay of initiating systemic treatment on cancer outcome as well as the risks associated with the procedure and the declining pregnancy rate per transfer with increasing age.

Another important consideration is the impact of subsequent pregnancy on breast cancer outcomes. Clinical studies are hampered by small numbers and the inability to reliably assess confounding prognostic factors. This is important since one Australian study reported up to 4.8% of women diagnosed under 45 years became pregnant after a breast cancer diagnosis and 2.6% had a live birth<sup>4</sup>. Pregnancy was associated with improved overall survival and there was no evidence that conception less than 2 years after a breast cancer diagnosis was different from women with a gap of more than 2 years.

In contrast to the concerns about fertility and the impact of pregnancy on survival after a prior breast cancer diagnosis, the management of breast cancer during pregnancy has immediate practical implications. Pregnant women require an accurate diagnostic assessment and timely management. The duration of pregnancy at the time of diagnosis often influences decisions about management. The teratogenic effects of ionizing radiation and cytotoxic drugs during the first trimester of pregnancy pose difficulties about diagnosis and management at this time. Imaging investigations during pregnancy are often more difficult to interpret because of physiological changes in the breast but mammography with abdominal shielding exposes the fetus to extremely low doses of ionizing radiation. Surgery is also feasible during pregnancy but radiation treatment to the breast is contraindicated. Numerous studies have evaluated the feasibility and safety of chemotherapy during the second and third trimesters. All studies are characterized by small numbers but there is no apparent increased risk of maternal or fetal complications. Normal physical, neurological and psychological development has been documented in long term follow-up studies of children exposed in utero to chemotherapy. In contrast, fetal abnormalities have been described in women taking tamoxifen during pregnancy and therefore the use of tamoxifen is contraindicated<sup>5</sup>.

Decisions about the management of the pregnant patient with breast cancer are characterized by the desire to maintain the pregnancy and the influence on pregnancy on the selection of treatments. The benefit of termination of pregnancy on outcomes is unknown and the sequencing of treatment modalities is not necessarily compromised by a diagnosis of breast cancer during the second and third trimesters. Management decisions for any individual patient therefore need to take into account the desire by the patient to continue the pregnancy, a careful explanation of the risks and uncertainties, and the need to adapt treatment modality sequencing to the duration of the pregnancy.

Although breast cancer associated pregnancy is reported to have a worse prognosis, stage-for-stage outcomes appear to be equivalent to non-pregnant women. The possible exception is those women presenting with advanced breast cancer during pregnancy where the clinical impression is one of more aggressive behaviour and greater resistance to treatment. Late stage presentation is often considered to reflect a delay of diagnosis but, given the relatively long natural history of breast cancer, other biological mechanisms are plausible. Support for this view is provided by epidemiological studies that report an adverse prognostic effect of pregnancy 2 years or less before a diagnosis of breast cancer<sup>6</sup>. During this preclinical phase of breast cancer development, pregnancy associated hormonal changes could plausibly play a role in breast cancer behaviour. High circulating insulin-like growth factor has been reported during pregnancy and this ligand, along with its receptor and other members of the insulin family of growth factors, are emerging as important players in breast cancer behaviour<sup>7</sup>.

Pregnancy associated breast cancer and decisions about pregnancy after a diagnosis of breast cancer are among the most highly emotive issues in the management of breast cancer. This problem has been exacerbated by limited data about management and outcomes. However, sufficient information has now accumulated to recommend that treatment guidelines should be adapted to fetal protection, not treatment avoidance. There is no proven role for therapeutic termination. Management should be individualized, taking into account gestational age, the patient's stage of disease and the patient's values. A multi-disciplinary team approach that includes both psychological support and genetic counseling is important for the optimal management of pregnancy associated breast cancer and for those women who seek pregnancy after a breast cancer diagnosis.

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## Ablation of fibroadenoma

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Cryoablation is a minimally invasive method to treat breast lesions. It is an office-based procedure that is performed under local anaesthesia with image- (usually ultrasound) guidance in a similar way to image-guided breast biopsy.<sup>1,2</sup> The equipment and technique for cryoablation (and other ablative methods) is not currently approved for use in Australia but is in clinical use in some parts of the world, particularly the USA. The aim of the procedure is to destroy the cells in breast lesions without the need for open surgical biopsy.

Background information about the technique and science behind cryoablation will be presented. A systematic review of the published evidence is in progress and key findings from this review will be presented including data on efficacy and safety of the procedure. Possible indications and contraindications for practice will be discussed from an international perspective, with emphasis on potential role in clinical practice in Australia.

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## SESSION 3: PROFFERED PAPERS

### Intra-operative ultrasound-guided hook-wire localisation for impalpable breast lesions

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#### Background and purpose

The management of women with screen-detected impalpable breast lesions requiring surgery for definitive diagnosis or treatment forms a large part of current breast surgical practice. It is therefore important for surgeons to have a reliable system for accurate localisation of these lesions. Several localisation techniques are in common use including pre-operative hook-wire localisation (HWL), radio-guided occult lesion localisation (ROLL) and marking the skin overlying the lesion (pre-operatively or intra-operatively.)<sup>1,2</sup> Consistent access to quality localisation services presents a challenge to many surgeons. A modification of the HWL technique using a portable ultrasound (US) unit allowing placement of the wire by the surgical team under general anaesthetic is described.

#### Methods

Patients undergoing HWL surgery were examined pre-operatively with a portable US unit and considered suitable for the procedure if the lesion was clearly visualised. Under general anaesthesia with the patient positioned for surgery, the lesion was identified with US and a hook-wire was placed through the lesion by a breast physician, also the surgical assistant. The skin immediately overlying the lesion was marked to assist with placement of the skin incision and measurements of lesion size, depth and position in relation to the wire tip were made. The lesion was excised by the surgeon and specimen imaging was performed if the lesion was not obviously palpable following excision.

#### Results

Intra-operative US-guided localisation of a series of 13 lesions (benign n=10 and malignant n=3) in 11 patients is reported. Data including lesion size, imaging features, percutaneous biopsy results and surgical histopathology results are presented. All lesions were removed without complication.

#### Conclusions

This small series has shown the intra-operative HWL procedure to be feasible and safe. The numerous advantages for the patient and surgeon that this technique has over traditional HWL are presented.

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#### Acknowledgement

The authors thank Cl A/Prof Owen Ung who contributed a case to the series.

# A multidisciplinary risk management clinic for women at high genetic risk of breast and ovarian cancer - Experience and evaluation

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## Background and purpose

A Risk Management Clinic (RMC) providing multidisciplinary care for women at high risk of breast and ovarian cancer was established in 2006 by the Familial Cancer Service at Westmead Hospital. This service has identified approximately 200 women with germline BRCA1 or BRCA2 mutations. Some of these women and others with a strong family history of breast/ovarian cancer were invited to attend the RMC. Details of eligibility criteria for invitation to attend and reasons for non-attendance have been previously presented.<sup>1</sup> The RMC is staffed by a cancer geneticist, a breast physician, a gynaecological oncologist and a clinical nurse consultant. Women undergo screening for breast and ovarian cancer and are provided with detailed information and advice about risk-reducing strategies including prophylactic surgery. Experience from the first year including evaluation data will be presented.

## Methods

Thirty-six women attended the monthly clinics during its first year in 2006. The average age of clinic attendees was 42 years (range 25–67). This included 16 BRCA1 gene mutation carriers, 14 BRCA2 gene mutation carriers and six women with a potentially high-risk family with an inconclusive or unavailable result from genetic testing.

A questionnaire was mailed to the 37 participants after they attended the clinic seeking feedback on the clinic and its services. The questionnaire sought information about reasons for attendance and satisfaction with various aspects of the clinic.

## Results

Twenty-six women returned completed questionnaires (response rate 72%). Respondents expressed a high level of overall satisfaction with the clinic with 96% stating they were satisfied or very satisfied with their experience. The most frequent reason for attending the clinic was to have screening tests performed (45%).

## Conclusion

The RMC, in its current form, is meeting many of the needs of women at high genetic risk of breast and ovarian cancer and will continue to provide this model of care.

## Reference

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## Acknowledgement

Karen Robinson is supported by a grant from the Cancer Institute NSW. The authors acknowledge the staff at the Peter MacCallum Cancer Institute Risk Management Clinic and the Royal Marsden Hospital for their assistance in the development of the clinic and the evaluation.

## Hormone receptor status in East African breast cancer patients - A different disease?

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### Background

African women with breast cancer have a worse prognosis than Caucasian women with breast cancer from developed countries. Evidence suggests that although many African or Afro-American women present with more advanced cancers, poorer outcomes are seen even when confounding factors such as stage of presentation and treatment availability are eliminated. Patients with breast cancers that express estrogen receptors (ER) and/or progesterone receptors (PR) have an improved prognosis. 60-70% of all breast cancers in the developed world express these receptors. Only one study has examined ER/PR status in African women in rural Africa. The aim of this study was to determine the hormonal receptor status in patients presenting to our institution in rural Kenya.

### Methods

Prospective data were collected on consecutive patients presenting to our hospital between July 2001 and March 2007. Tissue samples from patients with ductal carcinoma were freshly fixed in buffered formalin. Paraffin blocks were then made and transported to a regional pathology department for ER/PR analysis.

### Results

One hundred and twenty-nine patients presented with ductal carcinoma. The mean age at presentation was 48 years. Fifty-eight percent of our patients presented with locally advanced disease, with a mean symptom duration of 12 months. ER/PR status was determined in 120 of our patients, with only 24% being ER-positive/PR-negative and 34% ER- and/or PR-positive.

### Conclusions

East African women present at a younger age with far more advanced breast cancers and markedly lower hormonal receptor positivity than women from the developed world. These findings are almost identical to a previous study from Tanzania. This low hormonal receptor expression suggests that East Africans have genetically unique breast cancers and may help to explain their poor prognosis. Further work to investigate these differences is indicated. In addition these data may have implications for the design of adjuvant treatment regimens in Africa.

# Minimal access breast surgery - A single breast incision for breast conservation surgery and sentinel lymph node biopsy

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## Background and purpose

Minimal access breast surgery (MABS) is where the breast conservation procedure and sentinel node biopsy (SNB) is completed through a single incision. It can involve accessing the axillary SNB via the breast but may also allow access to the internal mammary nodes (IMN) or occasionally other sites. This study aims to demonstrate the utility, safety and efficacy of MABS.

## Methods

Review of 71 consecutive clinically node negative breast conservation surgery (BCS) cases, with successful SNB from the data base of a single surgeon between May 2006 and May 2007.

## Results

4 groups were identified: Group 1: single incision for breast and axillary SNB - 42 procedures, 124 axillary nodes removed (2.9 per case) with 14 positive (33%). Group 2: single incision on breast with axillary and IMN SNB - 8 procedures, 25 axillary nodes removed (3.1 per case) with 6 positive (75%). Group 3: separate incisions on breast and axilla (including 1 breast augmentation case with separate breast, axillary and IMN incisions) - 12 cases, 25 axillary nodes removed (2.4 per case) with 3 positive (25%). Group 4: single incision for BCS and IMN SNB but separate axillary incision - 9 cases, 20 axillary nodes removed (2.2 per case) with 2 positive (22%). Overall there were 19 cases that had IMN biopsy with 2 positive (10%). Reasons for separate incision were more medial and lower inner quadrant tumours, central tumours in a large firm breast, previous breast implants, and indeterminate node on ultrasound but cytology negative. Axillary aesthetic results are excellent with no scar whilst the breast aesthetics are no worse. Closure of breast plate is facilitated by the extra mobilization. Completion axillary dissection was done using MABS in 4 cases - all in upper outer quadrant.

## Conclusion

MABS is technically feasible in 70% of clinically node negative BCS cases and appears equivalent to separate incision axillary SNB. It gives superior aesthetic results.

## The breast care nurse practicum – A multidisciplinary approach to breast care nurse education and support

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The importance of education, ongoing professional development and support for Breast Care Nurses has recently been highlighted. This is particularly important for nurses working in isolation, and those in rural and remote areas. Working in collaboration with The College of Nursing, the NSW Breast Cancer Institute has developed the Breast Care Nursing Practicum for post-graduate nurses wishing to gain further clinical experience in breast cancer care.

The practicum is a five-day intensive course that is designed to build on nurses' theoretical knowledge of breast care gained during post-graduate study. The program is designed to bridge the gap between educational processes and real world experience by providing exposure to the practical and clinical aspects of the Specialist Breast Care Nurse role. Experience from the five courses in the first 12 months of the program will be presented.

The Practicum resulted in an increase in knowledge about breast cancer and an increase in confidence in caring for women with breast cancer. A need for ongoing support has been identified and the Practicum has been extended to include support and mentoring in the form of an email discussion group, teleconferencing and videoconferencing. Details of this new strategy will be discussed and future directions of the program for 2007/8 will be discussed.

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### Acknowledgment

The Practicum is supported by the Strengthening Support for Rural Women with Breast Cancer initiative, a project funded by the Commonwealth Department of Health and Ageing and coordinated by NSW Health, to improve support for women with breast cancer in rural and remote regions across Australia. The mentoring component is supported by the Commonwealth Department of Health and Ageing.

# Intraoperative ultrasound for determining clear histological margins during breast conservation therapy

David Clark

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Obtaining histologically clear margins in patients undergoing breast conservation therapy is important in terms of local recurrence and possibly for survival. Using intraoperative ultrasound for assessing margins improves the rate of tumour-free margins and avoids the removal of unnecessarily large volumes of normal breast tissue. Specimen ultrasonography was performed on the excised carcinomas of 232 patients in this prospective study conducted from January 2005 until December 2006. Clear histological margins were achieved in 206 patients (89%). Prior to the use of intraoperative ultrasound for this purpose, the rate was 72%. The method employed is reliable, rapid and leads to better cosmesis, improved patient satisfaction, lower morbidity and is cost-effective. Radiologically occult DCIS remains problematical in achieving clear margins.

## Results

There were 232 patients, with a mean age of 59 years, ranging from 22 to 92. The median age was 57 years. Of these patients, 105 had palpable cancers and 127 had subclinical cancers. The cancers were located and removed in all patients. Clear histological margins were obtained in 206 patients, as shown in Table 1.

The histopathologies of the cancers are shown in Tables 2 and 3.

**Table 1**

Clear US margins vs clear Histological margins

		Not Clear	Clear	% Clear
<b>Palpable</b>	<b>(105)</b>	11	94	89
<b>Impalpable</b>	<b>(127)</b>	17	110	88

**Table 2**

Histopathology vs clear Histological margins - palpable lesions

		Not Clear	Clear
<b>IDC Grade 1</b>	<b>(15)</b>	1	14
<b>IDC Grade 2</b>	<b>(35)</b>	3	32
<b>IDC Grade 3</b>	<b>(37)</b>	3	34
<b>ILC</b>	<b>(11)</b>	2	9
<b>DCIS</b>	<b>(1)</b>	0	1
<b>Other cancers</b>	<b>(6)</b>	2	4

**Table 3**

Histopathology vs clear Histological margins - impalpable lesions

		Not Clear	Clear
<b>IDC Grade 1</b>	<b>(39)</b>	4	35
<b>IDC Grade 2</b>	<b>(30)</b>	3	27
<b>IDC Grade 3</b>	<b>(28)</b>	4	24
<b>ILC</b>	<b>(11)</b>	1	10
<b>DCIS</b>	<b>(15)</b>	3	12
<b>Other cancers</b>	<b>(4)</b>	0	4

# Preoperative ultrasound of axillary lymph nodes in patients with breast cancer

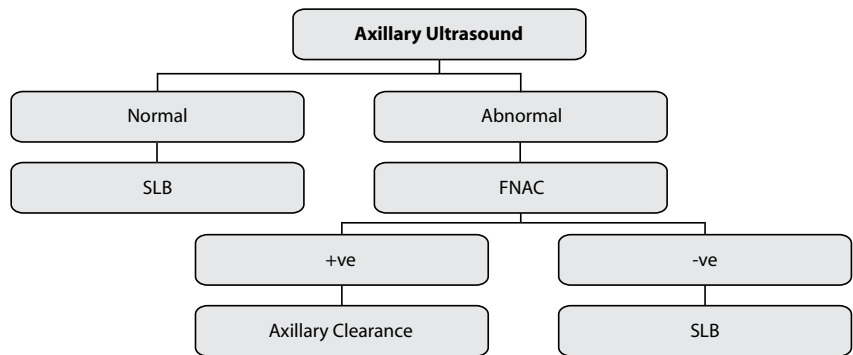
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## Background

The finding of a positive sentinel node often means progression to an axillary clearance either at the same operation or at a subsequent admission to hospital. Preoperative targeted axillary ultrasound could decrease the rate of sentinel node positivity in clinically node negative breast cancer patients.

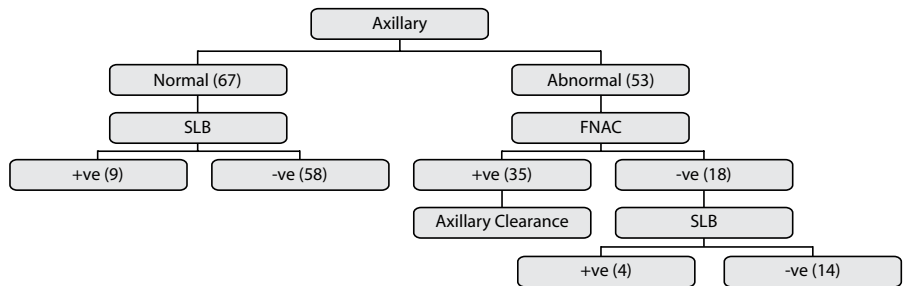
## Methods

All clinically node negative breast cancer patients had axillary ultrasound with or without fine needle aspiration cytology.



## Results

Only 13 of 120 patients had an unexpected positive sentinel node. 35 patients were upstaged, and thus had axillary clearances.



## Conclusion

Preoperative axillary ultrasound with fine needle aspiration cytology of abnormal nodes accurately stages patients preoperatively, decreasing the rate of conversion from sentinel node biopsy to axillary clearance.

## SESSION 4: METASTATIC DISEASE

*Sponsored by Novartis Oncology*

### Radiotherapy for breast cancer - Palliation

**David Joseph**

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Management of Breast Cancer cases contributes up to 30% of workload in radiotherapy departments. Up to 30-40% of total workload in departments has been palliation in the past but it is more like 20% in most modern units.

A significant proportion of this is palliation of breast cancer cases. The most common problems requiring palliation are bone metastases, brain metastases with specific problems including spinal cord compression, orbital metastases and meningeal disease.

Another area is the treatment of locally advanced/inflammatory cancers or local control in patients with metastatic disease exhibiting excellent response to systemic therapies. In these cases treatment is often given with the same technique and doses as radical intent cases and long term survival is possible.

Most patients with metastatic breast cancer will succumb to their disease but long term survival is common and is becoming more frequent because of the effectiveness of systemic therapies. Breast cancer palliation therefore needs to take into account the potential for relapse and late effects (of the situation with other solid tumours such as lung cancer).

The management of breast cancer palliation is multi disciplinary often involving specialised surgery (breast, plastic, neurosurgical, radiosurgery, orthopaedic), medical oncology, radiation oncology, palliative care teams.

The management of bone metastases depends on site, uni vs multifocality, other disease activity and may vary from surgery, stereotactic surgery, palliative localised RT, wider field RT, isotope therapy, systemic therapies (chemotherapy, hormone therapy, biologics, bisphosphonates).

RT is very effective in palliation of bone secondaries. There are differences of opinion regarding single vs multiple fractions and on the use of specialised techniques such as stereotactic radiosurgery.

A special area of bone metastases/neurologic is metastatic spinal cord compression (MESCC). This represents medical emergency requiring urgent intervention to prevent paraparesis. Studies show it is important to integrate spinal decompression with radiotherapy.

Brain metastases are also frequent and appear to be becoming more so because of the effectiveness of systemic therapies elsewhere (ex Herceptin). A number of modest randomised studies have investigated the role of surgery, whole brain radiotherapy (WBRT) and stereotactic radiosurgery. Patients with metastatic breast cancer to the brain may have prolonged survival (especially those with single metastases) so long term function is important.

Patients presenting with isolated supraclavicular/chest wall recurrences are often treated with radical intent (loco-regional RT). They benefit from systemic hormone therapy (if sensitive) and the role of chemotherapy, biologics is controversial.

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## Chemotherapy for metastatic breast cancer: Single agents or combinations?

**Robin Stuart-Harris**

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Few, if any, patients with metastatic breast cancer (MBC) are cured by medical therapy. Therefore, the impact of medical therapies on patients' quality of life is very important. Cytotoxic drugs were first used for MBC in the 1960s and initially the drugs were used as single agents. In the 1970's several trials suggested that combinations were superior to single agents and thus combinations became the standard of care. Although combinations are probably more effective, usually they cause greater toxicity than single agents and therefore combination regimens may impair the patient's quality of life more than single agents. A 1998 meta-analysis of 15 trials of single agent versus combination chemotherapy for MBC indicated that combinations were associated with a significantly higher objective response rate, better survival and a significantly lower risk of death, than single agents. However, this meta-analysis did not include taxanes and other new agents commonly in use today.

With respect to the efficacy of a treatment, oncologists tend to focus on response rates and survival, but patients focus on the duration of their survival and the quality of that survival. For some patients, particularly those with rapidly progressive visceral metastases, it is important to obtain disease control as rapidly as possible and thus for these patients, combination regimens are probably more appropriate than single agents. For other patients, particularly elderly or frail patients, single agents may be more appropriate and may produce disease control with a more acceptable toxicity profile than a combination regimen. Thus, no single strategy suits all patients and the selection of chemotherapy for MBC needs to be tailored to the individual patient.

# Phase II Combined Biological Therapy Targeting the HER2 Proto-Oncogene and the Vascular Endothelial Growth Factor (VEGF) Using Trastuzumab (T) and Bevacizumab (B) as First Line Treatment of HER2-Amplified Breast Cancer

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## Background

Activation/overexpression of HER2 is associated with up-regulation of VEGF in human breast cancer cells *in vitro*, and there is strong association between HER2 and VEGF expression *in vivo*, which predicts clinical outcome in primary breast tumors [Konecny, *et al.*, Clin Cancer Res 10: 1706–1716, (2004)]. In xenograft models, superior efficacy is observed when T is given in combination with B. In a phase I dose-escalation study of T plus B, we previously reported a recommended phase II dose of B 10mg/kg q 2 weeks plus T 4mg/kg loading dose, then 2mg/kg weekly (Pegram, *et al.* SABCS 2004). Pharmacokinetic (PK) analysis indicated co-administration of these two humanized monoclonal antibodies did not alter the PK of either agent. Clinical responses were observed in 5 of 9 patients in phase I, including one patient with prior disease progression on T. Taken together, these data support the use of combination therapies directed against both HER2 and VEGF for treatment of breast cancers with HER2 amplification.

## Methods

Phase II study objectives: to determine clinical efficacy of T plus B antibody combination, and to evaluate the safety profile of T plus B. Key eligibility: female patients (age 18-75), pathologically confirmed HER2-amplified (by FISH) metastatic or locally-relapsed, surgically-unresectable breast cancer, normal left ventricular ejection fraction determined by MUGA or ECHO, bidimensionally measurable disease, and signed informed consent. Key exclusions: any prior or concurrent chemotherapy in the metastatic setting, newly-diagnosed, untreated stage IIIB breast cancer, CNS metastasis, clinically significant cardiovascular disease, proteinuria, coagulopathy, bleeding diathesis, or anticoagulation, >3 different organ sites of metastasis, >50% parenchymal liver metastasis, or symptomatic pulmonary metastases.

## Results

At interim analysis, 37 of 50 patients dosed have preliminary response information. Patient characteristics: prior mastectomy - (89%), prior radiation - (47%), prior adjuvant/neoadjuvant chemotherapy - (54%), prior endocrine therapy - (49%), visceral metastasis - (62%). Grade III/IV drug-related adverse events: dyspnea (N=1), left ventricular dysfunction (N=1), HTN (N=7), and proteinuria (N=1). Most common grade I/II adverse events: fever/chills/headache/infusion reaction (N=14), fatigue (N=6), epistaxis (N=6), HTN (N=6), and AST or ALT increase (N=10). Thirteen cardiac adverse events (all grades, any causality, NCI-CTC version 2) have been reported, one of which was symptomatic: 7 grade 1, 5 grade 2, and 1 grade 4. Investigator reported, objective clinical responses (WHO criteria) have been documented in 20 of 37 (54%) evaluable patients. Eleven additional patients had stable disease at week 8. One third of the evaluable patients remained on treatment at the time of this report.

## Discussion

This is the first phase II trial of two humanized antibodies given in combination to human subjects. B in combination with T is clinically feasible and active in HER2-amplified recurrent or metastatic breast cancer. Stringent cardiac safety surveillance has been added under protocol amendment. These data support the use of combination therapies directed against HER2 and VEGF for treatment of breast cancers with HER2 alteration.

## SESSION 5: PROGNOSIS AND PREDICTION IN BREAST CANCER

### *Keynote address: Estimating prognosis*

**Mark Pegram MD**

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Because of the extreme biologic diversity of breast cancer, estimation of clinical prognosis in breast cancer is a formidable challenge. Forecasts of clinical prognosis are used in clinical decision making, particularly for selection of optimal systemic adjuvant therapy regimens, but also for approaches for local control such as surgery and ionizing radiation. Such information, when relayed to patients, can also have profound psychological consequences - particularly when estimates of mortality are contemplated.

Traditional estimates of clinical prognosis in breast cancer incorporate histopathologic categorization, tumor and lymph node staging, nuclear and/or histologic grade, measurement of markers of proliferation (mitoses, S-phase fraction, or Ki67 expression), presence or absence of steroid hormone receptor expression, and alteration of erbB2 (gene amplification and/or resulting protein overexpression). Unfortunately, despite all of these tumor characteristics and measurements, accurate assessment of clinical prognosis using the above conventional criteria remains problematic. This is due, at least in part, to the subjective nature of histopathologic classification and grading, potential sampling error in nodal staging, significant inter-laboratory variation in reagents used for testing proliferative potential, ER/PR, and erbB2 (and subjectivity in qualitative measurements of these factors), and finally the clinicians educated guess as to how to weigh each of these factors (as well as other co-morbid medical conditions) in determining overall prognosis. Consequently, it is not unusual for an individual patient to be given a wide range of forecasts of clinical prognosis from different medical professionals all considering the same clinic-pathologic data.

Recently, the estimation of clinical prognosis in breast cancer has been revolutionized by the advent of computer aided clinical decision making. The most widely used system to date is Adjuvant! Online ([www.adjuvantonline.com](http://www.adjuvantonline.com)). The computer algorithm generates not only prognostic information, but perhaps even more importantly, predictive estimates of the utility (or lack thereof) of various systemic adjuvant therapy modalities such as endocrine therapy and/or chemotherapy. Thus Adjuvant! allows the user to perform analyses that provide projections of the net benefit of adjuvant therapy for breast cancer. Because Adjuvant! was directly derived from mortality data and because details of local therapy (surgery and initial radiation) can strongly influence local relapse rates (more so than mortality), Adjuvant!'s estimates of mortality are more firmly based than those for relapse. Breast cancer outcome estimates made by Adjuvant! are for patients who have unilateral, unicentric, invasive adenocarcinoma of the breast, who have undergone definitive primary breast surgery and axillary node staging, and who have no evidence of metastatic or known residual disease. If they have had breast conserving therapy there should be plans for them to receive radiation therapy. They should not yet have received systemic therapy (neoadjuvant therapy), or radiation prior to their surgical staging. For patients with special histologic subtypes of pure tubular, pure papillary, or medullary histologies, or inflammatory breast cancer the help files should be consulted. The program will soon likely incorporate data from multiple large, prospective, randomized adjuvant trastuzumab trials for erbB2-positive patients.

The field of breast cancer classification is also being rapidly revolutionized by new molecular classification schemes based upon measurement of multi-gene expression profiles. Two platforms are now approved in the U.S., one a 21-gene multiplex Q-PCR assay (Oncotype DX™), and the other a 70 gene transcript expression microarray (MammaPrint®). Oncotype DX™ is a diagnostic assay that quantifies the likelihood of breast cancer recurrence in women with newly diagnosed, early stage breast cancer that is lymph node negative and estrogen receptor positive. In addition to predicting distant disease recurrence in patients treated with adjuvant Tamoxifen, Oncotype DX also assesses the benefit from chemotherapy. The assay – performed using formalin-fixed, paraffin-embedded tumor tissue – analyzes the expression of a panel of 21 genes and the results are provided as a Recurrence Score™ (0-100). The gene panel was selected and the Recurrence Score calculation was derived through extensive laboratory testing and multiple independent clinical development studies. The selection of the 16 cancer genes used for the Oncotype DX assay was based on the results of the three clinical trials, which demonstrated a consistent and strong statistical link between these genes and distant breast cancer recurrence. Five reference genes were identified to normalize the expression of these cancer-related genes. It should be noted however, that the mathematical algorithm for computation of the recurrence score gives the highest weight to steroid hormone related genes, genes on the erbB2 amplicon, and markers of proliferation. Advantages of this assay include its use of paraffin embedded material and standardization and accuracy of measurement of expression of individual genes. Potential disadvantages

include its high cost, and the uncertainty of the significance of an intermediate recurrence score value (the latter is being addressed in ongoing prospective randomized trials).

The *MammaPrint*<sup>®</sup> assay relies on a 70-gene transcript expression profile. By performing DNA microarray analysis on primary breast tumors of patients, investigators were able to identify a gene expression signature that was strongly prognostic for development of distant metastasis in lymph node negative patients. The 70-gene prognosis expression signature consists of genes regulating cell cycle, invasion, metastasis and angiogenesis. The gene expression profile was validated on a consecutive set of over 1000 patients (mainly European) and has been demonstrated to outperform all currently used clinical parameters in predicting disease outcome. *MammaPrint*<sup>®</sup> uses customized microarrays, manufactured by Agilent. Each microarray contains three identical sets of the 70 genes to be analyzed. This enables three independent measurements of the 70-gene profile, increasing confidence in the test result. In addition, the customized arrays contain several hundred carefully selected normalization genes. Finally, negative control genes are present on each microarray; these are DNA sequences to which no human mRNA can bind and are used to monitor various technical aspects of the microarray process. Special tissue handling is required for this assay in order not to allow RNases to degrade the RNA needed to perform the assay.

Ultimately, convergence of both molecular/genetic profiling and computer aided prognostication algorithms (such as Adjuvant! Online, genomic version) will likely markedly improve clinical decision making, thus sparing patients potential toxicities and costs from unnecessary systemic adjuvant therapies.

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## Will breast cancer genetic profiles replace formal pathology reporting?

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Decisions concerning the clinical management of a woman with breast cancer are being based on an ever-increasing number of data items. The small set of clinical and pathology measurements in use 20 years ago have been extensively supplemented by a sophisticated data set including receptor protein status and gene expression profiles. These advances are the result of research that is giving us a better understanding of cancer cell development and growth control at the DNA level. It is hoped that the end result for the patient will be that before treatment is initiated the nature of their cancer will be known in such detail that a specific treatment plan can be devised with a higher probability of success.

The prognosis for a woman with breast cancer is assessed principally from a set of macroscopic and microscopic pathology data such as histological grade, tumour size and axillary lymph node status. The decision whether or not a patient will benefit from systemic therapy is based on this information together with the oestrogen and progesterone receptor (ER,PR) status of the cancer which act as predictive factors. Given the heterogeneous nature of breast cancer, all this information is still insufficient to accurately assess the individual's risk of relapse or metastasis and as a result as many as 30% of women who receive systemic therapy for early breast cancer may not have needed it.

In order to improve this patient selection process, hundreds of proteins have been investigated in breast cancer tissue samples in the hope that these will provide more accurate predictive or prognostic information about the cancer. Most of these have not proved to be of use in routine practice. However, of the potentially useful molecular markers, the epidermal growth factor receptor family has proved to be one of the most valuable. There are four of these tyrosine kinase receptors, HER1-4, and HER2 (c-erbB-2) is the member of the family that appears to be of greatest importance in breast cancer as it is associated with a generally poor prognosis. HER2 is also however, the target for Trastuzumab, a humanised monoclonal antibody therapy which has produced a marked improvement in survival rates for patients with both early and metastatic breast cancer overexpressing the HER2 receptor on the cancer cell surface.

Individual genes in breast cancer have been studied for many years in an attempt to identify those responsible for growth control and metastasis. However, the completion of the Human Genome Project as well as the recent advent of DNA microarray technology and sophisticated data analysis software, have allowed the simultaneous analysis of thousands of genes in tissue samples. This has enabled breast cancers to be grouped according to their gene expression "profile" or "signature". These molecular analyses have already had a profound effect on our understanding of cancer growth. Among the information gained has been the identification of new breast cancer subtypes, the prediction of metastasis, response to therapy and prognosis, and the effect of various exogenous agents and hormones on cancer development. Large scale clinical trials are currently underway using this genetic information to select patients for chemotherapy. What is also required is a standardisation of laboratory techniques including specimen handling and data reporting. The "gene chips" used in genetic profiling are now commercially available from a number of companies and each chip may contain as many as 20,000 gene fragments to which the patient's cancer sample and normal tissue are hybridised.

The challenge for the breast pathologist is to integrate the information provided by the analysis of the proteins and genes in breast cancer cells with standard pathology data obtained by careful macroscopic and microscopic examination of the cancer specimen. There is also a need to correlate the new subtypes of breast cancer identified by genetic profiling with the existing histological classification advocated by WHO and others. This process is well advanced with the basal-like breast carcinoma identified first as a subtype with a specific genetic signature, but also recognised by the pathologist as having a characteristic set of microscopic features.

It is likely that in the very near future for every breast cancer there will be integration of information derived from clinical examination, pathology assessment of the tumour, receptor protein measurements and a genetic profile. From this information a treatment plan will be derived targeted specifically to the patient's cancer.

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## Assessing the genetic risk

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Breast cancer is usually associated with an accumulation of somatic (tissue) mutations in a series of essential cancer-related genes. There are some rare families, however, where a heritable (germline) mutation in one of these genes (eg BRCA1, BRCA2, p53, or PTEN) causes a high risk of cancer. These families usually have a stronger history of breast/ovarian cancer (and sometimes other cancers) affecting a number of individuals on the same side of the family, often at a relatively early age. The lifetime breast cancer risk for female carriers of BRCA1 mutations is estimated to be 60-80%, with a similar risk for BRCA2. Breast cancers attributed to germline BRCA1 mutations are often (not always) histologically distinct, characterised by high grade, high mitotic rate and lack of expression of ER, PR and HER2 (triple negative phenotype). BRCA2 related breast cancers have not been reported to have a specific phenotype. For women with a BRCA1 gene mutation and a new diagnosis of early breast cancer, treated with either mastectomy or conservation, the cancer outcome does not seem to significantly differ. However, the future risk of contralateral breast cancer may be as high as 60% over a lifetime, and sometimes this needs to be considered at the time of treatment decisions. Women who know they carry a BRCA1/2 mutation at the time of diagnosis are more likely to consider bilateral mastectomy and immediate reconstruction. In vitro, BRCA1 can regulate differential sensitivity to different classes of chemotherapy. Current studies may determine whether BRCA cancers are more sensitive to platinum-based chemotherapy. Inhibitors of the poly-adenosine diphosphate ribose polymerase 1 enzyme (PARPi) are being investigated as a specific therapy for BRCA cancers.

BRCA1 carriers also have an ovarian (and fallopian tube) cancer risk of 20-40% compared to 10-20% for BRCA2. Men with mutations in either of these genes are at increased risk of prostate cancer. Germline BRCA2 mutations may be associated with an increase in male breast cancer, pancreatic, gall bladder, bile duct and stomach cancers as well as melanoma.

Inherited mutations in other DNA repair pathway genes, such as ATM, CHEK2, BRIP1, PALB2 and others (known and as yet unknown) may cause a more moderate risk.

At a practical level, risk of cancer based on family history of breast and/or ovarian cancer can be assessed according to NHMRC/NBCC guidelines. In some families genetic testing may be used to identify a causative gene mutation, firstly in an affected family member. There are many families where this testing is "inconclusive". However, if a breast cancer susceptibility gene mutation can be identified in an affected family member, then other "at risk" adult individuals may be tested to clarify their risk status. Women at high genetic risk may be advised about early detection (including breast MRI) and risk reduction strategies.

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## Predictive indicators in breast cancer pathology

### Rosemary Balleine

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In recent years, advances in the understanding of breast cancer have made a major impact on the detail and significance of information provided in a pathology report. This includes new emphasis on features that are indicative of sensitivity to specific forms of treatment.

Currently the most direct indicators of treatment response identified in a tumour specimen are actual treatment targets or reflect the activity of molecular pathways that can be targeted. For example, presence of the hormone receptors ER and PR, is strongly associated with response to various forms of endocrine therapy. Amplification of the oncogene *HER2/neu* that is associated with response to *HER2* targeted agents, is the only other biomarker that is currently routinely assessed. However, the suite of individual biomarkers that are analysed will increase as additional targeted agents become available.

In addition to recognition of individual molecular targets, there is potential for subtypes of breast cancer with particular vulnerability to specific forms of treatment to be recognised by tissue pathology. For example, breast cancer occurring in *BRCA1* mutation carriers may be particularly sensitive to certain forms of chemotherapy as a consequence of defective DNA repair mechanisms in these tumours<sup>1</sup>. Recognition of the characteristic breast cancer pathology frequently seen in *BRCA1* mutation carriers<sup>2,3</sup> may therefore become a useful predictive indicator.

Features of breast cancer pathology are already an integral component of management planning. With further progress towards the goal of individualised cancer treatment, this role for pathology will increase.

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## SESSION 6: NEW APPROACHES IN DIAGNOSIS AND MANAGEMENT OF BREAST DISEASE

### *Keynote address: Partial breast radiation*

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Breast conserving therapy in women with operable breast cancer is now performed as a routine treatment. A series of well conducted randomized controlled trials with long follow-up have clearly demonstrated that treatment involving the complete excision of the primary tumour with whole breast radiotherapy is at least equivalent to mastectomy<sup>1</sup>.

There is also clear evidence that after BCS (Breast Conserving Surgery) RT to the breast is optimal management with data such as the EBCTCG meta-analysis demonstrating that RT reduces the risk of local relapse and improves overall survival<sup>2</sup>.

No randomized study has been able to conclude that radiotherapy can be avoided after BCS.

It is also clear though, that with the advent of widespread mammographic screening many women have small tumours detected early and that these have a very good prognosis. Clinicians have therefore attempted different maneuvers to allow good local control without giving all women whole breast RT after BCS. These efforts have included utilizing Tamoxifen in patients with small, node negative, tumours responsive hormone once again it appears clear that the addition of BCT still reduces the risk of LR by 70% what is different, however, is that we now see some patients with very low risk of LR despite avoiding BRT. A LR risk of < 20% at 5 years is now commonly seen (despite no BRT) and hence the question is asked why treat all the patients to benefit so few?

At the same time the potential side effects of BRT after BCS is questioned – especially the increase in cardiac events. The current update of the EBCTCG overview 2006 indicates that for women who have small, node negative, hormone sensitive tumours over the age of 50 there is only a small LR benefit and a slight negative survival effect from the addition of BRT to BCS<sup>3</sup>.

Also to be considered is the cost, financial, time effort, disruption of a 6 week course of BRT. It is not understood by many that significant numbers of women are denied optimal BCS because of lack of access and to avoid disruption to their lives. Many are forced to accept mastectomy because of this<sup>4</sup>.

These factors have led to an interest in the testing of partial breast RT as a potential way of allowing access to BCS with a minimum of disruption to their lives, but still avoiding the risks of LR.

It is well known that in the studies of BCS ± RT that the pattern of failure is 80%-90% in the index quadrant.

Recurrence elsewhere in the breast occurs equally whether or not BRT is given (also contralaterally).

Partial breast radiotherapy is already proven to successfully reduce the risk of LR in the index quadrant. This is clear from the EORTC Boost Trial where patients at high risk benefit most<sup>5</sup>. Why not apply this principle in low risk women with unifocal tumours after BCS as the primary treatment?

This hypothesis is worth testing in randomized trials. It is not an appropriate treatment to be routinely offered in the clinic. The potential benefits are considerable and include: Access to BCS, avoidance of cost and dislocation, avoid delay in local treatment (BRT often delayed for up to 6 months to allow systemic therapies), avoid toxicities of the whole RT. There are potential disadvantages of PBI<sup>6</sup>. Pathologic data from post-mastectomy specimens show a substantial risk of tumour more than 1–2 cm from the margin of the primary tumour<sup>7</sup>. Long term studies demonstrated that elsewhere failures do continue beyond 10 years of follow-up. However; studies like these<sup>7</sup> usually involved patients not suitable for BCS (who had simulated BCS often with +ve margins) and the ongoing recurrence 'elsewhere' is the same whether or not BRT was given!

It is very unlikely that partial breast radiation (alone) would be suitable for all women. Patients with different levels of risk of LR/patterns of risk need individualization of managements.

There are competing/complimentary approaches and technologies being investigated. These include immediate treatment at operation of the primary: Intraoperative RT with electrons (Eliot) or photons (Intrabeam). Techniques given at a variable time post operatively 'accelerated partial breast irradiation' where the treatment is delivered over 5 days utilizing BD fractionation of interstitial brachytherapy, mammosite brachytherapy or 3DCRT (NSABP B39 RTOG0413).

Eligibility for these trials vary. The group involved with one of these studies (TARGIT) recommends careful selection of patients with the study offered to patients considered to be at 'low risk' of LR. A major difference of the TARGIT Study compared to the other randomized studies is that TARGIT is testing a refinement to treatment rather than just PBI. In the TARGIT Study only patients found at post-operative review of pathology to be at 'low risk' have PBI alone. (IORT) Factors that indicate higher risk mean that the patient has whole breast RT and that in these patients PBI (IORT) was effectively a very accurate boost.

Patients more likely to be suitable for this approach have small, unifocal tumours, age > 50 years, post menopausal, free tumour margins, node negative, no lymphovascular invasion, Grade I, hormone receptor positive, non lobular, no EIC $\oplus$ , given systemic treatment (for enhanced local effect of PBI).

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## Keynote address: The evolution of the 21<sup>st</sup> century breast surgeon

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### The past

Breast surgery has undergone a revolution over the last 50 years. The development of randomised controlled trials in the 1960's and 1970's heralded a sea change from purely surgical management of breast cancer to a modern multidisciplinary approach, including the introduction of breast-conserving treatment. This era saw increased specialisation in breast surgery, with the emergence of specialised academic breast units.

Around this time the momentum for breast reconstruction was building up, with the description of three core procedures - latissimus dorsi, TRAM-flap and subpectoral reconstruction in 1976<sup>1</sup> and 1982.<sup>2,3</sup> By the 1980's, the world-wide introduction of breast screening was acting as a major catalyst for surgeons to learn new skills, to develop new services, and to specialise further. The introduction of a UK National Breast Screening Programme in the 1990's triggered off a chain of inter-related developments, including a National Cancer Policy, a robust quality assurance system and an audit of outcomes.<sup>4</sup> The multidisciplinary team rapidly became the core component of breast cancer units, developing and using a variety of emerging clinical practice Guidelines in different countries.<sup>5,6,7</sup> Increased specialisation was leading to better outcomes for patients. Improved survival was reported from high volume units<sup>8,9</sup> and high volume surgeons.<sup>10</sup>

By the close of the 20<sup>th</sup> century, breast surgery was at a crossroads. Consultants were becoming more specialised, services increasingly sophisticated and patients more demanding. Paradoxically, a career in breast surgery was becoming increasingly unpopular with trainees in the UK and in Australia.<sup>11,12</sup>

### The present

Three key factors are changing the face of breast surgical services at the start of the 21<sup>st</sup> century - public expectations, increasing specialisation and changes in workforce demographics and employment legislation. These changes are most acute in the UK and mainland Europe, but are beginning to affect both North America and Australasia. Public and healthcare provider expectations are impacting on the configuration and delivery of breast services. National and International Guidelines<sup>13</sup> are laying down standards which demand increased specialisation and which support greater patient involvement and choice. At the last UK election, the Government pledged that all women with breast problems would be seen within two weeks. This will be difficult to achieve without a change in working practice and the use of skill mix. Hospitals are appointing breast surgeons rather than general surgeons, and more than 50% of consultant posts for breast surgeons in the UK in 2006 specified experience in breast reconstruction with no on call commitment. Escalating litigation and indemnity costs are narrowing fields of surgical practice in a society with zero tolerance.

Increased specialisation is leading to a progressive loss of surgical skills. In the UK, 90% of general surgeons with an interest in breast surgery were treating more than 100 new cases of breast cancer per year in 2001, compared with only 5% in 1985. Breast referrals account for 25% of the total outpatient workload in general surgical departments, with 430 surgeons treating 44,000 new cases of breast cancer annually. As a result, less than 10% of breast surgeons' time is now spent performing elective general surgical operations.<sup>14</sup> In light of these changes, the Association of Surgeons of Great Britain and Ireland has recommended 'progress towards defined training in breast surgery', and has acknowledged the 'likelihood that breast surgeons would not in future be on the on call rota for general surgery'.<sup>15</sup>

Changes in workforce demographics, combined with a shorter working week and fewer opportunities for workplace training are leading trainees to choose specialties with controllable lifestyles, financial success and limited responsibilities.<sup>16</sup> Over 70% of new medical graduates are now women. The elective nature of breast surgery, coupled with new opportunities to learn oncoplastic reconstructive techniques, has led to a massive increase in recruitment into breast surgery training grades in the UK. There are now over 330 trainees with an interest in breast surgery, of which 40% are women. Forty-five senior trainees have completed Oncoplastic Fellowships, and many have been appointed as consultant oncoplastic surgeons, who are now passing on these skills to their own trainees. This is a model which is attracting considerable interest in mainland Europe and North America.

## The future

The next decade will see major changes in patient case mix and expectations, surgical technique, service configuration and training curricula. On the one hand, earlier detection and neoadjuvant treatment will minimise surgical intervention in a growing number of patients. New approaches to tissue replacement using tissue engineering, lipomodelling and minimal access techniques will reduce scarring and optimise cosmetic outcome. On the other hand, better identification of women at risk, more sophisticated imaging, and an increased desire for better aesthetic outcomes will increase demand for oncoplastic, risk-reducing, bilateral and cosmetic surgery.

Greater emphasis on 'patient choice' informed by publication of surgeon-related outcomes linked to national audits will lead to the growth of large multidisciplinary specialists centres, and the demise of small ones. Many of the core aspects of diagnostic and outpatient services will be provided by a multidisciplinary workforce, including surgeons, nurse practitioners, general practitioners, radiographers and others. A 'common trunk' core curriculum will provide the necessary training and certification for those surgeons and others carrying out diagnostic work and less invasive day case procedures. Those selected for higher level training will acquire a range of hybrid skills in corrective, prophylactic, oncoplastic, reconstructive, salvage and cosmetic breast surgery. This will lead to the emergence of a new specialty of breast surgery in the near future.

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# Digital mammography: Evidence and clinical implications; and other 'new' technology in breast imaging

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Digital mammography (DM) has been commercially available for at least one decade. Purchase cost is high (5-10 times that of a conventional mammography unit), and shifting from screen-film (SFM) to DM needs careful analysis of comparative accuracy and cost-effectiveness.

## Diagnostic accuracy

Physical measurements of image quality and comparative diagnostic studies suggest that DM is not inferior (and may be slightly better) to SFM as far as perceived information and diagnostic accuracy. Most comparative studies of screening SFM and DM suggest no significant difference in overall accuracy. A recent large study by Pisano et al<sup>1</sup> (the DMIST study) showed no overall difference for the two compared techniques but indicated a significantly higher sensitivity of DM for cancer detection in younger women and in women with dense breasts. A more recent comparative study of concurrent cohorts in screening in Florence<sup>2</sup> confirms that DM has a higher sensitivity in younger women with dense breast, but the improved detection is concentrated in cancers depicted as isolated microcalcifications<sup>2</sup> – the downside is that DM also had a higher recall rate<sup>2</sup>. Based on this evidence DM is likely to be at least as accurate as SFM, but probably has better accuracy (sensitivity) in subgroups (dense breasts, younger women). The implications of this are not clear because in the Florence study the additional cancer detection was mainly for microcalcifications (so possibly less aggressive cancers). Evidence on higher sensitivity needs to be confirmed in other settings – higher 'efficacy' of screening using DM is not supported by any scientific evidence (ie no evidence that it reduces mortality over and above SFM).

## Costs

Costs of DM are substantially higher compared to SFM. Purchase cost is determinant, whereas current cost is lower than SFM, as films are no longer used and images are archived electronically. Adopting a high workload per DM machine (e.g. 10,000 tests/year) will substantially reduce cost, although the break even point is still not reached<sup>3</sup>. Now that several firms are commercializing DM, if competition will lead to purchase cost reduction, the present situation might be reversed, with DM being cheaper than SFM.

## Workload for radiographers and radiologists

There is no evidence that radiographers working time to obtain a mammogram is reduced with DM (if comparison with SFM implies a dedicated daylight developer adjacent to the mammography unit<sup>3</sup>). Reduction of working time to obtain a mammogram often claimed for with the introduction of DM may be ascribed to suboptimal efficiency compared to SFM.

Increase of radiologist reading time with the introduction of DM has been repeatedly reported, being almost double<sup>3</sup> as compared to SFM (with films displayed on a rotating viewer, which of course implies the work of a clerk displaying films, and removing them after reading). This depends a) on a lower acquisition of images, b) on the adoption of a standard image sequence (including direct full screening magnification) which is employed also for fatty breasts where it should not be necessary, and c) on the better image details (magnification) which need to be analysed.

## Other applications of DM

- Computer assisted detection (CAD)

CAD has been developed prior to DM, with SFM films being digitized and then processed by a special algorithm to identify Regions Of Interest (ROI) for review. Although it had no success in Europe due to its high cost and impractical implementation, its value as an adjunct to conventional reading has been the object of several studies and there is no reason to expect CAD not to have the same diagnostic performance when applied to DM. Of course CAD use with DM, with the algorithm implemented as a software on the reading workstation, and ROI marks being displayed immediately on the monitor, is ideal.

CAD is relatively sensitive for screen detected cancers and interval cancers reviewed as screening errors (i.e. 'obvious' cancers that should have been recalled), but is not very sensitive for "difficult" cancers, such as interval cancer reviewed as minimal signs or screen detected cancer identified by only one of two readers<sup>4</sup>. Moreover, CAD is poorly specific with an average of one ROI being displayed per view. This means that out of 1,000 cases approximately 4,000 ROI are shown, of which not more than 20 correspond to cancer lesions, that is a ROI PPV of 0.5% and a specificity between 5 and 10%! This is translated into a relative increase of sensitivity as compared to single conventional reading of approximately 10%, and a relative increase in recall rate of approximately 10-12%. With the risk of radiologists discounting the value of CAD being annoyed by the excess of false positives.

Although a few controlled studies comparing single reading + CAD to double reading had conflicting results, the performance of single reading + CAD and double reading are quite similar when the average results of non controlled studies are considered, and the role of CAD as an alternative to double reading (currently recommended as a standard for screening by the European Union) is worth further research as it would allow a substantial reduction of costs. A prospective trial in the UK examining this issue with DM + CAD is due to report end of 2007 (CADET 2).

#### - Remote reading

Remote transmission of digitized images (e.g. for a second opinion) has been possible for many years, when digital photography and e-mail were introduced, but has not been used extensively. Transmission of DM images for remote delayed or immediate reporting (e.g. with centralized reading, or with remote mobile units) seems a more appealing option for the future, which nevertheless requires proper electronic equipment, dedicated lines or wireless connections. This option is particularly relevant in Australia because of its geographic vastness.

#### - Tomosynthesis

This is 'new' technique (in reality almost 50 years old) was formerly called "stratigraphy". X-ray source and detector are at the two ends of a rotating axis centred on a given level. All objects (and breast lesions) at that level are projected on the same site of the detector and are thus enhanced. Objects on other levels are projected on different portions of the detector and fade away. The technique is aimed at better analysis of dense breasts, as it would allow us to depict lesions which, on the standard 2-view mammography, are masked by the surrounding dense tissue. Clinical studies validating the technique in a clinical or screening setting are lacking, the technique is costly, time consuming and implies greater exposure. Definitely not ready for prime time, but clinical research in progress.

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## Novel paradigms in drug development in breast cancer

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Despite significant advances in the field of clinical oncology, including improvements in surgical techniques, radiation therapy, and defining active combination chemotherapy doses and schedules, many challenges remain in developing molecularly targeted agents with selective activity against malignant cells, thus sparing normal cells from collateral toxicities.

Advances in tumor biology have led to the emergence of unique therapeutic targets. Uncontrolled expression of growth factors and their receptors is one feature of tumor growth, frequently correlating with rapid disease progression and poor prognosis. One such family of growth factor receptors that has been extensively studied as a potential therapeutic target is the HER family. HER-family ligands, such as epidermal growth factor (EGF) directly stimulate tumor cell proliferation by binding to HER receptors. Receptor tyrosine kinases within the HER family are frequently overexpressed, amplified, or mutated in tumor cells. A high level of expression of HER receptors, particularly HER2, in tumors also allows ligand-independent activation of the receptor, stimulating tumor cell growth in the absence of ligand.

Trastuzumab (Herceptin®) - a recombinant humanized monoclonal antibody raised against HER2 - represents the first successful example of the clinical development of a highly specific agent targeted to an oncogenic protein. Many agents are currently being developed that target other HER family members. The small molecule inhibitors erlotinib (Tarceva™), gefitinib (Iressa®), and the monoclonal antibody cetuximab (Erbix™) all target HER1/EGFR, while pertuzumab (rhuMAB2C4) inhibits HER2 dimerization of HER2 with other members of the HER family. Finally, lapatinib represents a small molecule TKI which inhibits both HER1/EGFR and HER2 kinases. It has clinical activity in patients who have been previously treated with anthracyclines, taxanes, and trastuzumab. In summary, these agents prevent signaling through the HER family of receptors, leading to cytostatic and cytotoxic effects on tumors.

In addition to growth factors that stimulate tumor cell proliferation directly, many tumors overexpress vascular endothelial growth factor (VEGF), which stimulates the development and maintenance of tumor vasculature - an essential feature of tumor growth. VEGF, the central mediator of angiogenesis, binds and activates receptors found on normal vascular endothelial cells, promoting their survival, proliferation and migration. VEGF stimulates new blood vessel growth and functions as a key maintenance factor for immature tumor vasculature. Unlike normal vasculature, tumor vasculature is leaky, disordered, and frequently dependent on growth factors, such as VEGF, for survival. Due to its critical functions, VEGF has emerged as a prime target for anti-cancer therapy.

Several agents are in development that target VEGF or members of the VEGF family of receptors, including bevacizumab (Avastin™), PTK-787, VEGF-TRAP, Angiozyme®, and SU11248. The recombinant humanized anti-VEGF monoclonal antibody, bevacizumab is the most advanced agent in clinical development, with several ongoing phase III clinical trials in a variety of tumor types, including MBC. In earlier stages of disease, before tumor vasculature is firmly established and when tumors are more dependent on VEGF for vascularization, anti-VEGF therapy may be particularly effective.

Due to their critical roles in tumor growth, both HER receptors and VEGF represent important biologic targets for anticancer therapies. The distinct mechanisms of action of targeted biologic therapies are likely to have nonoverlapping side effect profiles and may therefore provide additive or synergistic effects in combination with a variety of therapeutic modalities: chemotherapy, radiation, and other biologic therapies. These agents are emerging as new therapeutic options in the treatment of breast cancer, and are currently being assessed in several randomized clinical trials.

Monoclonal antibodies and small molecules differ greatly with regard to their target specificity, pharmacokinetics, mechanism of action and potential for further engineering (e.g. to deliver toxic payloads, or to elicit anti-tumor immune responses). However, they need not be considered as mutually exclusive in cancer therapy. Exploiting their similarities and differences will likely offer many potential therapeutic options within each class, between classes, and through integration with other therapies such as chemotherapy, radiation, or other molecularly targeted approaches.

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## SESSION 7: PREVENTION, DETECTION AND DIAGNOSIS: COMPLEX AND CONTROVERISAL ISSUES

### Beyond randomised trials: Is there evidence of the effectiveness of breast screening in Australia?

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A meta-analysis of results of eight randomised controlled trials undertaken since the 1960s indicated that 40-74 year old women *invited* for screening in these trials experienced a 24% reduction in breast-cancer mortality.<sup>1</sup> An expert Group of the International Agency for Research on Cancer considered that these trial data were consistent with a 35% reduction in breast-cancer mortality in 50-69 year old women who *participated* in the screening.<sup>1</sup>

A review of evaluation studies of screening services introduced after these trials indicated a relative risk of breast-cancer mortality in screening participants of around 0.57, when compared with non-participants.<sup>2</sup> This equated with a reduction in breast-cancer mortality of 43%. However, after adjusting for the screening self-selection bias observed in the screening trials, the reduction was reduced in scale to approximately 32%.<sup>2</sup>

In a NSW study, where the association of population screening participation with reduction in population-based breast-cancer mortality rate was analysed by jurisdictional area, participation in BreastScreen NSW was found to relate to a reduction in mortality.<sup>3</sup> Results indicated that a participation rate of 70% would equate with a 32% reduction in breast-cancer mortality among 50-69 year olds. It follows from these results that complete BreastScreen coverage would lead to a reduction in excess of 40%.

The purpose of the present study was to evaluate effects on breast-cancer mortality of mammography screening through BreastScreen SA.<sup>4</sup> South Australia is one of the eight states of Australia, with a population of 1.5 million. The rollout of the population-based screening program (BreastScreen SA) followed a pilot project that commenced in 1989. By 1994, screening was widely implemented as part of a national government-funded initiative operating within each state. The SA program has provided biennial screening, with two-view mammography and double reading, since inception. It actively targets women aged 50-69 years, while allowing access to 40-49 year olds and women aged 70 years and older.

The relative odds (OR) of breast-cancer mortality in SA were investigated according to BreastScreen screening participation using a retrospective case-control design in which 491 breast-cancer deaths occurring in 2002-2005 among 45-80 year old South Australian females diagnosed after BreastScreen commencement (cases) were compared with 1,473 live controls (3 per death) selected at random from the State Electoral Roll after matching by date of birth.<sup>4</sup> These deaths applied to females listed on the State Electoral Roll (94%). Cancer Registry and BreastScreen records provided cancer and BreastScreen screening details.<sup>4</sup>

Breast-cancer risk estimates also were calculated by BreastScreen participation using weighted logistic regression analyses of data from a parallel population survey undertaken by telephone in 2006.<sup>4</sup> This included 1,684 females selected to be representative of South Australian females aged 40 years and over. The purpose was to gain comparative data by screening participation to assist interpretation of the case-control results.<sup>4</sup>

The OR (95% confidence limits) of breast-cancer death in BreastScreen participants compared with non-participants was found to be 0.59 (0.47, 0.74), due to a reduced risk of death in participants in age groups over 50 years.<sup>4</sup> Compared with non-participants, the OR was 0.70 (0.47, 1.05) for women last screened through BreastScreen more than three years before diagnosis of the index case, and 0.57 (0.44, 0.72) for those screened more recently, after adjusting for socio-economic status and health-service access. The adjusted OR tended to be lower again at 0.47 (0.34, 0.65) for women screened frequently in the pre-diagnostic period.<sup>4</sup>

The overall OR of 0.59 equated with a breast-cancer mortality reduction of 41%. The OR approximated 0.70 when corrected for the level of screening self-selection bias observed in the original field trials, equating with a cancer-mortality reduction of 30%. It was not clear, however, whether this adjustment was warranted. The population survey data did not point to a lower risk of breast-cancer death from selected breast-cancer risk factors among BreastScreen participants. Indeed, there were the contrary observations that BreastScreen participants were more likely than non-participants to report the following risk factors: family histories of breast cancer; use of hormone replacement therapy; and history of breast surgery for any reason.<sup>4</sup>

A similar proportion (about 20%) of BreastScreen participants and non-participants reported in the population survey that they had received screening mammography outside BreastScreen over the 15 years since BreastScreen SA was launched.<sup>4</sup> Depending on the frequency of this screening, it may have affected the results of the case-control study, although potentially by reducing rather than increasing the apparent screening effect.

The case-control results are consistent with a breast-cancer mortality reduction from participation in BreastScreen SA of between 30% and 40% or more, depending on the assumptions made about screening self-selection bias. The findings are in broad agreement with the results of the BreastScreen NSW evaluation, evaluations of European and United States screening services, and the original field trials.<sup>2,3</sup> A downward gradient in risk according to recency of last screen prior to cancer diagnosis, and frequency of recent screening, is also consistent with a BreastScreen effect.

Observational designs used for evaluation of breast-screening programs lack the scientific quality of the original randomised trials. Nonetheless they provide outcome markers that assist evaluation of screening programs in contemporary operational environments and comparisons with the original trial evidence upon which these programs were based

A further national evaluation of BreastScreen effects on breast-cancer mortality is likely to be implemented in 2007-08. Mammography data from Medicare Australia should be available to facilitate adjustment for mammography exposure outside BreastScreen, when assessing the BreastScreen effect. Micro-simulation models also could be used to estimate effects of BreastScreen screening and to model outcomes that would be expected under a range of policy options.

Routine surveillance data from the SA Cancer Registry show an increase in incidence of invasive breast cancer from the early 1990s, following the introduction of BreastScreen SA.<sup>5</sup> This increase appears to have been mostly a lead-time effect, rather than an over-diagnosis effect, in that the incidence rate is converging on, and has become very close to the rate projected from incidence-rate trends that preceded the introduction of BreastScreen SA. In other words, the incidence rate has returned to the level that might have been expected in the absence of BreastScreen screening. Nonetheless, the use of projections from historic trends to produce expected rates should be regarded with caution, particularly if projections cover long time frames when changes in a range of risk factors might have occurred.

Approximately 20% of screen-detected lesions in Australia comprise ductal carcinoma *in situ* (DCIS), where natural histories are not clear.<sup>5</sup> Although screen-detected DCIS is reported to have more aggressive features than other DCIS lesions,<sup>6</sup> the proportion that would progress to invasive cancer, if left untreated, is not known. Research into means of distinguishing between potentially non-progressive and progressive screen-detected DCIS should be a research priority.

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## False negative assessment (FNA) in women recalled for suspicious screening mammography

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The aim of screening is to detect mammography abnormalities associated with high risk of being a cancer, and thus worth of further diagnostic assessment. Diagnostic assessment is similar to clinical diagnosis, in that subjects referred to assessment have a suspicious lesion, the nature of which must be defined using a variety of diagnostic tools (detail or magnification mammography, palpation, ultrasonography, fine needle aspiration cytology or core biopsy (free-hand, US or stereotaxic directed), and open surgical biopsy). Diagnostic assessment is aimed at the highest sensitivity (identifying almost all cancers suspected at screening) and at a reasonable specificity, avoiding excessive or unwarranted intervention (e.g. open biopsy) in non-cancer cases. The latter aspect is relevant as the PPV of recall to assessment is commonly between 10 and 20%, i.e. the majority of subjects recalled to assessment are false positives (the harm of unnecessary intervention affects a larger proportion of women in screening).

Screening may fail in two ways a) it does not detect a cancer which is present at the time of screening, or b) recall and assessment fail to diagnose a cancer suspected at screen-reading. In both situations 'non-detected' cancers will surface as clinical before the next planned screening [interval cancers]<sup>1</sup> or will be detected at repeat screening, but the burden of responsibility might be greater for FNA. In fact, about half of cancers not detected at screening are evidently beyond the detection power of mammography, as shown by retrospective radiological review of interval cancers<sup>1</sup>, whereas cancers suspected at screening and misdiagnosed as benign at assessment are more likely due to an inadequate diagnostic process. While the sensitivity of screening, mostly due to the limitations of mammography, is unavoidably in the range of at most 75% (i.e. one in four cancers are not detected at screening<sup>2</sup>), the frequency of cancers misdiagnosed at assessment should be kept as low as possible (should be a small minority of missed cancers) to avoid a further decrease of screening efficacy (especially since these are cancers seen on screen-reading).

Assessment errors (or FNA) should be monitored, as a part of routine quality control of the screening programme - but in fact very few programmes have reported on this aspect of screening (for example, FNA rates from Australia have not been reported in the literature), while on the other hand many programs report overall interval cancer rates. Interval cancer rates commonly include all cancers undetected by a given screening "episode" and surfacing as clinical in the following interval, but cannot tell us the % that are due to FNA.

Such a quality assessment measure is not always performed in service screening, and the analysis of cancers missed due to false negative/benign assessment has been infrequently reported. Periodic review of interval cancers detected through linkage of the local cancer registry and of screening archives is currently ongoing as a measure of quality assessment in the Florence screening programme, and results have been recently reported<sup>3</sup>, and may be summarized as follows:

- From 339,953 consecutive screens, 11,624 subjects were recalled to diagnostic assessment (recall rate = 3.4%).
- Breast cancer was missed at assessment in 57 cases - a false negative assessment rate of 0.50% (0.37% - 0.62%) and a misdiagnosis in 4.1% (3.0% - 5.1%) of cancers occurring in women recalled after a positive screen.
- Two types of abnormalities were significantly more frequent in false negative assessment cases than cancers detected at assessment: mass with regular borders (21.1% vs. 5.6%,  $p=10^{-5}$ ), and asymmetrical density (22.8 vs. 5.4%,  $p=10^{-5}$ ).
- On review 56% of all false negative assessment cases were classified as benign or probably benign BI-RADS categories.
- False negative assessment occurred in 1.4% of early recalls following assessment and in 0.4% of initial assessment ( $p=0.0001$ ).
- Significantly fewer tests were performed when assessing missed cancers than detected cancers with the most significant difference noted for FNAC (29.8 vs. 96.0%,  $p=10^{-6}$ ).
- Mammography as the only evaluation on assessment (i.e. recalled from screening and had only further mammography views) was more frequent in missed cancers (31.5% vs 0.2%,  $p=10^{-6}$ ).
- The 57 missed cases were subsequently diagnosed at early recall (2 cases), at the next biennial screen (11 cases), or as interval breast cancers (44 cases), with a mean delay in diagnosis of 628 days.
- Tumour histology and indicators of pathological stage (tumour size and nodal status) did not significantly differ between cancers missed and cancers diagnosed on assessment. Implications on this issue are unclear.

In conclusion, false negatives on assessment might be reduced by adopting a more intensive diagnostic approach to assessment. It may be argued that they represent a minority of cancers in screened women, and public health efforts may be better directed at the larger proportion of cancers generally missed in screening. We argue that they represent screening failure and encourage screening programmes to audit cases of false negative assessment. Although we did not find evidence of a worse prognosis in cancers missed at assessment, the associated delay in diagnosis is substantial, and it is possible that this may impact long-term outcomes<sup>4</sup>.

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## The problem of the “Borderline” (B3) core needle biopsy result

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Breast core needle biopsies (CNB) are reported by the pathologist who will be in possession of the clinical and imaging findings related to the biopsy site. Identification of any targeted microcalcifications should have been performed by core radiography. Optimal fixation and processing, and H&E sections from 3 levels of the paraffin block are usually sufficient for initial examination. Subsequently further levels and immunohistochemical staining may be indicated to achieve a definite diagnosis. In the majority of cases a definitive diagnosis can be given and the biopsy is categorized as normal, benign or malignant. In the setting of mammographic assessment of women found to have a screen detected abnormality and also in the assessment of a symptomatic lesion, it is recommended that the pathology finding in the core biopsy be categorized using the B1-B5 classification. It is important that the category used by the pathologist is based upon the pathology findings in the biopsy independent of any clinical or imaging results. The categories used are summarized below:

B1 – normal tissue; used regardless of whether breast tissue is confirmed as being present. Microcalcifications may be seen for example in normal breast lobules. Normal tissue may also be seen in definite breast lesions such as a hamartoma or lipoma.

B2 – benign abnormality; used for a wide range of benign lesions such as fibroadenomas, sclerosing adenosis, duct ectasia, cysts and inflammatory lesions

B3 – lesion of uncertain malignant potential “borderline” – see below

B4 – suspicious; insufficient diagnostic material is present to make a definite diagnosis of ductal carcinoma in situ or invasive carcinoma, or a borderline atypical ductal hyperplasia/low grade ductal carcinoma in situ lesion

B5 – malignant; definite ductal carcinoma in situ (DCIS) and/or invasive carcinoma

The B3 “borderline” category includes a wide variety of lesions including atypical ductal hyperplasia, lobular neoplasia (atypical lobular hyperplasia and lobular carcinoma in situ) papillary lesions, radial scar/complex sclerosing lesion and fibroepithelial lesions with cellular stroma and features suggestive of phyllodes tumour. Although the B3 category may represent a small number of cases in practice (<10%), the implications of the use by the pathologist of this category are profound. The woman will inevitably require surgery in order to correctly categorise the pathology changes and reach a definite diagnosis. Furthermore it is likely that around 70% of these women will subsequently be found to have a benign lesion. The challenge then is to see whether it is possible to identify from an analysis of clinical, imaging and pathology findings, whether some women with a B3 diagnosis on core biopsy may be spared surgery. This decision should be based on an analysis of all the available data for the patient in a multidisciplinary team setting. The implication of the use of conventional versus vacuum-assisted core biopsy (VACB) in this context is also important in determining the likelihood of any residual changes being present in the breast. This may be important particularly in the assessment of a small papillary lesion removed piecemeal by VACB. Allowing the pathologist to discuss and/or demonstrate the pathology slides may be an important factor in determining a management plan. For example the diagnosis of atypical ductal carcinoma (ADH) may be predicated on the fact that the sample was small and that there are some features that would, if the area involved was larger, be diagnosed as low nuclear grade DCIS. Similarly a CNB may show lobular neoplasia involving multiple terminal duct lobular units or of pleomorphic type. In both these examples surgical excision is clearly indicated. On the other hand a small focus of equivocal ADH which is seen in a background of hyperplasia of usual type may present a more difficult decision process. A fibroepithelial lesion with a differential diagnosis of cellular fibroadenoma or benign phyllodes tumour may also represent a diagnosis with a low risk of malignancy on surgical excision.

It may be appropriate to further subdivide the B3 lesions into those with a significant risk of malignancy and those with a negligible risk. Whether this can be achieved will depend on the outcome of larger international studies.

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# Is prevention of breast cancer a reality?

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The short answer is yes. There have been four prevention trials of tamoxifen versus placebo and one using raloxifene (originally designed as an osteoporosis trial). As well, there are very rigorous data from the old adjuvant trials of tamoxifen that were (inadvertently) testing tamoxifen as a prevention agent for the unaffected breast. A systematic review of all these data shows a very clear treatment effect, with the incidence of new cancers reduced by about 40%<sup>1</sup>. We thus have proof of principle - why isn't everyone using tamoxifen in women at high risk of breast cancer?

First, we need to question the dangerous aphorism that prevention "is better than cure". Is that really true? IBIS 1 has recently been updated and thus has the longest follow-up of all the trials<sup>2</sup>. The update confirms the initial finding of a reduction in breast cancer incidence after 5 years of tamoxifen. Furthermore, it shows that the reduction in cancer risk persists over 10 years (ie after treatment has finished), but that the incidence of tamoxifen-related side-effects falls in the second 5 years. These are encouraging findings, yet it is sobering to look at the raw data. 3,500 women with increased risk of breast cancer were treated with tamoxifen for five years, and a total of 44 invasive cancers were prevented (or delayed). However, this was at the cost of 6 extra endometrial cancers, 49 extra thromboembolic events and 13 extra cataracts. Thus, treating well women to prevent a possible cancer exposes them to drug toxicity of some significance, and means that, while tamoxifen may be a useful preventative option, it should not be an automatic choice.

Naturally, as the risk of breast cancer increases, so does the cost benefit of tamoxifen for prevention. However, in a cruel irony, women with BRCA-1 mutations and an extreme risk of breast cancer almost invariably develop ER negative tumours, and the prevention trials only show an effect of tamoxifen on ER positive cancers. It is true that we do not yet know for certain that tamoxifen does not prevent cancers of the BRCA-1 phenotype.

It may be that estrogenic pathways are still important in the carcinogenesis of ER negative tumours. Certainly the impression that oophorectomy reduces breast cancer risk in women with inherited mutations of BRCA-1 suggests this<sup>3</sup>. However, these considerations make tamoxifen a less attractive option for such women, who may opt instead for prophylactic mastectomy.

Tamoxifen as a preventative agent is thus in a bind. For women at moderately increased risk of breast cancer, the reduction in breast cancer incidence is counterbalanced by toxicity concerns, while for those at very high risk, there is a real concern that it may not be effective. Take away the toxicity and the problem is at least partly resolved, and the results of testing an aromatase inhibitor as a preventative agent (IBIS 2) are eagerly awaited.

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## SESSION 8: CONTROVERSIES IN TREATMENT APPROACHES

### Immediate breast reconstruction

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#### Introduction

The fundamental goal of breast cancer surgery is to provide sound oncological treatment with good physical outcomes. Immediate breast reconstruction (IBR) has enjoyed increasing popularity as evidence of the oncological safety and the superior cosmetic results of this approach have emerged.<sup>1,2</sup> Although IBR may be conceptually appealing for both patient and surgeon, advice and subsequent decisions must be based on a sound understanding of the advantages and disadvantages of this often major surgical procedure. Ultimately, the decision to carry out IBR will be determined by the interplay of key sociodemographic, organisational, surgical and oncological factors.

#### Sociodemographic factors

Access to IBR is influenced by a wide range of factors which have been identified in the US,<sup>3</sup> the UK,<sup>4</sup> and Australia.<sup>5</sup> Key factors include patient age, disease stage, income, sociodemographic group, region of residence, rural location, ethnicity, availability of oncoplastic skills and status of hospital. Although IBR is still regarded as a luxury by many, recent UK Guidelines<sup>6</sup> spell out a woman's 'right' to be offered breast reconstruction, a directive which is putting pressure on breast units to provide this service. The economic arguments for performing one-stage IBR<sup>7</sup> as opposed to two-stage delayed breast reconstruction is strengthened by the need for fewer, costly revisional procedures following IBR,<sup>1</sup> but counteracted by the fact that significant numbers of women not offered IBR decline subsequent delayed reconstruction.

#### Organisational factors

The idea of a single stage reconstruction with one anaesthetic, one hospital stay and one recovery period is very appealing to the patient, the surgeon and the healthcare provider. Total bed days, convalescence, and time off work are all reduced. This is reflected in the lower total cost of IBR,<sup>7</sup> and the finding that the cost of IBR compares favourably with that of wide local excision and radiotherapy.<sup>8</sup> IBR also enables the surgical team to plan and organise the procedure, without being restricted by the scarring and other sequelae of previous surgery and adjuvant treatment.

The organisational disadvantages of IBR relate to the need to coordinate two surgical teams in those units where surgeons with joint oncoplastic skills are not available. Patients are under pressure to make decisions in a short time frame, and surgeons are under pressure to add additional major surgery to an already busy operating schedule. The oncoplastic surgeon is also under pressure to convey objective multidisciplinary advice in order to avoid the inevitable 'conflict of interest' which can colour opinions and advice about timing and technique.

#### Surgical factors

IBR enables the surgeon to plan and integrate incisions, to minimise scarring and to reconstruct the breast within its natural 3-dimensional skin envelope. As a result, the reconstructed breast is similar to the native breast, avoiding the need for contralateral procedures to achieve symmetry.<sup>1</sup> Scars can be minimised, lowered and concealed. Moreover, the amount of skin harvested during myocutaneous reconstruction can be minimised, avoiding the ugly 'patch' appearance associated with larger myocutaneous flaps. Dissection is facilitated by undisturbed tissue planes and axillary anatomy, in contrast to delayed reconstruction, where extensive scarring, poor quality tissues and tissue loss can hamper dissection and the creation of a like-like result.

The better cosmetic results achieved following SSM and IBR<sup>1,9</sup> are obtained at the risk of skin envelope necrosis, particularly in smokers.<sup>10,11</sup> Overall, IBR does not lead to increased complication rates compared with mastectomy alone.<sup>12</sup> IBR also plays a significant role in a woman's physical, emotional and psychological recovery from breast cancer,<sup>13</sup> but some women suffer from 'information overload' when making decisions about IBR.

#### Oncological factors

IBR is an oncologically safe option during mastectomy and does not increase the risk of relapse, or hamper the detection or management of local recurrences. During breast-conserving procedures, it enables very wide tumour clearance and reconstruction without cosmetic penalties<sup>15</sup> and without the adverse effects of radiotherapy.<sup>16</sup> The selection of patients for IBR at the same time as full mastectomy has become more complex since the demonstration of a survival benefit following the use of radiotherapy in node positive patients treated by mastectomy.<sup>17,18</sup> Unfortunately, complications increase substantially if

radiotherapy is administered after IBR using implants or expanders,<sup>19,20</sup> and less predictably after free TRAM,<sup>21</sup> pedicle TRAM,<sup>22</sup> and DIEP flap reconstruction.<sup>23</sup>

Recommendations for post-mastectomy radiotherapy are becoming increasingly relevant when considering IBR, in view of the reported adverse effects. The American Society of Clinical Oncology recommends the use of post-mastectomy radiotherapy for T3-T4 cancers, for locally advanced tumours, and in patients with 4 or more positive nodes.<sup>24</sup> Other groups are using radiotherapy for less extensive nodal involvement in the presence of other adverse tumour factors.<sup>25</sup> It seems likely that the use of radiotherapy post-mastectomy is likely to increase. Bearing this in mind, the routine use of sentinel lymph node analysis in the future will be helpful in selecting patients suitable for IBR, and this practice is increasing.<sup>25,26</sup> The chances of post-mastectomy radiotherapy being required in sentinel node negative patients based on findings that can only be known after mastectomy is very low.<sup>25</sup>

In future, IBR is likely to remain a popular choice for patients facing mastectomy. The majority will not require postoperative radiotherapy, and this number is likely to increase with earlier diagnosis. Three strategies are evolving to optimise the timing of breast reconstruction. Firstly, women with T0-T2 tumours with a negative sentinel node biopsy carried out before mastectomy are very unlikely to require radiotherapy, and can safely proceed with IBR. Secondly, following mastectomy and axillary clearance, a 'delayed-immediate' reconstruction can be performed in patients when full histopathological data excludes the need for radiotherapy. If radiotherapy is indicated, a temporary tissue expander can be inserted and replaced with an unirradiated autologous flap on completion of adjuvant treatment.<sup>26</sup> Lastly, neoadjuvant treatment can be carried out with the breast intact, and subsequent delayed mastectomy and immediate reconstruction can be performed with unirradiated tissues in those patients with an incomplete histopathological response.

Finally, most studies of IBR report no delay in the initiation of adjuvant chemotherapy compared with patients undergoing mastectomy alone,<sup>27,28</sup> as a result of retarded wound healing or infection. However, the use of pedicle and free TRAM flaps for IBR has been shown to delay the start of chemotherapy in a significant minority of patients.<sup>29</sup>

## Conclusion

IBR offers significant benefits to patients, surgeons and healthcare providers, and is the treatment of choice in the appropriate clinical setting. The future role of IBR will be determined by refinements in case selection and technique, coupled with the greater availability of oncoplastic skills.

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# Reconstructive surgery

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This paper will discuss breast reconstruction in general terms. The emphasis of the paper will be in the assessment of the patient and their expectations. This will, together with the availability of reconstructive tools blended with the patient's expectations, lead to a web of considerations before a decision is made. The aim of this is to try and enhance a woman's profile to perhaps correct other anomalies to make her feel some benefit from the breast reconstruction procedure.

## Post mastectomy radiotherapy 2007

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Post mastectomy radiotherapy has long been known to significantly decrease the risk of loco-regional recurrence. It was traditionally applied routinely post operatively to node positive breast cancer and if the primary tumour was 'large' treatment was given to the chest wall and nodal regions.

This approach fell into disrepute because of publications demonstrating significant toxicities – especially increased mortality due to cardiac events<sup>1,2</sup>. Other toxicities noted included brachial plexopathy, lymphoedema, radiation pneumonitis, rib fractures/fibrosis and second malignancies.

The other factor influencing the use of post mastectomy radiotherapy was the 'systemic approach'. The introduction of effective systemic adjuvant treatments; chemotherapy (CMF, AC) and hormonal (ovarian ablation, Tamoxifen), appeared to make loco-regional RT obsolete and unnecessary.

However, it soon became apparent that these systemic therapies, whilst clearly improving survival from breast cancer were relatively less effective at decreasing loco-regional recurrence. Debates on the role of post mastectomy radiotherapy in the 'systemic era' became 'heated'<sup>3,4,5</sup>.

A new interest in post-mastectomy radiotherapy was initiated after a series of publications clearly demonstrated not only significant improvement in loco-regional relapse but also survival advantage in the presence of systemic therapy<sup>6,7,8</sup>.

These publications led to a major shift in position, and the realization that loco-regional therapy could be very important, and that as systemic therapies became more effective at reducing metastatic progression, loco-regional radiotherapy not only reduces loco-regional recurrence by 70% but also had significant survival benefits<sup>9</sup>.

The overview of more recent radiation trials demonstrated that if the patient has a significant risk of loco-regional recurrence then loco-regional radiotherapy allows the avoidance of one breast cancer death (at 15 years) for every 4 local recurrences prevented.

A series of 'consensus' documents followed<sup>10</sup>. It is now apparent that optimal care for a patient with breast cancer really does involve a multi-disciplinary approach. We now see continuing improvement in prognosis as systemic therapies improve and from the appropriate use of loco-regional radiotherapy.

Current recommendations for consideration of post-operative RT include large primary ( $\geq 40$  mm) significant nodal involvement ( $\geq 4$  positive axillary nodes).

Updates of the EBCTCG overview (2006) suggest similar biologic effect for patients with 1-3 positive nodes and clinical trials are being performed to address this issue and the role of int. mammary L. node irradiation.

Modern radiotherapy techniques should further improve the therapeutic ratio – by avoiding as much as possible RT to the heart and coronary arteries. However, a lesson from the EBCTCG overview is that whilst loco-regional recurrence becomes apparent by 5 years and breast cancer mortality by 10-15 years, other death events may not be clear until 15-20 years later. Hence, newer systemic treatments (ex Taxanes, Herceptin) and new trends in RT (ex Hypofractionation), sequencing of modalities all need to be considered carefully.

Post mastectomy RT now clearly has an important role, but the individual patient needs to be considered. The individual's risk of loco-regional recurrence needs to take into account the patient's age, extent of surgery (including axillary management), tumour size, margins, extent of nodal involvement, lymphovascular invasion, systemic therapies. The options then need to be presented in a balanced fashion.

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## POSTERS

### Axillary lymphadenopathy in screening mammography - To see or not to see?

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#### Background and purpose

Screening Mammography reading classifications can leave radiologists and readers in a clinical dilemma when there is no concern of breast cancer in the screening mammogram but there is clearly another clinical problem that may or may not be known to the patient.

Bundaberg BreastScreen Clinical team and a local GP present this case as a nidus for discussion on the development of a consistent approach to the diagnosis and coding of axillary lymphadenopathy.

#### Method

Case Presentation: A 48 year old asymptomatic Australian woman of Caucasian descent presented for her third round of routine screening. Significant increase in size and density of bilateral axillary lymphadenopathy was the only concern noted. Both readers expressed concern that a clinical diagnosis be established or confirmed. The woman did not nominate a General Practitioner (GP).

She was recalled to our assessment clinic where no clinical abnormalities in breast, axilla, skin, joints or lymph nodes were detected. She was advised to see a GP for follow up but she could not access one in this area. The medical officer provided advocacy to a local GP and referral was accepted.

The GP noted her to be a well woman with no significant history. The GP performed routine tests for the exclusion of lymphoma, sarcoidosis, rheumatoid arthritis, glandular fever, CMV and Toxoplasmosis. All tests were negative.

Further testing proved both the woman and her husband were HIV +ve with low CD4 count. Neither was aware of their condition prior to this.

#### Conclusions

The BreastScreen coding was "No significant abnormality"! for the screen detected diagnoses of 2 cases of HIV. What do you do?

# Unusual presentation of lobular carcinoma of breast: A case report

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We report a case of a 67 year old female, presenting to a surgeon, with rubbery masses in the colon, small bowel, mesentery and ascitis which was clinically thought to be lymphoma. The ascitic fluid cytology disclosed malignant cells in poorly cohesive groups, clusters, linear formation and single cell arrangement. Occasional signet-ring cells were identified. The diagnosis of an adenocarcinoma with a probable primary origin in breast suspicious of lobular type was made.

The histological examination of the mesenteric lymph node tissue showed metastatic lobular carcinoma of breast confirmed with immunohistochemistry. On review, past medical history revealed a right mastectomy in 1998 for lobular carcinoma.

The salient cytomorphological features that would prompt the cytopathologist in the diagnosis of a lobular carcinoma of breast, in the absence of adequate clinical details is presented with a brief review of the literature.

# An investigation of gene expression in human breast cancer using tissue microarray

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## Background and purpose

One in eleven women will be diagnosed with breast cancer, the most common cause of cancer-related death in Australian women<sup>1</sup>. A number of genetic mutations have been identified in human breast cancer, yet the specific mutations required to act in concert to form breast carcinoma cells remain incompletely defined<sup>2</sup>.

## Methods

In this study, a gene expression profiling approach was used to uncover differentially expressed genes related to the disease and the pattern of regulation across the three grades of breast cancer development and progression. The investigation was undertaken using 12 breast archival invasive ductal carcinoma tissue samples of progressive grades, three of which were benign controls. From these samples, mRNA was extracted and gene expression profiles were determined using microarray hybridisation.

## Results

Results were analysed at significance levels of 0.01 and 0.05 to detect significantly differentially expressed genes in breast tissue compared to control tissue. In the analysis of the array data, a series of t-tests revealed that 184 genes were found to be significantly ( $P=0.01$ ) differentially expressed in at least one of the group comparisons, 42 of which were identified as being involved in processes previously implicated or associated with breast cancer. It was also discovered that 8 of these genes were significantly differentially expressed across more than one comparison of groups which included CLDN10, CXCL16, EPST11, LOC441259, CDC42EP3, ZAN, TCEA3 and PALMD.

## Conclusions

Investigating patterns of expression indicated that most of the differentially regulated genes showed up-regulation from controls to grade 1 tumours, then a drop in regulation in grade 2 tumours and a considerable up-regulation in the grade 3 tumours. One particular gene, the chemokine CXCL16 was the only gene found to be significantly differentially expressed ( $P=0.01$ ) in more than 2 comparisons, thus determining regulation of the gene in a greater number of grade 3 tissues would prove beneficial in potentially identifying this gene as a target for diagnostics and therapeutics. While the results of the study require validation, candidate genes for further investigation have been identified and future studies could now investigate these as potential targets for diagnostic and therapeutic development.

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# Review of fat necrosis cases in patients recalled from a breast screening program

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## Background and purpose

Fat necrosis frequently mimics carcinoma of the breast in its imaging features. The purpose of this study was to review indeterminate fat necrosis cases which were recalled in a breast screening program (BreastScreen Northern Sydney and Lower Central Coast).

## Methods

A review of the discharge letters of patients recalled for assessment was made with selection for the keywords "fat necrosis". The history and examination, imaging and pathology data were reviewed.

## Results

A total of 8,942 patients were recalled during a 3 year 5 month period from 1 January 2004 till 31 May 2007 with 30 patients selected for review, 9 patients gave a history of breast reduction surgery, 4 patients gave a history of trauma, 12 patients underwent assessments with fine needle or core biopsies, 2 patients had short interval follow-up.

## Conclusions

Patient recalled in our screening program with fat necrosis is relatively rare (30/8942=0.34%). 13/30 (43.3%) gave a history of trauma. 12/30 (40%) had biopsies. 2/30 (6.7%) had close follow-up. The mammographic and ultrasonic appearances of the manifestations of fat necrosis were analysed.

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## Inflammatory breast cancer: A long term single centre experience

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### Background and purpose

Inflammatory breast cancer (IBC) is an aggressive form of breast carcinoma with a high risk of subsequent distant metastases. The role of radiotherapy for this disease in a combined modality setting is evolving. We report treatment outcomes of the cohort of patients with IBC treated at our centre between 1989 and 2006.

### Methods

A retrospective review was performed. Patient demographics, mode of diagnosis, treatment modalities and cancer outcomes were analysed.

### Results

Sixty five patients with IBC were identified. The mean age at diagnosis was 50.3 years. Patients had variable follow-up periods between one month and seven years. Thirty two patients were still alive at the time of analysis. Over 50% developed metastatic disease and one in five was identified to have had loco-regional recurrence. Tri-modality treatment with chemotherapy, radiotherapy and surgery was the most common approach to treatment.

### Conclusions

Despite of poor overall prognosis, our experience suggests an improved outcome may be achieved with combined treatment with systemic and maximal local therapies for patients with IBC.

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# Dosimetric comparison of prone breast radiotherapy technique to the standard supine technique

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## Background and purpose

In breast cancer patients with pendulous breasts, prone-breast technique has been described as an alternative to the standard technique. The potential advantages are improved dose homogeneity and reduced normal tissue toxicity in large breasted women. We report the dosimetric comparison of a prone radiotherapy plan to a standard supine breast plan.

## Methods

The comparison plans using prone and supine positions on a same patient with large breasts have been generated using tangential fields. The plans were compared with regard to the dose-volume parameters.

## Results

Dose homogeneity within the target volume was better with the prone technique. The lung dose improved with the prone positioning and the volume of skin in high dose region was also reduced with this technique.

## Conclusions

An improved dose distribution towards the target tissue and organs at risk was observed using the prone breast technique suggesting potentially better toxicity and cosmetic outcomes.

A clinical trial including follow-up data on toxicity and cancer outcomes is recommended.

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## The prone technique for breast irradiation – Is it ready for clinical trials?

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### Background and purpose

Our aim was to determine whether a radiotherapy technique for treating breast cancer patients in a prone position could be developed as a means of reducing toxicity.

### Methods

At our centre, we designed a simple technique for simulation and treatment in the prone position. A specialised patient positioning device was designed to allow the breast to hang vertically downwards away from the chest wall and away from the contra lateral breast. Planning and treatment were performed, and clinical data on the first 40 patients treated were reviewed.

### Results

The commonest reason given by clinicians for choosing the prone technique was the large pendulous-breast shape. The treatment was well-tolerated. Dosimetric analysis revealed high levels of dose homogeneity. With a median follow-up of 11 months, one patient has developed metastatic disease, and one patient has locally recurred.

### Conclusions

This study shows that prone breast irradiation for patients with large or pendulous breasts can be readily developed in radiotherapy treatment centres and could be tested for efficacy in a large, multi-centre randomized trial.

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# Impact of more intensive information in cancer patients having radiation therapy: Results of a randomized phase III trial

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## Purpose

This study was conducted to determine the impact of intensive information addressing lifestyle and practical issues in addition to treatment-related information, on patients' anxiety levels. The secondary aim was to determine the impact of this information on patients' satisfaction levels.

## Materials and Methods

This prospective randomized trial consisted of patients with a pathological diagnosis of cancer having radical radiotherapy at Perth Radiation Oncology and Royal Perth Hospital. Patients were randomized to receive the more intensive information (including written information and a telephone call from the research nurse) or not to receive the more intensive information at the time of their initial consultation with the Radiation Oncologist. Study questionnaires measuring their anxiety (STAI form) were completed prior to their first consultation (baseline), at the time of simulation and at the completion of radiotherapy. A second questionnaire assessing their satisfaction with the information they had been given (ISQ) was completed at the time of simulation.

The 2-sample t-test was used to compare the anxiety scores between the 2 cohorts of patients. The chi-square test was used to compare the mean ISQ scores between the 2 cohorts. Multiple linear regression analysis was performed to look at the predictive value of baseline characteristics such as sex, tumour type, participation in a clinical trial and personality type according to their information needs.

## Results

One hundred and ninety eight patients were enrolled in the trial. On analysis, 38 of those patients had missing data and were excluded from the final analysis. Of the 160 patients analysed, 87 received the standard information and 73 received the more intensive information. There was no difference seen in patient satisfaction with the information given between the 2 groups. There was a significant reduction in state anxiety in both groups over time (ie following administration of information,  $p < 0.001$  and at the completion of the radiation therapy,  $p < 0.001$ ). There was no significant difference in trait anxiety over time.

## Conclusions

Extra information did not appear to improve patient satisfaction.

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