Eighth Scientific Meeting of the Australasian Society for Breast Disease

6-8 October 2011

HILTON ON THE PARK

MELBOURNE, AUSTRALIA

HANDBOOK & ABSTRACTS

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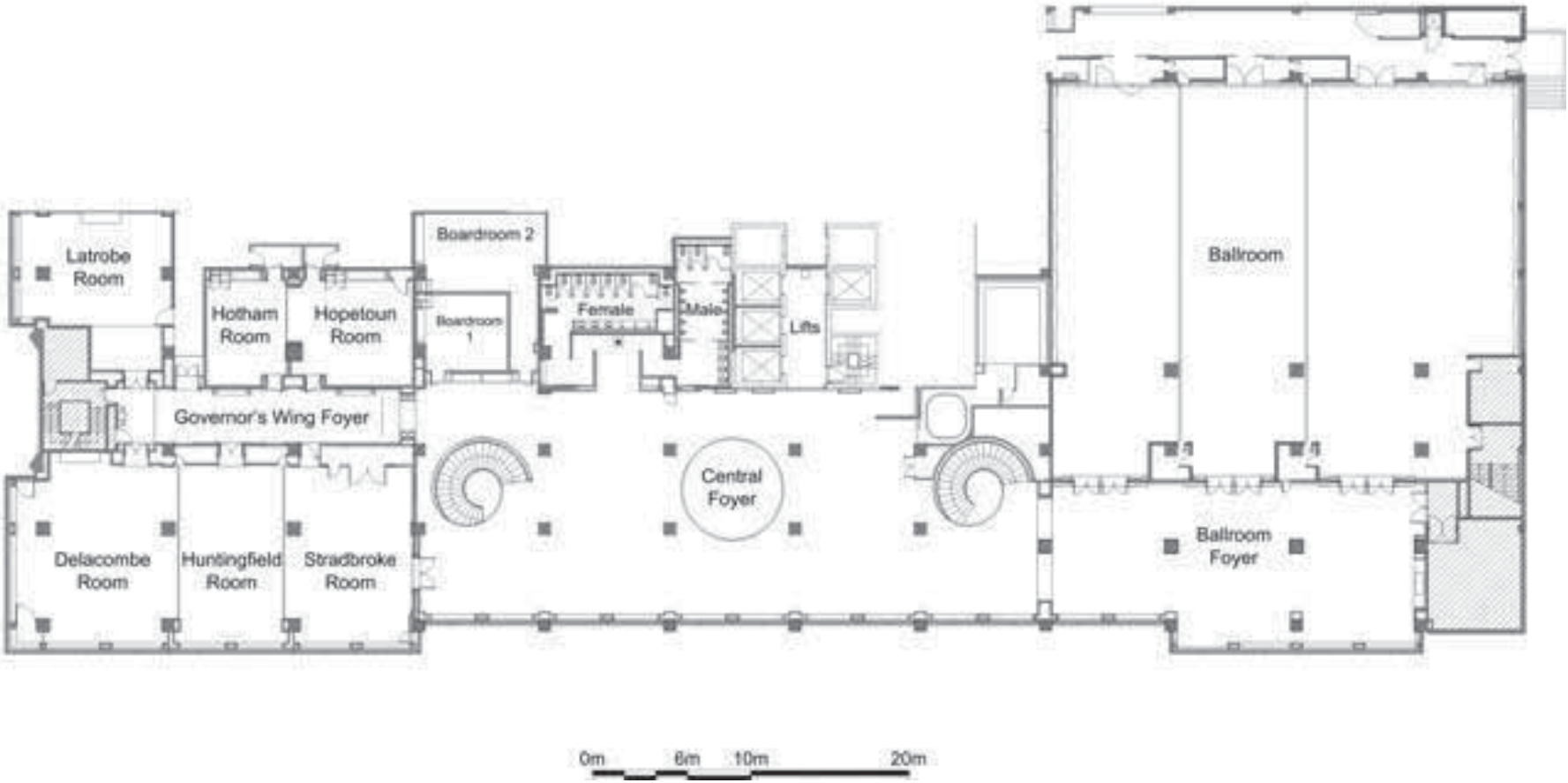

Contents

Section I

Welcome 4

Australasian Society for Breast Disease Executive Committee 4

Sponsors 5

Trade Exhibitors 5

Useful Information 6

Social Program 6

Keynote Speakers 7

Faculty Members 7

Presenters – Proffered Papers 10

Scientific Program 12

Section II

Abstracts 17

Notes

PBS Information:
Restricted benefit.
Treatment of hormone-dependent breast cancer in postmenopausal women.

Before prescribing, please review Product Information available on request from AstraZeneca.

Arimidex® (anastrozole) Indications: Early breast cancer – Adjuvant treatment of early breast cancer in postmenopausal women with oestrogen/progesterone receptor positive disease. **Advanced breast cancer** – First line treatment of advanced breast cancer in postmenopausal women with oestrogen/progesterone receptor positive disease. Treatment of advanced breast cancer in postmenopausal women with disease progression following tamoxifen therapy. Patients with oestrogen receptor negative disease and patients who have not responded to previous tamoxifen therapy rarely respond to Arimidex. **Dosage:** One tablet (1 mg) to be taken orally once a day. For early breast cancer, the recommended total duration of treatment is 5 years. For patients being switched to Arimidex from tamoxifen, the switch should occur after completion of 2 to 3 years of tamoxifen therapy. There are no data to support switching at earlier or later time points. **Contraindications:** Pregnancy (Category C), lactation, hypersensitivity to ingredients. **Precautions:** Not recommended for use in children or premenopausal women. Severe hepatic and renal impairment. Women with osteoporosis or at risk of osteoporosis should have their bone mineral density formally assessed by bone densitometry at the commencement of treatment and at regular intervals thereafter. Treatment or prophylaxis for osteoporosis should be initiated and monitored as appropriate. Use in combination with LHRH agonists. **Interactions:** tamoxifen, oestrogen containing therapies. **Adverse Reactions:** Very common – hot flushes, asthenia, arthralgia*, joint stiffness, arthritis*, headache, nausea, rash; Common – vaginal dryness/bleeding, hair thinning, allergic reactions, vomiting, diarrhoea, somnolence, Carpal Tunnel Syndrome, anorexia, increases in alkaline phosphatase, alanine aminotransferase and aspartate aminotransferase, hypercholesterol aemia, bone pain*; Uncommon – Trigger finger, urticaria, increases in gamma-GT and bilirubin, hepatitis; Others – see full PI. Based on Full Product Information approved 15th June 2009. Date of most recent amendment 1st November 2010* **PBS dispensed price:** Arimidex 1mg, $180.18. **References:** 1. Arimidex Approved Product Information (TGA approved 15/06/09, most recent amendment 01/11/10). 2. The ATAC Trialists' Group. *Lancet Oncology* 2008; 9(1): 45–53. 3. Cuzick J. 10 year analysis of the ATAC Trial. Poster presented at the 12th Milan Breast Cancer Congress. 16–18 June 2010. 4. Cuzick J *et al. Lancet Oncology* 2010; 11: 1135–41. AstraZeneca Pty Ltd, ABN 54 009 682 311, Alma Road, North Ryde NSW 2113. AU-ARI000280e. AZAE 0412.
AZAR5225. 09/11. AstraZeneca

*Please note changes in Product Information

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*Arimidex provides the benefits of AI therapy: efficacy, tolerability, and patient support.

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Section 1

Handbook

Welcome

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

The program will include sessions on optimising loco-regional management of DCIS, lobular cancer, new approaches to surgical management, controversies in radiotherapy, new modalities for screening, changing concepts of breast cancer subtyping and therapy, a novel hypothetical as well as several specialised workshops. I wish to acknowledge our distinguished international and local faculty; we are most grateful for your contribution to this Meeting.

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

If you are not a member of ASBD, please 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 and drop it into the box placed in the Meeting Office.

I hope you will enjoy all aspects of this Meeting.

Wendy Raymond
President

About the Australasian Society for Breast Disease

The Australasian Society for Breast Disease was constituted in 1997. Its primary goal is to promote multidisciplinary understanding and practice in the prevention, detection, diagnosis and management of breast disease and research into this area of medicine.

The Society has a nine-member Executive plus several co-opted members, providing for broad multidisciplinary representation.

The Society thanks current members for their support and involvement and welcomes new members from all disciplines involved in the area of breast disease. You can download a membership application form from our website: www.asbd.org.au or contact the Secretariat.

Contact details

Australasian Society for Breast Disease
PO Box 1124
Coorparoo DC Qld 4151
Tel: +61 (0) 7 3847 1946
Fax: +61 (0) 7 3847 7563
Email: info@asbd.org.au
Website: www.asbd.org.au

Executive Committee

A/Prof Wendy Raymond, Pathologist, President
Dr Kerry McMahon, Radiologist, Secretary/Treasurer
Dr Natacha Borecky, Radiologist
Dr Marie-Frances Burke, Radiation Oncologist (co-opted)
Dr Jacqueline Chirgwin, Medical Oncologist (co-opted)
Dr Roslyn Drummond, Radiation Oncologist
Dr Susan Fraser, Breast Physician
Dr James French, Surgeon (co-opted)
A/Prof Bruno Giuffre, Radiologist
Prof Sunil Lakhani, Pathologist (co-opted)
Dr Julia Leeds, BCNA Representative (co-opted)
Dr Lynne Mann, Surgeon (co-opted)
Dr Belinda Scott, Surgeon
Prof Robin Stuart-Harris, Medical Oncologist
Dr Daniel de Viana, Surgeon
Ms Solei Gibbs, Executive Officer

Previous Executive Committee members

Dr Geoffrey Beadle, Medical Oncologist
A/Prof Michael Bilous, Pathologist
A/Prof John Boyages, Radiation Oncologist
Prof Michael Friedlander, Medical Oncologist
Dr Colin Furnival, Surgeon
Prof Michael Green, Medical Oncologist
Dr Cherrell Hirst, Breast Physician
A/Prof Nehmat Houssami, Breast Physician and Clinical Epidemiologist
Ms Elspeth Humphries, BCNA Representative (co-opted)
Dr Michael Izard, Radiation Oncologist
Dr Jack Jellins, Scientist
Mr James Kollias, Surgeon
A/Prof Warwick Lee, Radiologist
Ms Veronica Macaulay-Cross, BCNA Representative (co-opted)
Mr William McLeay, Surgeon
Ms Lyn Moore, BCNA Representative (co-opted)
Dr Margaret Pooley, Surgeon
A/Prof Mary Rickard, Radiologist

Sponsors

Platinum Sponsor

AstraZeneca is a global, innovation-driven, integrated biopharmaceutical company.

Our mission is to make a meaningful difference to patient health through great medicines that bring benefit for patients and add value for our stakeholders and society.

We discover, develop, manufacture and market medicines for seven important areas of healthcare, which include some of the world's most serious illnesses: anaesthesia and pain management, cancer, cardiovascular, gastrointestinal, infection, neuroscience, and respiratory and inflammation.

Gold Sponsor

Novartis Oncology provides a range of innovative therapies and practical solutions that aim to improve and extend the lives of cancer patients. We aspire to develop new medicines that will transform the way cancer is treated, and are therefore committed to ongoing research and development in Australia and New Zealand.

Education Grants – Medical Oncology Trainees

Headquartered in Basel, Switzerland, Roche is a leader in research-focused healthcare with combined strengths in pharmaceuticals and diagnostics. As the world's largest biotech company and leading provider of cancer care products, Roche has a personalised healthcare strategy which aims to provide medicines and diagnostic tools that enable tangible improvements in the health, quality of life and survival of patients. In 2010, Roche invested over $9 billion (AUD) in research and development worldwide, including approximately $36 million (AUD) in pharmaceuticals in Australia.

Roche's innovative anti-cancer medicines include five products approved for use in Australia: Avastin (bevacizumab), Herceptin (trastuzumab), Xeloda (capecitabine), MabThera (rituximab), and Tarceva (erlotinib).

Bronze Sponsors

Trade exhibition

Booth no.	Company
1	Bard
2	Roche
3	Gate Healthcare
4	Hologic
5	Novartis Oncology
7	Allergan
8	AstraZeneca Oncology
9	SonoSite
10	Genomic Health / Healthscope
11	U Tech Medical
12	Genetic Technologies
13	GE Healthcare

Useful Information

Venue
Hilton on the Park
192 Wellington Parade
East Melbourne VIC 3002
Tel +61 (0) 3 9412 3167
Fax +61 (0) 3 9412 3192

Meeting Office
The Meeting Office will be open during the following times:

Thursday 6 October 2011	0730-1800 hours
Friday 7 October 2011	0730-1730 hours
Saturday 8 October 2011	0730-1500 hours

Speakers' Audiovisual Testing Room
The Speakers' Audiovisual Testing will be available in the Hotham room during the following times:

Thursday 6 October 2011	1500-1700 hours
Friday 7 October 2011	0730-1600 hours
Saturday 8 October 2011	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 Hilton Ballroom. Please advise potential callers to contact Hilton on the Park (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.

Social Program

Lunches
Lunches will be served in the Trade Exhibition area. Lunch service is by ticket only. Please ensure you have the correct tickets. Additional tickets are available at $45 per person.

Welcome Reception
Thursday 6 October 2011, 1830-2000 hours

Meet your fellow delegates for drinks and canapés in the HGA Harrison Room at the famous MCG. The MCG is located only a short walk away across the park opposite the Hilton. At the end of the path please turn slightly right and enter via Door 1. See map on Notice Board. Included for fulltime delegates and registered partners. Additional tickets cost $50 per person.

Tours are available of the MCG and the Sport Museum. Please contact the MCG direct for information.

Networking Drinks
Friday 7 October 2011, 1730-1830 hours

Following the last session for the day, catch up with your colleagues at drinks in the Trade Exhibition area. Included for fulltime and Friday delegates and registered partners only. No additional tickets.

Meeting Dinner
Sponsored by Novartis Oncology

Saturday 8 October 2011, 1930-2300 hours

Join your fellow delegates for an enjoyable night on the 'Streets of Melbourne'. To conclude the Meeting, the Hilton Ballroom will be transformed to depict some of the well-known streets of Melbourne. Savour tastes from Italy, Vietnam, China and Greece. The dinner will include pre dinner refreshments, dinner and drinks. Included for full time delegates and registered partners. Additional tickets: $125 per person. Cocktail wear.

Annual General Meeting

The Annual General Meeting of the Australasian Society for Breast Disease will be held in the Epicurean Room at 0730 hours on Saturday 8 October 2011. Breakfast will be served during the Meeting. Please reconfirm you attendance / nonattendance upon registration. Admission is free to members only.

Continuing Professional Development

RACS
This educational activity has been submitted to the Royal Australasian College of Surgeons' Continuing Professional Development (CPD) Program (1 point per hour, Category 4: Maintenance of Clinical Knowledge and Skills towards 2011 CPD totals).

RANZCR
The Royal Australian and New Zealand College of Radiologists will award points as follows:

- **7.5 points** may be claimed for attendance at the "Australasian Society for Breast Disease
- Scientific Meeting" to be held on the 6th October 2011.
- **7.5 points** may be claimed for attendance at the "Australasian Society for Breast Disease
- Scientific Meeting" to be held on the 7th October 2011.
- **6 points** may be claimed for attendance at the "Australasian Society for Breast Disease
- Scientific Meeting" to be held on the 8th October 2011.
- **A total of 21 points** can now be claimed for attendance on all three days of the Australasian
- Society for Breast Disease Scientific Meeting.
- For anyone who attends only part of this seminar, points may be claimed pro rata at **1 point**

RACGP
Breast Physicians and General Practitioners can access the RACGP website www.racgp.org.au to determine the QA points on an individual basis (Category 2) for Meeting attendance.

Faculty Members

Keynote speakers

Dr Krishna B Clough MD

Krishna Clough trained and graduated both as a surgical oncologist and a plastic surgeon. After spending many years treating both breast and pelvic cancers, parallel to offering reconstructive options to these patients, his activity is now solely devoted to breast surgery. He has focused on offering patients the benefits of a multidisciplinary approach whilst limiting the side effects of each of the treatment applied. His clinical research aims at developing a global surgical expertise for breast surgery, from non-palpable breast cancer, and sentinel node biopsy, to all types of breast reconstruction, including all possible surgical procedures for diagnosis, treatment and reconstructive surgery of the breast. He has focused his research on the extension of the surgical techniques for breast cancer patients and has developed an 'oncoplastic' approach for tumors that would not be suitable for standard conservative surgery, and has been teaching these techniques worldwide. After spending more than 15 years in the French public system, and achieving the position of chief of surgery at the Institut Curie in 1996, Dr Clough left the Institut Curie in 2004 to create the Paris Breast Centre, France's first Breast Center. The Paris Breast Center treats more than 500 new breast cancer cases per year and is one of the leading private institutions in France for treatment and education. He is the author or co-author of 105 original papers, one book, 10 book chapters, 26 didactic papers and more than 500 communications.

Professor Christiane K Kuhl MD

Christiane Kuhl is Chairman of the Department of Diagnostic and Interventional Radiology at RWTH Aachen University in Germany. She was previously Professor of Radiology and Vice Chair of the Department of Radiology at the University of Bonn, as well as the Director of the Division of Oncologic Imaging and Interventional Therapy. She received her medical degree from the University of Bonn Medical School and is a board-certified radiologist and neuroradiologist. Professor Kuhl's major fields of interest include higher-field MRI, breast imaging, and minimally invasive therapy. In addition to 23 review articles, about 240 citable scientific abstracts and 7 book chapters, she has authored 76 original articles. These latter yielded a total of 326 impact factors – a number that indicates the quality of the respective publications. She is associate editor and consultant to the editor of *Radiology*, and a member of the scientific editorial board of the *Journal of the German Radiological Society*, and a peer reviewer for *Journal of Magnetic Resonance*, *Journal of Clinical Oncology, European Journal of Cancer,* and *Nature Medicine*, among others.

Professor Ian E Smith MD, FRCP, FRCPE

Ian Smith is Professor of Cancer Medicine at The Royal Marsden Hospital and Institute of Cancer Research, London, UK. He is also Head of the Breast Unit at The Royal Marsden and was Medical Director there from 2000 to 2003. His initial medical training was in Edinburgh and then he came to the Royal Marsden for specialist training in cancer medicine. He also spent some time in Boston at the Dana Farber Cancer Institute. Over the years his principal clinical research interests have been in breast cancer, lung cancer and in new drug development. In the last decade he has become increasingly involved in neoadjuvant and adjuvant therapies, and in translational research. He is currently UK Principal Investigator for several international multicentre trials. He is chief investigator of the UK peri-operative POETICtrial and international co-chair of the FACE trial (letrozole v anastrozole). Professor Smith is recent past Chairman of the newly formed UK Breast Trials Intergroup and of the British Breast Group. He has been past Chairman of several national professional bodies including the Association of Cancer Physicians, the Royal College of Physicians Specialist Advisory Committee for Medical Oncology, and the NCRI Lung Cancer Clinical Studies Group. He has published and lectured extensively throughout his career and was given the Brinker Award for Scientific Distinction at the San Antonio Breast Cancer Conference in 2009.

Professor Lawrence J Solin MD, FACR, FASTRO

Lawrence Solin is Chairman of the Department of Radiation Oncology at the Albert Einstein Medical Center in Philadelphia, USA. He has contributed over 160 peer-reviewed publications to the medical literature, has presented more than 140 invited national and international lectures, and serves on nine journal editorial boards. He is a co-editor of the book, *Breast Cancer Management and Molecular Medicine: Towards Tailored Approaches*. He is Professor Emeritus at the University of Pennsylvania in Philadelphia. He has concentrated his research interests on breast conservation treatment with radiation for early stage breast cancer. His recent research has focused on the use of breast conservation treatment with radiation for ductal carcinoma in situ (DCIS), long-term outcomes after breast conservation treatment for invasive breast carcinoma and for DCIS, technical approaches to radiation treatment delivery, and biologically defined subsets of breast cancer. He maintains an active clinical practice in the area of radiation treatment for breast cancer. Professor Solin received his undergraduate and medical degrees from Brown University in Providence, RI. He completed his residency in Radiation Oncology at the University of Pennsylvania and Thomas Jefferson University, both in Philadelphia, PA.

Local faculty

Miss Caroline Baker MBBS, FRACS

Caroline Baker is a specialist breast surgeon and Director of Breast Services at Austin Health. She graduated with an FRACS from The University of Melbourne in 1994 in General Surgery, training via St Vincents Hospital. She then spent five years in the UK, most notably in Guildford at Royal Surrey County Hospital with Mr Mark Kissin, who inspired her to pursue a career in breast surgery. Miss Baker then spent a year at The Royal Marsden Hospital in London. Her special interests are in the genetic inheritance of breast cancer, sentinel node biopsy and immediate reconstruction.

Dr Natacha Borecky MBBS, Dip Rad (Belgium)

Natacha Borecky received her medical and radiological degrees from the University of Brussels, Belgium in 1995. After two years of training in Paediatric Radiology, Breast Imaging and MRI at the University Hospital in Lausanne, Switzerland, she passed her thesis on MRI of thoracic lymphangioma in children. During her radiological training, Dr Borecky developed a special interest in Breast Disease and became specialist in Breast Imaging. She is currently working as VMO Radiologist for NSW BreastScreen at the Westmead Breast Cancer Institute in Sydney and in rural areas. Dr Borecky is an educational affiliate of the RANZCR since 2008 and an Executive member of the ASBD since 2006.

Dr Meagan Brennan BMed, FRACGP, FASBP

Meagan Brennan is a Breast Physician and Clinical Senior Lecturer at the University of Sydney. Dr Brennan is in clinical practice in North Sydney and is a Staff Specialist Breast Physician at Westmead Hospital. Her clinical interests are management of women at high genetic risk of breast cancer and follow-up care after treatment for breast cancer. Dr Brennan is part of the research team at the Screening and Test Evaluation Program (STEP) at the School of Public Health. Her research interests are evaluation of diagnostic tests in the breast cancer setting and she is also leading a research project investigating the role of survivorship care plans.

Dr Jacquie Chirgwin
MBBS, MA (Oxon), FRCP (UK), FRACP, GAICD

Jacquie Chirgwin initially trained in the UK. Since 1990 she has been a Medical Oncologist at Box Hill and Maroondah Hospitals; for nearly ten years specialising in Breast Cancer only. She has a strong commitment to clinical trials and is currently the Chair of the Board of Directors of the ANZ BCTG. She is currently the leader of the Breast Tumour Group at North East Melbourne Integrated Cancer Service (NEMICS), and has a particular interest in Multidisciplinary Team care of Advanced Breast Cancer.

Professor Susan Clark
PhD, BSc (Hons1)

Susan Clark has a highly acclaimed international reputation for her work in mammalian epigenetics. She heads the epigenetics research group at the Garvan Institute of Medical Research in Sydney, Australia. She graduated in 1982 with a PhD in Biochemistry at the University of Adelaide and then spent ten years in the Biotechnology Industry before returning to basic research in gene regulation in 1992. Her studies over the last eighteen years have initiated profound questions about the importance of epigenetics in early development and in disease, especially in cancer. Professor Clark has made extensive ground-breaking discoveries relating to DNA methylation and chromatin patterns in normal and cancer genomes, that have led to new tests for early cancer detection. The techniques she pioneered in the early 1990s, including bisulphite sequencing, have revolutionised and now underpin a new era in epigenetics research. She has a number of awards including the RPAH Research Medal in 2002, Julian Wells Medal in 2003, Ruby Payne-Scott Award for contribution of women in science in Australia; "Biochemisch Analytik Preis" for outstanding contribution for Methylation analysis in 2004. In 2006 she was elected a Fellow of the World Technology Network for Biotechnology and in 2009 was awarded one of Australia's "Top Ten" National Health and Medical Research (NH&MRC) Project Scientists.

Dr Richard De Boer
MBBS, FRACP

Richard De Boer completed oncology training at the Royal Melbourne Hospital and undertook a 3 year clinical research fellowship at the Royal Marsden Hospital in London. His primary areas of clinical interest are in breast and lung cancer, with breast cancer interests focussing on endocrine therapy, treatment-induced bone loss and bone metastases, and biological predictors of response/survival. He is actively involved in clinical research, and is a member of the Australian New Zealand Breast Cancer Trials Group, and head of the Breast Trials group of Cancer Trials Australia. He has authored or co-authored articles appearing in journals such as the *Journal of Clinical Oncology, Annals of Oncology, The Breast* and *British Journal of Cancer*. Dr De Boer is Consultant Medical Oncologist at the Royal Melbourne, Western and Epworth-Freemasons Hospitals in Melbourne, Australia.

Dr Roslyn Drummond
MBBS, FRANZCR, MRACMA, FAChPM

Roslyn Drummond is Deputy Director of Radiation Oncology, and Senior Radiation Oncologist in the Breast Unit, at Peter MacCallum Cancer Centre and a Senior Fellow of The University of Melbourne. She has specialised in the radiation treatment of breast cancer since 1981, and is a member of a number of multidisciplinary teams treating breast cancer in the private and public medical sector in metropolitan Melbourne, as well as being a member of the ANZ Breast Cancer Trials Group, the Trans Tasman Radiation Oncology Group, EUSOMA, ESTRO and ASTRO.

Dr Susan Fraser
MBBS, FASBP

Susan Fraser has been a practicing breast physician in Cairns for 20 years. She is the current President of the Australasian Society of Breast Physicians. She has just completed a three year contract as Senior Breast Physician at Sydney Breast Clinic and Cairns Breast Clinic. Dr Fraser currently divides here time between working in Cairns and the Gold Coast and reads mammograms for BreastScreen Queensland and BreastScreen NSW.

Dr James French
MBBS, FRACS

James French is a specialist breast and endocrine surgeon. He is the head of breast surgery at the Westmead Breast Cancer Institute based in Westmead Hospital. He gained his fellowship in general surgery in 2002 and then completed 2 years of post fellowship training in Breast and Endocrine surgery. Dr French has particular interest in implant based breast reconstruction and has participated in numerous meetings where the focus has been on the aesthetic aspects of oncological surgery.

A/Professor Bruno Giuffrè
MBBS, FRANZCR

Bruno Giuffrè is Senior Staff Specialist Radiologist in Radiology Department at Royal North Shore Hospital and North Shore Private Hospital. His areas of clinical and research interest are Breast and Musculoskeletal Imaging and he has been instrumental in developing and supervising techniques and protocols for these disciplines at RNSH. He is also involved in many aspects of medical Informatics. His current projects include correlation of histopathology with MRI abnormalities of breast lesions and the correlation between MRI and Ultrasound abnormalities of joints with operative findings. He has extensive teaching experience with a wide variety of audiences from medical students to clinical colleagues.

Professor P Grantley Gill
MBBS, MD, FRACS

Grantley Gill is a general surgeon with a specialised interest in the management of breast cancer and surgical oncology. He is Head of the Breast and Surgical Oncology Unit at the Royal Adelaide Hospital and has a personal chair at the University of Adelaide and is the Surgical Coordinator for BreastScreen South Australia. He is Chair of the Royal Australasian College of Surgeons trial of sentinel node biopsy versus axillary clearance in early breast cancer and Chair of the Breast Multidisciplinary Management Group at the Royal Adelaide Hospital.

A/Professor Nehmat Houssami
MBBS (Hons), MPH, MEd, FAFPHM, FASBP, PhD

Nehmat Houssami is a Breast Physician, and Public Health Physician. She undertook medical training at the Sydney Medical School, and has practiced in dedicated breast services since 1990. She is Principal Research Fellow with the Screening & Test Evaluation Program, Sydney Medical School, and a consultant physician at the Royal Hospital for Women. The majority of her research has examined breast imaging, image-guided intervention, and impact of testing on clinical outcomes. She has experience in evaluating new technologies and in complex evidence reviews (meta-analysis) of diagnostic or prognostic testing. She has over 100 peer-reviewed publications, and is Editor for 'Imaging, screening and early diagnosis' with *The Breast*.

Dr James Kollias
FRACS, MD

James Kollias is a specialist oncoplastic breast surgeon, currently working as a senior consultant at the Royal Adelaide Hospital and BreastScreen SA. He is the current Chairman of the National Breast Cancer Audit Steering Subcommittee. His previous roles include chairman of the RACS Breast Section, Founding President of BreastSurgANZ, adviser to a number of working parties for the National Breast and Ovarian Cancer Centre and council member of ASBD. He has published over 80 manuscripts in scientific refereed medical journals and several book chapters pertaining to breast disease. Current interests include oncoplastic breast surgery, breast and endocrine surgical training, credentialling in breast surgery and audit.

Professor Sunil Lakhani
MD, FRCPath (UK), FRCPA

Sunil Lakhani is State Director, Anatomical Pathology, Pathology Queensland and Professor and Head of Molecular & Cellular Pathology in The School of Medicine, University of Queensland. He is Head of the Breast Group at the University of Queensland Centre for Clinical Research (UQCCR) and lead pathologist for North Brisbane Breast Screening Service. He has authored/edited a number of undergraduate and postgraduate textbooks and book chapters and published more than 175 scientific papers. He is a series editor for the 4th Edition WHO Tumour Classification Books and volume editor of the 4th Edition WHO Classification of Tumours of the Breast. Professor Lakhani is on the editorial board of *Breast Cancer Research, Journal of Pathology, Virchow's Archives* and *International Journal of Experimental Pathology*. He sits on a number of national and international advisory panels.

Adjunct A/Professor Warwick Lee
MBBS, BSc(Med), FRANZCR, DDU

Warwick Lee is the State Radiologist for BreastScreen NSW and Adjunct Associate Professor, Discipline of Medical Radiation Sciences, University of Sydney. He has been involved with BreastScreen - NSW for over 20 years in a clinical and training capacity. He is a member of the Breast Imaging Reference Group of the RANZCR and the National Quality Management Committee of BreastScreen Australia and is a Past President of the Australasian Society for Breast Disease.

Professor Geoffrey Lindeman
BSc(Med) MBBS(Hons) FRACP PhD

Geoff Lindeman is a clinician-scientist focusing on breast stem cell biology and translational breast cancer research. He is Joint Head of the Stem Cells and Cancer Division at the Walter and Eliza Hall Institute and also Heads the Familial Cancer Centre at The Royal Melbourne Hospital. His laboratory is studying molecular regulators of normal breast development and cancer, with a particular interest in breast stem cells, the breast epithelial cell hierarchy and cancer. Characterisation of the regulators and identification of novel biomarkers could provide novel therapeutic targets for the treatment or prevention of sporadic and hereditary breast cancer.

Dr David Littlejohn
MBBS, FRACS

David Littlejohn has worked as an Oncoplastic Breast Surgeon since 2000 in Wagga Wagga. He spent a year with Dr Dick Rainsbury in Winchester, United Kingdom, in 1999 learning oncoplastic techniques. He has been an invited speaker at previous ASBD's and ASC's on immediate breast reconstruction including Miniflap and therapeutic mammaplasty. He has been a member of the Breast Executive since 2004 and is the current chair of the Oncoplastic sub committee of BreastSurg ANZ.

Professor Guy Maddern
MBBS, PhD, MS, MD, FRACS

Guy Maddern is the RP Jepson Professor of Surgery at the University of Adelaide, Director of Surgery and Director of Research at The Queen Elizabeth Hospital, and Surgical Director of the Australian Safety and Efficacy Register of New Interventional Procedures in Surgery (ASERNIP-S). He is also a member of the Advisory Committee on Medical Devices (ACMD) of the Therapeutic Goods Administration (TGA), Chairman of the TGA Medical Devices Incident Review Committee (MDIRC), as well as Chairman of the South Australian Department of Health Committee on New Technology Assessment (HTAG). Professor Maddern was trained at the University of Adelaide and became a Fellow of the Royal Australasian College of Surgeons in 1989. He is a practising hepatobiliary surgeon based at The Queen Elizabeth Hospital, Adelaide, Australia.

Professor Bruce Mann
MBBS, PhD, FRACS

Bruce Mann is Director of The Breast Service at the Royal Melbourne and Royal Women's Hospital in Melbourne. His clinical practice is in breast disease and melanoma and his research interest relates to tailoring treatment to fit the disease.

Dr Kerry McMahon
MBBS, FRANZCR

Kerry McMahon is a radiologist with Queensland X-Ray in Brisbane where she has a special interest in Women's imaging. This includes mammography and Breast MRI, obstetric and gynaecologic ultrasound and bone mineral densitometry, and Pelvic/Gynaecology MRI. She is a graduate from the University of Qld, completing her radiology training at the Royal Brisbane Hospital and a fellowship year in Women's Imaging at the Edinburgh Royal Infirmary, Scotland. She has currently been in private practice with Qld X-Ray since 1999, and is a visiting consultant to BreastScreen Qld.

Dr Claire Phillips
MBBS, FRANZCR

Claire Phillips is a radiation oncologist at the Peter MacCallum Cancer Centre. She is a subspecialist in Breast Cancer and Neuro-oncology with a research interest in stereotactic treatment of choroidal melanoma. She trained in Melbourne and spreads her clinical time between the Peter MacCallum Cancer Centre and the Royal Melbourne Hospital. Dr Phillips is an active member of the Trans Tasman Radiation Oncology Group (TROG). She is co-chair of an international study of glioblastoma multiforme in the elderly and was local PI for the RAPID study of partial breast radiotherapy. Dr Phillips enjoys teaching medical undergraduates about her medical specialty and the multidisciplinary care of breast cancer.

A/Prof Wendy Raymond
MBBS, MD, FRCPA

Wendy Raymond holds appointments as a pathologist at Flinders Medical Centre / Flinders University, Breast Screen SA and in private practice at Healthscope Pathology in Adelaide. She has a longstanding interest in breast disease, having completed an MD on "Immunohistochemical markers in breast carcinoma" in 1991. She has co-authored several Australian guidelines in breast cancer management and has served on breast pathology/cytopathology quality assurance committees of the RCPA. Professor Raymond is the current President of the Australasian Society for Breast Disease.

Dr Angela Rutherford
BSc, PhD, MBBS, FRACGP, DRANZCOG

Angela Rutherford has been in General Practice in East Brunswick since 1988. Prior to medical studies, she obtained a PhD in science at the University of Melbourne, and has always been committed to evidence-based practice. Dr Rutherford has a particular interest in women with breast cancer, and has served on committees of BreastScreen Victoria, the National Health and Medical Research Council and the National Breast Cancer Centre. She was a member of the working parties which prepared the first Clinical Practice Guidelines for Early Breast Cancer, and Management of Advanced Breast Cancer.

Dr Paula Sivyer
MBBS, FRANZCR

Paula Sivyer is Director and Consultant Radiologist for Diagnostic Imaging for Women, an organisation committed to the practice of state-of-the-art diagnostic and interventional women's radiology with two practices based in Spring Hill, Qld. Dr Sivyer has dedicated her years in clinical practice to the pursuit of best quality patient outcomes through continuous education, pioneering techniques and investing in the advances in medical technology as they become apparent. Her particular interest is in breast imaging and intervention. Dr Sivyer has lectured extensively both in Australia and overseas and has published in the *World Journal of Surgery*.

Mr David Speakman
FRACS

David Speakman is a Consultant Breast Surgeon at the Peter MacCallum Cancer Centre (Peter Mac) and the Monash Medical Centre. He has sub-specialised in breast cancer treatments since completing his general surgical training. Specialist Fellowship appointments were at the Edinburgh Breast Unit in Scotland and at Peter Mac. Mr Speakman's special interests include minimally invasive surgery, sentinel lymph node biopsy, breast reconstruction and multidisciplinary breast care. He is heavily committed to educating both medical and allied health staff regarding breast disease. He is also the Director of the Monash Lymphoedema Service. He serves on the Medical Advisory Board of BreastScreen Victoria, the Australian and New Zealand Breast Cancer Trials Group, the NBCC and the Cancer Council. Mr Speakman has been the head of the Melanoma and Skin Cancer Service at Peter Mac since 2003. The service sees over 800 new melanomas each year and is a leader in providing a full range of multi disciplinary services. The unit has been involved in Sentinel Lymph Node Biopsy since 1996, was the lead institution in the TROG trial of Radiotherapy in Nodal Disease and also the first Australian site to test BRAF inhibitors, which are now changing outcomes in advanced melanoma. Mr Speakman is the Executive Director Clinical Services at Peter Mac.

Prof 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 February 1998, he took up the appointment of Senior Staff Specialist in Medical Oncology at the Canberra Hospital. He remains a Senior Staff Specialist in Medical Oncology, but is also Clinical Director of the Capital Region Cancer Service. He has particular interests in the management of both early and advanced breast cancer and the psychosocial aspects of cancer. Professor Stuart-Harris is the immediate past President of the Australasian Society for Breast Disease.

Dr Jacqui Thomson
MBBS FRACP

Jacqui Thomson graduated from the University of Western Australia in 1992 and moved to Melbourne following her intern year. She attained her FRACP in 2000 and currently holds appointments as a Medical Oncologist at Frankston Hospital and the Austin Hospital as well as a private practice in Frankston. Dr Thomsom is a member of MOGA, COSA, ASCO, ANZBCTG and MASCC. Her main professional and research interests are the management of early and late-stage breast cancer and reducing the side effects of breast cancer treatment.

Dr Daniel de Viana
MBBS, FRACS

Daniel de Viana is a medical graduate from the Queensland University, who completed his general surgery training through Princess Alexandra Hospital, Brisbane. He undertook postgraduate training in breast surgery and cancer management in the United Kingdom. He settled on the Gold Coast in 1999, initially working as Staff Breast Surgeon at the Gold Coast Hospital, and commenced private practice in 2000. Dr de Viana is a consultant at BreastScreen Southport, member of surgical review panel of BreastScreen Queensland, member of Executive Committee of the Australasian Society for Breast Disease, member of Royal Australasian College of Surgeons Breast Section, and member of the International Society of Breast Disease.

Miss Melanie Walker
MBBS (Hons), FRACS

Melanie Walker is a breast surgeon and a VMO at Alfred Hospital, Monash Medical Centre and Monash Breastscreen. She is in private practice in Frankston & East Melbourne (Breast Unit @ Mercy Private).

Presenters - Proffered Papers

Dr Helen Ballal
MRCS

Breast Fellow, Sir Charles Gairdner Hospital, Perth

Dr Elena Provenzano
MBBS, PhD, FRCPA

Pathologist, Focus Pathology, Melbourne

Mr Michael Puttick
BSc, MBBS, MD, FRCS

Surgeon, Department of Surgery, Auckland City Hospital, Auckland, New Zealand

Dr Richard Smith
MBBS

Surgical Registrar, Department of Surgery, Prince of Wales Hospital, Randwick, NSW

Venues

Thursday 6 October 2011

0730-1800 hrs	Registration Venue: Trade Exhibition area
1500-1800	Speakers' audiovisual testing Venue: Hotham Room
0900-1600	Workshop: Oncoplastic Surgery Venue: Hilton Ballroom 2 and 3
1500-1630	Workshop: Breast MRI for Radiologists Venue: Hilton Ballroom 1
1830-2000	Welcome reception Venue: HGA Harrison Room, MCG

Friday 7 October 2011

0730-1730 hrs	Registration Venue: Trade Area / Meeting Secretariat
0730-1600	Speakers' audiovisual testing Venue: Hotham Room
1730-1830	Networking drinks Trade Exhibition area

Saturday 8 October 2011

0730-1500	Registration Venue: Trade Area / Meeting Secretariat
0730-0845	Australasian Society for Breast Disease Annual General Meeting Venue: Epicurean Room, lobby level
0730-1300	Speakers' audiovisual testing Venue: Hotham Room
1930-2300	Meeting dinner Venue: Hilton Ballroom

The venue for all scientific program plenary sessions is the Hilton Ballroom.

GP Forum

Breast Matters
Wednesday 5 October 2011
1830-2130 hrs

Screening and diagnostic; triple assessment; breast disorders
Susan Fraser

New technologies; screening of high risk women
Natacha Borecky

Sentinel node biopsy; breast reconstruction
Melanie Walker

Biology, targeted treatment; EP/PR/HER-2; neoadjuvant treatment
Jacqui Thomson

Program

Please note that the program is subject to change.

Thursday 6 October 2011

0730 – 1900 hrs	Registration	
0900-1600	**Workshop 1: Oncoplastic Surgery** *In association with BreastSurg ANZ* *Sponsored by AstraZeneca Oncology*	
	Chair: Daniel de Viana	
	Introduction and getting started	James Kollias
	Oncoplastic surgery - Level 1 techniques: how to avoid breast deformities	Krishna Clough
	Reconstruction with tissue expanders and implants: Indications, technique and pitfalls	Daniel de Viana
	Oncoplastic surgery - Level 2 techniques: a quadrant per quadrant Atlas	Krishna Clough
	Latissimus Dorsi Flaps: How and when I do it	David Speakman
	Discussion	Panel
1030-1100	Morning break	
	The contralateral breast and nipple reconstruction	James Kollias
	How I perform nipple sparing mastectomy	James French
	My experience with skin sparing mastectomy	James French
	Acellular cadaveric dermal matrices	Belinda Scott
	Discussion	Panel
1230-1315	Lunch	
	Live surgery from Peter Mac	Krishna Clough and David Speakman
	Moderator: James Kollias	
	(The order of talks and the program may change depending on live surgery requirements)	
	How I do a TRAM flap	David Littlejohn
	Experience with superomedial pedicle breast reduction	Elisabeth Elder
	How I reconstruct a nipple	Richard Martin
	Case Presentations and discussion	Panel
1500-1630	**Workshop 2: Breast MRI for Radiologists**	
	Chair: Bruno Giuffre	
	Systematic image interpretation in breast MRI	Christiane Kuhl
	MR-guided interventions: Current techniques and success rates	Christiane Kuhl
1700-1830	**Minisymposium: DCIS – Optimising Loco-regional Management** *Sponsored by AstraZeneca Oncology*	
	Chair: Daniel de Viana	
	DCIS in MRI	Christiane Kuhl
	Changing surgical management of DCIS	Bruce Mann
	The role of radiotherapy and systemic therapy in DCIS	Lawrence Solin
	Panel / Questions	Faculty, Krishna Clough and Wendy Raymond
1830 – 2000	Welcome reception	

Friday 7 October 2011

0700-0830

Oncotype DX Educational Breakfast:
New perspectives and update on Clinical Utility Studies
Sponsored by Genomic Health

Chair: Bruce Mann
Speakers: Richard De Boer, Calvin Chao

0900-1015

Session 1: Lobular Cancer
Sponsored by AstraZeneca Oncology

Chair: Wendy Raymond

Welcome	Wendy Raymond
Diagnosis of lobular cancer in 2011	Sunil Lakhani
Should a diagnosis of lobular cancer change the surgical management?	James French
Should diagnosis of lobular cancer change the systemic treatment	Robin Stuart-Harris
Panel / Questions	Faculty and Christiane Kuhl

1015-1045 Morning break
Sponsored by Allergan

1045-1230

Session 2: Optimising Surgical Management
Sponsored by Novartis Oncology

Chair: James French

Keynote address: The debate around pre-operative staging with breast MRI	Christiane Kuhl
Keynote address: Why surgeons should favour neoadjuvant therapy	Ian Smith
What is an adequate excision margin?	Lawrence Solin
Axillary Reverse Mapping (ARM) in breast cancer patients requiring an axillary dissection: the SENTIBRAS multicentric French protocol	Krishna Clough
Questions	Faculty

1230-1330 Lunch

1330-1500

Session 3: Hypothetical – So We Think We Know How To Treat Breast Cancer: The perplexed patient

Moderator: Guy Maddern

Panel: Caroline Baker, Rick De Boer, Sunil Lakhani, Claire Phillips, Angela Rutherford, Sue Timms

1500-1530 Afternoon break

Session 4: Controversies in Radiotherapy Management

Chair: Roslyn Drummond

Keynote address: What will be standard of loco-regional radiotherapy in 2015?	Lawrence Solin
Mastectomy, immediate reconstruction and postoperative radiotherapy	Krishna Clough
Controversies of post-mastectomy radiotherapy	Lawrence Solin
Questions	Faculty

1730-1830 Networking drinks

Saturday 8 October 2011

0730-0845	ASBD Annual General Meeting	
0900-1030	**Session 5: Controversies in Breast Screening**	
	Chair: Kerry McMahon	
	Effect of digital imaging on recall and cancer detection	Warwick Lee
	Surgical QA for BreastScreen detected cancer	Grantley Gill
	Evolution of breast imaging: Beyond mammography	Christiane Kuhl
	The future role of tomosynthesis	Paula Sivyer
	Questions	Faculty
1030-1100	Morning break	
1100-1230	**Session 6: Proffered Papers**	
	Chair: Nehmat Houssami	
	Factors associated with underestimation of invasive breast cancer in women with core needle biopsy diagnosis of DCIS	Meagan Brennan
	Selected abstract presentations:	
	Use of Pre-operative MRI in DCIS of the breast	Michael Puttick
	Risk of additional axillary metastases after micrometastases in sentinel lymph node in a Western Australian population	Helen Ballal
	Local recurrence rates in young women with breast cancer following breast conservation treatment and mastectomy	Richard Smith
	PREDICT Plus: a population-based validation of a prognostic model for early breast cancer that includes HER2	Elena Provenzano
1230-1330	Lunch	
1330-1500	**Session 7: Changing Concepts in Breast Cancer**	
	Chair: Jacquie Chirgwin	
	Are triple negative cancers a distinct entity?	Sunil Lakhani
	Optimising chemotherapy for triple negative cancers	Ian Smith
	The importance of breast cancer stem cells	Geoffrey Lindeman
	DNA methylation sequencing identifies novel epigenetic markers in breast cancer	Susan Clark
	Questions	Faculty
1500-1530	Afternoon break *Sponsored by Sanofi*	
1530-1700	**Session 8: Looking to the Future: Optimising Treatment Outcomes** *Sponsored by Roche Products*	
	Chair: Robin Stuart-Harris	
	Optimal management of HER2 positive cancers	Ian Smith
	The future role of the breast surgeon	Krishna Clough
	Predictive assays – will these become routine?	Rick De Boer
	The future of adjuvant endocrine therapy	Ian Smith
	Questions	Faculty
	Awards for best proffered paper and best poster	
	Closing comments	Wendy Raymond
1930 – 2300	Meeting dinner *Sponsored by Novartis Oncology*	

Section 2

Abstracts

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WORKSHOP: ONCOPLASTIC SURGERY

In association with BreastSurg ANZ

Sponsored by AstraZeneca Oncology

Introduction and getting started

James Kollias

Oncoplastic breast surgery is a relatively new innovation embracing the concept of interdisciplinary surgical skills used to extirpate the breast cancer and immediately reconstruct the breast using various techniques to improve cosmetic and oncological outcomes. A number of techniques have been described involving volume replacement, volume displacement and various forms of skin sparing mastectomy. Obtaining experience in oncoplastic breast surgery requires a period of supervised training in a specialist centre, attending courses and/or performing basic procedures under the guidance of a surgical mentor. Working in conjunction with a peer with similar oncoplastic breast interests is recommended. Despite the recent enthusiasm for oncoplastic breast surgery, the current scientific evidence for the safety and efficacy of these techniques is not great. It is therefore essential to maintain a surgical log book of procedures performed including cosmetic outcomes and complications. The Oncoplastic Interest Group of BreastSurgANZ plans to develop a prospective database of oncoplastic procedures that can link to the National Breast Cancer Audit for the purposes of research and credentialing.

Oncoplastic surgery for conservative treatment of breast carcinoma: How to reshape each of the four quadrants

Krishna B Clough

The Paris Breast Center, France

Summary background data

When proposing breast conserving therapy (BCT), one has three goals: to achieve an overall survival identical to that obtained with mastectomy, to ensure optimal local control and to leave a normal breast. The last two objectives may result in a "clash of interest", particularly in patients with large, ill-defined tumours (invasive carcinomas with preoperative treatment, large DCIS or invasive lobular carcinomas) or poorly situated tumours. In such situations, clear resection margins can be difficult to obtain without altering the cosmetic results. In order to overcome this problem, one has two options: decline BCT because of a risk of major deformity, or use specific surgical techniques that allow reshaping of the breast in such complex situations. These operations have generally been designed under the term oncoplastic surgery (OPS).

Definition and methods

Reshaping of the breast after wide excision for BCT is needed in almost every case. In most patients this can be done in a very simple way, by undermining the gland from the skin, thus creating two glandular flaps that will close the defect. In some cases, recentralisation of the nipple-areola complex (NAC) will be necessary. These simple procedures (level 1 OPS) are easy to perform, do not require any plastic surgery training and should be performed by all breast surgeons.

Level 2 OPS is more complex and can be performed as a two team approach (breast surgeon and plastic surgeon). Ideally, we recommend that these operations should be performed by only one surgeon mastering these techniques. We have defined level 2 OPS as operations where breast reshaping is made difficult because of wide glandular resection, requiring excision of redundant skin and nipple areolar complex recentralisation. In most cases, this is performed as a unilateral operation. However, because of the large volume of excision, a contralateral symmetrisation is sometimes required to achieve breast symmetry. The indications for these techniques are patients for which conservative treatment is possible on oncologic grounds but where a standard lumpectomy would have led to a poor cosmetic result. Originally developed for cancers located in the lower pole of the breast, we have developed over the years, a wide range of techniques to allow reshaping of most tumour location. These techniques are defined according to the radius of the breast the tumour is situated on (i.e. from the 12 o'clock position clockwise) and will be described in detail. A series of 220 level 2 OPS operations will be presented, analysing both the operative results (complications, cosmetic results) and the oncologic results (tumor size and characteristics, re-excision and local recurrence rate).

Conclusions
Oncoplastic techniques allow extensive resections for conservative treatment of breast carcinoma and result in a favourable oncologic and aesthetic outcome. The indications for oncoplastic surgery are patients for which the ratio between tumour volume and breast volume is such that a standard excision would result in a high risk of positive margins, or a major distortion of the breast. Initially developed to allow wide breast excisions and prevent breast deformities, oncoplastic surgery has furthermore allowed us to extend the indications of breast conserving surgery to tumours that would otherwise be treated by mastectomy.

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Reconstruction with tissue expanders and implants: Indications, technique and pitfalls

Daniel de Viana

Reconstruction using the two stage tissue expander, implant technique provides a relatively simple option for women to restore their breast shape at a time when they are often burdened with other significant treatment decisions. It allows room for subsequent adjustment as well as patient input along the way in terms of breast volume and contour. Patient selection, essential steps in technique and personal experience will be discussed.

As with other reconstructive techniques it has its own limitations and potential complications, in particular those associated with any implant surgery. Patient education on achievable outcomes is important and the surgeon must be prepared for revisional surgery for some patients in the longer term. Nevertheless it is a fundamental technique in the reconstructive paradigm and a useful skill every oncoplastic surgeon should have.

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Latissimus Dorsi Flaps: How and when I do it

Dr David Speakman

Executive Director Clinical Services – Peter MacCallum Cancer Centre

The presentation will include the indications and contra indications for this form of breast reconstruction. There will be a description and video of the procedure including technical tips and tricks to assist harvesting of the flap and also its positioning. The use of the muscle only for partial breast reconstruction and the post operative management of the patient will also be covered.

The contralateral breast and nipple reconstruction

James Kollias

The breast is a paired organ such that the contralateral breast must always be considered in the context of breast cancer risk and changes to the primary breast cancer that may affect chest wall symmetry. In general, contralateral breast cancer is the least common form of breast cancer recurrence such that the contralateral breast should not normally be considered in terms of risk reduction or survival. In certain circumstances, the contralateral breast may assume importance due to issues of maintaining chest wall symmetry, favourable prognostic features of the initial breast primary, breast density that may affect surveillance and hereditary forms of breast cancer. Risk reducing surgery to the contralateral breast should therefore be considered on a case-by-case basis with the benefits and risks of surgery discussed with the individual patient.

Oncoplastic breast surgery and breast reconstruction surgery often require consideration of the contralateral breast in order to maintain chest wall symmetry. Volume displacement procedures such as therapeutic mammaplasty will lead to scarring and changes of the primary breast where a contralateral symmetrisation procedure will be required to improve cosmesis. Similarly, primary breast reconstruction often requires surgery to the contralateral breast (ie augmentation, reduction or mastopexy) to improve chest wall symmetry. Contralateral symmetrisation procedures are more common with implant-based methods of reconstruction. Various methods of nipple and areola reconstruction have also been described to improve chest wall symmetry. A number of techniques and case examples will be discussed to illustrate various aspects about these issues.

Skin reducing mastectomy and single-stage immediate implant reconstruction-lessons learned

*French J[1], Elder E[1], Brennan M[2], Lam T[3]

1. Specialist breast surgeon Westmead Breast Cancer Institute. Westmead NSW Australia
2. Breast physician Westmead Breast Cancer Institute Westmead NSW Australia
3. Plastic and Reconstructive surgeon Westmead Hospital Westmead NSW Australia

Background:
Skin reducing mastectomy (SRM) has the potential to offer the oncological advantages of a mastectomy, while at the same time allowing complete breast reconstruction (minus nipple areola reconstruction) in a single operation.

By using a Wise pattern incision both the vertical and horizontal dimensions of the breast skin envelope can be controlled. It however does present some technical challenges and risks related to the vascularity of the long random pattern upper flap.

Aim:
To describe the operation and report our experience with the first 25 cases, including the learning curve at a specialist breast cancer centre and to report patient satisfaction.

Methods:
Data were collected from the Westmead Breast Cancer Institute prospective database from between June 2010 July 2011. Information relating to patient and tumour demographics, complications and aesthetic outcome were collected and analysed. An approved patient telephone questionnaire was analysed to determine patient satisfaction.

Results:
15 patients underwent 25 SRM, 5 unilateral and 10 bilateral. Major complications resulting in implant loss occurred in 2 patients (4 breasts), a further 2 patients experienced superficial epidermolysis which required dressings only.

Conclusion:
SRM adds another option for carefully selected patients who either are contemplating or requiring a mastectomy and desire an immediate artificial reconstruction. We recommend that for surgeons not familiar with insertion of implants or experienced in tissue expander insertion that this operation be performed as a combined procedure between the oncological surgeon and reconstructive surgeon. When successful this operation results in a high degree of patient satisfaction.

How I do a TRAM flap

David Littlejohn

I first learnt TRAM flaps working with Dr Rainsbury in Winchester in 1999. He himself was also a novice at this technique at the time and we had great help from the plastic surgery department in Salisbury.

On returning to Wagga in 2000 at first I was reticent to continue doing TRAMs being worried about a perceived lack of support from peers. My opinion was changed by Dr Guy Hingston who was doing TRAMs in Port Macquarie. He was kind enough to mentor me through my first few in Wagga flying in for the days. I also visited Port Macquarie and operated with him. I describe my technique as it has evolved and what I have learnt along the way. How it varies with immediate, immediate-delayed and delayed reconstruction.

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WORKSHOP: BREAST MRI FOR RADIOLOGISTS

Systematic image interpretation

Christiane Kuhl

The Breast Imaging Reporting and Data System (BI-RADS) for MRI has been the first effort to standardize terminology in breast MRI. The system lists a number of descriptors for all sorts of breast MR imaging findings. Its main feature is that it distinguishes between "type of enhancement": mass like and non mass like enhancement. This distinction is important because it marks a crossroad of differential diagnosis: Whereas the descriptors for mass like enhancement serve to help distinguish benign and malignant solid tumors, e.g. fibroadenomas from breast cancer, the descriptors for non mass like enhancement can be used to distinguish DCIS or diffusely infiltration cancer from benign changes such as adenosis, hormonal stimulation, mastitis. So far, the PPV and NPV of the different descriptors are not yet established, such that the current BI-RADS lexicon helps describe, but not necessarily interpret breast MR images. The lecture is meant to help fill this gap by presenting the newest revisions and amendments of the BI-RADS MRI lexicon, and by a systematic review of BI-RADS descriptors in benign and malignant breast lesions.

MR-guided interventions: Current techniques and success rates

Christiane Kuhl

As it is the declared goal to use MRI in order to identify breast cancers at even earlier stages, the need to localize non-palpable lesions is ever increasing. Accordingly, the necessity to manage pre-operative marking or direct biopsy of MR-suspicious lesions has grown in parallel with the increasing availability of breast MRI and the increasing demand of pre-operative MR imaging. In general, three different concepts of MR-guided breast interventions have been pursued: MR-guided pre-operative lesion marking with consecutive excisional biopsy; 2. MR-guided core biopsy; 3. MR-guided vacuum assisted biopsy. Needle localizations are easily done even if performed with only limited equipment. Vacuum assisted core biopsy proves to be a very efficient and straightforward procedure for clarification of even small enhancing lesions. MR-compatible needles and core biopsy devices are available by a variety of vendors. We will present our experiences with MR-guided hook wire placement and MR-guided vacuum 9G core biopsy. Focus will be on the practical management of MR-guided biopsies, on success rates and the specific difficulties associated with MR guidance for biopsy of suspicious lesions.

MINISYMPOSIUM: DCIS – OPTIMISING LOCO-REGIONAL MANAGEMENT

Sponsored by AstraZeneca Oncology

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DCIS in MRI

Christiane Kuhl

Ductal carcinoma in-situ (DCIS) or intraductal cancer is considered to represent a direct precursor of invasive breast cancer. The constituents of DCIS, i.e. the individual DCIS cells, are clearly cancerous and exhibit the same cytological features, receptor status, and genomic deletion and expression profiles as their invasive sequela. However, as long as the lesion remains within the milk duct, it has no access to blood vessels or lymphatic channels, i.e. it cannot metastasize through these routes. Accordingly, this stage of disease can be considered benign, and is consistently curable by local treatment only (surgical excision with or without radiotherapy).[1]

The mammographic detection of DCIS is based on demonstration of microcalcifications. The typical fine linear calcifications are probably caused by necrosis secondary to the hypoxia that occurs in the central parts of a DCIS. DCIS are fed by diffusion from extra-ductal vessels only – there is no sprouting of vessels inside the milk ducts! Therefore, in ducts densely packed with DCIS, the diffusion distance may become too large. Hypoxia and calcified necrosis are therefore a frequent, but not obligatory finding in DCIS.

DCIS was a rare – and usually incidental – diagnosis before the advent of mammographic screening. With screening, well over 20% of cancers are now diagnosed as DCIS.[2] Accordingly, the success of mammography for diagnosing cancer in its pre-invasive stage is unprecedented in the entire field of oncologic imaging. Yet a number of issues remain.

First, not infrequently, calcifications develop in only part of the DCIS, whereas the major part may remain mammographically occult. Accordingly, women operated on a mammography-diagnosed DCIS may end up with inadequate resection margins positive for DCIS. This, in turn, requires surgical re-excision based on relatively gross spatial orientation information (suture markings of the specimen) and leads to additional, unplanned surgery.

Second, there are increasing concerns that mammographic screening causes over-diagnosis (and ultimately overtreatment) of biologically inert DCIS. This concern is fuelled by the observation that the increase of DCIS cases diagnosed with mammographic screening has not been associated with an appropriate decrease of early invasive cancers. The conclusion is that some – estimates range around 10%-25% – of the DCIS diagnosed by mammographic screening will never proceed to invasive cancer, but will remain dormant and never become a threat to a woman's life.

Third, there is probably also under-diagnosis of DCIS with mammography – in other words: There is reason to assume that mammography fails to identify DCIS in a substantial number of women. Very much unlike the intensive debate about overdiagnosis, this issue is virtually not discussed in the medical or scientific literature. Although it is held that the majority, if not all, invasive cancers proceed through the intraductal stage, still over 75%-80% of breast cancers will be diagnosed in the invasive stage – even in women undergoing annual mammographic screening. Accordingly, despite annual screening, the majority of the intraductal stages remain undiagnosed. Another piece of evidence for under-diagnosis is the fact that about half of invasive cancers appear as masses or architectural distortions without associated calcifications. It is unlikely that the respective intraductal precursors should have been associated with microcalcifications that vanished with the progression to invasive cancer. Since these DCIS – if they exist – did indeed progress to the invasive stage, one can conclude that mammography failed to detect prognostically relevant DCIS in a large number of women.

Over the past couple of years, it has become increasingly clear that MRI has a large role to play for diagnosing DCIS.[3] Still, the actual pathophysiologic correlate of contrast enhancement of DCIS is completely unknown. As with all in-situ neoplasias, DCIS represents a stage during which there is no direct structural connection between the intra-luminal cancer and the world beyond the basement membrane. There is no blood vessel infiltration into milk ducts, although an increased capillary cuffing is observable around ducts containing high grade DCIS.[4] Recent studies have confirmed that in contrast enhanced breast MRI, gadolinium compounds are indeed accumulated within the milk duct lumen that contains DCIS. These observations are in perfect agreement with clinical breast MRI studies, where we observe ductal enhancement or, in larger DCIS, enhancement of an entire ductal tree, yielding segmental enhancement. As the wording "ductal" indicates, what we observe appears to be enhancement within the milk ducts. This is different from inflammatory changes like those accompanying duct ectasia or secretory disease, where a peri-ductal signal increase is seen that produces a tram track type of contrast enhancement. Jansen's results indicate that enhancement in

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DCIS requires Gadolinium to diffuse from the intravascular to the extra-vascular, interstitial space and then – as a second step – from the extravascular to the intra-ductal space. This is in perfect agreement with the clinical observation that the enhancement kinetics of DCIS differ from those of invasive cancers. DCIS enhancement rates will remain below the typical enhancement thresholds of invasive cancers; a wash out signal time course in a DCIS is rare. This means that for diagnosing DCIS, current criteria related to enhancement kinetics are probably not useful, and current CAD software systems calibrated to the enhancement pattern of invasive cancers will consistently fail to highlight DCIS.

Since there is no gadolinium accumulation inside the normal milk duct, there must be a mechanism through which the intra-ductal accumulation is facilitated. Current thinking is that intraductal cancer release proteases which lead to a pathologically increased permeability of the basal membrane of milk ducts. This leakiness of basement membrane can be considered a first step in the preparation for invasive growth. They conclude that enhancement on MRI should constitute a biomarker for a DCIS' likelihood to progress to invasive cancer.[6] Again, this is in perfect agreement with the observation that the sensitivity of MRI for DCIS increases with nuclear grading of DCIS which, in turn, correlates with a DCIS' likelihood of progression to invasive cancer. DCIS lesions that exhibit strong enhancement on MRI, but no necroses, are obviously successful in maintaining their metabolic homeostasis – and in preparing extra-ductal spread. Demonstration of a DCIS in MRI is therefore based on a DCIS' well-being and its readiness to invade. This is in contrast to mammography, where the demonstration of DCIS is based on calcifications – in other words: on regressive changes associated with hypoxia and cell death. DCIS that exhibit no enhancement on MRI may be the ones that do not prepare invasive growth – because their basement membrane integrity is intact, and because they are not actively recruiting peri-ductal blood vessels.

In conclusion, with the systematic use of MRI for screening, we may improve the detection rate of prognostically relevant DCIS not associated with calcifications. We may avoid "under-diagnosis" of DCIS that is obviously occurring with mammographic screening alone. On the other hand, MRI may be used to guide treatment of DCIS because it may be useful to predict the natural behaviour of intra-ductal cancers.

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Changing surgical management of DCIS

Bruce Mann

DCIS was an unusual condition until the introduction of mammographic screening. It is now frequently diagnosed and its management is the subject of much controversy. While some view its detection and treatment as a means of preventing the development of breast cancer, others suggest that DCIS is massively overdiagnosed, and much of the treatment represents overtreatment.

Surgical management of DCIS is informed by minimal randomised trial data, and much of must recognise the uncertainties and controversies. A diagnosis of DCIS is only occasionally followed by the eventual death of a patient from breast cancer, and the main reported endpoint of treatment is local recurrence.

Surgical management of DCIS must be determined with this background of uncertainty. This presentation will explore some of these issues and draw conclusions on an approach to DCIS.

The role of radiotherapy and systemic therapy in DCIS

Lawrence J Solin, MD, FACR, FASTRO

The diagnosis of ductal carcinoma in situ (DCIS; intraductal carcinoma) has increased dramatically with the widespread use of screening mammography. In the asymptomatic patient, the most common mammographic finding is abnormal microcalcifications. DCIS is thought to be a non-obligate precursor for invasive breast carcinoma. Most women with newly diagnosed DCIS are eligible for surgical excision (lumpectomy), either with or without definitive radiation treatment, and mastectomy is rarely required. Thus, the decision for many patients with DCIS centers on whether or not to add definitive radiation treatment after lumpectomy.[1]

There are a number of reasons that support adding radiation treatment after lumpectomy for DCIS. Four randomized clinical trials have shown that adding radiation reduces the rate of local recurrence after surgical excision (lumpectomy) by about half, both for total local recurrence and invasive local recurrence. The risk reduction of approximately 50% with adding radiation treatment is consistent between randomized clinical trials, the Early Breast Cancer Trialists' Collaborative Group (EBCTCG) meta-analysis (see below), and retrospective institutional data, particularly where multivariate analysis has been performed. Retrospective clinical trials have not been able to define in a reproducible and reliable fashion those patients for whom the risk of local recurrence is sufficiently low that radiation treatment can be omitted. There are many reported retrospective, institutional studies of lumpectomy alone with radiation treatment. However, such retrospective studies serve as hypothesis generating, not hypothesis testing.

Very few patients with DCIS die from breast cancer or develop distant metastatic disease. Clinical trials have focused on endpoints that are measurable, for example, total local recurrence, invasive local recurrence, and the development of a contralateral breast cancer. Factors associated with local recurrence include the use of radiation treatment after lumpectomy, patient age, use of adjuvant tamoxifen, margins of resection, pathologic features of the primary tumor, and method of detection.

The first data have recently been reported from the Early Breast Cancer Trialists' Collaborative Group (EBCTCG) meta-analysis of the randomized trials of radiation treatment for DCIS.[2] This study analyzed patient-level data from four prospective, randomized clinical trials with 3,729 women randomized after lumpectomy to radiation treatment versus not. In the UK/ANZ (United Kingdom, Australia, and New Zealand) randomized clinical trial, a 2 x 2 factorial design was used to evaluate radiation treatment and tamoxifen in a single trial.[3] In the remaining three randomized trials, patients underwent simple randomization after surgical excision to radiation treatment versus not. A fifth randomized clinical trial from the Radiation Therapy Oncology Group (RTOG) reached its accrual goal, but did not have sufficient follow-up for inclusion in EBCTCG analysis.

The EBCTCG meta-analysis demonstrated that adding radiation treatment after lumpectomy reduced the 10-year rate of local recurrence (28.1% without radiation versus 12.9% with radiation; $P < .00001$), invasive local recurrence (15.4% versus 6.8%, respectively; $P < .001$), and DCIS local recurrence (14.9% versus 6.5%, respectively; $P < .001$). All subsets of patients gained with the addition of radiation treatment, independent of tamoxifen use, margin status, or extent of surgery. No differences were seen at 10 years for breast cancer mortality, overall mortality, or heart-related mortality (all $P > 0.1$). No increase in cardiac events was seen for patients with left-sided radiation treatment.

The EBCTCG meta-analysis identified a priori a subgroup of patients potentially at low risk for local recurrence as defined by the combination of low nuclear grade, negative margins of resection, and pathologic tumor size 20 mm or less. In this subset of potentially low risk patients, radiation treatment reduced the 10-year rate of local recurrence from 30.6% without radiation to 11.2% with radiation ($P = .001$). However, these patients may not be comparable to some retrospective studies. For example, the minimum negative margin width and the pathologic assessment of the tumor specimen were not as rigorous as in many single institution studies.

As suggested by retrospective studies, there are potentially patients at sufficiently low risk that omitting radiation treatment is a reasonable option. Such retrospective studies have used varying selection criteria. Nonetheless, population based studies in the United States have demonstrated that the use of lumpectomy alone (without radiation treatment) is increasing.

The Eastern Cooperative Oncology Group (ECOG) E5194 study was designed to identify prospectively potentially low risk patients for treatment with lumpectomy alone without radiation treatment.[4] In this registration study, there were two arms (not randomized); (a) low or intermediate grade DCIS, tumor size 2.5 cm or less; or (b) high grade DCIS, tumor size 1 cm or less. A minimum negative margin width of 3 mm or greater (or no tumor on re-excision) was required. Tamoxifen was optional beginning in the year 2000. However, the patients enrolled in this study were substantially more favorable than the protocol specifications. The median tumor sizes in the two arms were 6 mm and 5 mm, respectively. The

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minimum negative margin width was 5 mm or greater in 69% and 83% of the patients, respectively. At the 7 years, the rates of local recurrence were 10.5% and 18.0%, respectively.

For patients undergoing breast conservation surgery, the minimum negative margin width required from the lumpectomy surgical specimen remains uncertain. Retrospective data suggest that the minimum negative margin width is greater for patients undergoing lumpectomy alone without radiation treatment (e.g., 10 mm) compared to those patients who will be receiving radiation treatment (e.g., 1 mm or 2 mm). In a meta-analysis of local recurrence after lumpectomy and radiation for DCIS, Dunn et al recommended a minimum negative margin width of 2 mm.[5]

Two prospective randomized clinical trials have evaluated the role of tamoxifen in the setting of DCIS.[3,6] In the National Surgical Adjuvant Breast and Bowel Project (NSABP) B-24 study, the addition of tamoxifen was associated with a risk reduction in the rate of all breast events (ipsilateral plus contralateral) of 27% ($P < .05$), with a median follow-up of 13.0 years. In the UK/ANZ study, the addition of tamoxifen was associated with a risk reduction of 25% in the rate of all breast cancer events ($P = .002$), with a median follow-up of 12.7 years. These two studies are consistent in the benefit of risk reduction associated with adding tamoxifen. Subset analysis from the NSABP B-24 study indicates that tamoxifen is suitable for DCIS that is hormone receptor positive, not hormone receptor negative.

Future studies of DCIS will address systemic agents other than tamoxifen. The NSABP B-35 study randomized patients to tamoxifen versus anastrozole. This study has reached its accrual goal, although no outcome data have yet been reported. In the NSABP B-43 study, the role of trastuzumab is being evaluated for HER-2 positive DCIS. Single institution studies are evaluating the neoadjuvant use of other targeted agents, (e.g., trastuzumab, lapatinib).

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ONCOTYPE DX EDUCATIONAL BREAKFAST: NEW PERSPECTIVES AND UPDATE ON CLINICAL UTILITY STUDIES

Sponsored by Genomic Health

Bruce Mann, Richard De Boer, Calvin Chao

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SESSION 1 – LOBULAR CANCER

Sponsored by AstraZeneca Oncology

Diagnosis of lobular cancer in 2011

Sunil R Lakhani

Pathology Queensland: The Royal Brisbane and Women's Hospital, The University of Queensland Centre for Clinical Research and The University of Queensland School of Medicine

Invasive lobular carcinoma (ILC) is the commonest 'special type' of breast cancer. It poses difficulties for the surgeon and radiologist due to its diffuse infiltrative nature. Over the last decade, variants of ILC, in particular, the pleomorphic variant, have been identified that appear to have differing behaviour and prognosis. The behaviour of ILCs is also fascinating with a propensity to metastasise to serosal surfaces such as peritoneal cavity. The study of ILC using molecular methods is providing new insights into the biology that will hopefully lead to better and more targeted therapy for this tumour type.

Atypical lobular hyperplasia (ALH) and lobular carcinoma in situ (LCIS), collectively called lobular neoplasia (LN) are relatively uncommon but fascinating lesions. They were first described over 60 years ago and have been subject to extensive characterisation in the literature. However, despite this long time span, there remain problems and confusion surrounding the most appropriate terminology and classification for these lesions, their biological significance ('risk indicator' or 'precursor' for invasive cancer) and the best course of long-term management following diagnosis.

A diagnosis of LN has been perceived as a 'risk indicator' for subsequent carcinoma, rather than a true precursor. There is however, clear, epidemiological and molecular data to support a precursor role in the development of invasive carcinoma; hence LCIS is not a 'benign' disease. Molecular studies have been instrumental in highlighting the role of E-cadherin inactivation in the development of lobular lesions and in supporting the notion that ALH and LCIS are in fact non-obligate precursors for the development of invasive cancer rather than being simply risk indicators for invasive disease. This has significant implications for the management of patients, especially in the setting of a core biopsy diagnosis as part of mammographic screening. Unfortunately, there is a lack of data relating to identification of patients who are likely to progress.

Over the last few years, a pleomorphic variant of lobular carcinoma (PLC) has been described. In pleomorphic LCIS and ILC, neoplastic cells show the typical discohesiveness of lobular neoplasms; however, they are of high grade and sometimes show features of apocrine differentiation. Although molecular data on the PLC are scant, these tumours have overlapping genetic changes with both classic ILC and grade III invasive ductal breast carcinomas, harbouring recurrent loss of 16q and lack of E-cadherin expression, E-cadherin mutation, 1q+, 16p+, 11q- but also showing overexpression and amplification of Her-2 in a proportion of cases, p53 stabilisation and amplification of 8q24 (MYC). Preliminary data suggests that BRCA2 may play a role in the pathogenesis of some PLCs. In addition, anecdotal evidence suggests that PLC may have a more aggressive biological behaviour than ILC. Hence, PLCs are not merely high grade IDC that have inactivation of E-cadherin but are indeed a variant of ILC. PLCs are therefore likely to evolve along a similar molecular pathway to their classic counterpart, but in addition, acquiring a high grade phenotype through molecular changes typically associated with high grade tumours.

Lobular carcinomas mostly fall into the luminal A and luminal B molecular subtypes as defined by expression profiling but a subset also fall into the 'Molecular Apocrine' category. Interestingly, within an individual molecular category (e.g. Luminal A), the lobular cancers cluster separately to the ductal carcinomas, indicating that the morphological distinction is also seen at the molecular level despite the common intrinsic subtype designation.

Little is currently know about the other variants of lobular carcinoma.

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Should a diagnosis of lobular cancer change the surgical management?

James French FRACS

A pre operative diagnosis of infiltrating lobular cancer (ILC) on core needle biopsy presents certain unique challenges to the assessing surgeon and multidisciplinary team, with respect to recommendations for the surgical management of the breast and to a lesser extent of the axilla. The incidence of ILC seems to be rising (Fischer, 1975) and now constitutes up to 15% of all breast cancers. Concerns over its multifocal nature have lead to controversy over the surgical management in the past. Many authors have recommended mastectomy as the preferred option for the breast (Kinne, 1993). Authors as recently as 2003 have suggested that mastectomy is a safer option due to observed high rates of local recurrence following breast conserving surgery (BCS) + radiotherapy (Hussien, 2003). Furthermore, the incidence of bilateral disease in ILC has been reported in some series up to 30% (Silverstein, 1994). This has lead to some authors recommending consideration of bilateral mastectomy when faced with a diagnosis of ILC.

More recent data has demonstrated that ILC treated by breast conserving surgery with negative margins coupled with radiotherapy results in rates of local recurrence and survival comparable to the treatment of infiltrating duct cancers (IDC) (Viviana Galimberti, 2011).

Using modern surgical techniques there are a variety of options for the excision of an ILC - BCS (with the aim of minimizing breast distortion), oncoplastic surgery (OPS), that may entail major breast re-shaping with or without a contralateral symmetrising procedure, or mastectomy together with options for breast reconstruction and sequencing of such treatments with adjuvant therapies such as radiotherapy. Selection of the appropriate technique is complex, largely due to the difficulty of accurately estimating pre operatively the extent of the tumour. There is often poor correlation between the final tumour size on histopathology and the size found on clinical examination and by conventional imaging. This is because ILC frequently does not form a discrete mass, rather the cancer cells tend to spread in a single file fashion through the breast tissue, failing to induce the desmoplastic reaction that allows detection on mammography (Sakr, 2011). In addition ILC is more likely to be multicentric and multifocal (Lesser ML, 1982).

When compared to conventional imaging using mammography and US, magnetic resonance imaging (MRI) has shown improvement in size estimation (Mann, 2010) but still suffers from under and over estimations of size in some series. In a recent report (Heil, 2011), pre operative MRI had no impact on re excision rates following attempted BCS for women presenting with ILC (19% in MRI group vs 18% in non MRI group) and there was a trend toward an increase in primary mastectomy rates in the MRI group. In a review (Mann MR, 2008) demonstrated that MRI has an impact on surgical management, resulting in a change in management in 28.3% of patients with ILC of which 88% were judged necessary based on pathology.

Following BCS, involved margins have been reported in up to 60% in patients being treated for ILC, resulting in high rates of second surgery either by re excision or conversion to mastectomy (Silverstein, 1994). A recent publication, suggests that use of OPS may limit the rate of margin involvement in BCS for patients being operated on with ILC, especially if the tumour is located in the central or lower quadrants of the breast (Sakr, 2011).

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While neoadjuvant chemotherapy (NAC) might seem to be an enticing concept for downsizing tumours to make them amenable for BCS, NAC fails to have the same impact on ILC as it does for IDC. Rates of complete pathological response are a disappointing 2%, compared with 12% for IDC, while conversion rates to successful BCS following NAC were 20% compared with 41% for IDC (Straver, 2010), making NAC a discouraging strategy.

Use of intra operative assessment for sentinel lymph node biopsy (SLNBx) has generated some controversy for axillary staging in ILC due to the bland nature of the metastatic cells in the lymph node. It has been a widely held view that this limits the sensitivity of both frozen section and imprint cytology when assessing lymph node status. However a paper published in 2009 found no significant difference in sensitivity, specificity or accuracy of frozen section when assessing SLNBx in patients presenting with ILC compared to IDC (Horvath, 2009).

While this uncertainty in the pre and intraoperative staging of the breast in women presenting with ILC may seem depressing, it should serve as a salient reminder to the surgeon for the need to carefully and adequately inform women of the pitfalls and limitations of current imaging techniques and the resultant implications. Patients should be fully warned of the increased likelihood of not being able to obtain clear margins in a single BCS episode and the subsequent need for further surgery. This is particularly important when employing more complex strategies; for example, when combining BCS with breast reduction surgery. It is very disappointing for both surgeon and patient if widely involved margins on histopathology result in a need to convert to a mastectomy + reconstruction following a satisfying aesthetic result from an OPS re shaping procedure.

In summary a diagnosis of ILC should not automatically trigger a recommendation for mastectomy +/- reconstruction, rather it should serve as a warning to both surgeon and patient that achieving clear surgical margins while retaining an acceptable aesthetic result may prove to be difficult. The surgeon in concert with the radiologist should evaluate all the pre operative staging information not withstanding the limitations of this assessment, which in turn should form the basis of an informed discussion with the woman about the surgical strategy to be employed in the local management of her breast. Painting a realistic picture of BCS pre operatively will hopefully lessen disappointment should this strategy not be successful.

It is unlikely that the use of pre operative MRI will limit the need for second surgery, but it may well increase the rate of recommending primary mastectomy. The use of pre operative NAC is unlikely to convert non-conservable tumours to being suitable for BCS. Intra operative assessment of SLNBx specimens should be the same as for women presenting with IDC.

Should a diagnosis of lobular cancer change the systemic treatment?

Robin Stuart-Harris

Infiltrating duct cancer (IDC) is the commonest histological type of breast cancer and accounts for approximately 75% of all breast cancers. Infiltrating (or invasive) lobular cancer (ILC) is the second commonest variety of breast cancer and accounts for 5-15% of all breast cancers. Several subtypes of ILC exist, but the classic (pure) and the pleomorphic forms are the commonest. Classic ILC is often multicentric and widespread. The cells are loosely cohesive and often in single file. The diagnosis of ILC is confirmed by the lack of staining for the cohesion molecule, E-cadherin. Classic ILC is usually ER and PgR positive and very rarely HER2 positive. Compared with IDC, ILC tends to be larger, lower grade, have a lower Ki-67 index and is more commonly ER and PgR positive and HER2 negative. On gene profiling, classic ILC is a luminal A tumour whereas IDC may be of other varieties. The metastatic pattern of spread of ILC is often very different to IDC.

Few studies in either metastatic or early breast cancer (EBC) have separated out patients with ILC from the majority with IDC. However, data are available for ILC and chemotherapy from neoadjuvant studies. Overall, ILC is much less likely to respond to neoadjuvant chemotherapy than IDC and some have suggested that neoadjuvant chemotherapy should not be used in ER positive, HER2 negative ILC (Purushotham et al. 2010). This is because neoadjuvant chemotherapy is more effective in smaller tumours, tumours that are hormone receptor negative, tumours that are higher grade and have a higher Ki-67 index, whereas ILC tends to be larger, is usually strongly hormone receptor positive and has a lower Ki-67 index.

Two studies of adjuvant therapies which separated outcomes according to ILC or non lobular histology have been published recently. The first was a retrospective analysis of 254 EBC patients who received FEC 100 chemotherapy. The outcomes for relapse free survival (RFS) and overall survival (OS) were similar in the 45 ILC and the 209 non ILC patients (Liem X et al 2011). The authors concluded that patients with ILC may gain some benefit from adjuvant chemotherapy. The second study in 2115 EBC patients, split patients into lobular (mixed) (498) and IDC (1617) histologies. In the patients with ILC, there was no difference in OS between those that received adjuvant endocrine therapy (AET) plus chemotherapy and those that received AET alone. However, in the patients with IDC, OS was significantly better in those that received both AET and chemotherapy than in those that received AET alone (Truin et al. *The Breast* 2011). The results of this study suggest that patients with ILC gain little benefit from adjuvant chemotherapy over and above AET, unlike those with IDC. Lastly, one study has examined outcomes in EBC patients receiving AET or not, according to histology (Rakha EA et al. 2008). Without AET, the survival of patients with ILC was worse than those with IDC. However, with AET, the survival of patients with ILC was better than those with IDC.

Classic ILC is a relatively uncommon but distinct form of breast cancer. ILC is usually strongly hormone receptor positive but HER2 negative. ILC responds poorly to chemotherapy but responds well to AET. AET provides greater benefit than adjuvant chemotherapy in ILC and AET is the adjuvant treatment of choice in ILC. However, some potential benefit from adjuvant chemotherapy in patients with ILC cannot be excluded.

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SESSION 2: OPTIMISING SURGICAL MANAGEMENT

Sponsored by Novartis Oncology

Keynote address: The debate around pre-operative staging with breast MRI

Christiane Kuhl

In the field of oncologic surgery, an accurate local staging, i.e. the delineation of local disease extent, is considered of key importance to guide treatment decisions in patients with operable cancers, in particular patients who are operated on with curative intention. Imaging studies are used to provide an accurate road map for the surgeon to help him or her obtain clear margins – which, in turn, is considered essential in order to avoid recurrent disease. It is well established that breast MRI is by far superior to mammography, with or without concomitant ultrasound, for the local staging of breast cancer. MRI allows the most accurate delineation of the size and the local extent of cancer, including the depiction of multifocal or multicentric or contralateral disease. MRI offers the highest sensitivity for demonstrating intraductal extensions around invasive cancers. Due to its very high negative predictive value, MRI can be used to confidently exclude the presence of breast cancer, and, thus, avoid unnecessary surgery. For all these reasons, MRI should be considered an integral part of the work up of patients who undergo breast conserving treatment for breast cancer. And yet, the technique is only slowly adopted in clinical practice. Arguments against the use of breast MRI include costs, frequency of false positive diagnoses, lack of availability of minimally invasive biopsy capabilities, lack of evidence by randomized controlled clinical trials, and, last, fear of overtreatment. In this lecture, these concerns are explained, discussed and weighted against the advantages of pre-operative breast MRI for breast cancer staging.

The point is made that pre-operative MRI serves two different purposes: (1) Mapping the extent of the known breast cancer (index cancer) which makes her a BI-RADS6 patient; (2) identifying additional cancers in the remaining parts of the same or the contralateral breast.

Whereas the first issue is “local staging”, the second issue could actually be considered “high risk screening”. Whereas there is indeed sufficient evidence to support the use of breast MRI for planning surgery of a known cancer (issue 1), this is not true for the second purpose (screening for additional cancers in the same or the other breast).

It is important to realize that even before the advent of breast MRI, it has been known that in about 30% of women staged only through mammography, residual breast cancer foci remain in the breast if breast conserving treatment is administered – this is indirectly proven by the fact that in women undergoing lumpectomy alone (without radiation therapy), over 30% of women will recur due to microscopic or macroscopic residual disease. This residual disease is obviously sufficiently treated by radiation therapy, because this will reduce the risk of local recurrence siginificantly down to about 5%, making breast conservation plus radiotherapy an equivalent choice to mastectomy in terms of long term survival.

Now with breast MRI, it appears that we are able to depict these additional cancers – the presence of which we could only suspect based on cancer recurrence rates.

Accordingly, the management of these additional cancers should be chosen with caution. As long as women receive whole breast radiotherapy, there is reason to assume that these additional cancers may not always require surgical treatment. Randomized clinical trials are needed to set up guidelines that help us decide on the management of these additional lesions.

In any case it is wrong to use guidelines that were developed based on mammographic staging data to guide management. For example, whereas there is (weak) evidence available to recommend mastectomy in case of mammographically diagnosed multicentric disease – there is no such guideline for MRI-detected multicentric cancer. Overtreatment (unnecessary mastectomy) will occur if old guidelines (established for mammographic staging) are used for a new situation (staging with MRI). Guidelines that require mastectomy for multicentric breast cancer are based on mammographic diagnoses alone.

Keynote address: Why surgeons should favour neoadjuvant therapy

Ian Smith

Neoadjuvant medical therapy before surgery has been around for 25 years but its definitive role in breast cancer treatment remains to be established.

The main clinical role for neoadjuvant therapy is downstaging to render inoperable cancers operable, or more commonly to reduce the need for mastectomy and allow conservative surgery. Neoadjuvant endocrine therapy with aromatase inhibitors downstages to allow breast conserving surgery in around 50% of patients (Eiermann, Paepke et al. 2001; Smith, Dowsett et al. 2005). Neoadjuvant chemotherapy also can achieve downstaging to avoid mastectomy but in a smaller number of patients; this may relate to caution among surgeons in younger women where long-term local control is crucial.

Experimental data suggest that neoadjuvant medical treatment might improve survival. This concept has not been accurately tested for endocrine therapy. Most of the data for neoadjuvant chemotherapy suggest no difference in survival compared with the adjuvant route but a recent long-term follow-up of the B-18 trial suggests that there might be a long-term improvement in disease-free survival and overall survival with neoadjuvant chemotherapy for patients under the age of 50 (Rastogi, Anderson et al. 2008).

An important potential research role for neoadjuvant therapy is as a short-term surrogate marker for long-term outcome. In this context it is clearly established that patients who achieve pathological complete remissions have better long-term outcome than those who do not (eg (Rastogi, Anderson et al. 2008), and although triple negative breast cancer is considered to have an adverse prognosis, this is not the case when patients with this histological sub-type achieve a pCR (Liedtke, Mazouni et al. 2008). Improved pCR rates with neoadjuvant trastuzumab in addition to chemotherapy reflect improved survival with adjuvant trastuzumab in large trials and recent trials have shown that combined Trastuzumab and Lapatinib in combination with chemotherapy are more effective than Trastuzumab and chemotherapy alone. The same has been shown for the combination of Trastuzumab and Pertuzumab. It remains to be seen if these results are confirmed in currently running adjuvant trials.

The problem with pCR is that it is achieved in only a minority of patients treated with chemotherapy and very rarely indeed in patients treated with neoadjuvant endocrine therapy.

Recent clinical research has therefore been directed towards establishing whether short-term molecular markers can be used to predict long-term outcome. In the IMPACT neoadjuvant endocrine therapy trial comparing anastrozole with tamoxifen with combination (the neoadjuvant equivalent of the adjuvant ATAC trial), anastrozole achieved a significantly higher mean fall in Ki67 than the other two arms, correctly predicting the ATAC trial outcome and suggesting that Ki67 might be a useful short-term surrogate measure.

Based on the same trial the degree of Ki67 suppression following a mere two weeks of neoadjuvant endocrine therapy predicted for disease-free survival (Dowsett, Smith et al. 2007) and a major Phase 3 randomised trial, POETIC, is currently running in the UK with the aim of seeing whether these results could be validated and extended. Similar preliminary findings have been found for Ki67 suppression following chemotherapy and studies to validate are also underway.

In conclusion, it is likely that short-term preoperative endocrine therapy and chemotherapy followed by core biopsy to assess molecular response will become increasingly used in planning individualised treatment for women with early breast cancer.

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What is an adequate excision margin?

Lawrence J Solin, MD, FACR, FASTRO

For the patient with early stage invasive breast carcinoma undergoing breast conservation treatment, surgical excision (lumpectomy) of the primary tumor is typically followed by definitive radiation treatment.[1-3] When definitive radiation treatment is applied, the goal of surgical excision is not to remove every last tumor cell. Rather, the goal of the surgical excision is to debulk the primary tumor to the point where definitive radiation treatment has a high probability of controlling any residual microscopic disease within the breast. Thus, surgical excision requires a great deal of judgment to balance the competing needs of removing sufficient tissue for adequate local tumor control, but not removing so much tissue as to adversely impact on the cosmetic outcome. In contemporary practice, local recurrence is a very low risk, typically of the order of about ½% per year (or less), which translates into a local recurrence rate of about 5% at 10 years.

The lumpectomy specimen is inked by the surgical pathologist to assess the tumor margins. Optimal evaluation of tumor specimen includes orienting the specimen relative to margins, so that any inadequate margin can be assessed pathologically. A number of approaches have been described for assessing margins, including using different ink colors or using shaved margins.[3]

Although a negative margin (or negative margins) of resection is the goal of the lumpectomy, the optimal minimum negative margin width has been the subject of controversy.[1,3,4,5] For the patient with early stage invasive carcinoma, negative margins indicate that there is a high probability of local tumor control when the radiation treatment is applied thereafter. Negative margins imply a prespecified minimum negative margin width. A specific minimum negative margin width is established by the treatment team, and used by the pathologist in the description of the lumpectomy specimen. Various minimum negative margin widths have been described for invasive carcinoma, including no tumor cells on ink, or a minimum negative margin width of 1, 2, 5, or even 10mm. The definition of no tumor cells on ink as a negative margin is used in the National Surgical Adjuvant Breast and Bowel Project (NSABP) studies.

In judging an optimal definition of minimum negative margin width, the published data are constrained by the fact that no randomized clinical studies have been done, and a randomized trial is pragmatically impossible. Many individual institutions have defined their respective internal standards with corresponding local control, thus representing the limitations of the published literature.

Retrospective institutional studies have established in a convincing and reproducible manner that a negative margin is associated with better local control than a positive or inadequate margin.[4,6,7] Some institutions have used a third category of a close margin, with intermediate local control results between negative and positive margins.

Houssami et al have published a meta-analysis of clinical studies evaluating surgical margins relative to local control.[4] This study is a comprehensive literature review with rigorous statistical analysis. Houssami et al demonstrated that negative margins are associated with improved local control relative to close or positive margins. For any prespecified minimum negative margin width (e.g., 1 mm or 2 mm), the local recurrence was lowest with negative margins, intermediate with close margins, and highest with positive margins. There was a suggestion that local recurrence decreased as the prespecified minimum negative margin width was increased from 1 mm to 5 mm (test for trend P = .097), even when restricted to negative margins (local recurrence at 10 years, 7.7% versus 5.5% versus 3.8%, respectively). However, these results were rendered not statistically significant when adjusted for the use of a radiation treatment boost or hormone therapy, both of which have been shown in randomized clinical trials to reduce the risk of local recurrence.

The decrement in the local recurrence associated with not having a negative margin is difficult to estimate. In the study by Houssami et al, the decrement in 10-year local recurrence between positive and negative margins was on the order of 5-8%.[4] Extrapolating from the Early Breast Cancer Trialists' Collaborative Group, a 5-8% decrease in local recurrence should translate into an approximately 1-2% decrease in breast cancer mortality at year 15, which would be essentially impossible to demonstrate in a retrospective study.

Those studies which have reported results for close or positive margins of resection have typically restricted these patients to minimal or focal margin involvement, not diffuse involvement. Diffuse margin involvement is an indication for further surgery, either re-excision or mastectomy. The significance of the geography (or orientation) of close or positive margins of the lumpectomy specimen is a matter of considerable controversy. Some authors have suggested that a close or positive margin anteriorly (near the skin) or posteriorly (near the chest wall) does not have the same significance as circumferential margins within the breast parenchyma.

Selected patients age 70 years or above have been suggested as being eligible for treatment with lumpectomy plus hormones, without radiation treatment. In this setting, negative margins are required. The minimum negative margin width in this setting is generally unchanged (e.g. 1 mm or 2 mm).

There is little information published on the minimum negative margin width for the patient undergoing accelerated partial breast irradiation (APBI). In this setting, the ASTRO Consensus Guidelines recommended a minimum negative margin width of 2 mm.[8]

In the setting of DCIS, Dunne et al performed a meta-analysis for the minimum negative margin width for patients undergoing lumpectomy plus radiation treatment.[9] When compared to a minimum negative margin width of 5 mm or greater (reference group), there was no statistically significant difference for a minimum negative margin width of 2 mm (odds ratio 1.51; $P > .05$). In contrast, there was a statistically significantly increased risk of local recurrence for a minimum negative margin width of 1 mm or no tumor cells on ink (odds ratios of 2.89 and 2.59, respectively; both $P < .05$). Based on these results, Dunne et al recommended a minimum negative margin width of 2 mm when radiation is given after lumpectomy. For those patients undergoing lumpectomy alone without radiation for DCIS, a larger minimum negative margin width is generally recommended, typically 10 mm.

In the setting of mastectomy, defining negative margins can be substantially more difficult. The pectoralis fascia is often considered as a physical barrier. Some guidelines (e.g., NCCN) recommend considering post mastectomy radiation treatment for close or positive margins.[10] The minimum negative margin width in the setting of mastectomy is poorly established, but some studies have suggested a minimum negative margin width of 5 mm as adequate (i.e. not requiring post mastectomy radiation treatment).

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Axillary Reverse Mapping (ARM) in breast cancer patients requiring an axillary dissection: the SENTIBRAS multicentric French protocol

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We proposed and published a new anatomic classification of the axilla, dividing the lower axilla (Berg's level I/ II) into 4 zones (A, B, C, D) determined by the intersection of the lateral thoracic vein (LTV) (vertically) and the second intercostobrachial nerve (ICBN) (horizontally). In a series of 242 breast cancer patients where the breast sentinel node was precisely mapped, we demonstrated in a previous publication that the sentinel node was always medial (zones A and B) and almost never lateral.

The next step was to localize and harvest the arm sentinel node, then to assess in which conditions the arm sentinel node could be kept when performing an axillary dissection. In order to answer that question, Dr C. NOS developed a prospective multicentric French trial, the SENTIBRAS protocol. The main objective of this protocol is to evaluate the feasibility and reproducibility of an isotopic ARM procedure in breast cancer patients who require an axillary dissection AD (N1 patient, secondary AD for positive sentinel node).

Isotopes are injected in web spaces of the ipsilateral hand in order to detect lymphatic drainage of the upper limb. The surgeon seeks out radioactive nodes in zone D (above the 2nd ICBN and lateral to the LT V) and removes them. All others radioactive or non radioactive nodes of the AD are removed for a total of 3 different samples: P1= radioactive nodes from the D zone, P2= radioactive nodes from the ABC zone, P3= non radioactive nodes from the ABCD zone.

The secondary objectives of this study are to calculate the incidence of metastatic disease within P1, P2 and P3, and to evaluate the morbidity associated with AD. For these purposes, patients will be followed at 1, 2 and 5 year intervals.

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SESSION 3: HYPOTHETICAL – SO WE THINK WE KNOW HOW TO TREAT BREAST CANCER: THE PERPLEXED PATIENT

Moderator: Guy Maddern

Panel: Caroline Baker (Surgeon), Rick De Boer (Medical Oncologist), Sunil Lakhani (Pathologist), Claire Phillips (Radiation Oncologist), Angela Rutherford (General Practitioner), Sue Timms (Consumer)

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SESSION 4: CONTROVERSIES IN RADIOTHERAPY MANAGEMENT

Keynote Address: What will be the standard of local-regional radiotherapy in 2015?

Lawrence J Solin, MD, FACR, FASTRO

Over the past decade, radiation treatment for breast cancer has undergone a number of major changes.[1-5] These changes have included increasing options for radiation treatment fractionation, improvements in the technologic delivery of radiation treatment, and increasing insights into the molecular and biologic approach to breast cancer. These advances have substantially improved local regional control for patients with breast cancer, and have increased the options for radiation treatment delivery. Over the next five years, these trends will continue, with increasingly tailored and individualized programs of radiation treatment.

The last decade has witnessed an explosion of knowledge for the molecular and biologic nature of breast cancer.[1,4,5] This information includes a knowledge of the basic understanding of the biology of various subtypes of breast cancer as well as those molecular features that predict systemic recurrence. Integrating the biology of breast cancer into local regional treatment will be a major focus over the next few years.

Recent studies have looked at the relationship of biologic subtypes to local regional control. Some, but not all, studies have suggested an increased risk of local regional recurrence associated with tumors that are hormone receptor negative, triple negative, or HER2 positive. Early studies have also evaluated the potential for gene expression profiling to predict for local regional recurrence.

In the coming years, the individual selection of local regional treatment for specific patient subgroups based on biologic stratification will become increasingly important for selecting and individualizing local regional treatment. Some possibilities might include selecting patients for breast conservation treatment versus mastectomy, selecting patients after lumpectomy for adding definitive breast radiation versus not, and selecting patients after mastectomy for post mastectomy radiation treatment versus not. One might envision using molecular approaches for identifying those patients who might need increased radiation dose, wider boost fields, or inclusion of nodal fields. Advances in breast imaging, particularly molecular imaging, could lead to substantial improvements in the individualization of target volume definition for radiation treatment.

Radiation treatment equipment has undergone vast improvements over the last decade. The net effect is the ability to deliver increasingly more sophisticated radiation treatment plans in a shorter period of time on a daily basis. While not only improving patient convenience, the more rapid delivery of treatment has also led to more radiation treatment options. The increasing ability to perform gaiting will allow increasing protection of normal tissues with a corresponding reduction in normal tissue complications. At the present time, however, target volumes must be covered appropriately, rather than reducing local regional control.

An increasing knowledge of radiation dose fractionations has been developed through randomized clinical trials. Radiation fractionation options at the present time includes standard whole breast fractionation using a daily dose of 1.8 or 2 Gy per day, as well as more accelerated whole or partial breast radiation fractionation options. One accelerated whole breast fractionation option that has gained wide acceptance is 2.66 Gy per day to 42.56 Gy as published by Whelan et al.[6] Clinical randomized trials are ongoing to evaluate the role of more limited fields using accelerated partial breast irradiation (APBI).[7] One large randomized clinical trial of APBI has been reported.[8] In the future, the menu of radiation fractionation options will range from no radiation to accelerated fractionation regimens delivered over 1-4 weeks to standard whole breast radiation delivered over 6–8 weeks.

In summary, by the year 2015, there will be less standardization of local-regional radiotherapy, and more individualization based on an increasing knowledge of breast cancer biology and improvements in radiation treatment technology. Substantial gains have been seen in local regional treatment, including radiation treatment. The result will be an increase in the individualization of treatment of patients, while maintaining the current high rates of local regional control, decreasing the risk of complications, and decreasing the time commitment for selected subgroups of patients.

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Mastectomy, immediate reconstruction and postoperative radiotherapy

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Summary background data:

Indications for post mastectomy radiotherapy (RT) are expanding, as RT has demonstrated to be beneficial both in terms of local and distant control for selected patients. A counter effect is that patients scheduled for postmastectomy RT are often discouraged from immediate breast reconstruction (IBR) because of the adverse effects of chest wall radiotherapy on the cosmetic results of the reconstruction.

Our goal was to demonstrate the feasibility of a new protocol for patients who demand IBR and for whom postmastectomy RT is planned. Most of these patients present with a large breast cancer: they are offered preoperative chemotherapy; if tumour response is not sufficient for breast conservation, we perform breast and nodal RT prior to surgery, then a mastectomy with axillary dissection and immediate breast reconstruction.

Material and methods:

Between December 1990 and September 2005, 24 patients with a large breast cancer not eligible to upfront breast conserving surgery (median clinical size: 55 mm) were treated with upfront chemotherapy (71% of patients) or hormone treatment (29% of patients), followed by breast and nodal radiotherapy (100% of patients), then mastectomy and IBR 6 weeks after completion of RT. All reconstructions were performed with a myocutaneous flap (autologous latissimus: 14 cases, latissimus and implant: 7 cases, TRAM: 3 cases).

Results:

Median follow-up was 6 years (9-187 months). Overall survival was 79%, and disease free survival was 67%. Only one patient (4%) developed a local recurrence 4 years after mastectomy: she was treated with wide local excision and systemic treatment, and the reconstructed breast was conserved.

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37% of patients developed a complication either at the donor site of the flap or on the chest wall. Out of these, 25% were reoperated during the first postoperative month.

Cosmetic results were evaluated both by the surgeon and the patient: 69% of patients had a very good or good result, 23% a fair result, and 8% a poor result.

87% of patients were satisfied with the operation and all outlined the psychological benefit of having an IBR despite a multidisciplinary treatment.

Conclusions:

Patients who are not candidates for breast conservation after neoadjuvant treatment and are scheduled for mastectomy and postoperative radiotherapy can have their radiotherapy delivered prior to mastectomy. Our study demonstrates that this option is feasible, and allows IBR with excellent cosmetic results. In this pilot study, the oncologic results were in accordance with a standard protocol of postoperative radiotherapy, with excellent local and distant control rates. This sequence of treatments should be assessed by further studies, but seems a promising approach for patients who do not respond to neoadjuvant treatment and are willing to have a mastectomy with IBR.

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Controversies of post-mastectomy radiotherapy

Lawrence J Solin, MD, FACR, FASTRO

Post mastectomy radiation treatment is often a consideration for patients who undergo mastectomy for invasive carcinoma of the breast. Those patients who undergo mastectomy typically have advanced disease, and are not eligible for breast conservation treatment. A number of guidelines have been proposed for deciding which patients are candidates for post mastectomy radiation treatment.[1-3] Post mastectomy radiation treatment is generally recommended for patients with four or more positive axillary lymph nodes, close or positive margins of resection, T4 tumors, or T3 tumors with positive axillary lymph nodes. For patients who have T3 tumors with negative axillary lymph nodes, the use of post mastectomy radiation treatment is less well established.

Patients with T1-2 tumors and 1-3 positive axillary lymph nodes comprise a large percentage of the patients undergoing mastectomy. The indications for post mastectomy radiation treatment in this subset of patients are not well established. SWOG 9927 was the only large randomized clinical trial restricted to this subset of patients, but unfortunately failed to meet its target accrual. Therefore, direct randomized clinical trial data are not available for this large and important population of patients. The information from which to judge the efficacy of post mastectomy radiation treatment instead comes from subset analyses of large randomized clinical trials as well as from the Early Breast Cancer Trialists' Collaborative Group (EBCTCG) meta-analysis. Subset analyses from the Danish Breast Cancer Trial and the British Columbia randomized clinical trials have both demonstrated an improvement in survival associated with post mastectomy radiation treatment for patients with 1-3 positive lymph nodes.[4, 5]

The Early Breast Cancer Trialists' Collaborative Group (EBCTCG) meta-analysis is a large source of information for the value of post mastectomy radiation treatment.[6] The EBCTCG meta-analysis includes over 8,000 women in 20 randomized clinical trials evaluating post mastectomy radiation treatment. The EBCTCG shows a gain with post mastectomy radiation treatment of 22.5% in local regional recurrence by year 5 for patients with 4 or more positive axillary lymph nodes, which is associated in turn with a gain in breast cancer mortality of 7.3% at 15 years. For patients with 1-3 positive axillary lymph nodes, the 5-year gain in local-regional treatment is 16.1%, and there is an associated 15-year gain of 8.1% in breast cancer mortality. The avoidance of one local-regional recurrence by year 5 leads to the avoidance of one breast cancer death by year 15. There was no evidence of a different effect from adding post mastectomy radiation treatment for patients with 1 versus 2 versus 3 positive axillary lymph nodes.

To adjust for the potentially confounding variables of systemic therapy and surgical technique, the EBCTCG evaluated a subset of patients with a full axillary lymph node dissection and having received adjuvant systemic chemotherapy to be more consistent with contemporary treatment regimens. In the subset of patients with 1-3 positive axillary lymph nodes, the 5-year gain in local regional recurrence was 10.1% with post mastectomy radiation treatment, and the 15-year gain in breast cancer mortality was 3.3%.

The absolute gain for post mastectomy radiation treatment can be estimated for an individual patient based on her baseline risk of local regional recurrence without radiation treatment. In estimating the gain, adding post mastectomy radiation treatment reduces the baseline risk of local regional recurrence without radiation treatment by about 2/3. The gain in breast cancer mortality is approximately 1/4 of the gain in local regional recurrence. Variables to be considered for estimating baseline risk include the number of positive axillary lymph nodes, tumor size, patient age, use of systemic therapy, and the margins of resection.

Published models have limited ability to estimate the baseline risk of local regional recurrence without post mastectomy radiation treatment based on all important clinical and pathologic variables. Nonetheless, the number of positive axillary lymph nodes appears to be the strongest predictor of local regional recurrence, and estimates can be approximated based on the number of positive axillary lymph nodes alone. Patients with 4 or more positive axillary lymph nodes have a baseline risk of local regional recurrence after mastectomy of about 30% or more. Adding post mastectomy radiation treatment improves the absolute risk of local regional recurrence by about 20% at 5 years, thereby leading to an absolute gain in breast cancer mortality of about 5% by year 15. Similarly, patients with 1-3 positive axillary lymph nodes have a baseline risk of local-regional recurrence without post mastectomy radiation treatment of about 15%. Adding post mastectomy radiation treatment leads to an absolute gain in local-regional recurrence of about 10% by year 5, leading in turn to a gain in breast cancer mortality of about 2-3% by year 15. This magnitude of gain for local-regional recurrence and breast cancer mortality is favorable for most patients in clinical practice.

Retrospective studies have tried to estimate the risk of local-regional recurrence using finer combinations of number of positive axillary lymph nodes and primary tumor size to more closely approximate the risk for individual patients.[7, 8] Large retrospective data sets, such as the Eastern Cooperative Oncology Group and the MD Anderson Cancer Center, have provided valuable information. On balance, such studies have demonstrated that both tumor size and positive axillary lymph nodes are related to the baseline risk of local regional recurrence without post mastectomy radiation treatment,

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although the number of positive lymph nodes is the stronger factor. Adding systemic chemotherapy improves the baseline rate of the local-regional recurrence, although there is no evidence that more contemporary chemotherapy regimens (e.g., containing doxorubicin) improve the baseline rate of local regional recurrence without post mastectomy radiation treatment compared to earlier chemotherapy regimens (e.g., CMF).

In summary, post mastectomy radiation treatment is indicated for patients with 4 or more positive axillary lymph nodes. In contrast, there is only indirect evidence of the value of post mastectomy radiation treatment for patients with 1-3 positive axillary lymph nodes. There is no prospective randomized clinical trial for this subset of patients, although indirect evidence comes from the EBCTCG meta-analysis and subset analyses of prospective randomized clinical trials.

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SESSION 5: CONTROVERSIES IN BREAST SCREENING

Effect of digital imaging on recall and cancer detection

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The implementation of digital mammography (DM) within an organised Mammographic Breast Cancer Screening program such as BreastScreen NSW is expected to provide benefits related to image quality, transfer and storage of images, reduced dose and improved productivity. However, the quality of the program must be maintained to at least the levels achieved with screen film mammography (SFM). Key performance indicators of a program that allow comparison between DM and SFM are recall to assessment rates and cancer detection rates. A Program aims to achieve high cancer detection rates while maintaining low recall to assessment rates.

The results of 4 prospective clinical trials were published from 2001 to 2005[1-4] with the last 2 studies, the Oslo II[3] study and DMIST[4], demonstrating improved performance and equivalent performance respectively in cancer detection rates and recall to assessment rates. These studies provided evidence for the confident introduction of digital mammography into screening programs.

Since 2007, there have been 11 published papers retrospectively comparing DM with SFM5-15 with some conflicting results. Comparison between such studies may be difficult due to study design and screening practices[16]. However, all studies demonstrated either equivalent or significantly improved cancer detection rates with DM. 5 of the 11 studies demonstrated significantly increased recall rates[7,9,11,14,15,] four studies demonstrated significantly reduced rates[6,8,10,12] and in 2 studies, there was no change[5,13]. In 7 studies, there was no change in positive predictive value (PPV) of recall to assessment[7, 8, 10, 11, 12, 13,] in 2 studies PPV increased[5, 6] and in two studies, PPV decreased[9, 14].

The impact on screening outcomes of the implementation of digital mammography at BreastScreen NSW – Sydney South West has been assessed[17]. Cancer detection rates were equivalent for DM and SFM. Recall rates were significantly higher for DM compared to SFM for all screening examinations, although the increase was small (6.22% and 5.48% respectively, $p<0.0001$). However, recall rates (RR) for initial rounds were equivalent for DM and SFM (11.94% and 11.51% respectively) and there was only weak evidence for increased RR for DM in subsequent rounds (4.4% vs 4.12%, $p=0.07$). PPV for DM and SFM were also equivalent.

High recall rates, especially for initial screens, are a particular problem for BreastScreen NSW. However, there is no clear correlation between the time of introduction digital mammography into a Screening and Assessment Service (SAS) and the increase in recall rates. The lack of correlation is evident when the time point of introduction of digital mammography is plotted against trend charts of SAS recall rates. It is proposed that other factors such as pressure on readers to maintain high cancer detection rates and related quality assurance activities have a greater effect on recall rates than the introduction of digital mammography.

Conclusion: Cancer detection rates with DM are equivalent to those with SFM. The effect of DM on recall to assessment rates is variable, but should not be overstated when other factors may have a greater impact on recall to assessment rates.

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Surgical QA for BreastScreen detected cancers

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BreastScreen Australia is a publicly funded public health program, the aim of which is the reduction in breast cancer mortality through early detection. Using screening mammography in the target age group 50-69 years. Surgeons are currently involved in the assessment of screen detected abnormalities and subsequently in treatment. (Open biopsy is not part of most screening programmes.) Surgeons have defined separate role in each of the assessment and treatment pathways.

There are 173 NATIONAL ACCREDITATION STANDARDS (NAS) which are utilised in the assessment and the awarding of accreditation status to individual programs. Standards are grouped into clusters at each of three levels which are ranked according to their importance for screening outcomes, the most important relating to cancer detection and timeliness.

Regarding the ASSESSMENT CLUSTER, two NAS (2.7.1 and 2.8.1-4) are of immediate relevance to surgeons. NAS 2.7.1 states that more than 75% are diagnosed with invasive cancer or DCIS without the need for diagnostic open biopsy, whilst 2.8.1 complements this by insisting on a minimal biopsy rate following assessment. Services must demonstrate that all members of the multidisciplinary team have relevant training and qualification at the appropriate expertise in breast assessment. In order to meet these formalised requirements, participation of surgeons in multidisciplinary assessment protocols are essential in achieving these targets and services must demonstrate protocols are in place to manage discordant results.

The key NAS relevant to SURGICAL MANAGEMENT are those relating to small cancers <15mm diameter (2.2.1). Thus ALL women with IMPALPABLE LESIONS undergoing open biopsy must have specimen radiography performed (2.21.2) and more than 95% of impalpable lesions must be correctly identified at first open biopsy. 2.21.3 This requires a combination of effective imaging and surgery and can be rendered difficult by the complete removal of calcifications and small cancers at biopsy. Achievement of these NAS can be difficult in regional/rural programs.

The TIMELINESS cluster of the NAS are rated of very high importance by consumers and time to open biopsy (3.7.3-4) is susceptible to surgical influence. In practice this is rarely achieved except in the rare circumstance where open biopsy is part of the program and the assessment outcome is coordinated by surgeons. The various aspects of timeliness are a major problem for most programs and are frequently a result of radiological and/or administrative issues rather than surgical ones.

The NAS requires receipt of surgical histopathology information and the primary treatment information by the service and surgeons are best placed to provide this. Thus screening outcomes (radiology/pathology/surgery) of all lesions resulting in surgery must be reviewed and correlated by each service. Other aspects of treatment are not part of the NAS. However some published data from BreastScreen indicate that breast conserving surgery should approach 70% of women with screen detected cancers. The NAS require that surgeons develop and maintain their skills through continuing education and recertification.

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Evolution of breast imaging: Beyond mammography

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Regarding the early diagnosis of breast cancer, population based mammographic screening has been shown to help reduce breast cancer mortality. Mammographic screening, reduced post-menopausal hormone intake and the development of new, targeted therapies all contributed to the reduction of breast cancer mortality that has been observed in the last couple of years. Still – breast cancer is one of the most frequent cancers overall, and it continues to be the leading cause of cancer death in women, indicating that there is room – and need! – for improvement. Magnetic resonance imaging (MRI) of the breast has been introduced a decade ago. Over recent years, it has become increasingly evident that breast MRI is by far the most powerful breast imaging technique that is currently available. Across all different clinical and screening scenarios, MRI has been shown to be superior to mammography – be it for diagnosing primary or recurrent, invasive or intraductal, familial or sporadic breast cancer, irrespective of a woman's breast density. And yet is the technique only slowly adopted in clinical practice. Arguments against the use of breast MRI include costs, frequency of false positive diagnoses, lack of evidence by randomized controlled clinical trials, and, last, fear of overtreatment. In this lecture, these concerns are reviewed, discussed and weighted against the advantages of screening and diagnostic applications of breast MRI.

The point is made that on the long run, the main advantage of breast MRI over mammography will not be its higher overall sensitivity for breast cancer – but its tendency to identify biologically active disease. In other words: In view of the heated discussion around overdiagnosis and overtreatment of cancer in general and breast cancer specifically, the future question with regards to breast cancer screening methods will no longer be: "How many breast cancers do we detect by a screening method?" but "What type of breast cancers do we detect?". The following pathophysiological considerations fuel this statement:

It is well established that breast cancers that are diagnosed through mammographic screening have a better prognosis than those detected by clinical examination: Mammography tends to detect slowly growing cancers, a well known effect referred to as "length time bias", of which overdiagnosis is an extreme form. On the other hand, it is well established that breast cancers detected through MRI screening exhibit adverse biological profiles. Accordingly, whereas mammographic screening has a bias for detecting slowly growing cancers, MRI screening has a bias for detecting rapidly growing cancers.

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The reason for this difference lies in the different pathophysiological basis of breast cancer detection in mammography and MRI:

Mammography detects breast cancers by revealing structural changes that go along with impeded neoplastic growth (calcifications due to necrosis, architectural distortions due to local fibrosis which is secondary to hypoxia). Accordingly, breast cancer detection in mammography is mainly based on the depiction of regressive changes associated with slowed growth. This is different for DCE breast MRI, where cancer is detected due to local contrast enhancement. Enhancement of a DCIS or of an invasive cancer depends on a locally increased vessel density, an increased vessel permeability and – in the case of DCIS – an increased permeability of the ductal basal membrane. Accordingly, breast cancer detection in MRI is based on pathophysiological changes that are indicative of cancer proliferation, infiltrative growth and metastasis. In fact, the more angiogenesis or protease activity a cancer or DCIS exhibit, the higher the likelihood that it will be detected by MRI. Accordingly, detection of a DCIS or of an invasive cancer in MRI is biased towards cancers that are successful in maintaining an adequate supply of oxygen and nutrients and thus in maintaining metabolic homeostasis and metastatic potential. In addition, local contrast enhancement is an in-vivo biomarker for DCIS protease activity, because an increased ductal basal membrane permeability is required to allow a gadolinium chelate to accumulate within the milk ducts. It is well established that protease activity is an essential initial step in the process of invasive growth of DCIS, and of metastatic growth of invasive cancer.

Accordingly, we propose that overdiagnosis of prognostically irrelevant, biologically inert cancer (with all its important medical and socio-economical implications) is closely related to the very basis of mammographic breast cancer detection, and can hence be considered a modality-inherent, unavoidable side effect of mammographic screening.

In contrast, overdiagnosis may not be an inevitable consequence of MRI screening. We propose that in spite of the higher overall sensitivity of MRI and in spite of the higher cancer detection rates that have been published with MRI screening, overdiagnosis could even be reduced if MRI alone was used for breast cancer screening. This will probably be especially true for the diagnosis of DCIS.

The future role of breast tomosynthesis

Dr Paula Sivyer

The nature of the approach taken in breast imaging determines the success or failure of patient outcomes. While mammography remains the premier imaging modality for early detection of breast cancer, other imaging modalities such as breast ultrasound and MRI have long been recognised as valuable additional options for reassuring and comprehensive breast imaging, dependent on clinical context. Breast tomosynthesis represents a new development in breast imaging technology that, implemented effectively, has the potential to greatly enhance the accuracy of diagnoses and recommendations based on mammography. It is important for the medical profession to understand the benefits of tomosynthesis as an adjunctive breast imaging modality and to include breast tomosynthesis as a valuable tool in the available arsenal of breast imaging options.

If we argue that the medical profession needs to hold as its goal in breast imaging that all breast cancers should be found in the pre-clinical phase, then we must acknowledge the different nature of the contributions that each imaging modality can make towards achieving that goal. The multiple imaging modalities available must be used appropriately for their individual and combined contribution to accurate pre-clinical diagnosis. Moreover, the diagnostic pathway must be accurate, cost-effective and accessible, not exclusive to large urban centres.

We must also accept that size matters. Despite all the recent advances in imaging, pathology, surgery and adjuvant therapies, the critical issue affecting patient outcomes (mortality and morbidity) is: lesion size at diagnosis. In general, the smaller the lesion when identified, the better the prognosis in the long term.

Mammography is the imaging modality of choice for early detection of breast cancer and has been proven to reduce mortality from breast cancer when implemented as a screening program. Unfortunately, it is a reality that mammography is not a one-size-fits-all solution for the problem of

early breast cancer detection. Gaps or failures in detection arise due to the heterogeneous nature and what may be termed bad behaviour of breast cancer as a disease. Younger patients and patients with dense and/or complex breast parenchyma present particular challenges for mammogram imaging, due to the superimposition of breast structures on compression. Ambiguity can arise between differential diagnoses of normal superimposed breast parenchyma that gives a false appearance of abnormality and normal superimposed breast parenchyma that obscures a genuine abnormality in need of further investigation. This ambiguity erodes the sensitivity and specificity of mammography as a screening modality. Breast tomosynthesis has the potential to address these limitations in mammography.

Breast tomosynthesis is the tomographic application of digital mammography (Poplack et al, 2007). That is, positioning and compression of the breast is performed as for acquisition of a digital mammogram however rather than a single exposure taken in a single plane, tomosynthesis involves multiple exposures taken as the x-ray tube moves through a 15 degree arc. These images comprise the digital data set which is then reconstructed as a series of 3D sections through the breast.

In conjunction with high resolution low-dose digital mammography, corresponding breast tomosynthesis provides a reassuring and comprehensive review of breast tissue under x-ray imaging. Modalities such as ultrasound and breast MRI also retain their place within the breast imaging arsenal depending on clinical context.

Park et al (2007) argued the potential benefits from using breast tomosynthesis as a 3D imaging modality adjunctive to digital mammography include:

> *A lower recall rate, higher positive predictive value for a biopsy recommendation, and higher cancer detection rates...*

Poplack et al supported this position following a study of 98 women with abnormal screening mammogram results who underwent breast tomosynthesis by consent. As a result of the improved ability to differentiate between overlying breast structures, the study found breast tomosynthesis was associated with an identified recall reduction rate of 40%. In essence, breast tomosynthesis applied in conjunction with high-resolution low-dose digital mammography can improve accuracy of recommendations for patients to proceed to biopsy or other imaging modalities.

Our approach to breast tomosynthesis at Diagnostic Imaging for Women has been open minded. We have invested in the Hologic Selenia Dimensions tomo-capable unit at the newly-launched state-of-the-art women's imaging satellite site at St Andrew's War Memorial Hospital. We have developed strict protocols on the premise that we carefully consider tomo application and clinical context in the case of each and every patient. Our initial expectation was that tomosynthesis would be of most value in the detection and evaluation of mass lesions and/or architectural distortion. However, we have observed in practice that there is a marked improvement in the depiction and morphologic analysis of microcalcification on tomo application, particularly in patients with dense breast parenchyma. The benefits conferred by appropriate use of breast tomosynthesis in conjunction with digital mammography have led to a reduction in the number of lateral views undertaken as part of workup, reducing patient compression discomfort and radiation exposure.

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SESSION 6: PROFFERED PAPERS

Factors associated with underestimation of invasive breast cancer in women with core needle biopsy diagnosis of DCIS

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Background

When ductal carcinoma in situ (DCIS) is seen on core-needle biopsy (CNB), it may represent invasive breast cancer that is underestimated (understaged). Studies have shown that 0—59% of diagnoses of DCIS on CNB will demonstrate invasive cancer at excision histology.[2–6] Underestimation is of clinical importance as it is a key factor that increases the need for re-operation[7] (frequently for sentinel lymph node biopsy) and it interferes with the ability of patients and clinicians to effectively plan treatment. An ability to predict which lesions showing DCIS on CNB represent underestimated invasive breast cancer would be of clinical interest however previous research studies have examined single or a limited number of variables (such as size and histopathology features) and have shown inconsistent findings.[2–6]

Aims

The aims of this research were

(1) To perform a systematic review of the published literature reporting outcomes for women with a CNB diagnosis of DCIS and invasive breast cancer at excision histology;

(2) To report a pooled precise estimate for the prevalence of underestimation in this setting;

(3) To explore preoperative variables that may predict invasive breast cancer at excision histology.

Methods

Eligible studies were identified by searching MEDLINE and reported data on DCIS/invasive cancer underestimates (overall and according to preoperative variables). Study-specific and pooled percentages for DCIS underestimates were calculated. By using meta-regression (random effects logistic modeling) the association between each study-level preoperative variable and understaged invasive breast cancer was investigated.

Results

Literature review revealed 52 studies that reported outcomes for 7,350 cases of DCIS using findings at excision histologic examination as the reference standard. Thirty six studies also reported data on all CNBs in their series (49,365 CNBs): there was a median 8.3% of CNBs reporting DCIS on CNB across these studies (interquartile range 4.4%–12.0%). The prevalence of invasive breast cancer in women with a CNB diagnosis of DCIS was 25.9% (1,736 underestimates).

Preoperative variables significantly associated with underestimation included

(a) clinical variable: palpability;

(b) imaging variables: larger lesion size (greater than 20mm), mammographic mass (rather than calcification without mass) and mammographic features highly suspicious of malignancy (BI-RADS 4 or 5);

(c) biopsy variable: using a 14-gauge automated device rather than 11-gauge vacuum-assisted device;

(d) histology variable: presence of high-grade features on CNB.

Conclusion

About a quarter of DCIS diagnoses on CNB represent understaged invasive breast cancer. Several preoperative variables are significantly associated with understaging and these can be used to assist in treatment planning. This may increase the likelihood of surgical treatment being completed in a single operation and provides women and treating clinicians with additional information to guide pre-operative discussion.

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Selected Abstract presentations:

Use of pre-operative MRI in DCIS of the breast

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Background and Purpose

Most DCIS is diagnosed on a screening mammogram, but this can underestimate the extent of DCIS. Breast MRI is a more sensitive imaging technique than mammography. The aim of this study was to evaluate whether a pre-operative MRI would more accurately gauge the extent of disease within a breast, thereby informing surgical decision making.

Methods

Consecutive patients with a single area of DCIS who were being considered for breast conserving surgery were offered an MRI. Information was recorded on how the MRI had influenced the patient management and the size of the lesion on imaging was compared with the final pathological result. Any additional biopsies required were noted.

Results

32 patients were included. 2 refused MRI. In 1 patient no lesions were seen. In 13 patients the MRI made no difference. The MRI result altered the management of 17 patients. In 4 patients the MRI influenced the decision to have a mastectomy rather than breast conserving surgery. 3 others were able to have BCS but a larger resection was required. In one patient a more conservative resection was safely carried out.

However, in 4 patients the MRI underestimated the size of the lesion and 2 of these patients subsequently required a mastectomy. In 4 others, the MRI overestimated the size of the lesions leading to possible overtreatment. As a result of the MRIs an additional 8 biopsies were performed, 1 of which revealed an invasive cancer. The other 7 were benign.

Conclusions

Pre-operative MRI in DCIS of the breast can yield useful information but at significant cost.

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Risk of additional axillary metastases after micrometastases in sentinel lymph node in a Western Australian population

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Background and Purpose

The presence of micrometastases in sentinel nodes (SN) in patients with early breast cancer has been shown to be associated with a poorer prognosis. The management of micrometastases remains controversial and the rate of non sentinel lymph node involvement in an Australian population is difficult to ascertain from the literature.

Methods

A retrospective review of a prospectively collected pathology database at Sir Charles Gairdner Hospital identified all patients with a positive axillary SN between January 2001 and Dec 2010. Data on further axillary surgery and standard histopathological fields were collected and analysed.

Results

187 women with a positive SN were identified. 30% had micrometastases or isolated tumour cells only. This proportion was constant over the 10 year period. 81% of these patients went on to axillary dissection, and 24% had their disease upstaged to macroscopic metastases. This compares to 39% of people with macroscopic disease that had further nodes involved on dissection. There was a non-significant trend for tumour type to predict further disease in patients with micrometastases (p=0.07).

92% of patients with a positive SN underwent intra-operative assessment. 70% of the false negatives were found to have micrometastases or ITC on final histology.

Conclusion

We have demonstrated a higher rate of non-sentinel lymph node metastases in patients with micrometastases than reported in the literature (7.2% - 20%). In a number of our patients who were upstaged, the final axillary status may have influenced the choice of adjuvant therapy. Given the current debate about the management of positive SN and the poorer prognosis of those with micrometastases it is important not to ignore further study into the management and outcome of this group of patients.

Local recurrence rates in young women with breast cancer following breast conservation treatment and mastectomy

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Background and Purpose

Breast cancer (BC) is less common in "young" women (defined as 40 years age or less), but is associated with more aggressive biological features, higher risk of local recurrence (LR) and poorer survival. Our aim was to determine if young women with operable BC treated at our centre have an unacceptable incidence of LR following breast conservation therapy (BCT) compared to mastectomy (M).

Methods

The POWHCC breast cancer database was retrospectively reviewed between January 1995 to December 2008. 2245 eligible women with BC undergoing primary breast surgery were identified. LR rate was compared between young women and women over 40 years, and according to type of surgery. Data was analysed using a competing risk model to account for distant recurrence and death as competing events for LR.

Results

Median follow-up is 5.8 yrs. Of 2245 women, 249 were ≤ 40 years age, of whom 127 underwent BCT and 122 M. There were 17 local recurrences (6.8%), including 12 BCT and 5 M. In women > 40 years LR was 2.8% (56, including 42 BCT and 14 M). LR incidence was significantly higher in women ≤ 40 (p=0.001). On multivariate analysis significant predictive values for LR risk were positive margins (p=0.029), age ≤ 40 (p=0.001) and no adjuvant systemic therapy (0.037). There was a trend for BCT (p=0.057). The interaction between age and type of surgery performed on LR was borderline significant (p=0.07).

Conclusions
Our results are consistent with the literature that young women with operable BC have a greater risk of LR. There was a significant positive effect on LR with use of adjuvant systemic therapy. Due to small number of events in the young women group, no definite conclusions can be made about the optimal type of surgery for them.

PREDICT Plus: a population-based validation of a prognostic model for early breast cancer that includes HER2

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Background and Purpose
Predict (www.predict.nhs.uk) is an online, breast cancer prognostication and treatment benefit tool developed using UK cancer registration data. The aim was to estimate the prognostic effect of HER2 status, include it in a new version of the model (Predict+), and to compare the 10-year survival estimates from Predict+ with the original Predict model, Adjuvant! and the observed 10-year outcome from a British Columbia dataset used previously to validate Predict and Adjuvant!.

Methods
Estimates for the prognostic effect of HER2 status were based on 14,017 breast cancer patients from 15 studies in the Breast Cancer Association Consortium. Relative hazard estimates for HER2 positivity were obtained separately for ER positive and ER negative disease and incorporated into Predict. The validation study comprised 1653 patients identified from the Breast Cancer Outcomes Unit (BCOU) database in British Columbia. 10-year predicted OS and BCSS were calculated for each patient using Predict+, Predict and Adjuvant! by investigators blinded to actual patient outcome. Predicted outcomes from all three models were compared with observed outcomes from the dataset.

Results
The total number of deaths predicted by Adjuvant! (n=492) was within 6.1% of that observed (n=524) compared to 8.8% for Predict (n=478) and 8.4% for Predict+ (n=8.4). The total number of breast cancer specific deaths predicted by Adjuvant! (n=311) was within 14% of that observed (n=360) compared to 3.6% for Predict (n=347) and 2.5% for Predict+ (n=351). In patients with HER2 positive tumours (n=203), the total number of breast cancer specific deaths predicted by Predict+ was within 4.0% of observed compared to 20% for Predict and 29% for Adjuvant!.

Conclusion
This study reports the first clinical breast cancer prognostication tool (Predict) that includes HER2 status and demonstrated a marked improvement in 10-year BCSS estimates using Predict+ compared to the original Predict model and Adjuvant! for patients with HER2 positive tumours.

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SESSION 7: CHANGING CONCEPTS IN BREAST CANCER

Are triple negative cancers a distinct entity?

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Breast cancer is the commonest malignancy in women. It is a heterogeneous disease with multiple sub-types, variable size, grade, metastatic potential and with varying prognosis. The examination of the standard H&E section is still an efficient, cost-effective and powerful mode of providing information to inform classification and hence clinical management. None-the-less, the developments in our understanding of the molecular and cellular basis of cancer initiation and progression is providing tools for refining breast cancer taxonomy and is opening up new avenues for the treatment of breast cancer.

Recently, microarray technology, looking at the genomic profiles and expression of thousands of genes simultaneously has been used to sub-classify breast cancer into biological subclasses and a new taxonomy has been introduced including ER+ luminal tumours and ER- HER2 and Basal-like cancers. These so called basal-like cancers overlap with triple negative breast cancers (TNC).

TNC account for 10-15% of breast cancers depending on criteria used to assess positivity on ER and PR. There is overlap with characteristics associated with basal cancers in that they tend to occur in younger women, are mostly high histological grade, are more common in African-American women and are more aggressive than other molecular subtypes in their clinical behaviour and outcomes.

Although there is a clear and large overlap between TNC and basal-like cancers, there is no doubt that TNC encompass a heterogeneous group of tumours including basal and non-basal high grade as well as some grade 1 cancers despite an association with high histological grade. A range of morphological variants have also been demonstrated to be TNC including the ductal carcinomas which are basal-like, metaplastic carcinomas and the more indolent salivary gland-like cancers such as adenoid cystic carcinomas. Tumours arising in patients with BRCA1 germline mutations are also mostly TNC and a proportion is basal-like.

Hence TNC are by no means a distinct entity and comprise a heterogeneous group with varying histology and clinical behaviour.

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Optimising chemotherapy for triple negative cancers

Ian Smith

Triple negative breast cancer is a recently established entity defined on the basis of tumours which are ER negative, PgR negative and HER2 negative. There is considerable but not complete overlap with molecularly defined basal-like cancers, and indeed TN breast cancer represents in itself a heterogenous group of cancers with an overall worse prognosis than other types and with a higher risk of early relapse.

Standard adjuvant anthracycline chemotherapy is less effective for TN than for other breast cancers (Tan, Marchio et al. 2008). There is good evidence that the addition of a taxanes to anthracycline improves the outcome for TN breast cancer (Hayes, Thor et al. 2007).

Overall neoadjuvant chemotherapy achieves a higher clinical response rate in TN than in non-TN breast cancer and yet overall survival is worse. This apparent paradox is explained by the fact that patients with TN breast cancer who achieve pCR do just as well as pCRs for other types but the majority who do not do significantly worse than for other types. (Liedtke, Mazouni et al. 2008)

TN breast cancer has phenotypic features resembling BRCA1-mutated cancers. Experimental data suggest that the latter may be particularly sensitive to cisplatin and carboplatin since their deficiency in homologous recombination may prevent repair of DNA breaks caused by these agents. Clinical studies have therefore been started with these drugs in triple negative disease with evidence of promising activity as neoadjuvant single agent therapy (Silver, Richardson et al.). Likewise a very high pCR rate of 83% with neoadjuvant Cisplatin has been reported in BRCA1- positive breast cancers (Byrski, Gronwald et al.). The UK TNT trial is currently comparing docetaxel with carboplatin as first-line chemotherapy for metastatic relapse with a cross-over design. Phase II studies have suggested that other newer agents may have increased efficacy as neoadjuvant therapy for TN breast cancer including ixabepilone alone or in combination with cisplatin.

Sub-set analysis of trials involving bevacizumab with chemotherapy have likewise shown specific benefit for patients with TN breast cancer.

So far however no convincing data have emerged to suggest that the selection of chemotherapy for TN breast cancer should be different to that for other sub-types, outside the context of clinical trials.

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The importance of breast cancer stem cells

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Our group has identified normal breast epithelial populations that are highly enriched for basal/breast stem cells, daughter luminal progenitor cells and mature luminal cells. Although breast stem cells were found not to express female steroid hormone receptors, they were exquisitely sensitive to hormone signalling. Stem cells become inactive following endocrine ablation or anti-estrogen therapy. Conversely, exogenous hormones or pregnancy result in stem cell expansion, suggesting a cellular basis for increased breast cancer risk with HRT or in the early years following pregnancy, respectively. It is likely that hormone receptor-positive luminal cells produce factors (that include RANKL) in response to hormones, which in turn activate breast stem cells. We speculate that chemoprevention can be achieved by switching off breast stem function.

The luminal progenitor (rather than basal/stem cell) subset shares many similarities with basal-like breast cancer. Moreover, in BRCA1 mutation carriers, who are prone to develop basal-like breast cancer, luminal progenitor cell exhibit aberrant growth and differentiation properties. Our findings suggest that luminal progenitors are the likely 'cell-of-origin' for basal-like breast cancer. Targeting this population may therefore represent a strategy for the prevention of BRCA1-associated (and possibly sporadic) basal-like breast cancer.

The cancer stem cell (CSC) hypothesis proposes that established tumours are organised in a hierarchical fashion, analogous to normal tissue, and contain a subpopulation of cells with tumour propagating ability. CSCs need to acquire key stem cell properties (such as self-renewal capability). Breast CSCs have now been identified by several groups using xenograft models. Our laboratory has studied mouse models of mammary tumorigenesis and found that a subset (but not all) appear to conform to the CSC hypothesis. By understanding normal breast stem cell biology and identifying markers in CSCs, it should prove possible to identify novel therapeutic targets for breast cancer therapy.

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DNA methylation sequencing identifies novel epigenetic markers in breast cancer

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Despite the completion of the Human Genome Project[1] we are still far from understanding the molecular events underlying epigenetic change in cancer. Even though it is now accepted that tumour suppressor genes, with CpG island-associated promoters, are commonly hypermethylated and silenced in cancer, we do not understand what triggers this process or where it occurs during carcinogenesis[2]. Since most archival cancer samples are from formalin-fixed paraffin embedded tissue (FFPET), the DNA extracted is often limiting and degraded presenting challenges for genome-wide DNA methlyation studies. We have optimized MBDCap-Seq, a method whereby methylated DNA isolated by the MBD2 capture technique (MethylMiner™) is sequenced using next generation Illumina sequencing. We used MBDCap-Seq3-4 to identify novel DNA methylation changes in triple negative breast cancers and matched lymph node metastasis as part of a collaborative NBCF program grant. We have built a comprehensive breast cancer methylation map using computational approaches. This technique permits interrogation of CpG rich sequences and as such allows differential methylation detection of novel promoters and enhancer sequences that may not be covered by conventional techniques. We are now in the process of validating these changes in a larger cohort of breast cancer samples to determine diagnostic and prognostic significance.

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SESSION 8: LOOKING TO THE FUTURE: OPTIMISING TREATMENT OUTCOMES

Sponsored by Roche Products

Optimal management of HER2 positive cancers

Ian Smith

Around 20% of early breast cancers amplify/overexpress the trans-membrane growth factor receptor HER2 and the development of the monoclonal antibody trastuzumab (Herceptin) targeted against the external domain of HER2 represents the biggest advance in breast cancer therapy in the last decade.

Four major trials (NSABP-B31,NCCTG- N9831,HERA and BCIRG006, involving over 11,000 patients) have all shown that the addition of 1 year's trastuzumab to chemotherapy either sequentially (HERA) or concurrently (all the other trials) very significantly improved disease free survival and overall survival. These trials have all involved anthracycline-containing chemotherapy but the BCIRG006 trial has also shown that a non-anthracycline containing schedule (taxotere, carboplatin and trastuzumab) has similar efficacy. Only one much smaller French trial (PACS004) involving 540 patients has failed to show benefit.

Key questions still remain. The first concerns duration of therapy. All the major trials empirically selected 1 year's treatment with Herceptin. A very small Finnish trial however (FinHER) with a mere 232 patients has shown that a similar degree of DFS and OS benefit can be achieved with a mere 9 weeks of trastuzumab given upfront with docetaxel or vinorelbine and with anthracyclines given subsequently. A series of currently running trials are now assessing in more detail short duration treatment. In contrast the HERA trial is comparing 2 year with 1 years treatment with Trastuzumab. So far no results from this randomised comparison are available.

The second question concerns sequential or concurrent use of trastuzumab with chemotherapy. The HERA trial suggests that sequential trastuzumab after completion of chemotherapy is effective but a small French trial (PCS004) involving 440 patients suggests no significant benefit in DFS or OS with sequential trastuzumab. The only trial to compare concurrent with sequential trastuzumab directly, NCCTG-N9831, suggests a small but significant benefit in favour of concurrent usage, in combination with paclitaxel, and it is now generally accepted that the concurrent approach is preferable. The development of adjuvant trastuzumab has been a major step forward in the treatment of breast cancer with an estimate that this approach may prevent nearly 28,000 women from developing recurrent disease over a ten year period in the 5 major EU countries alone (France, Germany, Italy, Spain and the UK).

Recent evidence suggests that other anti-HER2 therapies in addition to trastuzumab may improve outcome further. lapatinib is an oral tyrosine kinase inhibitor, acting on the internal domain of both HER1 and HER2 receptors and has clinically useful activity in the treatment of metastatic breast cancer. In the neo-ALTTO trial, lapatinib has been compared with trastuzumab alone and in combination, all in association with paclitaxel. The combination has shown a significantly superior pathCR rate (20% v 28% v 47% respectively) (Baselga 2010, S3-3). It will be interesting to see whether the benefits from this combined anti-HER2 therapy approach will be translated into long-term outcome in the parallel ALTTO adjuvant trial. Pertuzumab is a monoclonal antibody acting on the external domains of the HER2 and HER3 receptors and inhibiting heterodimerisation.

Pertuzumab, like lapatinib, has been shown to have clinical activity in trastuzumab- resistant to metastatic disease. In a neoadjuvant trial pertuzumab has been compared with trastuzumab alone and the combination together, all in association with docetaxel. This trial also included a fourth neoadjuvant arm of pertuzumab and trastuzumab alone (NeoSphere). As in the neoALTTO trial. NeoSphere has shown a significantly improved pathological complete remission rate for the combination with chemotherapy compared with the two monoclonal antibodies given alone with chemotherapy (24% v 29% v 46% respectively), again suggesting potential benefit of combined anti-HER2 therapy. This combination is currently being assessed in metastatic disease in the Cleopatra trial and adjuvant therapy trials are about to start.

An intriguing additional finding the NeoSphere trial was that 17% of patients treated with trastuzumab and pertuzumab alone without chemotherapy achieved a pathCR and this shows that 29% of patients whose tumours were also ER negative (Gianni L 2010, S3-2). This raises the exciting possibility that some patients with HER2 positive breast cancer may be curable with combined anti-HER2 therapy without the use of chemotherapy. The challenge now is to define in advance which patients these might be and to investigate further the role of upfront endocrine therapy in combination with anti-HER2 treatment for patients with ER positive, HER2 positive cancers.

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The future role of the breast surgeon

Krishna Clough

Predictive assays – will these become routine?

Rick De Boer

The question is not 'if they will' but 'when they will'!

The heterogeneity of breast cancer is well documented. Understanding this heterogeneity and using it to inform treatment decisions holds the promise of allowing physicians to deliver better outcomes to breast cancer patients. We continue to develop and modify classification systems to try and account for this increasing complexity and to try and better predict tumour behaviour. Nevertheless, whatever system is used, determining the correct treatment pathway for the individual patient remains a challenge, and it is clear that many patients receive unnecessary overtreatment. This is particularly so in patients with ER positive disease where the risk of recurrence and potential benefits of chemotherapy have to be balanced with the potential of adverse events, and the understanding that many patients derive no additional survival benefits from the chemotherapy.

Breast cancer remains the only major cancer where certain treatment is routinely determined by specific predictive factors, and molecular diagnostics are already a key part of clinical practice. Predictive biomarkers such as oestrogen (ER) and progesterone (PR) receptors and c-erbB-2 oncoprotein have become a staple in breast cancer reports. These tests are based on immunohistochemistry (IHC) and fluorescent in situ hybridization techniques (FISH) which have previously dominated the breast cancer diagnostic testing landscape.

More recently, a number of diagnostic tests based on the gene expression in breast cancer tissue have entered the market for breast cancer diagnostics. These tests are generally centralised laboratory assays that utilise algorithms and statistical data analysis to inform results. Gene signatures have been developed in different contexts of the disease to try and predict outcome or treatment response better than the standard clinico-pathological parameters currently used.

Perhaps the most important practical contribution of genomics to breast cancer management has been the development of multi-gene assays (e.g. Oncotype Dx, MammaPrint, Genomic Grade Index) that can distinguish low and high risk prognostic groups among ER-positive, early stage breast cancers[1,2].

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The first prognostic signature was developed by comparing the expression patterns of tumours from patients who developed distant metastases to those who did not. The 70-gene signature (MammaPrint, Agendia, The Netherlands)[3] was validated in node negative and node positive women, is available as a diagnostic test and is now being tested prospectively in a clinical trial (MINDACT: Micro-array In Node-negative Disease may Avoid ChemoTherapy) against standard pathological parameters for predicting outcome.

Reliably predicting a patient's response to tamoxifen and whether chemotherapy is also required is a significant clinical need and was the basis of the development of the Oncotype DX assay (Genomic Health, USA)[4,5]. This is a quantitative RT-PCR diagnostic test to measure the mRNA levels of 16 cancer genes (plus 5 reference genes) related to ER, HER2, proliferation and tumour invasion. Importantly at a practical level, the test is applicable to formalin-fixed paraffin embedded tumour material. A resulting 'recurrence score' (RS) quantifies the likelihood of the development of a distant recurrence in node negative, ER positive breast cancer patients treated with tamoxifen. This test is also in clinical trials eg TAILORX. The American Society of Clinical Oncology and the National Comprehensive Cancer Network have included the Oncotype DX assay in their guidelines as an option to predict whether certain patients will benefit from chemotherapy[6,7]. Further work has been done examining the Oncotype DX assay in hormone positive, node positive patients, and newer data have been generated suggesting that Oncotype DX may potentially guide locally advanced breast cancer neo-adjuvant treatment strategies in ER+ patients. Clinical impact studies in the USA have shown that the use of Oncotype DX recurrence scores to guide treatment decisions results in an approximate 30% shift away from chemotherapy[8]. More recently, impact studies have been performed in Europe, and a Melbourne-based Australian study looking at the impact of the Oncotype test in the multi-disciplinary setting has successfully recruited its goal of 150 patients and results will be presented at the upcoming San Antonio Breast Cancer Symposium.

Although genomics are a promising technology, certain limitations exist and predictive diagnostic tests for breast cancer have not yet been fully accepted for choosing treatment. These assays are, in general, applicable to only a subset of cancer patients and are not yet standardised. They demonstrate significant variability and, since tissue is homogenized, all sense of tissue topography and heterogeneity is lost. The development and validation of any predictive biomarker or assay must satisfy multiple criteria to be considered fit for their intended purpose of guiding patient treatment decisions. Specifically, they must be standardised to assure reproducibility, substantiated with clinical results across prospectively-designed studies of sufficient size, and proven to show independent value beyond traditional measures.

Nevertheless, as these tests become more widely utilized, they will form the basis of individualized treatment for breast cancer patients. With these improved risk assessment tools thousands of women each year could be spared from the harmful short- and long-term side effects associated with chemotherapy.

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The future of adjuvant endocrine therapy

Ian Smith

Tamoxifen as adjuvant therapy is still one of the most effective drugs in cancer medicine, reducing the absolute risk of death by around 10% and the relative risk by nearly 50% 15 years after diagnosis. Recent trials have shown the aromatase inhibitors (AIs) in postmenopausal women achieve a modest but significant further reduction in the risk of recurrence, and in the case of letrozole, improved survival (Regan, et al.2011). It is important to note however that tamoxifen will continue for many years to remain an effective and important endocrine therapy for post menopausal women who cannot tolerate AIs or who have low-risk disease.

An important question for the next 5 years is whether all the AIs have similar clinical efficacy. So far the MA27 trial has shown no difference in efficacy between adjuvant exemestane and anastrozole (Goss et al 2010). The FACE trial is comparing letrozole with anastrozole in 4,000 node positive patients but results are not yet available.

A key question for the next 5 years concerns duration of adjuvant endocrine therapy. The MA17 trial has shown convincingly that extended adjuvant therapy with letrozole for patients still in remission 5 years after tamoxifen very significantly reduces the risk of further recurrence (Goss et al. 2005) and these results have been confirmed in two other trials, for exemestane (NSABP-B33) and for anastrozole (ABCSG-6A). The MA17 trial has shown that the gain with letrozole increases with duration of use, and a further randomization is now being carried out at the 10 year mark. Recently the MA17 trial has shown an even greater benefit for younger women, premenopausal at diagnosis but postmenopausal after 5 years (Goss 2010). Intriguingly, this sub-group analysis also showed a benefit for women started on letrozole some time after stopping tamoxifen (up to 6 years), reflecting the long natural history of breast cancer. Important questions of duration of endocrine therapy remain to be answered, including whether there is a similar gain for extended adjuvant therapy beyond 5 years in patients starting on an aromatase inhibitor, and which patients are most likely to benefit.

CYP 2D6 is a P450 gene coding for the metabolism of tamoxifen to the more active metabolite, endoxifen. Retrospective pharmacogenomic studies initially suggested that the 5-10% of patients who were homozygous for variant inactive CYP 2D6 alleles may have achieved less benefit with tamoxifen. Recently however two large retrospective studies on the BIG1-98 (letrozole v tamoxifen) trial and the ATAC (anastrozole v tamoxifen) trial have both shown no difference in outcome for women with wild type versus variant alleles (Jones SE 2010; Rae JM 2010). For the next few years it is therefore unlikely that pharmacogenomics are going to play an important part in endocrine therapy. Increased body mass index (BMI) is associated with poorer breast cancer prognosis. An exploratory analysis in the ATAC trial has confirmed an increased risk of recurrence with increasing BMI, but has also shown that the gain of anastrozole over tamoxifen is lost in women with higher BMI (>25) (Sestak, et al.2010).

A possible hypothesis for this observation is that anastrozole is not sufficiently potent to inhibit the additional aromatase associated with high amounts of adipose tissue. Further similar analyses from patients treated with each of the aromatase inhibitors are so far showing conflicting results. It is possible however that in the next 5 years BMI is going to become an important criterion for determining selection of adjuvant endocrine therapy. Tamoxifen remains the mainstay of adjuvant endocrine therapy for premenopausal women. In the next 5 years the SOFT trial should hopefully answer two important further questions: (i) does the addition of ovarian suppression to tamoxifen improve outcome; (ii) is ovarian suppression and an aromatase inhibitor superior to ovarian suppression with tamoxifen? A recent sub-set analysis of the ZIPP trial has shown no additional gain for Goserelin added to tamoxifen compared with tamoxifen alone (Sverrisdottir A 2010). Likewise in the ABCSG-12 trial there is so far no significant difference between adjuvant anastrozole and tamoxifen, both given with Goserelin, in premenopausal women (Gnant).

Fulvestrant (Faslodex) is an oestrogen receptor antagonist which down regulates cellular levels of ER. For a time it appeared no more effective than standard endocrine therapies, but a recent trial (CONFIRM) has shown a dose response effect with 500mg im monthly achieving significantly longer progression-free survival than the standard 250mg dose (Di Leo, Jerusalem et al.). Likewise Fulvestrant 500mg has been shown to be significantly superior to anastrozole in first-line treatment of metastatic breast cancer in terms of time to progression (Robertson, Llombart-Cussac et al. 2009).

The greatest problem continuing to face endocrine therapy is resistance to treatment. Recent trials have suggested improved efficacy for patients with ER positive, HER2 positive cancer with the addition of trastuzumab to anastrozole or lapatinib (Kaufman, et al. 2009) or lapatinib to letrozole (Johnston, et al. 2009). Similar results are beginning to emerge for other targeted therapies including for example the mTOR inhibitor everolimus given in conjunction with tamoxifen (Bachelot T 2010).

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Finally, the use of short duration pre-operative endocrine therapy to predict long-term outcome based on molecular markers after treatment eg, Ki67, is likely to have a major role in selecting both adjuvant endocrine therapy and chemotherapy, and this approach is currently being investigated in the POETIC trial.

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POSTERS

Accuracy of vacuum-assisted breast biopsy

Dr Shalini Amukotuwa, Dr Jane Fox, Dr Ann Lynch, Dr Jill Evans

Monash Breastscreen

Lesions identified on screening mammography, which are suspicious for malignancy or of an indeterminate nature, require sampling for histological evaluation. Where ultrasound fails to detect the lesion, this sampling is performed under stereotactic guidance. At our population breast screening service, which screens over 40 000 women per year, we previously performed all of these stereotactic biopsies with an automated 14 G needle. However, due to the potential for underestimating the severity of disease, it is now current best practice to sample these lesions using a vacuum-assisted breast biopsy device, thereby increasing the area sampled. In line with this best practice, we have gradually introduced vacuum assisted breast biopsy (VABB) into our service, using the 9 G Suros device, since February 2009. In this 26 month period, 119 procedures have been performed, mainly for biopsy of microcalcifications. Due to the high cost involved, VABB has been reserved for lesions deemed to be difficult to target with a standard 14 G needle and those which are diffuse, in which sampling error is likely to be an issue. In this retrospective study, we compared the histology of the VABB specimen with the histology of the surgical resection specimen for the 56 lesions found to be malignant on biopsy. The histological upgrade and downgrade rates were calculated. 5/56 (9%) of lesions were upgraded from in situ carcinoma on biopsy to invasive tumour on surgical resection, comparable with the rates quoted in the literature, and in all cases the invasive component was less than 5 mm. There were 2 downgrades where benign lesions were found at surgical resection, despite malignant histology on VABB. Our results support the use of VABB to optimize sampling for accurate pre-operative diagnosis of breast lesions.

Proliferating trichilemmal cyst of the breast with atypical cytological features

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Background and Purpose

Proliferating trichilemmal cysts are relatively common occurring within the scalp of elderly women. Proliferating trichilemmal cysts of the breast, however, are rare. These cysts are benign with low chance of malignant transformation. Few cases have been published describing the cytological features of these cysts. Cytology reveals varying degrees of atypia with small, basaloid or squamoid cells abruptly associated with keratin globules. The features can mimic squamous cell carcinoma.

Methods and Results

Fine needle aspiration of the breast lump was performed with preparation of smears. These showed sheets of atypical epithelial cells with foamy histiocytes, multinucleate cells and fibrotic material with evidence of fat necrosis. A cell block was acellular. A specific diagnosis was not made with recommendation for excision based on the atypia in the epithelial cells present.

A subsequent excisional biopsy showed a well circumscribed multi-cystic lesion within the subcutaneous tissue lined by stratified squamous epithelium with absence of a granular layer. The cyst contained dense keratin, cholesterol clefts and multinucleate giant cells with features in keeping with a proliferating trichilemmal cyst.

Conclusions

The cytological features in this case are in keeping with previous cases reported in scalp lesions. While benign, a small number of these cysts undergo malignant transformation. While rare, proliferating trichilemmal cysts of the breast do occur and complete surgical excision is required. Cytological features are thus important to recognise. No previous cytological diagnoses of this rare breast lesion have been reported.

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Long-term outcomes of sentinel lymph node biopsy in large and small breast tumors

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Background

Guidelines exist for the use of Sentinel Lymph Node Biopsy (SLNB) for small, unifocal, and clinically negative axilla. The accuracy of SLNB in higher-risk tumors, larger than 30mm and multifocal tumor, is unknown, and is part of the considerations of the SNAC2 Trial.

The aim of this study was to predict some of the outcomes of the SNAC 2 trial by looking at a selected cohort with 5 years follow up

Methods

A retrospective review of a prospectively collected data on the NBCA was performed. Consecutive patients, of a single surgeon at a tertiary referral Breast unit with a minimum of 5-years post-operative follow-up, who underwent SLNB was assessed. Blue dye alone was used for SLN mapping.

"SNAC2 Criteria" tumors were tumors >30mm, or multifocal tumor, N0 Clinically. These tumors where compared to "SNAC 1 Criteria" tumours, defined as <30mm, unifocal, N0 clinically.

Results

102 Patients where included. Average tumor size was 29.3mm (2 – 138mm). There were 41 "SNAC2 Criteria" tumors and 61"SNAC 1 Criteria" tumors. Mean number of SLN taken = 2.21,(2-8) with the Mean number of axillary (non-sentinel) nodes removed = 6.14 (1-21).

Successful SLN mapping occurred in 93.4% (57/61) of "SNAC 1 Criteria" and 63.4% (26/41) of "SNAC2 Criteria". Tumors were significantly larger when mapping was unsuccessful (50.2mm v 24.5mm, p= 0.002).

For SLNB, the overall negative predictive value (NPV) = 80.6%. The NPV for small and large tumors was 97.4% and 58.6% respectively.

"SNAC2 Criteria" 5-year DFS and OS was 80.5 %and 90.2% respectively. For "SNAC1 Criteria" DFS and OS was 96.7% and 100%.

Conclusion

"SNAC2 Criteria" patients are more likely to have unsuccessful mapping and a lower NPV. Non-mapping of SLN is more likely to occur in larger size tumors and thus the accuracy of SLNB in these tumors cannot be guaranteed.

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A decade of experience of intraoperative analysis of the sentinel node in breast cancer

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Background

Sentinel node biopsy is a standard way of staging the axilla in breast cancer but conventional treatment requires a delayed axillary dissection when metastatic disease is found. Intra-operative analysis of the sentinel node during breast cancer surgery obviates the need for a second operation in patients who need an axillary dissection. Frozen Section is a sensitive way of analyzing the sentinel node. Intraoperative node analysis by frozen section has been routine practice in our region for over 10 years. This study aims to identify the sensitivity and negative predictive value of this practice.

Methods

A review of patients entered into The Auckland Breast Cancer Register. Patients who underwent a sentinel node biopsy as part of their breast cancer surgery were identified. Intra-operative analysis was carried out by frozen section and all nodes also underwent conventional assessment with H&E staining. Results were compared and false positive and false negative rates were calculated.

Results

Data were available on 3218 Sentinel Node procedures carried out between 2000 and 2009. 960 patients went on to have an axillary dissection, 804 immediately as a result of intra-operative node analysis. In 19 cases there was a discrepancy between the intra-operative analysis and the H&E staining. These were all false negatives and there were no false positives. This gives a sensitivity of 98% and a negative predictive value of 99% for intra-operative analysis.

	Positive H&E	Negative H&E	
Positive intra-operative analysis	804	0	804
Negative intra-operative analysis	19	2259	2278
	823	2259	3082

Conclusions

Intra-operative node analysis is sensitive and specific and can save the need for a second operation for a large number of patients.

Management of isolated tumour cells, micrometastases and the solitary positive sentinel lymph node in breast cancer

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Background

Sentinel Lymph Node Biopsy (SLNB) is now the standard way of staging the axilla in breast cancer. Conventionally, an axillary node dissection (AND) is performed when there is a positive SLNB. However the optimal management of the axilla when isolated tumour cells (ITCs) or micrometastases (MMs) are found is still not clear. There are also a number of cases where only the sentinel node is positive and an unnecessary AND is performed.

Methods

Records from the Auckland Breast Cancer Register were retrieved for patients who had an operation between 2000 and 2009. Those in whom there were ITCs, MMs or a single positive node were studied. Tumour size and grade were analysed size to see if there were factors for predicting a solitary positive SLNB.

Results

Data was retrieved on 3218 SLNBs. 51 patients had ITCs in a SLNB. Of these 7 went on to have AND but no other positive nodes were found. 17 patients had a limited axillary node sample without finding any further tumour.

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63 patients had MMs in a Sentinel node. Of these 43 had AND with no further positive nodes being found.

264 patients had a solitary sentinel lymph node. There was no statistical difference between these patients and those with multiple positive nodes with regard to tumour stage and grade.

Conclusions

If MMs or ITCs are seen in the sentinel node, further axillary surgery is not required. However, if there is a solitary positive sentinel lymph node then it is not possible to determine the status of the rest of the nodes on basis of tumour size and grade.

Sentinel node biopsy with blue dye alone – a cohort with 5year follow up

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Background and purpose

"Blue dye alone" sentinel node biopsy is said to have a higher false negative rate than combined with nuclear medicine, including missing both some axillary and all extra axillary sentinel nodes. The clinical implications of non mapping, or missing extra axillary metastasis are not well studied.

Aim

To analyse whether negative sentinel node mapping with blue dye lead to worse patient outcomes.

Methods

The study included data on 170 consecutive patients with early breast cancer operated on by one surgeon between 2004-2006. All underwent blue dye injection.

Outcome measures: Choice of adjuvant systemic therapy, locoregional and distant recurrence, and mortality. Comparison was between patients who had an identifiable axillary blue node, and those who had no axillary sentinel node identified.

The median follow up for the group was 62 months.

Results

53 patients had no axillary sentinel node mapping, all proceeded to level 1 or 2 axillary dissection. The rates of systemic therapy, local and distant recurrences and mortality were not significantly different between the 2 groups. There were 7 recurrences in the group with no axillary mapping compared to 12 recurrences in the group with axillary sentinel node identified.

Conclusion

Blue dye alone as a sentinel node mapping technique seemed to lead to similar treatment decisions and recurrence as using both blue dye and scintigraphy.

References:

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Intraoperative assessment of sentinel nodes in breast cancer by One-step Nucleic Acid Amplification (OSNA) versus imprint cytology.

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Background and purpose

Sentinel node based management of the axilla has become standard of care in early breast cancer. Low-volume nodal metastatic disease is associated with poorer prognosis and increased benefit from systemic therapy. Nevertheless, the value of completion axillary clearance in micrometastatic nodal disease has recently been questioned.

Intraoperative sentinel node assessment reduces costs by avoiding second surgery and has beneficial psychological effects. However, frozen section and imprint cytology have high interobserver variability and false negative rates approaching 52%.

OSNA is a quantitative assay using reverse transcription loop mediated isothermal amplification to detect mRNA levels of the breast cancer marker CK19. It is reported to have >95% specificity and sensitivity in detecting nodal metastasis compared to formalin fixed paraffin embedded sections.

This ongoing study evaluates OSNA versus imprint cytology for detecting micro and macro lymph node metastasis to determine its intraoperative suitability.

Methods

Consenting patients with breast cancer undergoing sentinel node biopsy at Westmead Hospital are included in this ongoing prospective study. Of a targeted 200 nodes, 87% have been collected. Each node is examined in 2 mm thick slices, with imprint cytology performed on each cut surface and every second slice submitted for OSNA. Results are compared with permanent histology on each second slice, sectioned at 200 um intervals stained with H&E or AE1/3 antibody.

Results

Preliminary results show a trend towards higher sensitivity for OSNA than for imprint cytology when compared to final histopathology. Nodes weakly positive by OSNA were largely negative by imprint cytology. Formal histology disclosed malignant cells in some but not all of these.

Conclusions

OSNA is a simple technique with high accuracy and an acceptable turnaround time. Sensitivity appears greater than for imprint cytology and possibly histology. It has great potential for use in hospitals where on-site pathology is unavailable.

Notes

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