Australasian Society for Breast Disease

NINTH SCIENTIFIC MEETING

12-14 SEPTEMBER 2013

CAIRNS CONVENTION CENTRE
AUSTRALIA

HANDBOOK & ABSTRACTS

Heading sculpture by Dr. Alex Sandor Kolozsy. C.D.V.A. Sculptor from Sculpture By the Sea '06

Australasian Society for Breast Disease

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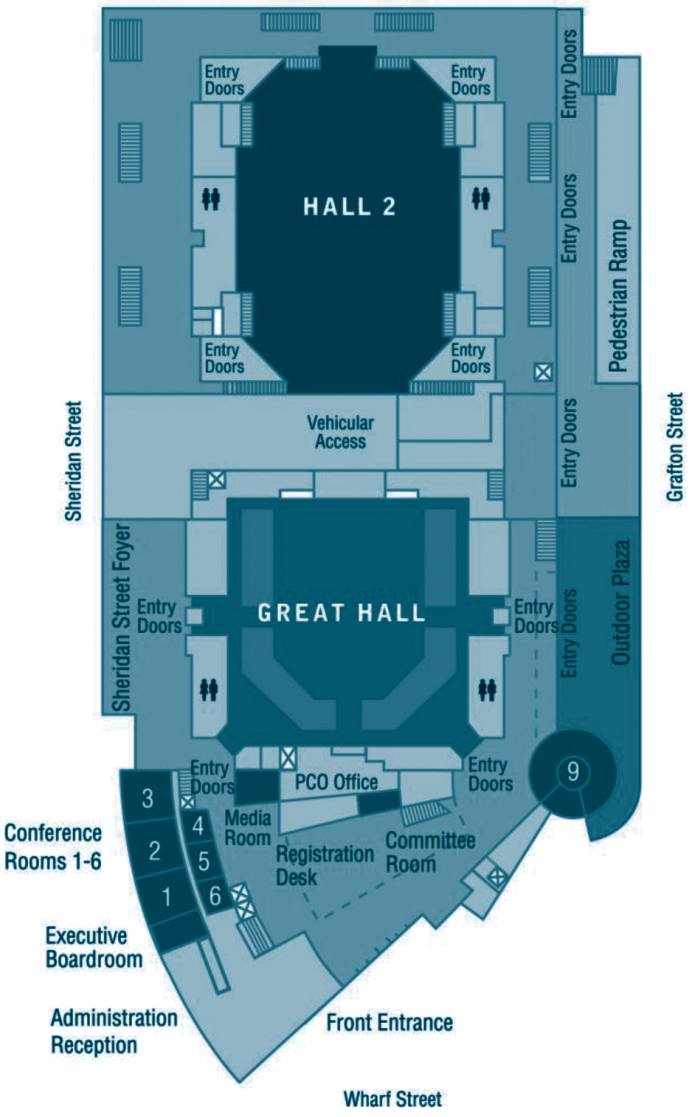
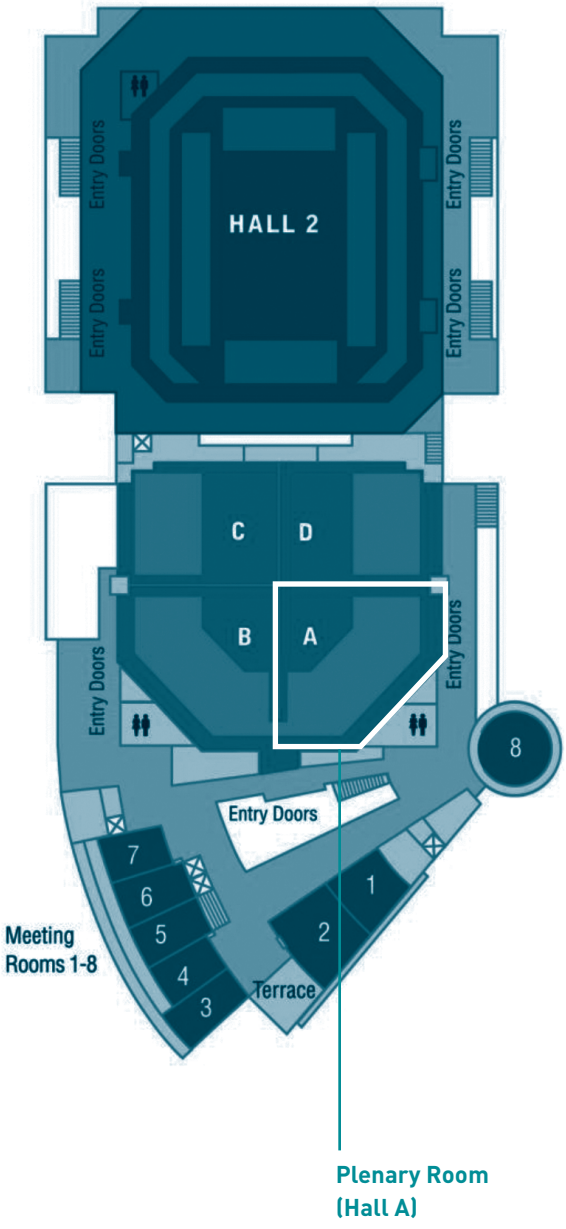
Handbook

Cairns Convention Centre Floorplan

EXHIBITION LEVEL



MEZZANINE LEVEL



Welcome

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

This multidisciplinary Meeting is designed for health care professionals to advance their knowledge of pathology classifications and epidemiology of breast cancer and the latest techniques in investigation and management of breast cancer. The program will include sessions on management of the axilla, lifestyle factors in breast cancer, emerging imaging modalities, pathology of borderline lesions and the latest WHO Classification, high risk disease, neoadjuvant therapy and new chemotherapeutic agents, as well as workshops on tomography and oncoplastic surgery. We are fortunate to have such a distinguished international and local faculty.

I wish to thank our sponsors Roche Products, Hologic, AstraZeneca, Novartis Oncology, Allergan and Genomic Health as well as all the exhibitors for their support. It would not be possible to hold this Scientific Meeting without this support. 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 the scientific program of this Meeting as well as the social interaction with your colleagues.

Yours sincerely

DANIEL DE VIANA
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
P.O Box 1124 Coorparoo DC, Qld 4151
T: +61 (0) 7 3847 1946 **F**: +61 (0) 7 3847 7563
E: info@asbd.org.au **W**: www.asbd.org.au

EXECUTIVE COMMITTEE

DR DANIEL DE VIANA, Surgeon, President
DR KERRY MCMAHON, Radiologist, Secretary/Treasurer
DR MEAGAN BRENNAN, Breast Physician (co-opted)
DR ROSLYN DRUMMOND, Radiation Oncologist
PROF STEPHEN FOX, Pathologist (co-opted)
DR SUSAN FRASER, Breast Physician
DR JAMES FRENCH, Surgeon
A/PROF BRUNO GIUFFRE, Radiologist
MR WAYNE JONES, Surgeon (co-opted)
PROF BOGDA KOCZWARA, Medical Oncologist
PROF SUNIL LAKHANI, Pathologist
A/PROF WENDY RAYMOND, Pathologist
DR CATHERINE SHANNON, Medical Oncologist (co-opted)
DR YVONNE ZISSIADIS, Radiation Oncologist (co-opted)
MS SOLEI GIBBS, Executive Officer

PREVIOUS EXECUTIVE COMMITTEE MEMBERS

DR GEOFFREY BEADLE, Medical Oncologist
A/PROF MICHAEL BILOUS, Pathologist
DR NATACHA BORECKY, Radiologist
A/PROF JOHN BOYAGES, Radiation Oncologist
DR MARIE-FRANCES BURKE, Radiation Oncologist
DR JACQUELINE CHIRGWIN, Medical 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
DR JULIA LEEDS, BCNA Representative (co-opted)
MS VERONICA MACAULAY-CROSS, BCNA Representative (co-opted)
DR LYNNE MANN, Surgeon
MR WILLIAM MCLEAY, Surgeon
MS LYN MOORE, BCNA REPRESENTATIVE (co-opted)
DR MARGARET POOLEY, Surgeon
A/PROF MARY RICKARD, Radiologist
DR BELINDA SCOTT, Surgeon
PROF ROBIN STUART-HARRIS, Medical Oncologist
PROF SHIH-CHANG (MING) WANG, Radiologist

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TRADE EXHIBITION

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Useful Information

VENUES

Cairns Convention Centre
Cnr Wharf and Sheridan Streets,
Cairns Qld 4870
T: +61 7 4042 4200
F: +61 7 4052 1152
W: www.cairnsconvention.com.au

Cairns Hilton
34 Esplanade,
Cairns Qld 4870
T: +61 (0) 7 4052 6752
F: +61 (0) 7 4031 1167
W: www.hilton.com

MEETING OFFICE

The Meeting Office will be open during the following times:

Thursday 12 September 2013	08:30 - 18:00 hours
Friday 13 September 2013	07:30 - 17:30 hours
Saturday 14 September 2013	07:30 - 15:00 hours

T: +61 7 4042 4300, +61 7 4042 4301

SPEAKERS' AUDIOVISUAL TESTING ROOM

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

Thursday 12 September 2013	11:30 - 17:00 hours
Friday 13 September 2013	07:30 - 16:00 hours
Saturday 14 September 2013	07:30 - 13:00 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 Registration counter. Please advise potential callers to contact Cairns Convention Centre (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 Rainforestation Meeting is smart casual and flat shoes are recommended.

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 12 September 2013, 18:45 - 20:00 hours

Meet your fellow delegates for drinks by the waterfront at Cairns Hilton. Hilton is located only a short walk from the Cairns Convention Centre. Included for fulltime delegates and registered partners. Additional tickets cost $60 per person.

NETWORKING DRINKS

Friday 13 September 3013, 17:00 - 18:00 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

Saturday 14 September 2013, 18:15 - 23:00 hours

To conclude the Meeting, an unforgettable evening has been organised at the Rainforestation Nature Park in the tropical rainforest of Kuranda. Dinner will include pre dinner refreshments, dinner and drinks, and entertainment. Included for full time delegates and registered partners. Additional tickets: $130 per person.

Coaches will depart from the Cairns Hilton at 18:15 hours. Return coaches will be staggered.

Annual General Meeting

The Annual General Meeting of the Australasian Society for Breast Disease will be held at 7.30am on Saturday 14 September 2013. As breakfast will be served during the Meeting, please confirm your attendance/non attendance. 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 2013 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 9th Scientific Meeting" to be held on the 13 September 2013.
- **6 points** may be claimed for attendance at the "Australasian Society for Breast Disease 9th Scientific Meeting" to be held on the 14 September 2013.
- **A total of 13.5 points** can now be claimed for attendance on all three days of the Australasian Society for Breast Disease Scientific Meeting.
- **A total of 8.25 points** may be claimed for attendance at the "Tomosynthesis for Radiologists Workshops' to be held on 12 September 2013.
- For anyone who attends only part of this meeting, points may be claimed pro rata at **1 point per hour for lectures or 3 points per hour for workshops.**

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.

LIVING WELL BEYOND BREAST CANCER

Far North Queensland locals are invited to attend Breast Cancer Network Australia's (BCNA) free information forum, held 1000-1500 hrs on Saturday 14 September 2013 at the Cairns Convention Centre. Speakers include Dr Susan Fraser, Dr Carrie Lethborg, Ms Raelene Boyle and Ms Julie Hassard.

Faculty Members

KEYNOTE SPEAKERS

Prof Andrew D Baildam

MD, FRCS, FEBS

Andrew Baildam trained in general surgery and surgical oncology, and obtained an MD for research in molecular biology of breast cancer. He then trained in plastic and reconstructive breast surgery at a time when seamless cancer surgery with reconstruction was highly innovative. As consultant surgeon in South Manchester and to The Christie hospitals, Andrew was joint creator of the training courses at the Royal College of Surgeons of England, developed the UK's oncoplastic breast surgical training fellowships and chaired the national cross-specialty Breast Training Interface Group. His experience of oncoplastic and reconstructive breast surgery is extensive. He has particular skill in risk-reducing mastectomy and breast reconstruction for women at high personal breast cancer risk by virtue of family history or BRCA1/2 gene mutations. Professor Baildam is the immediate past President of BASO~The Association for Cancer Surgery, and is now Professor of Breast and Oncoplastic Surgery to the Barts and The London hospitals, University of London.

Prof Kathy Pritchard

MD, FRCP(C)

Kathy Pritchard is one of Sunnybrook & Women's best-known academic physicians. She graduated from Medicine at Queen's University in Kingston, Ontario and trained in internal medicine and medical oncology at the University of Toronto. Professor Pritchard is on staff at Sunnybrook Odette Cancer Centre (OCC) where she was Head of Medical Oncology from 1987-1999 and of Clinical Trials from 1987 - 2007. Professor Pritchard was also Chair of the Breast Cancer Site Group of the NCIC Clinical Trials Group from 1984 - 2007. She is currently a Professor of Medicine and the Departmental Division Director of Medical Oncology at the University of Toronto and is cross-appointed in the Department of Oncology, at McMaster University. She has been the Clinical Director of the Ontario Clinical Oncology Group (OCOG) since 1998. Professor Pritchard's interests are in adjuvant and hormonal therapy of breast cancer, clinical trials design, translational research and the career development of oncologists. Her expertise is demonstrated by her 250 publications and many invited lectures across Canada, North America, and internationally. She has been a member of the Board of Directors of the American Society of Clinical Oncology (2007 – 2010) and of the Canadian Breast Cancer Foundation, Ontario Division (2010-2012). Professor Pritchard was awarded the O. Harold Warwick Prize for Cancer Control in Canada in 2005 by the Canadian Cancer Society and the National Cancer Institute of Canada for her work in clinical and translational trials in breast cancer, named the Cosbie Lecturer for 2006 and awarded the ASCO Statesman Award in 2011.

A/Prof Puay Hoon Tan

MBBS, FRCPA, FAMS, FRCPath, MD

Puay Hoon Tan is currently the Head of the Department of Pathology at the Singapore General Hospital (SGH), a position assumed since July 2005. The Pathology Department oversees 10 clinical laboratories with 450 staff, and is busy preparing to physically relocate to a new state of the art pathology facility within the campus grounds in 2013.

Dr Tan has a busy surgical pathology diagnostic practice, and participates actively in research and teaching. She leads the breast pathology research agenda in the Department, and with colleagues in the breast pathology team, organises an annual breast pathology course that has registrants from the region and beyond. She serves in the Executive Councils of the International Society of Breast Pathology and the International Society of Urologic Pathology. She is a Volume Editor for the 4th edition of the World Health Organisation Classification of Tumours of the Breast, and is on the Editorial Boards of several key Pathology journals.

Dr Anne A Tardivon

MD

Anne Tardivon is a radiologist dedicated to breast imaging at Institut Curie in Paris. She is the past President of the French Society of Breast Imaging (SOFMIS) and associated member of the College des Enseignants de Radiologie de France (CERF). At the European level, she is member of the Board of the European Society of Breast Imaging (EUSOBI), was the Chairman (2006) and responsible of a categorical course for breast imaging (2008-2009) at the European Congress of Radiology. Dr Tardivon's major fields of interest include development and validation of new imaging technologies, high-risk group surveillance strategies, expertise in national guidelines, and teaching in multidisciplinary settings. She is the author or co-author of 83 articles and one book. She is the breast imaging editor for *European Radiology* and reviewer for *Radiology, European Journal of Radiology* and *Breast Cancer.*

LOCAL FACULTY

Dr Marie-Frances Burke

MBBS FRANZCR

Marie Burke is the Director of Medical Services at Premion, the largest provider of private Radiation Oncology services in Queensland. She is a past Secretary/Treasurer of Australasian Society for Breast Disease. Currently, she is on the Faculty of Radiation Oncology Council of the Royal Australian and New Zealand College of Radiologists, and is on the board of the Breast Cancer Association of Queensland. Dr. Burke has been involved in guideline development in the National Breast and Ovarian Cancer Centre. Her major interests are in the management of breast and gynecologic cancers.

Prof Chen-Pin Chou

MD

Chen-Pin Chou is Chief of the Breast imaging section of Kaohsiung Veterans General Hospital in Kaohsiung, Taiwan. He is on attending staff in breast, GI and GU radiology. Professor Chou is an instructor in radiology at the National Yang-Ming University School of Medicine, Taipei, Taiwan
Professor Chou has a personal interest in contrast-enhanced breast tomosynthesis, breast MRI and breast biopsy.

Dr Richard De Boer

MBBS, FRACP

Richard De Boer completed oncology training at the Royal Melbourne Hospital and undertook a three 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 mechanisms of endocrine-resistance. 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 and Epworth-Freemasons Hospitals in Melbourne, Australia.

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, current President 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.

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 & ASTRO.

Dr Elisabeth E Elder

MBBS, PhD, FRACS

Elisabeth Elder graduated from the Karolinska Institute in Stockholm, Sweden in 1992, where she also completed her surgical training together with a PhD in tumour biology in 2002. She gained her Australian FRACS in 2008 and is now a staff specialist in breast surgery at the Westmead Breast Cancer Institute and clinical senior lecturer at the University of Sydney. She is a member of the oncoplastic subcommittee of BreastSurgANZ.

Dr Lisa Erzetich

MBBS, FASBP

Lisa Erzetich graduated from the University of Queensland in 1982 completing her residency at the Royal Brisbane Hospital. Following this she commenced in General Practice in 1988. Dr Erzetich joined The Wesley Breast Clinic in 1991 on a part time basis becoming a full time Breast Physician in 1998 and is also a Fellow of the Australasian Society of Breast Physicians. In 2002, Dr Erzetich became Deputy Director of The Wesley Breast Clinic and in May 2003 took over as Director. She is currently on the Board of Directors of the Australasian Society of Breast Physicians.

Prof Stephen Fox

BSc (Hons), MBChB, FRCPath, FFSc, FRCPA, DPhil

Stephen Fox is Director of Pathology at the Peter MacCallum Cancer Centre and Professorial Fellow at the University of Melbourne. He moved in February 2006 from the University of Oxford where he was Clinical Reader in Pathology. Professor Fox took an Honours degree and Medical degree at the University of Bristol, UK before completing Pathology training in Oxford. He holds a DPhil in Medicine at the University of Oxford and Fellowships of both the Royal College of Pathologists Australasia and UK. His current research is focused on predictive markers of response to therapies in several tumour types using protein and DNA-based assays.

Dr Susan Fraser

MBBS, FASBP

Susan Fraser has worked as a Breast Physician for 24 years. She has worked in roles including diagnostic breast assessment, BreastScreen reading and assessment, breast surgical assisting and post cancer follow up care. She is the current President of the Australasian Society of Breast Physicians. Dr Fraser currently works bteween Cairns, her home and Breastcare on the Gold Coast and continues to read and assess for BreastScreen Queensland and 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.

Dr Michael Gattas

MBBS, FRACP

Michael Gattas is a graduate of Sydney University. He is a Physician who works full time as a Clinical Geneticist in Brisbane. He has been a staff specialist at the Queensland Clinical Genetics Service since 1996. Dr Gattas was mainly responsibility for familial cancer patients in this service until he started his private practice in 2004. He is a regular attendee at the multidisciplinary breast cancer meeting held at the Wesley Hospital in Brisbane. He has an active interest in delivering clinical genetics services by videoconference technology. Dr Gattas provides Clinical Genetics advice to Sullivan Nicolaides Pathology, and has previously been a member of the Ethics Committee of the Royal Children's Hospital in Brisbane.

A/Professor Bruno Giuffrè

MBBS, FRANZCR

Associate Professor 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.

Dr Anthony Green

MBBS, FRACS

Tony Green has been a surgeon in Far North Queensland for 30 years. 20 years ago he developed a special interest in Breast surgery and 10 years ago trained and specialised in Oncoplastic breast surgery - especially implant breast reconstruction. He was a founding member of the RACS Breast Executive Committee and is a member of BreastSurgANZ. He was very involved in the promotion and rolling out of the BreastScreen program in rural/regional Australia particularly Queensland. Dr Green was on the NHMRC Committee which produced the Guidelines for the management of Breast Cancer in Australia and has been on many committees/projects for the NBOCC. He remains an advisor for Cancer Australia.

Mr Wayne Jones

BHB, MBChB, FRACS

Wayne Jones graduated from the University of Auckland and completed his General Surgery Fellowship in New Zealand. He did a Melanoma Fellowship in Auckland then a Breast Surgery Fellowship in the United Kingdom. He has been a consultant surgeon since 1998. He is involved with a variety of committees and professional associations and contributes to furthering the understanding of cancer treatment through participation in research studies and trials. Mr Jones is the Head of the Breast Unit at Auckland Hospital and a partner at Breast Associates, a specialist clinic providing complete breast care. Until recently he was the Clinical Director of General Surgery at Auckland Hospital.

Prof Bogda Koczwara

FRACP, MBioethics

Bogda Koczwara is a medical oncologist and the Director of Medical Oncology at Flinders Medical Centre in Adelaide. Her clinical interests revolve around management of breast cancer, in particular in young women, survivorship care, psychooncology and supportive care and she has a particular interest in strengthening of the interface between specialist and primary care for cancer patients especially in rural Australia. Professor Koczwara leads the Survivorship Program at the Flinders Centre for Innovation in Cancer and has recently convened the inaugural Flinders Survivorship Conference. She is the Lead in Survivorship for the South Australian Health and Medical Research Institute Comprehensive Cancer Consortium.

Prof 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).

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.

Dr Peter Laniewski

ASPS, ASAPS, FRACS

Peter Laniewski has fellowships in General Surgery and Plastic and Reconstructive Surgery. He studied at the Royal Marsden Hospital in London, consolidating an interest in breast reconstruction and cosmetic breast surgery. He has been working as a plastic surgeon in North Western Sydney focusing on delivering improved access to breast reconstruction. He is a VMO at Westmead Hospital and several Private Hospitals. His private practice are based at Bella Vista and Erina. Apart from breast and skin cancer surgery his interests include non-surgical facial rejuvenation, facial aesthetic surgery and rhinoplasty.

Dr Joseph Ling

MBBS (Hon), FRACP, FCSANZ

Joseph Ling is a cardiologist who has been practising general adult cardiology in Cairns for the last 15 years. He graduated from University of New South Wales and completed his cardiology training in John Hunter Hospital. He performs his own echocardiographic studies.

Dr David Littlejohn

MBBS, FRACS

David Littlejohn is a specialist breast oncoplastic surgeon performing the full range of breast cancer surgery including breast oncoplastic procedure such as miniflap and therapeutic mammaplasty as well as immediate and delayed breast reconstruction. Dr Littlejohn has been practising oncoplastic breast surgery in Wagga Wagga for 13 years and is a member of the Executive Committee of the Breast Section of the Royal Australian College of Surgeons and a founding member of Breast Surgeons NSW and BreastSurgANZ and is the current chairman of the oncoplastic committee.

Prof Bruce Mann

MBBS, PhD, FRACS

Professor Bruce Mann is Director of The Breast Service at the Royal Melbourne and Royal Women's Hospital in Melbourne. He completed Surgical training at The Royal Melbourne Hospital and Fellowship training at Memorial Sloan Kettering Cancer Centre. He has been involved in many clinical trials and much clinical and translational research, with his main research interest being tailoring treatment to the disease and the patient.

Dr Richard Martin

FRACS, MBChB

Richard Martin is the Chair of the Younger Fellows Committee and Deputy Chair of the SEC (Skills Education Committee) of the RACS. He is on the Oncoplastic Committee and Post Fellowship Training Committee of BreastSurgANZ. He performs all level 1 and level 2 oncoplastic procedures including TRAM flaps, LD flaps, Therapeutic mammaplasty, lipofilling and uses acellular dermal matrices as part of his routine practice.

A/Prof Wendy Raymond

MBBS, MD, FRCPA, FIAC

Wendy Raymond holds appointments as a consultant pathologist at Flinders Medical Centre / Flinders University of South Australia, 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 immediate past President of the Australasian Society for Breast Disease.

Dr Catherine Shannon

MBBS (Hons), FRACP

Catherine Shannon is Director of Medical Oncology at the Mater Adult Hospital Brisbane. She is a member of the Executive of the Australasian Society for Breast Disease and the breast cancer advisory committee for Cancer Australia. She has a special interest in breast and gynecological malignancy. She is the director of the oncology trials unit for Mater Health Services and honorary senior investigator for Mater Research. She is the principal investigator on a number of clinical trials in breast and gynecological malignancy and a member of the Australasian collaborative research groups for Breast, gynecological and lung malignancies. Dr Shannon has extensive experience with clinical trials of new drugs for the treatment of malignancy. Her special interests include the management of breast cancer in young women and pregnant women and she has published in this field.

Dr Kylie Snook

BMed (Hons), FRACS

Kylie Snook is a Consultant Breast Surgeon in Sydney. After completing her general surgical training through Northern Sydney Area Health Service she undertook two years of post-fellowship training in Breast and Oncoplastic Surgery in Guildford, UK. Dr Snook is a VMO at the Mater, North Shore Private and Hornsby Ku-ring-gai Hospitals and Northern BreastScreen. She is a member of Breast SurgANZ, ANZ Breast Cancer Trials Group and the Association of Breast Surgeons UK. She regularly participates in breast cancer education for medical professionals, patient groups and the broader community. Dr Snook's interests include oncoplastic breast surgery, intraoperative analysis of sentinel nodes and research into patients undergoing breast reconstruction.

Dr Yvonne Zissiadis

MBBS, FRANZCR

Yvonne Zissiadis is a Radiation Oncologist with a special interest in breast cancer. She completed her Radiation Oncology training at Peter MaCallum Cancer Institute following which she took up a Research Fellowship at the Breast Cancer Institute in NSW. Following that Dr Zissiadis was appointed Consultant Radiation Oncologist at the Prince of Wales Hospital, Sydney. She then undertook a second fellowship at the Massachusetts General Hospital, Boston before returning to take up a Radiation Oncology consultant position at Royal Perth Hospital. She now works for Genesiscancercare, both privately and at Royal Perth Hospital where she is currently Head of Department. Dr Zissiadis has been a long term and active member of the Trans Tasman Radiation Oncology Group participating in many of their breast cancer trials. She also has a lectureship at Edith Cowen University, with whom she is collaborating on exercise in breast cancer trials.

PRESENTERS - PROFFERED PAPERS

Dr Jesse Beumer

MBBS, MSSc.

General Surgery Trainee. Royal Adelaide Hosipital & University of Adelaide

Mr Christopher Kelly

B MRS(RT), Adv Dip Adv Prac (Breast Localisation and Simulation)

Breast Specialist Radiation Therapist, Crown Princess Mary Cancer Centre, Westmead, NSW

A/Prof Elizabeth C Penington

MD, MBBS, BMedSci, FRACS (Gen & Paed)

Surgeon, Bendigo

Dr Guillermo A Regalo

BSc, MBBS

Postgraduate Fellow, John Hunter Hospital, N.S.W

Mr Matthew Samarin

Medical student, Flinders University of South Australia

Dr Sanjeewa Seneviratne

MBBS, MD, MRCS

PhD Student, Waikato Clinical School, University of Auckland, New Zealand

Ms Daisy Veitch

PhD Candidate, Faculty of Industrial Design, Delft University of Technology, The Netherlands

Dr Geoffrey Yuet Mun Wong

MBBS

Resident Medical Officer, Department of Breast, Endocrine and Surgical Oncology. Royal Adelaide Hospital.

Venues

THURSDAY 12 SEPTEMBER 2013

08:30 - 18:00	**Registration** Venue: Registration Desk
11:30 - 17:00	**Speakers' audiovisual testing** Venue: Media Room
09:30 - 12:30	**Workshop: Tomosynthesis for Radiologists** Venue: Meeting Room 2
12:30 - 16:30	**Workshop: Oncoplastic Surgery** Venue: Hall A
13:30 - 16:30	**Workshop: Tomosynthesis for Radiologists** Venue: Meeting Room 2
18:45 - 20:15	**Welcome reception** Venue: Cairns Hilton gardens

FRIDAY 13 SEPTEMBER 2013

07:00 - 08:45	**Educational breakfast session: Genomic Assays in Breast Cancer - A Step towards Personalised Medicine** Venue: Meeting Rooms 1 & 2
07:30 - 16:00	**Speakers' audiovisual testing** Venue: Media Room
17:00 - 18:00	**Networking drinks** Trade Exhibition area Venue: Halls C & D

SATURDAY 14 SEPTEMBER 2013

07:30 - 15:00	**Registration** Venue: Registration Desk
07:30 - 08:45	**Australasian Society for Breast Disease Annual General Meeting** Venue: Meeting Room 8
07:30 - 13:00	**Speakers' audiovisual testing** Venue: Media Room
18:15 - 23:00	**Meeting dinner** Venue: Rainforestation, Kuranda

The venue for all scientific program plenary sessions is Hall A.

Program

Please note that the program is subject to change.

THURSDAY 12 SEPTEMBER 2013

09:00 - 17:00	**Registration**	
09:30 - 12:30	**Workshop: Tomosynthesis for Radiologists** *Sponsored by Hologic*	
12:30 - 16:30	**Workshop: Oncoplastic Surgery** *In association with BreastSurg ANZ* Co-chairs: Daniel de Viana and Wayne Jones	
	Incisions and decisions for level 1 oncoplastic techniques	Richard Martin
	Decision making in implant reconstruction (1v2 stage, implant selection)	Anthony Green
	How I do it: Total skin sparing mastectomy	Elisabeth Elder
	How I do it: Tissue expanders	Andrew Baildam
	How I do it: One stage implant reconstruction	David Littlejohn
	Matrices: State of the art or over-rated?	Wayne Jones
	Nipple problems with Total Skin Sparing Mastectomy	Daniel de Viana
	Options for nipple reconstruction	Andrew Baildam
	Decision making for the contralateral breast	Peter Laniewski
	How I do it: Symmetrisation	Peter Laniewski
	Lipofilling: Getting started	James French
	TRAM versus DIEP: How we choose?	Peter Laniewski
15:30 - 15:45	**Afternoon break**	
15:45 - 16:30	Dealing with the surgical disaster in reconstructive breast surgery	Andrew Baildam
	3D analysis of breast morphology: A systematic review of current literature	Farid Meybodi
	Experience with large breast reductions using the central breast pedicle technique	Ananda K Ponniah
	Cases and discussion	
13:30 -16:30	**Workshop: Tomosynthesis for Radiologists** *Sponsored by Hologic*	
17:00 - 18:30	**Minisymposium: Management of the Axilla** Chair: Wayne Jones	
	Radiologist's view	Anne Tardivon
	Surgeon's view	Andrew Baildam
	Pathologist's view	Puay Hoon Tan
	Panel – Anne Tardivon, Andrew Baildam, Puay Hoon Tan, Roslyn Drummond	
18:45 – 20:15	**Welcome drinks** (at Cairns Hilton)	

FRIDAY 13 SEPTEMBER 2013

07:00 - 08:45	**Educational breakfast session: Genomic Assays in Breast Cancer - A Step towards Personalised Medicine** *Sponsored by Genomic Health*	
	Capturing Tumor Biology Beyond Traditional Factors	Richard de Boer
	Incorporating Genomic Assay in Clinical Practice	Bruce Mann
09:00 - 10:45	**Session 1: Breast Cancer – Different Mechanism, Different Approach** *Sponsored by Roche Products*	
	Chair: Daniel de Viana	
	Welcome	Daniel de Viana
	Keynote: Obesity, metabolic factors and breast cancer	Kathy Pritchard
	Breast cancer in the older woman	Richard De Boer
	Changing patterns of breast disease in Asia	Chen-Pin Chou
	Breast cancer genetics beyond BRCA	Michael Gattas
	Discussion / questions	Faculty
10:45 - 11:15	**Morning break**	
11:15 - 12:45	**Session 2: Defining the Disease** Chair: Wendy Raymond	
	Keynote: New imaging modalities	Anne Tardivon
	Keynote: Implications of the "New" WHO Morphological Classification of breast cancer	Puay Hoon Tan
	Next generation technology	Sunil Lakhani
	Predictive biomarkers in the context of neoadjuvant therapy for breast cancer	Stephen Fox
	Discussion / questions	Faculty
12:45 - 13:45	**Lunch** *Sponsored by AstraZeneca*	
13:45 - 15:00	**Session 3: Prevention and Screening Strategies** Chair: Bruno Giuffre	
	Keynote: Risk reducing mastectomy and reconstruction for high risk women	Andrew Baildam
	Reinventing Breast Screening for the 2020s	Anne Tardivon
	Screening in women with dense breasts	Anne Tardivon
	Discussion / questions	Faculty
15:00 - 15:30	**Afternoon break**	
15:30 - 17:00	**Session 4: Benign Diseases Symposium** Chair: Susan Fraser	
	Should the pathologist report atypical hyperplasias?	Puay Hoon Tan
	Optimal treatment of the atypical core biopsy	Bruce Mann
	Diagnosis of biphasic lesions	Puay Hoon Tan
	Phyllodes tumour	Kylie Snook
	The emerging role of Breast Physicians	Susan Fraser and Lisa Erzetich
	Discussion / questions	Faculty
17:00 - 18:00	**Networking drinks**	

SATURDAY 14 SEPTEMBER 2013

07:30 - 08:45	**ASBD Annual General Meeting**	
09:00 - 10:30	**Session 5: Contemporary Management of the Aggressive Cancer** Chair: James French	
	Breast cancer surgery: What you should ask the radiologist	Anne Tardivon
	Current neoadjuvant interventions	Kathy Pritchard
	Optimising cosmesis in high risk breast cancer	Andrew Baildam
	Changing indications for radiation therapy	Marie Burke
	Discussion / questions	Faculty
10:30 - 11:00	**Morning break** *Sponsored by Allergan*	
11:00 - 12:30	**Session 6: Proffered Papers** Chair: Wendy Raymond	
	Sentinel node biopsy and large (≥3cm) breast cancer	Jesse Beumer
	A cardiac sparing technique for breast cancer radiation treatment	Christopher Kelly
	Intra-operative ultrasound refines breast conserving surgery for palpable breast cancers	Guillermo Regalo
	Risk factors associated with mortality from breast cancer in Waikato, NZ – A Case Control Study	Sanjeewa Seneviratne
	Development of a realistic model for teaching breast examination	Daisy Veitch
	Use of blue dye in Sentinel Lymph Node Biopsy: time to reevaluate	Geoffrey Wong
	Audit of fine needle aspiration cytology of breast versus histopathological outcome in a busy hospital setting: valuable tool or an anachronism?	Matthew Samarin
	Closure of the axillary fascial space avoids the need for drainage in axillary dissection	Elizabeth C Penington
12:30 - 13:30	**Lunch** *Sponsored by Novartis Oncology*	
13:30 - 15:00	**Session 7: Managing the Extremes – interactive case presentations** Chair: Sunil Lakhani	
	Borderline and atypical lesion management	
	High risk disease management	
	Panel: Wendy Raymond, Andrew Baildam, Bruce Mann, Kathy Prichard, Yvonne Zissiadis, Joseph Ling	
15:00 - 15:30	**Afternoon break**	
15:30 - 16:45	**Session 8: Beyond Primary Treatment** Chair: Catherine Shannon	
	What's new in adjuvant hormonal therapy?	Kathy Pritchard
	Breasts, bones and bisphosphates	Richard De Boer
	Addressing needs of Cancer Survivors - What, Who and How	Bogda Koczwara
16:45 - 17: 00	**Awards for best proffered paper and best poster** Closing comments	Daniel de Viana
18:15 – 23:00	**Meeting dinner** (at Rainforestation, Kuranda)	

Section 2

Abstracts

Workshop: Tomosynthesis for Radiologists

Sponsored by Hologic

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Workshop: Oncoplastic Surgery

In association with BreastSurg ANZ

INCISIONS AND DECISIONS FOR LEVEL 1 ONCOPLASTIC TECHNIQUES

Richard Martin

We will discuss the surgical decision making involved in the application of level 1 oncoplastics and consider those that would be better suited to a second level technique.

IMPLANT BREAST RECONSTRUCTION

Anthony Green

Once a patient has decided they would prefer an implant reconstruction and number of decisions need to be made:

- The size and shape of the implant/expander
- Saline vs silicone
- 1 vs 2 stages
- Skin/nipple sparing
- The other breast
- Bilateral mastectomy

The pros and cons of these and other general considerations will be presented and discussed.

TOTAL SKIN SPARING MASTECTOMY – HOW I DO IT

Elisabeth Elder
Westmead Breast Cancer Institute

Total skin sparing mastectomy, or nipple-sparing mastectomy (NSM), involves the removal of all macroscopic breast tissue with preservation of the entire skin envelope including the nipple areola complex (NAC). The aim is to optimise the aesthetic result after an immediate breast reconstruction using a one- or two stage implant based approach or autologous tissue.

Several studies have shown that NSM is oncologically safe and provides improved patient satisfaction and quality of life in carefully selected patients, with recurrence rates comparable to conventional mastectomy and breast conserving therapy for early breast cancer or risk-reducing mastectomy in the context of increased breast cancer risk. The nipple may be excised in a second procedure if there is evidence of occult nipple involvement (<5%).

Appropriate patient selection is crucial. The procedure is contraindicated in cases of known skin involvement, including inflammatory cancer, and careful assessment of preoperative imaging is essential to ensure there is a free plane of tissue overlying the tumour. Smoking, vascular comorbidity including diabetes and postmastectomy radiotherapy increase the risk of complications. The procedure is particularly suited for smaller breasted women typically A-C cup with no or minimal ptosis. A minor degree of ptosis can be corrected using a circumvertical incision, raising the nipple position no more then 2-3 cm. For larger breasted women with a sternal notch to nipple distance of less than 25 cm, a skin-reducing mastectomy with nipple preservation can occasionally be achieved.

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The incision is preferentially placed in the inframammary fold (IMF) or inferolaterally to facilitate simultaneous axillary sentinel node biopsy. In women with a large areola, a hemiareolar incision may be used. Previous incisions may also be used to reduce the overall scar burden. Radial incisions, particularly involving the areola circumference should be avoided, as it is associated with an increased risk of ischemic complications as well as deviation of the NAC.

The mastectomy flaps are raised in the same plane as for a conventional mastectomy, i.e at the level of the anterior mammary fascia - a too superficial dissection risks disrupting the subdermal plexus resulting in ischemia, a too deep dissection risks leaving breast tissue behind. The central ducts of the nipple may be cored out for oncological reasons but leads to loss of nipple projection. It is important to avoid dissecting outside of the breast boundaries and to preserve the subcutaneous reflection of the IMF.

A cohesive gel implant (or nearly filled tissue expander) is placed subpectorally. A biological mesh, such as Biodesign mesh by Cook® may be attached laterally and inferiorly to achieve total cover and reduce the risk of implant displacement.

HOW I DO IT: TISSUE EXPANDERS

Andrew Baildam

For many women who undergo therapeutic as well as those undergoing risk reducing mastectomy, the relative 'simplicity' of an implant-based reconstruction makes this the first choice, and they opt for immediate sub muscular tissue expander placement. The cosmetic key is the match of the skin envelope surface area to surface area of the expanded muscle pocket. The use of an immediate fixed-volume permanent implant is an attractive ideal but this rarely gives acceptable cosmesis, and the aesthetic result of the two-stage process for most women is far better than a one-stage operation. Even the use of acellular dermal matrices (ADM) in experienced hands increasingly is done with tissue expansion as a first procedure, with permanent implants placed subsequently.

Careful preoperative breast evaluation is done in the clinic. Preoperatively breast assessment with accurate skin measuring and marking is essential, photographs are taken and there is agreement between the woman and surgeon as to the proposed postoperative breast size. For unilateral reconstruction where contralateral symmetrisation surgery is not wanted, a discussion must take place that focuses on the limitations of expander/implant based breast reconstruction with respect to ptosis as well as maximum breast volume. Tissue expanders work best for the breast with only moderate ptosis and a weight of no more than 550g, but ideally < 450g .

The patient is positioned on the operating table with partial flexion of elbows and hands tucked into the waistband. The incision follows the carefully marked preoperative skin mark-up, which has been accurately measured, planned and discussed with each patient. Subcutaneous fat is preserved to keep the deep dermal vasculature, and the breast parenchyma removed from this layer by gentle dissection below the layer of Scarpa's fascia. The skin and subcutaneous tissue should not be buttonholed but removed in parallel and flaps should be of consistent thickness extending to the pectoralis fascia. Resection of the breast gland is achieved by dissecting along the plane of the subtle Scarpa's fascia that separates the fibro-fatty and glandular tissue of the breast from the subcutaneous fat, which should be preserved deep to the dermis. Removal of the subcutaneous fat results in a high incidence of skin damage, particularly if the subdermal vascular plexus is breached. The pectoralis fascia is preserved wherever possible and the breast tissue removed and weighed. The inframammary fold is preserved – its removal will remove lower breast edge definition and may allow the implant to 'submarine' below the bra line into the lower anterior chest wall.

The subpectoral space is opened by sharp dissection of the lateral border of pectoralis major, and the submuscular pocket developed by sharp and blunt dissection using an illuminated retractor and direct vision. The medial border of pectoralis minor is mobilised, and the muscle freed up laterally and opened out from behind pectoralis major. When the muscular pocket is closed over the expander this medial edge of pectoralis minor is sutured to the lateral edge of pectoralis major, and this increases the surface area of the muscle cover as well as providing lateral support to the prosthesis. The submuscular pocket is extended under the upper part of rectus abdominis and the external oblique muscles to recreate the breast lower pole fullness. The tissue expander is placed in the pocket with full aseptic precautions, partially inflated and the subcutaneous mastectomy space closed over a closed vacuum drain. The skin is closed with multiple layers of subcutaneous and intradermal absorbable sutures and wound dressing strips applied.

After recovery and healing, the tissue expander is inflated cautiously with injectable saline in the outpatient clinic over several weeks or months, and the woman encouraged to use simple skin creams and massage to promote skin softening and elasticity in the neo-breast mound.

After full tissue expansion several months later, the tissue expanders are removed and replaced with permanent implants. At full maturation of expansion, permanent implants can be chosen from the extensive ranges now available, with consideration to filler materials, surface textures, size, shape and volume. Permanent implants are specifically ordered for individual women according to breast horizontal width, breast height and projection. For some, round dome-shaped implants are appropriate, for others there is a range of anatomically shaped implants in a wide variety of heights and projections.

This second operation involves accessing the expander pocket either through part of a previous scar or through the inframammary fold, and removing each expander. Shaping of the pocket capsule can be done with bipolar scissors and this helps in forming breast ptosis and filling in and smoothing out areas that may not have expanded fully. Use of implant sizers is helpful prior to permanent implant placement, orientation and closure. Women are sat up on the operating table to judge size, shape and symmetry of the breast reconstructions, and adjustments made accordingly.

For immediate insertion of tissue expander at the same time as mastectomy there are options for the mastectomy scars - essentially they are modifications of either horizontal/oblique incisions or of the Wise pattern approach. There are also multiple expander shapes and sizes available as well as adjustable permanent implants, such as the Becker 35 and the Natrelle 150. For delayed reconstruction with expanders I prefer an inframammary fold short incision, away from the healed mastectomy scar, with dissection of the submuscular pocket from below using a lighted retractor and bipolar scissors. Previous radiotherapy is a relative but not absolute contraindication to an expander/implant based reconstruction. But an expander can be placed as an immediate step in a woman for whom post mastectomy radiotherapy is planned, as a temporising solution, with a definitive flap based reconstruction done as a delayed procedure at a time remote from the radiotherapy.

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HOW I DO IT: ONE STAGE IMPLANT RECONSTRUCTION

David Littlejohn

Skin sparing mastectomy and immediate "one stage implant" reconstruction is becoming a popular choice for patients. Patient selection, operative techniques and outcomes and complications are discussed.

MATRICES: STATE OF THE ART OR OVER-RATED?

Wayne Jones

NIPPLE PROBLEMS WITH TOTAL SKIN SPARING MASTECTOMY

Daniel de Viana

Total skin sparing mastectomy also known as nipple-sparing mastectomy can provide excellent cosmetic outcomes in the prophylactic and oncologic setting and has been popularized in recent times. The technique creates a potential for complications not experienced with traditional mastectomy such as nipple margin issues, nipple necrosis, nipple symmetry problems and other cosmetic issues. These will be discussed along with strategies to avoid or at least minimize them.

OPTIONS FOR NIPPLE RECONSTRUCTION

Andrew Baildam

Nipple reconstruction is precise but easy, a small technique that with pigmenting tattoo and done well, transforms a featureless reconstructed chest wall mound into something familiar that the eye can accept naturally as 'breast'. The existence of many different techniques and the lack of any dominant one shows that there is no one ideal method. Nipple areolar complexes, NACs, come in all shapes and sizes and a range of colouration. The NAC gives the breast reconstruction a more natural appearance and restores symmetry, allowing the woman to perceive the breast as intact. Goals are position, size, projection, appearance and colour.

The position to place a NAC can be difficult as it involves a compromise between the best location on the most prominent part of the breast mound, and the visual impression of symmetry when regarding both breast together. No reconstructed breast will be precisely a mirror image of its natural counterpart. When there is doubt above all the NAC should not be placed too high; lowering a NAC surgically is very difficult and leaves an obvious scar, whereas raising a NAC is easier as well as cosmetically more forgiving.

Modern surgery has innovated a number of ways of creating varying volume and projections of NAC buds, followed by artistic design and colouring of the areola. Initially methods involved a surgical projection bud coupled with a skin graft, often from the upper inner thigh. But the pigmentation of skin grafts fades, there is a donor site scar, and the

NAC bud shrinks. Shrinkage occurs more so after implant based breast reconstruction than after autologous tissue breast reconstruction.

The commonly used NAC bud flaps are the box flap or asymmetric trefoil flap. Both need to be protected for a month after surgery by a sponge ring to discourage shrinkage, and can be created slightly larger than required to allow for some flattening. There are some techniques of nipple sharing, but these should be used with caution, for concern at damaging the natural contralateral nipple.

The ideal time for NAC reconstruction is 3 months after mound creation, sufficient time to allow maturation and some ptosis in the reconstructed breast. The technique should be chosen on an individual basis, and complications are rare.

DECISION MAKING FOR THE CONTRALATERAL BREAST

Peter Laniewski

Treating the 'other' side is often overlooked. The appropriately educated patient will usually elect to have additional surgery to achieve symmetry and balance. I have outlined the varying techniques which best achieve harmony and a happy patient.

HOW I DO IT: SYMMETRISATION

Peter Laniewski

LIPOFILLING: GETTING STARTED

James French

Lipofilling has been utilised since the early 1980's in a variety of clinical settings but fell out of favour due to high rates of reabsorption of the fat. In 1997 Coleman described a technique, which has been widely adopted across parts of the USA and Europe. In breast cancer it is commonly used to fill defects in the breast post wide excision and to re contour breast mounds post implant based reconstruction. It is thought to work by activating adipose derived stem cells along with fibroblasts endothelial cells. There is some controversy as to whether or not there is a risk of promoting cancer recurrence.

Equipment needed to set up to perform lipofilling will be demonstrated as well as a short video showing harvesting, preparation and injection of the fat.

Lipofilling's oncological safety is yet to be scientifically validated, but is a promising technique which is cheap to set up and easy to learn.

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TRAM VERSUS DIEP: HOW WE CHOOSE?

Peter Laniewski

Choosing between a DIEP or a Tram is simple, Because a DIEP is a refinement of a Tram flap the DIEP is always the preferred option if technically possible. There are however circumstances where a Tram may be preferred.

DEALING WITH THE SURGICAL DISASTER IN RECONSTRUCTIVE BREAST SURGERY

Andrew Baildam

This presentation looks at the issues surrounding failed or suboptimal outcomes from previous breast surgery. Patients can be affected from the perspectives of oncology, aesthetics and psychological damage, and for individual patients sometimes all three co-exist. Sometime every surgeon finds unexpected - but explicable - complications that seriously affect outcome adversely; less common is the suboptimal result of reconstructive or aesthetic surgery attributable to poor planning, technical issues or inexperience. Patients can be devastated by poor aesthetic and functional outcomes and seek not only explanation and restitution but also redress. A failed flap for breast reconstruction may occur rarely in an individual surgeon's practice, but for the affected woman failure has occurred 100% - for her this can be catastrophic, and a pivotal episode in her failure not only to rehabilitate after breast cancer treatment but also to adapt with confidence to normal every day living.

We have seen breast surgery move away from its general surgery roots over the last decade in the UK and occupy the ground more familiar to plastic and reconstructive surgery. Awareness of the aesthetic aspects of surgery is not central to the 'general surgeon' who deals with emergency and elective gastro-intestinal surgery, but crucial for the oncoplastic practice of the modern breast surgeon.

Management of the affected patient consists of the management of some – occasionally most - of these – oncology, aesthetics, complications, scars, displacement, asymmetry, flap failure and skin loss. Careful evaluation of each component problem allows creation of a surgical treatment plan to address the maximum extent of the issues with the least risk for additional complications and further adverse outcomes. A woman must not be subjected to a high-risk strategy when she has already had complications leading to poor outcomes. She may feel not only that she has had to bear the diagnosis and treatment of breast cancer, but has been left mutilated by the results of her operations. Corrective surgery often requires two or more operations staged and carefully planned, and outcomes reliably anticipated. Patient expectations must be addressed and any intervention should at all cost be 'low risk' for further injury. Wherever possible keep a 'surgical lifeboat' in reserve should further intervention fail.

Litigation, especially against the first surgeon, is not uncommon. Any plan for care has to be agreed openly with realistic expectations on both sides, the patient and the surgeon undertaking the revision. Most of all, the revising surgeon must not become a part of the ongoing problem. A number of actual clinical scenarios will be presented.

Successful resolution for individual patients can result in high levels of satisfaction and restoration of self-image, and repair of social and domestic relationships. Failure can result in escalation and further distress and should be avoided at all costs. A failed expander/implant reconstruction patient will be seriously harmed if a subsequent flap based reconstruction also fails. Consider too the risk of donor site breakdown and long term morbidity, should a flap fail. There are particular groups at higher risk of surgical complications than others, especially smokers, diabetics or women with high BMIs. For these women the simplest solution is the expedient one. This may mean some compromises in achieving goals and outcomes. The surgeon should never allow the overly demanding patient to 'take the risk' of a likely major complication when the surgeon has advised against a particular course of action. The response should be 'whilst you may be willing to take that particular risk, as your surgeon I'm not prepared to'.

Finally the best way to manage poor outcome is to anticipate when that likely may be a danger, and plan to avoid getting the patient into a situation in one's own practice in the first place where catastrophe is likely to strike. For example, the young woman with a highly aggressive breast cancer in whom an immediate flap coupled with skin-sparing mastectomy fails, will not only have aesthetic complications, but necessary chemotherapy will be delayed, and that will directly affect her chance of disease free survival.

3D ANALYSIS OF BREAST MORPHOLOGY: A SYSTEMATIC REVIEW OF CURRENT LITERATURE

Farid Meybodi*, Tessa Morgan, James French, Meagan Brennan, Elisabeth Elder
Westmead Breast Cancer Institute

Background

3D photography (3DP) is a new method that aims to objectively quantify breast morphology. It is based on the simultaneous capturing of the breast surface by multiple cameras and its 3D generation. The software program then generates a virtual chest wall and enables the user to extract data about volume, surface, symmetry and anthropometric measures.

Objective

To define the advantages, disadvantages and clinical application of this technology based on a literature review.

Method

Studies describing 3DP were identified from PubMed with manual cross-referencing. Full text papers in English describing utilisation of this technique in the field of breast surgery were included.

Results

40 studies were identified from July 2002 to May 2013 that met the inclusion criteria. These studies represent a total of 1263 3DP for breast morphology assessment. Papers were published by 17 centres from 10 countries. The technique was most commonly used by plastic surgeons for breast augmentation 316/1263. 3DP was used for assessment of volume (70%) anthropometry (35%), symmetry (27%) and breast surface (10%). Most of the studies (97%) found 3DP to be useful in breast assessment.

Conclusion

3D breast assessment appears to a useful and accurate tool for objective evaluation of breast morphology. Currently, it is mostly utilised in aesthetics compared to oncoplastic surgery. However, the technology has potential to be used in everyday practice for breast analysis, planning of surgery, simulation, patient education and longitudinal studies in the reconstructive setting.

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EXPERIENCE WITH LARGE BREAST REDUCTIONS USING THE CENTRAL BREAST PEDICLE TECHNIQUE

Ponniah A.K.*[1], Ong L.S., Martin R.[2]

[1] Breast Centre, Sir Charles Gairdner Hospital, Perth, WA

[2] Breast Centre, Mount Hospital, Perth, WA

There are many breast reduction techniques for the treatment of macromastia. The wise skin pattern is commonly used for large volume reductions however it is sometimes criticised for producing a "boxy" breast shape. The skin and breast volume are usually reduced concurrently, and women with significant ptosis are at risk of a "flat, boxy" final shape if too much glandular volume is resected.

We describe a "central pedicle" wise pattern reduction which produces a more conical breast shape. The skin is resected in a stepwise fashion prior to the final volume reduction, allowing for more accurate tailoring of the final breast shape and eliminating the potential for a disastrous over resection of volume.

The central pedicle can be used safely in gigantomastia, where a massive reduction in breast volume is required, but is particularly useful in the ptotic "empty" breast to maximise projection.

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MANAGEMENT OF THE AXILLA: A RADIOLOGIST'S VIEW

Anne Tardivon, MD
Department of Radiology, Institut Curie, Paris, France

Concerning the pre-operative staging of the axilla in patients with breast cancer, imaging has two main issues: 1) to improve selection of N0 patients for a sentinel lymph node (SLN) procedure and 2) to select among N+ patients those for an ALND excision with preservation of lymph nodes (LN) draining the arm (ARM technique). In N0 patients, the combination of ultrasound and fine needle aspiration is the reference technique with a sensitivity and specificity around 80% and 98% respectively (meta-analysis of Houssami et al, FNA or core biopsies, median prevalence of N+ = 47.2%)[1]. The PPVs of ultrasound criteria for selecting LN for FNA are variable (37% for one abnormal cortical lobulation versus 85% for multiple, 10% for cortical thickness < 2 mm versus 88% for thickness > 4mm); adjunct of US elastography seems to improve sensitivity and specificity of B mode[2-3]. Because of high specificity and PPV values, axillary US + FNA is an accurate triage test but its utility and cost effectiveness are clearly related to the probability of metastatic LN (cancer size and tumor profile). In case of normal axillary US examination, the principal question is to perform or not systematic FNA (PPV around 30% for normal LN at US). If yes, identifying the sentinel LN is mandatory and preliminary results evaluating contrast-enhanced US (intradermal injection of microbubbles) demonstrated that 39% of SLN were detected after injection only [4-5]. So, in this N0 breast cancer population, studies (clinical and economical) are necessary to optimize patient selection for axillary staging. It has been demonstrated that 98% of SLN were located medially alongside the lateral thoracic vein, 87% under the second inter-costo- brachial (ICB) nerve and 11.5% above[6]. In N+ patients, the aims of imaging are 1) to evaluate the number of suspicious LN and 2) to localize them precisely in the axilla for triage patients between a classical ALND and an ARM dissection (patients with less than 4N+ and all located under the second ICB nerve)[7]. These landmarks are easy to identify during a CT examination (indicated in N+ patients) if the acquisition protocol is optimized (chest exploration at a late venous phase after contrast medium injection, ipsilateral arm at 90-110°, MIP reconstructions in coronal plane). By using the following criteria for suspicion of metastatic LN: short axis > 5 mm with no hilum or abnormal margin or with a contrast uptake > + 20UH compared to the opposite side, the PPV to predict LN metastases is around 83% and 95% to predict the number of metastatic LN (≤ 3N+ versus > 4N+)[8]. MRI with Gadolinium contrast agents does not provide superior results compared to CT. Diffusion or spectroscopy MR techniques are limited by a relatively low spatial resolution and are unable to detect small metastases in normal-sized nodes. Using USPIO (Ultrasmall SuperParamagnetic Iron Oxide) agents, interesting results have been published with specificity ranges over 95%. In normal and benign reactive LNs, the contrast agent is captured by the macrophages and generates a loss of signal (no signal on T2* sequences) whereas there is no capture of USPIO agents in metastatic areas. The limitations are related to the cost and the need for injecting USPIO many hours before the MRI examination[9-10] . PET/CT is not indicated for patients at early stages of the disease; in advanced-stage breast cancers, PET/CT coupled with US increases the specificity for detecting metastatic LN, US correcting the relatively low sensitivity of PET [11].

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MANAGEMENT OF THE AXILLA – A SURGEON'S VIEW

Andrew Baildam

For both surgeon and the patient with breast cancer the current management of the axilla presents a dilemma. A decade ago the standard of care for most women with invasive breast cancer was full axillary node clearance, ANC. A few centres offered random axillary four node sampling, but up to 24% undergoing sampling are incorrectly staged compared to ANC. For most the completeness and security of ANC allowed it to hold the monopoly on axilla surgery. That began to change when it was recognised that increasing numbers of women were no longer presenting with lymph node metastases at the time of diagnosis, and that for a greater proportion of women not only was ANC unnecessary, it was also often accompanied by sometimes very unpleasant sequelae. These ranged from dysaesthesia, to intercostobrachial nerve neuralgia, through to numbness, and full-blown arm lymphoedema, and shoulder dysfunction. Axillary surgery began to change with the onset of several game-changing clinical studies and trials, and the innovation of new techniques to stage the axilla.

The first innovation in decades was the development of the axillary sentinel node biopsy technique (ASLNB), using Patent Bleu V dye, a radioisotope tracer, and both together. Despite variability in selection criteria and technique, a SLN is consistently identified in approximately 96 percent of cases, and predicts the status of the remaining axillary LNs in ≥95 percent of cases in most series[1-2]. The false negative rate of SLND was originally reported as 5 to 10 percent (sensitivity 90 to 95 percent), but lower rates are achievable. Around 40 percent of patients with a positive sentinel lymph node (SLN) will be found to have further disease in the remaining axillary nodes. SLN metastases are categorized as isolated tumour cells, micrometastases, or macrometastases, depending upon the size of the largest tumour deposit in the sentinel node. Extranodal spread is prognostically important. There is debate about the prognostic value of the size of the SLN micrometastases (≤0.2 mm versus larger) to determine the likelihood of involvement of axillary non-SLNs.

After proof of principle was established, and the technique found to have acceptably high sensitivity and specificity, the UK ALMANAC trial addressed both training and collection of data to support ASLNB[3].

ASLNB is now the standard of care for women with invasive breast cancer, with no further procedure advised for women whose ASLNB shows no evidence of metastases.

For women with positive sentinel lymph nodes ANC has been the preferred option both for complete staging and therapeutics. This is changing: the ACOSOG Z-0011 trial, looked at no further axillary surgery for women with low burden axillary metastases, and compared this approach with ANC[4].

Essentially Z-0011 is a trial that compares surgical ANC with radiotherapy to remaining nodes after positive sentinel node removal. The need for a completion ALND in patients with a positive SLND showing micrometastases or macrometastases in less than three nodes has been questioned. The SLN is the sole metastatic node in up to 60 percent of cases overall, and in almost 90 percent of patients who have only micrometastases. Completion ANC may not be necessary in selected patients with a positive SLND in less than three nodes because the need for systemic therapy is clear and the risk of an axillary recurrence is low. The Z-0011 trial was designed to address the need for completion ANC for patients with T1 or T2 tumours that were clinically node negative and had less than three positive sentinel nodes; all patients were treated with post-operative radiotherapy.

The results of the trial concluded that at a median follow-up of 6.3 years, there were no significant differences in survival or locoregional recurrence between the SLND plus ANC group versus SLND alone. The five-year overall survival was similar whether women were treated with SLND plus ANC or with SLND alone (91.9 versus 92.5 percent, respectively) (HR 0.79, 90% CI 0.56-1.10). Recurrence rates in the ipsilateral axilla were similar between the two arms with four recurrences (0.9 percent) in the SLND alone arm compared with two recurrences (0.5 percent) in the SLND plus ANC arm.

The ACOSOG Z-0011 trial was criticized for a number of important issues and it is likely that further similar studies are undertaken before this approach becomes widespread, but already it is the new standard of care in North America. It is demonstrating a radiation effect, not 'no further axillary treatment' in women with low burden nodal metastases. Meanwhile further interest will be in the as-yet unpublished results of the EORTC AMAROS study, where women with positive ASLNB were randomised to go on to ANC or to have axillary radiotherapy instead.

The preoperative standard of care for all women with suspected breast cancer is axillary ultrasound scan, with fine needle aspiration cytology or core biopsy for those with any suspicious or equivocal findings. This can identify women with positive nodes who can decide to proceed with ANC rather than sentinel node biopsy, thus avoiding the need for a second operation. But axillary ultrasound is very observer dependent, and variable in specificity and sensitivity.

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MANAGEMENT OF THE AXILLA – A PATHOLOGIST'S VIEW

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The pathologist's role in the management of the axilla of a woman with breast cancer is manifold, and can be broadly viewed from the preoperative, intraoperative and postoperative perspectives.

Preoperative confirmation of positive axillary nodal status can obviate the need for intraoperative sentinel lymph node biopsy, as axillary dissection can then proceed directly during therapeutic surgery. Clinically enlarged or radiologically abnormal axillary lymph nodes detected during preoperative evaluation of a woman diagnosed with breast cancer can be pathologically assessed using imaging guided biopsy or fine needle aspiration[1]. This approach is also useful in documenting nodal metastases prior to commencing neoadjuvant systemic chemotherapy. Depending on the expertise available at the institution and the preferences of the assessment team, either core biopsy or fine needle aspiration cytology (FNAC) may be used to examine such lymph nodes. The FNAC procedure has advantages of being able to accommodate more passes and potentially reach anatomically challenging positions of the axillary lymph node, but requires cytologic expertise for interpretation. Corebiopsy histology is readily handled by histopathologists familiar with light microscopic evaluation, but may suffer from sampling error. The modality used should be the one that yields the most accurate and reliable results based on overall institutional experience.

Intraoperatively, the pathologist is often called upon to render diagnostic conclusions of sentinel lymph node(s) biopsied. A positive result leads to formal axillary dissection, while a negative intraoperative finding on the sentinel lymph node(s) will allow the patient to avoid axillary surgery. While there are emerging views regarding the necessity of further axillary lymph node dissection even in the presence of metastasis to sentinel lymph nodes[2], traditionally sentinel lymph nodes are examined intraoperatively through either frozen section, imprint or scrape cytology, and more recently using a molecular tool most widely represented by the one stop nucleic acid amplification (OSNA) method[3]. The OSNA technique is based on polymerase chain reaction detection of cytokeratin 19 positive cells, considered synonymous to carcinoma cells, within the lymph node.

Each intraoperative method of sentinel lymph node evaluation has different sensitivity and specificity rates, depending on the respective familiarity, experience and expertise of pathologists in its application. Cytologic methods tend to have the widest range of sensitivity in view of the diverse cytologic expertise in different laboratories. Frozen section is a frequently used method of intraoperative sentinel lymph node assessment in many institutions, but there are technical challenges that may lead to micrometastatases being underdiagnosed. False negative rates of sentinel lymph node biopsy range from about 5% to 40% in the literature. The OSNA method may avoid the subjectivity of cytologic and frozen section interpretation, but the length of time per run (turnaround time), as well as the costs incurred, may be deterrents to its routine use. If the entire node is used for OSNA evaluation, there will be no residual tissue to serve as permanent section histology, in which case the size of the metastasis will not be available, although some general guide on the corresponding nodal metastatic groupings in relation to the OSNA result categories is available[3].

Subsequent permanent histology of sentinel lymph nodes is based on an approach of focused assessment in order to allow detection of isolated tumour cells, micrometastases and macrometastases. Step or serial sections are often used to discover the presence or otherwise of metastatic deposits though the detection of micrometastases or isolated tumour cells through additional deeper levels does not have significant clinical impact on recurrence or survival[4]. Immunohistochemistry using antibodies to cytokeratins can be applied to increase the sensitivity of discovering carcinoma cells within the sentinel lymph node, but this is not regarded as a standard requirement in sentinel lymph node assessment[5].

For women whose sentinel lymph node biopsy is negative intraoperatively, there will be no further axillary dissection that needs to be pathologically handled. For those whose sentinel lymph node(s) yielded a positive result, axillary contents will be delivered to the laboratory for assessment. Here, the pathologist needs to diligently harvest all the lymph nodes present in the axillary fat, accurately count the numbers and submit entire lymph nodes, either whole when they are small, or sectioned into not more than 2mm thick slices for larger nodes with embedding of all the slices so that any metastases larger than 2mm (macrometastases) can be identified. Failure to evaluate all nodes present in an axillary dissection can result in overlooking macrometastases in up to 40% of positive lymph nodes[4].

Histologically, the number of positive lymph nodes and the size of the largest metastastic focus need to be recorded. Presence of extranodal extension is also an important parameter that has to be conveyed in the final pathology report[6].

Pathological staging of axillary lymph nodes is based on the TNM/AJCC system, with pN0 being node negative, pN0(i+) indicating presence of isolated tumour cells which are defined as a cluster of not more than 200 tumour cells or measuring up to 0.2mm in size, pN1mi referring to micrometastasis measuring up to 2mm in size, and pN1 corresponding to metastases in up to 3 lymph nodes, pN2 implicating 4 to 9 positive lymph nodes, and pN3 refers to 10 or more positive lymph nodes.

Immunohistochemistry can be used to verify that abnormal cells observed in the lymph nodes are metastatic carcinoma cells. Sometimes, histiocytes in subcapsular sinuses may mimic cancer cells and vice versa. Presence of epithelial keratin expression by these cells can affirm their metastatic carcinoma nature. A situation where immunohistochemistry may be particularly useful is in post-neoadjuvant chemotherapy where previously positive lymph nodes may be depleted of carcinoma cells by chemotherapy effect, and where residual carcinoma cells may be difficult to detect or may have altered morphology, such that they can resemble histiocytes and thereby be unnoticed.

In summary, axillary lymph node staging is a powerful prognostic parameter, and is regarded as the single most important factor for the majority of breast cancers apart from the basal-like subtype that tends to spread haematogenously and may skip the regional nodes[4]. The pathologist provides crucial information on the pathologic status of the axilla that allows appropriate treatment decisions.

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Session 1: Breast Cancer – Different Mechanism, Different Approach

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KEYNOTE: OBESITY, METABOLIC FACTORS AND BREAST CANCER

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Across North America and much of the developed world, the incidence of overweight and obese men and women is markedly increasing. An elevated body mass index (BMI) is associated with a wide variety of cancers, most strongly with endometrial cancer, but definitely also with breast cancer[1].This is particularly evident with estrogen receptor (ER) positive breast cancer[2] and with breast cancer in postmenopausal women. However, BMI does not appear to be a factor in the development of ER negative breast cancer, although there are data implicating obesity with the occurrence of triple negative breast cancer[3].

In addition, obesity is associated with poor survival rates once breast cancer is diagnosed. A wide variety of studies show overweight and/or obesity to be related to a variety of breast cancer outcomes including recurrence, both distant and local, and death from breast cancer[4-5],regardless of tumour ER and progesterone receptor (PgR) status[6]. Serum sex hormone levels including estrone and estradiol are higher in overweight women[7]. This is true for both bioavailable and free estradiol, as well as total estradiol measures[8].In postmenopausal women, most estrogen is produced by aromatase, an enzyme which is present in the adipose, muscle, brain and other tissue in women. The aromatase inhibitors (AIs) as a class suppress estrone and reduce estrogen production dramatically[9]. The AI letrozole is likely most effective at this[11].In the adjuvant setting, aromatase inhibitors are significantly better than tamoxifen at reducing recurrence and marginally better at improving survival for all BMI levels in the three largest studies: ATAC[11],BIG 1-98[12], and TEAM[13]; although the reverse is seen in the ABCSG-12 Trial[14]. Thus selectively prescribing tamoxifen vs. an AI in relation to weight does not seem to be indicated.

In addition, there are a variety of non-estrogen-related pathways that may link weight to breast cancer. These include insulin, leptin, IGF-1, IGF-2, c-reactive protein, and various inflammatory factors[15]. Elevated insulin levels have been shown to be associated with poor breast cancer outcomes in a variety of studies[16-18]. Insulin may interact with both insulin receptors and IGF-1 receptors in human breast cancer and the presence of these receptors in such breast cancers is associated with a worse survival. Some analyses suggest that insulin may be a more important mediator than estradiol of the association of BMI with postmenopausal breast cancer risk[17]. Fasting glucose is also associated with breast cancer outcomes, with higher fasting glucose levels being associated with both distant disease-free and overall survival even when adjusted for age, tumour size, node status, grade hormone receptor chemotherapy and hormone therapy[19]. It has been shown in randomized trials that body weight can be reduced by lifestyle changes and by metformin[20]. The Women's Intervention Nutrition Study showed that weight loss could be achieved by dietary counseling and was associated with improved disease free survival[21]. The Women's Healthy Eating and Living (WHEL) Study, showed that weight loss could be achieved although it was transient[22]. In the Lifestyle Intervention Study in Adjuvant Treatment of Early Breast Cancer (LISA) study[23],a randomized controlled trial in Canada, it was shown that a telephone intervention relating to diet and activity can result in significant weight loss. The investigators plan to explore this approach further. Physical activity has been shown in a variety of case control and randomized studies to be associated with improved breast cancer outcome, as well as improved insulin and glucose levels[24]. Weight loss results in reduced estrogens in overweight or obese breast cancer survivors, particularly in those who are postmenopausal. Weight loss also reduces other biomarkers that may be associated with both obesity and poor breast

cancer prognosis[25]. At the furthest extreme, bariatric surgery also produces weight loss. Peculiarly, even before weight is lost, various markers including insulin and glucose improve following bariatric surgery[26]. In a variety of studies, intentional weight loss by whatever means has been associated with reduced risk of developing breast cancer[27].

Metformin is a widely utilized treatment for type 2 diabetes as it is well tolerated and has been used on millions of patients in whom it reduces insulin and is associated with weight loss. It is not associated with any impairment in quality of life. It impacts favourably on breast cancer biology by reducing insulin, and Ki-*67 levels* in tumours. In addition, insulin mediated cell destruction such as apoptosis is increased by the use of metformin as shown by the TUNEL assay. In a meta analysis of metformin and breast cancer risk, in both cohort and case-control studies it has been suggested that the use of metformin is associated with a reduced risk of developing cancer[28]. However, a meta analysis in randomized control trials was not suggestive of any effect. The NCIC Clinical Trials Group Trial MA.32, a large randomized trial of metformin versus placebo in the adjuvant setting has now been completed and results are awaited.

In conclusion

1 Obesity is associated with an increased risk of postmenopausal, primarily hormone receptor positive breast cancer and with poor breast cancer outcomes regardless of menopausal or hormone receptor status.
2 Obesity-related prognostic effects may be mediated by physiologic factors at the level of the whole organism, in the tumour microenvironment or both. Key physiologic mediators include estrogen, insulin/IGFs, adipokines, and inflammatory factors. Insulin may act via fetal insulin/IGF-1 receptors on breast cancers to activate PI-3 kinase signaling.
3 There is increased evidence that the tumour microenvironment is altered in obesity, and that tumour-associated macrophages and a range of cytokines may play a role.
4 Potential interventions include weight loss, lifestyle, and pharmacologic interventions such as metformin.

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BREAST CANCER IN THE OLDER WOMAN

Richard De Boer

Breast cancer is the most common cancer in women accounting for 23% of all female cancer and 14% of cancer deaths globally[1]. Breast cancer is also a disease of aging with an incidence rate of approximately 82 new patients per 100,000 in women aged less than 65 years versus 404 per 100,000 for those aged 65 years and older[2]. The average age at diagnosis is currently 61 years and the average age at death is 68 years.

Although many men and women aged 65 years and older are healthy and have long life expectancies, they are considered to be the aging population. Retirement age has long been considered to start at 65. This has led medical and health-policy researchers to consider individuals aged 65 years and older as the aging population.

Despite a growing level of interest by clinical researchers with regard to this age group, the management of breast cancer in elderly patients has been largely ad hoc and to a large degree this is due to a lack of evidence-based clinical trial data for older patients with breast cancer. Indeed, many breast cancer clinical trials have excluded elderly individuals, either on the basis of age alone, co morbidity, or both[3-4]. There have been some efforts to specifically target the elderly population in terms of adjuvant therapy, but these trials have been few and far between[5-6]. There have also been some collaborative efforts to develop consensus guidelines to guide treatment[7].

Diagnosis of breast cancer at an older age is generally associated with more favourable tumour biology as indicated by increased hormone sensitivity, less HER2 overexpression, and lower tumour grades[8]. Nevertheless, elderly patients are less likely to be treated according to standard treatment guidelines and this can result in inferior disease outcomes[9]. The reason for this undertreatment are complex but one reason is the presence of increasing levels of co-morbidities in the elderly with the resulting fear that patients will be unable to tolerate standard therapies, whether they be surgical or chemotherapy-based. This has led to a bias towards endocrine therapy alone or no active treatment in this group of patients. To overcome the impact of co-morbidities, collaboration with geriatricians and comprehensive geriatric assessment are critical[10]. Assessment of patients prior to commencing treatment and understanding not just their medical issues, but also their social and environmental problems will allow a clearer picture to develop of the patient and enable more informed treatment recommendations to be made.

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This presentation will focus on the elderly patient with breast cancer, and in particular the medical oncology side of the treatment paradigm. The problems in managing these patients will be discussed, as will the importance of treatment of the whole patient and not just focusing in on the chronological age. It will be emphasized that the goals of treating breast cancer in older patients are not different from those in younger patients. Unfortunately, the data we rely on to inform our recommendations come primarily from retrospective studies or sub analyses from general population studies, and there is a critical need to further develop prospective clinical trials for this older population of patients with breast cancer, a population that is increasing rapidly.

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CHANGING PATTERNS OF BREAST DISEASE IN ASIA

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Asia is the most populous continent, with its 4.2 billion inhabitants accounting for over 60% of the world population. The rapidly rising incidence of breast cancer in Asia area represents an important global health problem. Prevalence or incidence proportion of breast cancer in the Asia could be different from those in Western countries. Breast cancer mortality in Asia countries is almost two-fold higher than in Western countries. Many factors can impact different morbidity and mortality of breast cancer patients between Asia and Western countries. Lack of awareness, different social/cultural factors, early on-set breast cancer and low mammogram screening rate could be important factors responsible for unfavorable prognosis of breast cancer. The conspicuous difference is that the peak incidence of breast cancer is between 40 and 50 years in the Asian countries, but the peak incidence in the Western countries is between 60 and 70 years. In China, more than 1/3 of the breast cancers are diagnosed between the ages of 40-49. In Taiwan, the median age at diagnosis of breast cancer is about 45- 49 years. In India, almost 48% breast cancer are below age 50 and a disturbing trend with increasing numbers of breast cancer is noted in the age 25-40.

Breast self examination (BSE) has shown no clinical impact on patient's survival in Asia. A prospective, randomized, controlled Shanghai study investigating the BSE group and the control group was done between 1989 and 1991.There was no difference in mortality rate from breast cancer between BSE group and the control group in this study. Screening programs of breast cancer using mammogram have been well established in Western countries and were recently launched in some Asian countries. There are several different guidelines about the age and interval of screening mammography. As the debate on the age of breast cancer screening continues, the U.S. Preventive Services Task Force (USPSTF) revised the recommendation beginning at age 50 for women with an average risk of breast cancer. The recommendation changes are very controversial and should not be adopted in Asian countries due to early-onset breast cancer in Asia. Mammography screening results in the early detection of more favorable pathology staging and a higher overall survival in Asian women. Singapore national breast cancer screen program was launched in 2002. Screening mammogram was found to be the only significant factor associated with presentation at an early stage, as compared to a symptomatic patient[1]. The diagnosis and management of early and advanced breast cancer are totally different. Breast cancer screening and early breast cancer detection would change the current patterns of common breast imaging findings, patient clinical presentations, and methods of surgery for breast cancer in Asia.

Mammography screening rates in the United States have exceeded 70% eligible candidates in 2010. Screening rates are much lower among Asian countries. Dense breasts can make mammograms more difficult to interpret. There are other controversies of mammogram screening because of higher false negative cancer detecting rate in women with dense breasts. Breast sonography could be earlier in thin dense breasts. Additional breast sonography done by certified medical specialists and dedicated breast sonography machine may be helpful for women with such dense breasts. A study performed at Chinese rural areas between 2009 and 2011[2] showed ultrasound is more sensitive than mammography in detecting breast cancer in women under 55 years with high-density breasts. Dr. Huang and colleagues conducted a 5-year study with 79,691 Taiwanese women, aged 40-49 between 2003 and 2008[3]. Most of the enrolled women had heterogeneously dense breasts. Women enrolled in the study were randomized into two screening groups (mammogram or ultrasound on alternate year) and one non-screening group. In the first year, the detection rate of breast cancer using mammography and ultrasound were 0.34% and 0.22%, respectively. The detection rate in the second year was 0.36% on subsequent mammogram and 0.16% on subsequent ultrasound screen. The combination of mammography with ultrasound screening was able to find four times of breast cancer than annual incidence. In Japan, a local study at Miyagi tried to use breast sonography for age 30-39 women. The breast sonography study showed promise of asymptomatic breast cancer detection for young women but low cost-effectiveness ratios. One randomized controlled trial (called J-START) for women aged 40-49 is currently taken in Japan. The J-START assess the effectiveness of sonography in women aged 40–49, with a design to intervention group (both of mammography and sonography) and control group (mammography only). Asian studies of breast sonography screening have prompted manufacturers and government authorities to seek out a more suitable imaging modality, or combination of modalities, to deliver breast care in Asia.

A sonography guideline for dense breast for age 40-49 women is still under discussion. Besides, the most common disadvantage of breast sonography is that more than 80% of sonographic breast lesions biopsied turn out to be benign. Recent newly-developed diagnostic tools are helpful for Asian women with dense breasts to improve the breast cancer detection. Elastosonography has improved ultrasound's specificity by utilizing sonography imaging to measure the internal compressibility and mechanical properties of a breast lesion. Elastosonography has been a potential tool to avoid unnecessary biopsy during screening. In Taiwan, several studies about 3D breast tomosynthesis and contrast-enhanced mammogram for dense breast are undergoing to know the effectiveness and efficacy of new-developed diagnostic tools in Asia.

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In Asia, education and socioeconomic status are not the only barriers to early detection of breast cancer. Some well-educated women still reject breast screening tests and early surgical treatment because of rumors about harms related to screening mammogram and surgery, pain during mammogram, less family support for unmarried woman, and accessibility of mammography. In order to provide convenient health services and meet the health requirements of disadvantaged groups, Taiwan set up mobile mammography vans for door-to-door service, in order to provide community screening with high quality equipment and professional services. Women with abnormal screening mammogram are registered on a national data system and these women would be visited by community health workers. Evidence-based education in public health issues is also an important issue in addition to the diagnostic tools and surgery.

The patterns of breast disease in Asia have greatly changed in recent years because of screening and women's awareness. There are still many issues including shortage of manpower needed to be solved when applying the national screening methodology. In Asia, the current and future availability of specialists who perform breast cancer screening and long-term management of early breast cancer will be a critical question. Asian Breast Disease Association (ABDA) promotes members networking as a platform for information and knowledge sharing for more for health providers including surgeons, oncologists, pathologists and radiologists.

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BREAST CANCER GENETICS BEYOND BRCA

Michael Gattas

A family history of breast cancer has long been known to be a risk factor for developing breast cancer. Mutations in the *BRCA1* and *BRCA2* genes are found in less than 20% of high risk families. A definition of high risk, moderate risk, and low risk is readily available using the Cancer Australia on line tool, called FRA-BOC[1].

Some of the less common genes associated with breast cancer include, TP53, PTEN, ATM and CHEK2. These seem to explain a small proportion of high risk families. Published data using next generation genome sequence technology in the non BRCA families is lacking. The kConFab study[2] amongst others will hopefully provide some answers as to the cause of familial clustering for breast cancer.

Issues that are appearing in this era include: discovery of many variants of unknown significance, mutations for which penetrance data is lacking, an inadequate number of genetics specialists to see patients, a lack of molecular genetics expertise, direct to consumer testing[3], and testing for polygenic risk.

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Session 2: Defining the Disease

KEYNOTE: NEW IMAGING MODALITIES

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Two full-field digital mammography techniques are emerging with promising results: tomosynthesis (TS) and contrast-enhanced mammography (CEM). Tomosynthesis is based on the acquisition of multiple low-dose mammograms at different angle views that allows 3D reconstruction of the entire breast volume (mm thickness slices). The major goal of TS is to cancel fibro-glandular superimpositions increasing lesion detection and characterization with a decrease in false positive findings. The commercial field is now rich with different acquisition types: angulation range, number of views, continuous versus "stop and shoot" modes, reconstruction algorithms, grid or not). Estimated TS radiation dose per incidence is 1 to 1.2 x one standard view. Ongoing developments include TS-guided biopsy devices and the possibility of having a standard view during TS acquisition (Combo mode or synthetic reconstructed view) avoiding a double irradiation for the patients (TS and standard mammography). The first results of TS performance in screening populations have been published (Oslo; Malmö and STORM trials); all showing that the association of standard mammography + TS provides +2 cancers for 1000 screened women with a decrease in recall rates of 15-17%. The reading time is doubled (Oslo trial). At the end of this year, the complete results of the Oslo trial will be available and we'll see if the reading arm "TS + combo view alone" provides the same performances than as that of TS + mammography. Most of the TS-detected cancers are architectural distortion or spiculated masses in not only heterogeneous dense breasts (51-75%) but also in 25-50% density breasts. The major question is if TS would not be responsible of over-diagnosis (majority of grade I cancers and prevalent cancer detection rate effect with a single round. So, next screening rounds using TS are mandatory to evaluate this[1-3].

CEM relies on the detection of abnormal focal area with increased microvessel density like breast MRI. This imaging technique requires a modified full-field digital mammographic unit with implementation of a copper filter, an extension of the voltage range (45-49 kV) and injection of an iodinated contrast medium to the patient. Dual energy acquisition (one image at low energy and the second one at high energy) is the standard method to generate angiographic images and the two breasts (2 views per breast) can be explored during the first 10 minutes after injection. Interpretation is based on a binary response: contrast uptake present or not. First published series have demonstrated the potential interest of this technique in terms of problem solving approach (superimposition versus true lesion, location of cancers seen on a single view, correlation between MRI and ultrasound and mammography findings), characterization of ambiguous focal asymmetries on standard mammographic views, differentiation between scar vs local recurrence in treated breasts and in the local extent of breast cancer[4]. In a published prospective study of 148 breast lesions (84 malignant and 64 benign), the adjunct of CEM significantly increased the diagnostic accuracy compared to mammography and ultrasound alone. In the local extent of breast cancer, CEM was less sensitive than MRI for additional malignant foci only but significantly more specific with a lower number of false positive results. CEM False negative results were observed for DCIS (but some were detected through calcifications on low energy views) and invasive lobular carcinomas. Compared to MRI, this technique offers many advantages: no problems of contrast uptake background after injection, easy to implement, to perform (10 minutes) and to interpret with optimal understanding for the medical community (mammographic views); it may be useful in patients with contraindications for MRI[5]. At this time, the diagnostic performance of the low energy view compared to the standard mammography seems equivalent[6]. Potential indications of CEM are breast cancer screening in specific groups such as patients with very dense breasts, at intermediate risk of breast cancer (clinical trial on going at Memorial Hospital of New York)[7]. At this time, standardized interventional procedure

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is in progress and new developments are under evaluation such as contrast-enhanced acquisition coupled with TS.

Other emerging modalities (breast dedicated nuclear imaging and Automated 3D whole breast US) will be also presented.

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KEYNOTE: IMPLICATIONS OF THE "NEW" WHO CLASSIFICATION OF BREAST CANCER

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The 4th edition of the World Health Organisation (WHO) Classification of Tumours of the Breast was published in June 2012[1]. With 5 volume editors and 90 contributing authors from 24 countries, this latest volume represents a timely update from the prior 3rd edition of 2003[2]. It is also a stand-alone volume focusing on breast tumours, in contrast with the previous edition which was combined with tumours of the female genital tract. While many of the entities have remained in the classification, some key changes have occurred that represent an evolving understanding of disease that drives taxonomy, underpinned by a pragmatic, broad consensus approach towards categorisation of pathological entities that are clinically meaningful.

In the 3rd edition, **metaplastic carcinomas** were classified according to whether only epithelial elements were present versus both epithelial and mesenchymal components being identified within the tumour. In the 4th edition, a descriptive approach is adopted, with entities documented according to their histological pattern and components, with recognition of specific subtypes such as the low grade adenosquamous cancer and the fibromatosis-like metaplastic cancer which have relatively good prognoses[1]. Myoepithelial carcinoma, referred to in the 2003 WHO histological classification table as malignant myoepithelioma and categorised as a myoepithelial lesion, is grouped with metaplastic carcinoma in the 2012 edition. The rationale behind these aforementioned changes is prompted by the histological heterogeneity of tumours encompassed under metaplastic carcinomas which may not be as well served with a dichotomous historical

division into epithelial and mixed epithelial/mesenchymal categories. The previous approach does not ease recognition of specific clinicopathological entities that have relatively indolent biological behaviour with potentially better clinical outcome that diverges from more aggressive metaplastic tumours. Myoepithelial carcinoma shows both myoid and epithelial differentiation, and is microscopically difficult to distinguish from spindle cell metaplastic carcinoma with which it shares close morphological and immunophenotypical characteristics. Whether there is a substantive difference in prognosis between spindle cell metaplastic carcinoma and myoepithelial carcinoma is also uncertain[1]. It was therefore a practical decision to migrate it to metaplastic carcinoma in the 4th edition.

Mucinous carcinomas were categorised with other mucin producing cancers in the 3rd edition, the latter including extremely rare entities such as mucinous cystadenocarcinoma and columnar cell mucinous carcinoma. Both these rare entities have been removed in the 4th edition, as it was considered that the majority of pathologists would not encounter them in their practice. Discussion on carcinomas with signet ring differentiation is expanded in the 4th edition, with 2 main groups identified – that with intracytoplasmic vacuoles which can be observed in lobular and ductal cancers, and the other form that resembles diffuse signet ring gastric carcinoma. Mucinous carcinomas remain as a key special subtype of breast cancer in both 2003 and 2012 editions.

The classification of **neuroendocrine breast tumours** is revised and updated. In 2003, primary neuroendocrine tumours of the breast were defined as those that morphologically resembled neuroendocrine tumours in the lung and gastrointestinal tract. A threshold for the proportion of tumour cells demonstrating neuroendocrine differentiation was pegged at 50%, and there was also explicit exclusion of ductal NOS (not otherwise specified) tumours which disclosed scattered neuroendocrine positive cells. In 2012, this group of neuroendocrine breast tumours is expanded to include conventional invasive breast cancers, both ductal NOS and special types, that manifested neuroendocrine differentiation on histochemistry or immunohistochemistry without setting a cutoff for the proportion of neuroendocrine positive tumour cells. Neuroendocrine breast tumours in the new classification followed terminologies established in the WHO classification of gastrointestinal tumours[3] – well differentiated neuroendocrine tumour (which resembles carcinoid), poorly differentiated neuroendocrine tumour (synonymous with small cell carcinoma), and invasive breast carcinoma with neuroendocrine differentiation. The move away from the 2003 classification of solid neuroendocrine carcinoma, small cell carcinoma, large cell neuroendocrine carcinoma and metastatic carcinoid, to the 2012 groupings according to widely accepted neuroendocrine taxonomy, allows alignment to universal convention and simplifies the classification into one that can be readily understood and applied.

In 2003, it was acknowledged that literature reports of **invasive papillary carcinoma** likely included both in situ and invasive forms. In 2012, the definition of invasive papillary carcinoma is refined and the restrictive definition implies that true invasive papillary carcinoma in its pure form is extremely rare. Clarification that encapsulated papillary carcinoma should be regarded as in situ (Tis) disease pending further data on their biological nature is provided. Additionally, invasive carcinoma observed accompanying encapsulated papillary carcinoma should be separately subtyped histologically according to morphology, and the invasive tumour size evaluated on its own without incorporating that of the encapsulated papillary carcinoma.

Criteria for **medullary carcinoma** enumerated in the 2003 edition included syncytial architecture in over 75% of the tumour, absence of tubular/glandular structures, diffuse lymphoplasmacytic stromal infiltrate, moderate to marked nuclear pleomorphism of carcinoma cells, and complete histological circumscription of the tumour. It was acknowledged however, that the reproducibility of the diagnosis of medullary carcinoma is low due to difficulties in applying the microscopic criteria. Atypical medullary carcinoma

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was described as a tumour with syncytial architecture, and showing only 2 to 3 of the other criteria. It was recommended that morphological criteria for diagnosing medullary carcinoma ought to be strictly adhered to, in order to preserve its apparent favourable prognosis. Since then however, it has been found that low reproducibility in applying the criteria has promoted a conceptual shift in the 2012 edition to amalgamating these tumours into a group of cancers with medullary-like features, encompassing medullary carcinoma, atypical medullary carcinoma, and invasive carcinoma with medullary features. It was also noted that the relatively improved prognosis of medullary-like cancers is related to the presence of lymphoplasmacytic infiltrates [4-5].

Additional changes in the 2012 edition include disposing of ductal intraepithelial neoplasia (DIN) and lobular intraepithelial neoplasia (LIN) terminologies, redefining the significance of flat epithelial atypia, recognising solid papillary carcinoma as a separate entity among papillary breast lesions. Haemangiopericytoma (currently referred to as solitary fibrous tumour) is deleted from the 2012 edition as it is vanishingly rare in the breast. Myoepitheliosis and adenomyoepitheliosis which were conditions described in 2003 have been merged into myoepithelial hyperplasia. Newly included lesions are the atypical vascular lesion and nodular fasciitis.

In summary, while the framework of breast tumour classification is generally maintained between the 2003 and 2012 WHO editions, there are changes which have an impact on the manner in which we classify some of the tumours. These modifications are premised on new information and understanding of various disease entities, as well as a sensible rational approach towards categorisation that can be readily applied by practising pathologists across broad geographic zones globally.

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NEXT GENERATION TECHNOLOGY

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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. Among women with breast cancer in western countries, 30%-40% will develop metastatic disease. The examination of the standard H&E section is still an efficient, cost-effective and powerful mode of providing data 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.

Over the last two decades, a large number of new technologies have become available to probe the molecular profiles of cancers and their precursors. These methods include analysis of DNA (aCGH, next generation sequencing, SNP), expression profiling and RNAseq, proteomic analysis, methylation profiling, study of non-coding RNA and exosomes. These methods are providing an unparalleled insight into the workings of cancer cells.

A big challenge is the bioinformatics tools and expertise needed to integrate the information and hence provide a detailed map of the networks important in the development and maintenance of the cancer cell and its propensity to survive and disseminate to distant sites.

The knowledge from these new technologies promises to change our basic understanding of cancer biology and unravel new targets for prevention and treatment of breast cancer.

PREDICTIVE BIOMARKERS IN THE CONTEXT OF NEOADJUVANT THERAPY FOR BREAST CANCER

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It is recognised that only a subset of patients benefit from particular modalities of therapy, with response dependent on the individual patient. Predictive factors are needed to forecast such responses that are best undertaken in a clinical trial setting. These have mostly been performed in the adjuvant context requiring several thousand patients and extended follow up. More recently it has become appreciated those similar randomised neoadjuvant trials where chemotherapy and/or hormonal therapy are administered to patients before definitive surgery is a powerful model for the identification of prognostic and predictive markers. These trials require relatively small numbers of patients and have an accelerated timeline such that hypotheses for any particular marker can be ascertained within 1-2 years since tumour response is used as a surrogate of survival. In addition, tumour biopsy material that is available before and after systemic therapy in patients at diagnosis and definitive surgery provides valuable material to study the interaction between biological markers and treatment. We have used this approach to identify predictive markers for patients with ductal carcinoma *in situ* (DCIS) for which we are currently unable to predict *individual* patient's risk. Using a training set of 95 tumours from women with pure DCIS, we immunostained for proteins involved in cell survival, hypoxia, growth factor and hormone signaling shown to be important in invasive breast disease. A generalised linear regression with regularisation and variable selection was applied to a multiple covariate survival analysis with recurrence-free survival that identified COX2 to be a predictor of recurrence. COX2 was then validated in an independent cohort of 58 patients with pure DCIS. The clinical role of a COX-2 targeting agent was then tested in a proof-of-concept neoadjuvant randomised trial. COX-2 expression was an independent prognostic factor for early relapse in the training ($p=0.0001$) and independent validation cohort COX-2 ($p=0.002$). There was no significant interaction with other clinicopathological variables. A statistically significant reduction of Ki-67 expression after treatment with exemestane ± celecoxib was observed ($p<0.02$) with greater reduction in the combination arm ($p<0.004$). Concomitant reduction in COX-2 expression was statistically significant in exemestane and celecoxib arm ($p<0.03$) only. COX-2 may predict recurrence in patients with DCIS aiding clinical decision-making. A combination of an aromatase inhibitor and celecoxib has significant biological effect and may be integrated into treatment of COX2 positive DCIS at high risk of recurrence.

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Session 3: Prevention and Screening Strategies

KEYNOTE: RISK REDUCING MASTECTOMY AND RECONSTRUCTION FOR WOMEN AT HIGH PERSONAL RISK OF BREAST CANCER

Andrew Baildam

Over the last two decades there has been a substantial rise in our knowledge of inherited breast cancer. Women at very high levels of risk of the disease can be identified, but how to manage them is both a dilemma and a controversy. There are new recommendations for reducing breast cancer risk using hormonal medications, but the level of risk reduction still falls far short of that after surgical removal of breast tissue. Until another reliable risk-reducing measure is developed, risk-reducing surgery will remain a mainstay of management in women at very high risk who want to reduce substantially their chances of developing breast cancer. The presence of a significant family history is the strongest risk factor for the development of breast cancer. Even at extremes of age, the presence of a *BRCA1* mutation confers significant risks. A 25-year-old woman who carries a mutation in *BRCA1* has a greater risk of developing breast cancer in the following decade than a woman aged 70 years in the general population. About 4–5% of breast cancer is thought to be due to inheritance of a high-penetrance, autosomal-dominant, cancer-predisposing gene.

Many women consider or undergo risk-reducing mastectomy (RRM) if found to be mutation carriers for *BRCA1* or *BRCA2*. The efficacy of surgical procedures for reducing the risk of breast cancer is controversial, although it would appear that the residual risk of breast cancer depends on the amount of residual breast tissue following the surgical procedure. It would be ideal to perform a prospective randomized clinical trial where women with the same risk were randomized to either intensive surveillance or risk reducing surgery, but it would be difficult to recruit women to such a type of trial and so it is unlikely to happen. Uptake rates even for BRCA mutation carriers vary enormously across countries and cultures. Protocols should be in place to deal with requests for RRM at all cancer genetics and oncoplastic clinics.

The first study to demonstrate that women with a high risk of breast cancer can significantly reduce their subsequent incidence of the disease with RRM was published in 1999[1]. This was followed by a Dutch study that confirmed risk reduction in those at highest risk, *BRCA1/BRCA2* carriers[2]. Current evidence would suggest that RRM is associated with an approximately 90–95% reduction in risk[3].

Data from Manchester, show that 6% of women who are at 1 in 4 (31/902) lifetime risk or above seek further advice about RRM and 1.8% (16/902) have undergone surgery; this rises to 6% (49/798) in those at 40-45% lifetime risk. Although the uptake in *BRCA1/2* carriers tended to be early, there was a continued increase in uptake so that by 7 years the actuarial uptake for RRM for *BRCA1* carriers was 60% and 43% for *BRCA2* carriers.

The mean expected rate of breast cancer for our cohort of high-risk women is 1 % annually, reflecting a lifetime risk that ranges from 25% to 80%. To date although RRM can reduce risk of breast cancer, it has not been proven to have a survival benefit.

Most European centres that undertake RRM do so within a multidisciplinary team of geneticists and specialised surgeons, and management is done along the lines of adopted protocols. The first imperative is to establish specific risk calculations for individual women, and to determine whether there is the possibility of gene testing if there is a known breast cancer related gene mutation within the family. The family history needs confirmation – the presentation of a fraudulent family history in order to obtain surgery inappropriately is sometimes encountered. There are specific computer programs available to calculate risk, including Tyrer–Cuzick, Cyrillic and BRCAPRO.

After a psychological assessment, at least two detailed surgical consultations are needed to discuss the types of mastectomy and breast reconstruction procedures available and their techniques, limitations, outcomes and potential complications. Many women may have little understanding of the extent and nature of risk-reducing surgery, with or without breast reconstruction. They may initially regard RRM as a relatively minor cosmetic procedure, and this may be reinforced by family or friends. The objective of surgery must be explained - to reduce the incidence of breast cancer, relieve anxiety and ultimately diminish breast cancer mortality. Any procedure should reduce risk in a way that balances risk reduction with aesthetic outcome and function, and quality-of-life concerns.

The most complete resection is achieved by traditional total mastectomy. For most the idea of simple total bilateral mastectomy without breast reconstruction does not achieve a balance between risk reduction and cosmetic outcome. Mastectomy with breast reconstruction can be offered to almost all women, with careful evaluation of the breast and body shape to advise on the most appropriate reconstruction options for each individual. Conservation of the natural NAC is controversial, as its preservation confers a small but unknown increase in residual risk. If preserved, loss of NAC sensation or even NAC loss from ischaemia may rarely result; nevertheless, a high proportion of women do opt for NAC preservation, and there is no evidence thus far to suggest that this is inappropriate. There are relative contraindications to surgery, especially if individual risk cannot be substantiated, a gene test result is imminent, or surgery is not the woman's own choice but that of her partner or family, or reasons for choosing surgery are 'cosmetic'rather than 'oncological'.

Innovations in breast surgery over the last few years have resulted in a wide range of mastectomy approaches and incisions, and a full repertoire of reconstruction techniques. These should be presented and discussed in detail at the surgical consultation. Women who opt for RRM with reconstruction have the choice of skin-sparing mastectomy techniques together with immediate reconstruction using expander/implants or myocutaneous flaps, chiefly the latissimus dorsi (LD) flap or the lower abdominal DIEP flap. LD flaps can be used alone if there is sufficient tissue on the back to transfer into the breast defect, the autologous LD flap, or it is used more commonly, with an implant to increase volume and projection when fatty tissue overlying and adjacent to the LD muscle is inadequate.

For a majority the relative 'simplicity' of an implant-based reconstruction makes these the first choice, and many women opt for an immediate submuscular tissue expander placement. There are three main surgical approaches used: horizontal/ oblique, Wise pattern incisions and peri/ circumareolar approaches, similar to the Benelli mastopexy-type incision.

The need of more and better breast reconstruction options after mastectomy has resulted in the increase in the number and types of different reconstructive techniques to achieve the best aesthetic outcomes based on an individualised approach based on a woman's breast size, desired outcome and technical feasibility. The use of acellular dermal matrices and similar materials highlights the way that such surgery is developing. The placement of an acellular dermal matrix can also be used in combination with fat grafting to achieve softer breast reconstructions.

After risk reducing surgery, women should have a prolonged follow up protocol and should be reviewed annually at a multidisciplinary clinic. Long term aesthetic outcomes and patient satisfaction should be assessed, and if necessary surgical interventions may be needed to sustain or to improve the aesthetics. Problems do arise and when necessary other members of the team should be involved. Clinical examination by palpation of the breasts is considered to be adequate, as remaining breast tissue is very superficial in all types of surgical procedure.

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REINVENTING BREAST CANCER SCREENING FOR THE 2020S

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Breast cancer screening programs have been implemented in many countries as long as 30 years ago (Sweden). Screening organizations vary among countries: centralized versus decentralized organizations, age ranges (starting at 40, 47 or 50 years to 70, 74 years), interval time between rounds (every 2 or 3 years) but fundamental principles are common: training of radiographers and radiologists, quality control of mammographic units, second reading and evaluation of program efficiency. If breast cancer is well-identified as the first female cancer in the public, violent and continuous controversies have recently emerged in newspapers about over-diagnosis (and so over-treatment), false positives and inefficiency to detect early and to treat aggressive cancers. The recent positive conclusions of the Euroscreen working group and of the independent panel in UK are good news in this general context[1-2]. These attacks arise paradoxically in a context of increasing general interest about individual risk evaluations (genetic tests, environmental factors, "personalized" medicine concept) where population subgroups in "rich" countries ask for specific screening strategies. The worsening economic background is clearly a new dimension to consider for the near future; for example, Sweden has sold more than half of its breast cancer screening units to a private company (Unilabs). So, from my personal point of view, the priority is to consolidate our national screening programs by communicating clear and detailed information to women about the aims of screening and the status of our knowledge about this disease; this is also very important for obtaining participation of women to clinical trials evaluating different screening strategies as many new imaging techniques are emerging and evolving rapidly. For a 2020s perspective point of view, the major points for breast cancer screening are: replacement or not of mammography by a new test? Will it be an imaging technology or not? Shall we be able to stratify general population in terms of breast cancer risks? Concerning replacement of mammography, tomosynthesis is clearly the most promising and advanced technology (radiation dose similar to 2D mammography, ongoing quality control procedures) with several on-going clinical trials in screening populations[3-4]. Several questions are waiting for answers: value of the synthetic mammographic view compared to standard 2D technique? One versus two TS incidences? Need for a second reading process? Increased risk of over-diagnosis? The alternative to TS could be imaging technologies without radiation such as ultrasound or MRI. US has several limitations: no detection of isolated calcifications, operator-dependency, no second reading process; difficult quality control of US units. Automated 3D whole-breast ultrasound technology is still developing; the acquisition time of one breast is around 20 minutes and the reading time is incompatible with screening workflows; medical community has to be trained whereas the learning curve is very short for TS. It could be an adjunct in the subgroup of women with very dense homogeneous breasts at TS. MRI, because of its limited access and its costs would not be the emerging test in the general population but may become the screening technique in populations with intermediate risks if shorter acquisition protocols are developed and if possible without contrast agents. The alternative for this intermediate risk group could

be contrast-enhanced mammography alone (clinical trial on going) or associated to TS. 2020 is too near from now but the fantastic progress in genomics offer new perspectives in terms of early detection of cancer such as detection tumor DNA, circulating chromatin or cells in blood or serum, and of individual assessment of breast cancer risk using large-scale genotyping technologies[5-6]. In these new research fields, the amount of collected information to treat, to archive and to transfer in medical decisions is the major problem to resolve rapidly in terms of human and informatics resources. Understanding of the early phases of development of cancers is another important research field and it seems urgent that imaging integrates the networks of large biomedical databases not only as providers of tissue samples but also as a real medical specialty.

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SCREENING IN WOMEN WITH DENSE BREASTS

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Different questions are debated in in the medical community concerning breast density: 1) is breast density a significant risk factor of cancer? 2) Because of mammography sensitivity decreases with the amount of breast dense tissue, is it necessary to add or to propose other imaging modalities? So, in women with dense breasts, do we have to implement a specific screening strategy in terms of age at the first round, interval between two rounds (annual, bi-annual) and with which imaging modalities (one, multiple etc...)? For most of our colleagues, breast density is a significant risk factor and for others not, the latter emphasizing that its measurement is not scientifically correct and that it is not possible to separate fibrous from glandular tissues using mammography[1]. It is important to note that the different reported values of relative risks (RR) are related to the choice of the reference category of breast density. Thus, in the meta-analysis published by Mac Cormack et al in 2006, a breast density > 75% is associated to a RR mean value of 4.64 [3.64-5.91] with a reference value of breast density < 5% (RR = 1)[2]. If now we consider that the standard risk in the general population (RR= 1) is a breast density ranged from 25 to 49% (type 2, BI-RADS classification, 49.7% of 50-74 year-old women in the French screening program), the mean RR value for very dense breasts would be around 2. Some published papers have evaluated the risk factor density with this reference category of 25-49% with differentiation between pre- and post- menopausal women. In the premenopausal group, reported mean RRs are 1.62 [1.51-1.75] for a breast density (50-75%) and 2.04 [1.84-2.26] for very dense breasts (density > 75%; in post-menopausal women, reported RRs are 1.35 [1.28-1.42] and

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1.51 [1.35-1.68] respectively[3-4]. So to summarize, more there is dense breast tissue, more the risk of breast cancer increases but the level of risk is modest and concerns premenopausal women. Concerning the imaging strategy to apply in women with dense breasts, studies have been conducted to evaluate other technologies. Implementation of digital mammography has improved cancer detection in dense breasts. Clearly, one may reasonably consider that tomosynthesis (TS) will be the next step (see abstract about new imaging modalities). For ultrasound, the ACRIN trial 6666 (performance of ultrasound (US) screening in patients at high risk, heterogeneous group) has shown that a single US round yielded an additional 1.1 to 7.2 cancers per 1000 women but with a substantially increase in the number of false positives. In a recent publication, adjunct of US in asymptomatic women with negative mammograms added 1.45 cancers per 1000 women (1.95 in the subgroup < 50 years and 2.21 in the subgroup with dense breasts); the US generated invasive assessment was 1.9% (422/22 131)[6]. So, US could be implemented in screening but its performance will depend on the US homogeneity of breast tissue; if we consider that TS will be the screening reference method in a near future, only women with very dense and homogeneous breasts at TS will benefit from additional US. We have to wait for technical improvement of automated 3D US (at this time, acquisition time of 20 min...) to see if this technique may replace 2D handhold US. Modeling studies suggest starting screening at 40 years for women with very dense breasts, every 2 years to obtain a positive benefits/arms balance[7]. There are no prospective clinical trials concerning MRI screening in patients with dense breasts and without significant other risk factors. Nevertheless, the American Cancer Society in its last recommendations considers that dense breasts may be a potential indication for MRI screening[8]. Interestingly, it seems that the risk would not be related to the density level but to the degree of background enhancement at MRI[8]; so, a perfused dense tissue would be at more risk that a "quiet" dense tissue without enhancement (9). MRI screening must be discussed only in women with dense breasts AND with other associated risk factors such as family history of breast cancers, personal history of atypical epithelial hyperplasia or breast cancer (ex: 40-49 year old woman + very dense breasts + a first-degree relative with breast cancer < 59 years => RR = 4). A lot of work is still needed to make more precise the real level of risk in women with dense breasts! Breast density just begins to be incorporated and tested in risk models and new automatic and reproducible quantification methods using digital mammography or MRI are available and will help to give interesting data in a near future especially in the individual longitudinal follow-ups of breast density over time.

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Session 4: Benign Diseases Symposium

SHOULD THE PATHOLOGIST REPORT ATYPICAL HYPERPLASIAS?

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Atypical hyperplasia of the breast encompasses both atypical lobular hyperplasia and atypical ductal hyperplasia[1]. These conditions are regarded as risk lesions, in that their diagnosis carries an increased risk of subsequent breast cancer development in the affected woman of 4-5x that of the general population.

Atypical lobular hyperplasia (ALH), together with lobular carcinoma in situ (LCIS), are classified under the umbrella term of lobular neoplasia. Both ALH and LCIS are characterized by a population of uniform small non-cohesive cells with or without pagetoid extension along the ducts. ALH and LCIS differ histologically according to the extent of the proliferation, with LCIS also implicating a higher risk of subsequent breast cancer development of about 8-10x that of the general population. Often, precise distinction between ALH and LCIS is difficult and the lesions appear as a continuum of changes which lend support to the usage of lobular neoplasia as an overall unifying term. Briefly, classic LCIS is diagnosed when the discohesive lobular neoplastic cell population distends and/or distorts more than half the acini of a lobule; lesser degrees of involvement are referred to as ALH. A unique immunophenotypical feature of lobular neoplasia is the loss of expression of the intercellular adhesion molecule, e-cadherin, which has been used as a supportive adjunctive diagnostic trait.

ALH is often discovered as an incidental lesion as it does not form a mass nor is it associated with calcifications. Its diagnosis on core biopsies does not mandate further excision – close radiological correlation is needed to ascertain if histological findings are concordant, in which case no further action, apart from continued surveillance related to its risk status, is required. ALH found in excisions warrant follow-up. LCIS on core biopsies often lead to excision, and if it represents the worst lesion on excision, the recommendation is for surveillance and patient counseling for risk reduction[2].

Atypical ductal hyperplasia (ADH) is defined by the presence of monomorphic, evenly placed epithelial cells within the terminal duct-lobular unit, closely resembling low nuclear grade ductal carcinoma in situ. ADH was encountered in 4% of benign breast biopsies prior to the mammographic era, but among radiologically detected breast abnormalities, ADH is observed in about 10% of such benign biopsies, often associated with calcifications.

Histologically, ADH is diagnosed only when a low grade ductal carcinoma in situ (DCIS) is being seriously contemplated. In contrast to low grade DCIS, the lesional extent of ADH is limited, being not more than 2mm in overall size or involving less than 2 duct spaces. Larger lesions with similar cytoarchitectural alterations are diagnosed as low nuclear grade DCIS. This distinction of ADH from DCIS is arbitrary and represents a pragmatic threshold that avoids diagnosing very small low grade lesions as DCIS, hence preventing overtreatment. Debates regarding overdiagnosis in mammographic breast screening programs have often revolved around diagnoses of low grade DCIS which tend to be indolent biologically.

Finding ADH on core biopsy requires further excision to rule out the possibility of a larger lesion which fulfills criteria of low grade DCIS. Some authors have advocated using descriptive terminology of an 'atypical intraductal proliferative lesion' on core biopsy pending complete histological evaluation and final categorization on excision.

ADH observed in excision specimens does not require specific action apart from continued surveillance due to the risk its presence poses for subsequent breast cancer

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development. ADH at the surgical margins of an excision however, may indicate a larger lesion that is not completely sampled. In such situations, clinicoradiological correlation is recommended to determine if further excision to fully assess the lesional extent is required.

Both ALH and ADH belong to the low grade neoplasia family of lesions that include flat epithelial atypia (FEA), LCIS, DCIS of low nuclear grade, and low grade invasive breast cancers[3].

Should the pathologist report atypical hyperplasias?
The diagnosis of atypical hyperplasia in the breast, especially on core biopsies, often evokes feelings of frustrated uncertainty by the managing clinical team, as there is no universal prescription of whether further excision will be beneficial. Nevertheless, atypical hyperplasias represent important lesions that ought to be recognized and communicated in pathology reports, as there may be undersampling of low grade DCIS in the context of ADH observed on core biopsy; and ALH on core biopsy may merely be an incidental lesion that distracts from the true radiological abnormality which may or may not have been sampled, underscoring the critical importance of radiologic-pathologic correlation. The finding of ALH on core biopsy also spurs the search for associated lesions of the low grade neoplasia family.

While FEA is not strictly an 'atypical hyperplasia', its diagnosis on core biopsy provokes discussion that parallels that of atypical hyperplasia. Part of the confusion may be related to prior reference to FEA as being equivalent to DCIS of the clinging type[4] which led to overtreatment decisions. There was also the concept that FEA is a precursor lesion that could be regarded as having a risk value similar to atypical hyperplasia, and that FEA on core biopsy should be followed with open excision[5]. The 4th edition of the WHO classification of breast tumous has clarified that FEA is a likely precursor of ADH, and that the risk for subsequent breast cancer development following a diagnosis of FEA is substantially lower than that accompanying ADH or ALH[1]. Finding FEA on core biopsy therefore, should prompt radiologic-pathologic correlation to determine if the radiologically detected lesion has been appropriately explained on pathology. Open excision is not mandated. A multidisciplinary decision is needed to determine the subsequent course of action. FEA on excision biopsy does not require specific management modifications.

Atypical hyperplasia (ADH, ALH) as the worst lesion on excision specimens warrants continued surveillance, usually with mammography, and patient counseling for risk reduction.

In order to harness the true clinical relevance of the diagnoses of ALH and ADH, there is need for pathologic accuracy and consistency in their recognition. This translates to having reproducible criteria that can be readily followed by practicing pathologists. Mimics such as florid usual ductal hyperplasia and myoepithelial hyperplasia for ADH and ALH respectively, need to be excluded. On the other end of the spectrum, ADH should be distinguished from low grade DCIS through careful morphological appraisal of cytoarchitectural changes and lesional extent. Similarly, ALH should be separated from LCIS, in particular morphologic subtypes such as pleomorphic, necrotic and mass forming LCIS with presumably more aggressive.

OPTIMAL TREATMENT OF THE ATYPICAL CORE BIOPSY

Bruce Mann

Aim of treatment is to alter the natural history of the disease, to reduce mortality and to reduce morbidity. Optimal treatment will achieve both of these goals at minimum cost to the patient and the health care system.

Atypical lesions include atypical ductal hyperplasia, atypical lobular hyperplasia, papillomas, radial scars and lobular carcinoma in situ. All have been associated with an increased risk of a subsequent malignancy that may be ipsi- or contra-lateral, and have been variably associated with upstaging to either DCIS or invasive cancer on surgical excision. Atypical core biopsy is a management challenge because the lesion itself is not dangerous, but because of the risk of a more serious lesion in the vicinity.

Multiple series have demonstrated that upstaging does occur. Some particular lesions may be associated with a lower rate of upstaging that means that observation is reasonable. New technologies may allow percutaneous excision of selected atypical lesions to safely omit surgical excision.

These issues will be reviewed.

DIAGNOSIS OF BIPHASIC LESIONS OF THE BREAST

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Biphasic lesions of the breast refer to conditions composed of a dual population of epithelial and mesenchymal/mesenchymal-like cells. There is a wide spectrum of lesions that fall within this definition ranging from benign epithelial-myoepithelial neoplasms such as pleomorphic adenoma, spindle cell adenomyoepithelioma; to metaplastic carcinoma with mesenchymal-like elements; and the unique group of fibroepithelial tumours encompassing the fibroadenoma and phyllodes tumour. This discussion focuses on the diagnosis of fibroepithelial neoplasms.

The fibroadenoma is a common benign fibroepithelial neoplasm, occurring mostly in women of reproductive age. Its microscopic diagnosis is based on growth of both epithelium and stroma in either pericanalicular or intracanalicular growth patterns. Hyalinisation, myxoid change and calcifications can occur. Focal or diffuse stromal hypercellularity (especially in women aged < 20 years), bizarre multinucleated giant cells (which do not have any biological significance) can be seen. Mitotic figures are uncommon, but can be observed in young or pregnant patients.

The cellular fibroadenoma shows hypercellular stroma and may resemble the benign phyllodes tumour. Complex fibroadenoma contains cysts >3 mm in size, sclerosing adenosis, epithelial calcifications, or papillary apocrine hyperplasia[1]. Juvenile fibroadenoma occurs predominantly in adolescents, showing increased stromal cellularity, a pericanalicular growth pattern and usual ductal hyperplasia featuring delicate micropapillary epithelial projections. Juvenile fibroadenoma can assume enormous sizes, referred to by some as giant fibroadenomas. However, other authors have restricted 'giant fibroadenoma' to massive fibroadenomas with usual histology, with sizes exceeding 5 cm[2-3].

Atypical ductal or atypical lobular hyperplasia, when confined within the fibroadenoma without involvement of surrounding breast epithelium, is apparently not associated with an increased relative risk for subsequent development of cancer[4].

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Cellular fibroadenomas and benign phyllodes tumours fall into the same spectrum of benign fibroepithelial lesions, sharing similar histologic features, with both possessing a low potential for local recurrence[5-7]. This differentiation is particularly difficult in core biopsies, and if the differential diagnosis includes phyllodes tumour, the lesion would be best classified after excision[8-9].

Histological clues favouring a diagnosis of phyllodes tumour on core biopsies of cellular fibroepithelial lesions are fragmentation, pleomorphism, increased mitoses and percentage of stroma, and older age[10-13]. Multidisciplinary discussion is encouraged for prioritizing cases for immediate surgical management.

The phyllodes tumour is characterized by double-layered epithelium arranged in clefts surrounded by hypercellular stroma, with elaboration of prominent fronded leaf-like structures. They are classified into benign, borderline and malignant grades based on a constellation of histological features: degree of stromal hypercellularity, mitoses, cytological atypia, stromal overgrowth and nature of the margins[14]. Most are benign, but recurrences are not uncommon and a relatively small number of patients develop haematogenous metastases, particularly following a diagnosis of malignant phyllodes tumour. Depending on the bland or overtly sarcomatous characteristics of their stromal component, these tumours display a morphological spectrum mimicking cellular fibroadenomas and pure stromal sarcomas.

Phyllodes tumours account for 0.3–1% of all primary breast tumours and constitute 2.5% of all fibroepithelial tumours. They occur predominantly in middle-aged women (average age 40–50 years) about 15–20 years older than for fibroadenomas. In Asian countries, phyllodes tumours may occur at a younger age (average age, 25–30 years). Malignant lesions develop about 2–5 years later than benign ones.

Clinically, patients present with a unilateral, firm, painless breast mass. Very large tumours (> 10 cm) may stretch the skin with striking distension of superficial veins. Tumours of 2–3 cm in diameter are becoming more common due to mammographic screening, but the average size remains around 4–5 cm. Histologically, there is an enhanced intracanalicular growth pattern with leaf-like projections. Because of the structural variability of phyllodes tumours, selection of one block for every 1 cm of maximal tumour dimension is appropriate. Histological examination of the interface with normal breast tissue is critically important to ascertain the invasive or pushing nature of the borders. In rare examples, adjacent fibroadenomatoid change or periductal stromal hyperplasia can be difficult to distinguish from the infiltrative border of a phyllodes tumor. Phyllodes tumours should be graded according to the areas of highest cellular activity and most florid architectural pattern.

Benign phyllodes tumours are more cellular than fibroadenomas. The spindle-cell stromal nuclei are monomorphic and mitoses are rare, usually less than 5 per 10 high-power fields[14]. Stromal cellularity may be higher in the zone immediately adjacent to the epithelium, sometimes referred to as periepithelial or subepithelial stromal accentuation. Presence of occasional bizarre stromal giant cells should not be taken as a mark of malignancy[15]. Margins are usually well-delimited and pushing, although very small tumour buds may protrude into the surrounding tissue. Such expansions may be left behind after surgical removal and are a source of local recurrence.

Malignant phyllodes tumours are diagnosed when there is a combination of marked nuclear pleomorphism of stromal cells, stromal overgrowth defined as absence of epithelial elements in one low power microscopic field containing only stroma, increased mitoses (≥10 per 10 high power fields), increased stromal cellularity which is usually diffuse, and infiltrative borders. Malignancy is also diagnosed when malignant heterologous elements are present even in the absence of other features. Owing to overgrowth of sarcomatous components, the epithelial component may only be identified after examining multiple sections with diligent sampling of the tumour.

Borderline phyllodes tumour is diagnosed when not all the adverse histological characteristics found in malignant lesions are present. While borderline phyllodes tumours have the potential for local recurrence, they usually do not metastasize.

The main differential diagnosis for benign phyllodes tumour is fibroadenoma having an accentuated intracanalicular growth pattern accompanied by stromal cellularity. This distinction is arguably arbitrary and a matter of judgement. A phyllodes tumour should have more cellular stroma along with formation of leaf-like processes. The degree of hypercellularity that is required to qualify a phyllodes tumour at its lower limit is difficult to define, but stromal cellularity should be mostly present throughout the lesion, or closely accompanying the leafy fronds, to qualify as benign phyllodes tumour. Sometimes, separating a cellular fibroadenoma from benign phyllodes tumour can be very challenging. As this differentiation may not be significant because of similar clinical outcomes in terms of reported recurrences [5-7,16], it is recommended that a diagnosis of fibroadenoma is favoured when there is histologic ambiguity, to avoid overtreatment. Some authors advocate using the term 'benign fibroepithelial neoplasm', with explanation of the diagnostic difficulty as needed.

Malignant phyllodes tumour may be confused with pure breast sarcoma. In such cases, the diagnosis depends on finding residual epithelial structures. The clinical impact however, of these two entities appears to be similar. Metaplastic carcinoma is also a differential, but immunohistochemical demonstration of epithelial differentiation helps resolve the diagnosis.

As the histologic features of phyllodes tumours fall into a continuum, some are difficult to precisely grade. Since malignant lesions are the most likely to cause metastasis and death, it is important to identify this group. So defined, one study revealed that malignant phyllodes tumours demonstrated a metastatic and death rate of 22% whereas no distant metastases were seen in borderline and benign tumours over the same follow-up duration[16]. Strict diagnostic criteria for diagnosing malignant tumours should be used in order to avoid overtreatment.

Local recurrences can occur in all phyllodes tumours at an overall rate of 21%, ranging from 10%-17%, 20%–25% to 23%–27% for benign, borderline and malignant tumours respectively. These recurrences often mirror the microscopic pattern of the original tumour or show dedifferentiation with microscopic upgrading (in 25%–75% of cases)[16]. Many histological features have been reported to possess predictive value for local recurrences, and status of surgical margins appears to be the most reliable. Other less consistent predictors include stromal overgrowth, classification/grade and necrosis[14,17]. A recent study found that a formula incorporating stromal atypia, mitotic rate, overgrowth and surgical margins was able to predict recurrence free likelihood for the individual patient (www.phyllodes.com)

Distant metastases, seen almost exclusively in malignant phyllodes tumours, have been reported in nearly all internal organs, but the lung and skeleton are the most common sites of spread[18]. Most metastases consist of stromal elements only. Axillary lymph node metastases are rare, but have been recorded[19-20]. Local recurrences generally develop within 2 years, while most deaths occur within 5 years of diagnosis.

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PHYLLODES TUMOURS

Kylie Snook

Phyllodes tumours are uncommon lesions of the breast representing 2-3% of all fibroepithelial tumours and less that 1% of all breast tumours. Women age 35-55 are more commonly affected although there have been reports of phyllodes tumours in men. Phyllodes tumours can be difficult to distinguish clinically from a fibroadenoma (which is 50 times more common), but accurate diagnosis is important due to their propensity to recur locally and potential to metastasize.

Apart from Li-Fraumeni syndrome, there are no known predisposing factors for the development of phyllodes tumours. Current evidence suggests that phyllodes tumours develop when the interaction between epithelium and stroma is lost such that growth

of stroma becomes independent of the growth of epithelium. Stromal proliferation, angiogenesis and matrix alterations seem to be involved in progression to malignancy.

The WHO Classification recommends classifying phyllodes tumours into benign, borderline and malignant lesions based on histological criteria (mitotic activity, stromal cellular atypia, stromal overgrowth and tumour margins). Unfortunately the pathological findings do not always reflect the clinical behaviour of the tumour.

Phyllodes tumours commonly present as a rapidly growing solitary painless breast mass. Around 20% present as an impalpable lesion found on screening mammography. Clinical findings are usually indistinguishable from that of a large fibroadenoma – a firm, well-circumscribed, rounded or lobulated lesion. As they enlarge they can cause breast distortion or enlargement, or cause ulceration of the skin due to pressure necrosis.

There are no imaging features that can accurately distinguish a large fibroadenoma from phyllodes tumour. Diagnosis is often made after surgical biopsy, when the entire lesion is examined. Phyllodes tumours can be difficult to distinguish from fibroadenomas on fine needle aspiration and core biopsy due to the heterogenous nature of the lesions.

The treatment of phyllodes tumour is surgical excision. There are conflicting data with regard to the optimal margin of excision. Traditionally a margin of 1cm was recommended for all phyllodes tumours. More recently it has been shown that negative margins (or even involved margins) in the treatment of benign phyllodes tumours are associated with a low recurrence rate. It is accepted that borderline, malignant and recurrent lesions require a negative margin to reduce the incidence of local recurrence, but there does not appear to be a relationship between positive margins and the development of metastatic disease.

As the diagnosis of phyllodes tumour is often made after surgical excision, re-excision of margins for borderline or malignant lesions is recommended for security. Mastectomy +/- reconstruction may be necessary for very large lesions or those lesions which cannot be removed with an acceptable cosmetic result despite oncoplastic techniques. Routine axillary nodal assessment is not recommended as phyllodes tumours, like sarcomas spread via the haematogenous route and rarely spread to the axillary lymph nodes.

The WHO reports an overall recurrence rate of 21% (17% benign, 25% borderline, 27% malignant lesions) with an overall metastatic rate of 10% (benign 0%, borderline 4%, malignant 22%). The most common sites for metastases are lung, soft tissue, bone and pleura.

There is no clearly defined role for adjuvant chemotherapy or radiotherapy for non-metastatic phyllodes tumours. Some studies have shown better local control with radiotherapy especially in borderline and malignant cases.

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THE EMERGING ROLE OF BREAST PHYSICIANS

Susan Fraser and Lisa Erzetich

Breast Physicians like their counterparts in the United Kingdom have existed in Australia and New Zealand for over 30 years. Over this time they have evolved to meet the rapidly expanding workforce requirements in the area of breast medicine. Breast Physicians provide holistic care for women with both benign and malignant breast diseases.

The Australasian Society of Breast Physicians has about 50 members and has developed its own training program and Fellowship examination.

The roles of Breast Physicians include:

- Working in BreastScreen Australia facilities as part of the multidisciplinary team – reading mammograms and as clinicians in assessment clinics, examining patients and performing a range of breast interventional biopsies.
- Working in diagnostic breast clinics where again they can be examining patients, performing breast ultrasound, doing biopsies, film reading and counselling.
- Working with breast surgeons in their private rooms or in public hospital breast outpatients clinics engaged in post cancer care – 'survivorship' – or seeing new diagnostic patients.
- Assisting breast surgeons in the operating theatre where they are exposed to the full range of breast surgery and oncoplastic breast procedures.

These varied roles have emerged as the demand for high quality breast diagnostic, screening and post cancer follow up has skyrocketed due to heightened awareness of breast cancer and breast disease and increased incidence of breast cancer in our population (incidence 1 in 14 in the 1980s to 1 in 8 currently lifetime risk).

Breast Physicians are well placed to be advocates for their patients by virtue of their extensive knowledge and expertise across all the disciplines of breast disease and management. In addition, Breast Physicians have evolved to meet the huge workforce demands on breast surgeons and manage the large number of women with benign breast disorders (most diagnostic / symptomatic breast clinics see 90 patients with benign disorders for every 10 with breast cancer who require surgical referral and care).

Session 5: Contemporary Management of the Aggressive Cancer

BREAST CANCER SURGERY: WHAT YOU SHOULD ASK THE RADIOLOGIST FOR?

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Collaboration between radiologists and surgeon is very important to optimize breast cancer – conserving surgery especially in T0 cancers and when oncoplastic surgery techniques are required. The goal is to obtain a one –step surgical procedure with free margins in patients.

Concerning imaging reports: Because many patients underwent multiple imaging examinations (Mx, US, MRI, second-look US etc...) and not rarely in different sites, a GLOBAL report is required explaining clearly how the cancer was detected and with which technology. Concordance between results of the different modalities must be clearly validated. This point is crucial when multiple cancers are diagnosed within the same breast and moreover when they are not detected by the same imaging modalities.

Concerning the location and tumor size: The quadrant distribution is clearly poor and the surgeon should ask for: type of the surrounding normal tissue (fatty or dense), tumor distribution using clock face system (ex: between 3 and 4.30), cancer size (mass) in a radial orientation and in an antero-posterior axis (from the skin and the major pectoralis muscle). For large or multiples clusters of malignant calcifications, tumor extent must be evaluated on magnification orthogonal views only with measurements of the cranio-caudate and transverse maximal diameters (lateral margins for the surgeon).

Concerning the number of cancers: Teach your radiologists to avoid the terms of multifocality or multicentricity and train them to speak about multiple cancers! The radiologists'job is to provide you the precise spatial distribution of each cancer or suspicious associated lesions! Ask for a diagram! This latter will be very useful for discussing percutaneous biopsy strategies (which lesions to biopsy and how?). As for calcifications, in relatively close lesions between them, the global lateral margins (CC and Lateral/Medial axes) have to be evaluated.

Concerning multiple cancers (same breast): Ask for clips during interventional procedures! This approach is well-established for breast cancer requiring neo-adjuvant therapy but not in most of other breast cancer situations. These clips help for a fast and very comprehensive staging using orthogonal mammograms. In case of discordant results (for example: very suspicious MR lesion with benign biopsies under US-guidance) clips are very useful for validating the location concordance of lesions in the different imaging modalities.

Concerning MRI (local staging): The decision to perform a breast MRI examination in a breast cancer patient is the concern of surgeons, the patients and not only the radiologists! MRI benefit/harms balance has to be discussed not only between professionals but also with the patients. As MRI detects additional equivocal findings in approximately 25% of breast cancer patients, second-look imaging (mammography and US) is crucial for the final imaging staging. Thus, 1) ideally, the radiologist that performs MRI has to perform this final workup (global report) and 2) has to be familiar with breast–conserving surgery principles to measure correctly volume excision in patients with multiple lesions.

Lymph node staging: In typically malignant lesions (BI-RADS category 5), the radiologists must explore the axilla before the diagnostic biopsies to avoid false positive results (benign reaction after core biopsies). The surgeons have to explain to the radiologists

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where are preferentially located the sentinel lymph node(s) in the axilla for improving the pre-surgical staging.

Concerning needle localization procedures: The surgeons must be precise in their request for pre-operative needle localizations! In patients that underwent vacuum-assisted biopsies with a clip placement, the radiologists need the diagnostic mammography for validating its good positioning within the breast (possible displacement along the compression axis during stereotactic procedures; so, the information about the incidence and biopsy approach must be notified in the report). Also, when multiple hook wires are necessary to circumscribe calcifications or multiple masses, the surgeon must be precise in discussing with the radiologist the planed lateral margins of the surgical excision. In case of oncoplastic procedures, information about the need or not for a single puncture approach is mandatory (the radiologist chooses the shortest way to target the lesions; so in patients with multiple lesions, different approaches may be decided with consecutive surgical difficulties if a single quadrant surgical approach is chosen - extensive skin dissection to recover hookwires).

In conclusion: The surgeon is not a radiologist and the radiologist is not a surgeon! Comprehensive and common language is required between them for improving patient care.

CURRENT NEOADJUVANT INTERVENTIONS

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Systemic neoadjuvant interventions include chemotherapy, targeted therapy such as Herceptin, and endocrine therapy. In theory, systemic therapy given in advance of surgery for breast cancer might seem likely to provide superior endpoints in terms of disease-free and overall survival, but this has never been shown in randomized trials to be the case. Large randomized studies such as NSABP B-18[1], which randomized women with operable breast cancer to receive four courses of AC (cyclophosphamide, doxorubicin) before or after surgery and the NSABP B-27[2] which randomized patients with operable breast cancer to receive:

1) AC before surgery with no further chemotherapy,
2) AC and taxol before surgery or
3) AC before surgery and taxol afterward

have each shown no difference in survival regardless of chemotherapy being given before or after surgery. In the NSABP B-27 study, the addition of the taxane either before or after surgery did provide improved disease-free survival (DFS).

In these studies, the achievement of a pathologic complete response (pCR) is associated with better survival, but the pCR is likely only a marker of better outcome, not the cause of it. In theory if one could identify early non-responders and switch their systemic treatment to a more effective one a better outcome might be achieved. In studies such as the Aberdeen trial[3] however, patients did better when switched from their initial anthracycline to a taxane, whether they were responding well to the initial anthracycline or not. Therefore, the use of the anthracycline response to guide subsequent chemotherapy was not shown to be particularly helpful. There have been few other trials of this nature. The design of such trials is difficult since it involves randomizing patients to receive changes in chemotherapy guided by poor or good early responses versus undergoing a standard chemotherapy algorithm regardless of response. Such a randomization may be intuitively unattractive, therefore the ethical and logistic issues associated with such a trial are challenging.

It has become very clear that patients with ER positive disease are also less likely to have a pCR to endocrine therapy[4]. Does this mean they should not be treated with endocrine therapy, which seldom results in a pCR in part because disease recedes more slowly? Indeed patients with ER positive disease are less likely to have a pCR after chemotherapy which does not necessarily mean that they will ultimately do more poorly. Reports from these types of trials are also plagued by definitions of pCR, which may include complete regression of invasive tumour in the breast, complete regression of invasive tumour in the breast and nodes, or complete regression of all invasive tumour and of all **ductal carcinoma in situ** (DCIS)[5].

One advantage that is clearly shown is that giving neoadjuvant chemotherapy in both NSABP B-18 and NSABP B-27 resulted in a higher percentage of patients being able to have breast conserving surgery (BCS) rather than mastectomy. However, this is somewhat offset by a higher risk of in-breast recurrence in both of these trials even though BCS was always followed by breast irradiation[1-2]. Furthermore, of course in the locally advanced breast cancer setting, starting out with systemic therapy prior to surgery and radiation can reduce a technically unresectable tumour to one in which complete clearance of the tumour and all its margins may be possible. In patients with large or locally advanced breast cancer this is clearly a superior approach and in this setting multidisciplinary coordination is crucial for decision making. Outside of the locally advanced technically unresectable setting, however, neoadjuvant systemic therapy is not mandatory but rather optional. There is no question, however, that observing patients during the course of neoadjuvant systemic therapy with baseline and repeated biopsies and/or imaging may provide a powerful model for exploring new therapies.

Trials such as the NOAH Study[6] in which patients were randomized to receive neoadjuvant and post-surgical Herceptin versus no Herceptin, showed not only improved pCR rates due to the neoadjuvant Herceptin, but improved event-free survival and overall survival for the HER-2 treated population. Pathologic complete response rates with the addition of Herceptin were nearly double (43% vs. 23%) in the patients who received neoadjuvant as well as adjuvant Herceptin. However, whether similar long-term endpoints would have been achieved by giving Herceptin only in the adjuvant setting is unclear. The NeoALLTO trial has shown higher pCR rates for the combination of Herceptin and **lapatinib but this was accompanied by higher toxicity and less ability to deliver the regimen**[7].

In conclusion, systemic neoadjuvant therapy is indicated for locally advanced and/or inflammatory breast cancer. With resectable tumours, neodjuvant therapy results in more likelihood of breast conserving surgery at the price of a higher rate of in-breast recurrence. The neoadjuvant model while intriguing for the exploration of new systemic approaches, is currently only as effective as adjuvant therapy in terms of long term distant disease recurrence and survival outcomes. A multidisciplinary approach for decision making is clearly advantageous in all of these settings.

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OPTIMISING COSMESIS IN HIGH RISK BREAST CANCER

Andrew Baildam

This talk will present the developing techniques of oncoplastic breast surgery, and to summarise the published literature on its oncological safety and outcomes.

Wide excision of a cancer can involve the removal of significant breast volume, and be followed by radiotherapy: poor aesthetic outcomes after breast cancer surgery are a problem. The total package of oncoplastic breast surgery has been defined as provision of appropriate cancer resection, skin-sparing techniques, total and partial reconstruction with a full range of techniques - both immediate and delayed - for wide local excision and mastectomy, and correction for any resultant breast asymmetry using implants/expanders, reduction or mastopexy for the contralateral breast.

Breast conservation with oncoplastic techniques extends the role of breast conservation for some women with larger breasts or larger tumours who otherwise would of necessity undergo mastectomy. Paramount is the need to plan and execute placement and closure of scars carefully and to weigh optimally the oncological and aesthetic outcomes.

Approaches involve breast volume displacement or replacement, often with modification of the appearance also of the opposite unaffected breast to pursue symmetry. Extensive replacement requires total breast remodelling, as in the therapeutic mammoplasty, or in the round block technique of central segmentectomy including the nipple areola complex. Therapeutic mammoplasty often requires contralateral breast reduction. Recent work has concentrated on innovation of highly complex local flaps, extending further the range of techniques.

Published series are small, non-randomised and short in terms of follow up, but find early low recurrence rates.

Breast cancer oncoplastic surgery is an innovative, progressive and sophisticated subspecialty with new cross-specialty training opportunities. What it lacks are published randomised controlled trials, which directly compare surgical techniques, and easily reproducible objective measures of functional and aesthetic outcome.

CHANGING INDICATIONS FOR RADIATION THERAPY

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It has become increasingly evident over time that improved loco-regional control translates into survival benefits for women with breast cancer[1].

Traditionally, radiation has been an integral component of treatment for loco-regional control in women having breast-conserving surgery, and in women after mastectomy who have a T3 or T4 tumor, four or more nodes involved or positive surgical margins.

A number of recent prospective randomized controlled trials have been potentially practice changing with respect to the use of regional nodal irradiation (RNI).

The first of these is the NCIC-CTG MA.20 trial[2]. The goal of this study was to determine whether adding RNI to modern systemic therapy improved survival with acceptable limited toxicity in patients treated with breast conservation therapy. In this trial, 1832 women with node positive (90%, 85% with 1-3 positive nodes) or high risk node negative (tumor size > or = to 5cm, or > or = 2cm and fewer then 10 nodes dissected, Grade 3 histology, ER – disease or lymphovascular space invasion) undergoing breast conservation therapy (BCT) with axillary dissection were randomly assigned to whole breast radiation (WBI) of 50 Gy in 25 daily 2Gy fractions, with our without RNI. Boost irradiation to the primary site (10Gy in 5 fractions) was allowed. In the group receiving RNI, the nodal areas targeted were the supraclavicular, infraclavicular, ipsilateral, internal mammary nodes in the 1st-3rd interspaces, and high axillary lymph nodes (Level III). These nodal areas were concurrently treated to 45Gy in 25 daily 2Gy fractions. The internal mammary nodes could be treated with either modified wide tangents, or a mixed photon-electron direct field matched to the tangent.

Adjuvant chemotherapy was received by 91% of the patients in both arms, and in > 90% of cases, was anthracycline-based. Adjuvant hormonal therapy was received by 71% of the patients.

The primary outcome of the study was overall survival (OS). Secondary outcomes included loco-regional recurrence rates, disease free survival (DFS) distant metastases DFS, toxicity and cosmetic outcomes.

A preliminary report of a planned interim analysis was presented at the 2011 meeting of the American Society of Clinical Oncology (ASCO).

At a median follow up of 62 months, the addition of RNI to whole breast radiation was associated with a significant decrease in isolated loco-regional recurrence (96.8 V 94.5%) and distant DFS (92.4 V 87%). There was a significant improvement in 5 year DFS from 84 to 89.7%, favoring the WBI plus RNI arm. There was a strong trend towards improved OS with the addition of RNI, with 5 year OS of 92.3% V 90.7% for WBI alone.

The addition of RNI to WBI was associated with an increase in radiation dermatitis (50 V 40%), radiation pneumonitis (1.3 V 0.2%) and lymphoedema (7.3 V 4.1%). These were all statistically significant.

Adverse cosmetic outcomes increased with time in both groups of patients, but more so in those patients treated with RNI (36 V 29%).

Based upon these data the risks and benefits of RNI should be discussed with all patients with positive nodes who are undergoing BCT. Patients with 1-3 nodes however represent a heterogeneous group, with some patients having only microscopic disease in only one node. Further study is necessary to determine whether low risk 1-3 node women will benefit from RNI.

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The other interesting question raised by this trial is whether or not it is necessary to irradiate the internal mammary nodes. In this study only 1 patient treated with WBI alone relapsed in the IMNs. Treatment of these nodes may be associated with increased radiation dose to heart and lung, which may be clinically significant, as documented by the increased risk of pneumonitis in this study. The question of IMN radiotherapy remains unanswered therefore at this point, and is an issue requiring further investigation.

Finally, this study also raises the question of the role of radiation in the post-mastectomy setting for patients with 1-3 nodes involved. This question remains unanswered.

The second, potentially practice changing trial to be recently reported is the EORTC AMAROS trial[3].

Results of this trial were presented at ASCO 2013. The goal of this trial was to compare the efficacy of axillary radiotherapy (ART) with that of axillary lymph node dissection (ALND), the standard treatment advised in the case of a positive sentinel node biopsy (SNB).

In this trial, 4806 patients with clinical T1c-T2, N0 breast cancers were enrolled. Breast conserving therapy was performed in 82% and mastectomy in the remainder. All patients had SNB. Those patients with positive sentinel nodes were then randomised to ALND or ART. The ART consisted of 50Gy in 25 fractions. Irradiation of Level I and II nodes was mandatory, and Level III and the medial supraclavicular fossa was optional. The two treatment arms were comparable regarding age, tumour size, grade, tumour type, and adjuvant systemic treatment. Adjuvant systemic treatment was given 90% of cases.

The ALND group comprised 744 patients. No further positive disease was found in 67% patients. Further positive disease was found in 33%, with 8% having 3 or more nodes involved. The ART group comprised 681 patients.

With a median follow up of just over 6 years, the 5 year axillary recurrence rate after a positive SNB was 0.54% after ALND V compared with 1.03% after ART. The axillary recurrence rate after a negative SNB was 0.8%. There were no significant differences between treatment arms regarding OS (93.3% ALND, 92.5% ART) and DFS (86.9% ALND, 82.7% ART).

The 5 year rate of lymphoedema was significantly more in the ALND arm (28% V 14%). There was a non-significant trend towards more early shoulder movement impairment after ART. There were no other differences in Quality of Life.

The conclusion of the study was that ALND and ART both provide excellent and comparable regional control in patients with a positive SNB, with less toxicity from ART.

These results may lead to a trend to less surgery and more radiation in axillary management. Longer follow up is required however, as the lymphedema risk after ART may increase with time.

These studies both point to changing indications for radiation therapy, with potential expanded indications for regional nodal radiation.

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SENTINEL NODE BIOPSY AND LARGE (≥3CM) BREAST CANCER

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Background
Sentinel node biopsy is an accurate method for staging the axilla in early (small) breast cancers. However, data for the role of this technique for large breast cancers remains limited. With evidence for sentinel node biopsy lacking, the current practice for staging axilla in setting of large cancer is to instead undertake an immediate axillary clearance with associated increased morbidity.

Method
From the Royal Adelaide Hospital Sentinel Node database and the Sentinel Node Biopsy versus Axillary Clearance (SNAC) trial database, 100 subjects were identified with clinically node negative, large(≥3cm) primary breast cancer who had undergone sentinel node biopsy and immediate axillary clearance. The pathology results from the sentinel node and axillary specimens were analysed.

Results
Average tumour size was 3.91cm (range 3-10cm) and 65 of 100 cases had metastatic disease in the axillary nodes. A sentinel node was successfully identified in 93/100 cases with an average of 1.75 sentinel nodes sampled. 62% (58/93) were sentinel node positive and 43% (43/100) had a positive non-sentinel node. The false negative rate following successful sentinel node identification was 4.9% (3/61).

Conclusion
Sentinel node biopsy is an accurate tool for staging the axilla with a false negative rate comparable to that seen in small tumours. 38% of women studied could have avoided axillary clearance. However, the high rate of nodal metastasis in those with larger cancers implies that the absolute numbers of women at risk of harbouring non-sentinel node disease will be significant, therefore further prospective investigation is warranted.

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A CARDIAC SPARING TECHNIQUE FOR BREAST CANCER RADIATION TREATMENT

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Background
Historically left-sided breast cancer radiation treatment has been associated with an excess risk of cardiac deaths[1], and every additional 1Gy mean cardiac dose results in a relative increase in cardiac events of 7.4%[2].

Method
A deep inspiratory breath hold (DIBH) technique was introduced as a method of reducing the volume of heart in breast / chest wall tangential radiation treatment at CPMCC in 2010, one of the few centres using this technique in Australia. This study evaluates the impact of DIBH on cardiac radiation dose.

Results
A total of 51 patients underwent an attempt at radiation treatment simulation by DIBH as well as the conventional 'free breathing' (FB) approach between December 2010 and April 2013. Thirty eight patients proceeded to treatment delivery by DIBH. Thirteen patients did not undergo treatment by DIBH, either because DIBH did not reduce the cardiac dose (6 patients) or because they were not able to follow instructions for DIBH (7 patients). For the 38 patients who underwent DIBH, the simulated size of the heart measured as a volume varied between FB and DIBH by 72% - 115%. The mean irradiated heart dose calculated by simulation was 6.2Gy by the DIBH technique and higher by the FB technique for all 38 patients. It was a mean of 7.0Gy for the 13 patients treated by FB. Six of 38 patients underwent fluoroscopic imaging of one radiation field during treatment on at least two occasions. For the six patients as a group, the heart moved between 1 and 6mm during the fluoroscopic imaging.

Conclusions
DIBH is a suitable technique to reduce the cardiac volume irradiated for some patients with left sided breast cancer. We are now exploring the best method of measuring cardiac position during treatment, and how we can help more women cope with this procedure.

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INTRA-OPERATIVE ULTRASOUND REFINES BREAST CONSERVING SURGERY FOR PALPABLE BREAST CANCERS

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Background and purpose
Excision of a breast cancer with a tumour-free margin is the principle aim of breast-conserving surgery. Tumour-involved margins of up to 41% are reported with palpation-guided excision. Satisfactory cosmetic outcome is an important secondary aim, with poor cosmesis associated with excision volumes greater than 85cm^3. Intra-operative ultrasound (US) has the potential to reduce positive margin rates and tissue volume for palpable breast cancers. The purpose of this study is to report outcomes of a five-year experience in the use of this technique.

Methods

A retrospective review was conducted of 176 consecutive patients with a palpable breast cancer, undergoing breast-conserving surgery between 2008-2012. All patients underwent intra-operative US localisation followed by specimen US. Sonography was performed by a breast surgeon or breast sonographer. Specimen volumes were calculated and compared to an optimum specimen volume.

Results

Thirty-eight (22%) patients had involved margins on final pathology, with 15 (9%) showing invasive carcinoma, and 23 (13%) having DCIS. The rate of tumour-involved margins was higher for lobular carcinoma (29%) than invasive ductal carcinoma (6%). Of those with positive margins, 93% underwent re-excision, with 40% having residual cancer at resection. Specimen interrogation resulted in 25 patients having additional tissue excised. Two had cancer, and four DCIS, in the marginal tissue. The median value for specimen volume was 60cm3, with 23% of patients having excision volumes greater than 85cm3.

Conclusions

Use of intra-operative US localisation coupled with specimen interrogation demonstrated a low rate of positive margins. For the majority of patients, specimen volumes remain lower than those associated with cosmetic dissatisfaction. Intra-operative ultrasound is a useful adjunct to breast conserving surgery.

RISK FACTORS ASSOCIATED WITH MORTALITY FROM BREAST CANCER IN WAIKATO, NZ – A CASE CONTROL STUDY

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Background

New Zealand (NZ) has the seventh highest age standardized breast cancer mortality in the world[1]. Maori women fare even worse with a 60% higher mortality rate compared to NZ European women[2].

We performed a case control study to identify key characteristics associated with death from breast cancer in Waikato, NZ.

Methods

Women diagnosed with breast cancer during 2002-2010 were identified from the Waikato Breast Cancer Register and NZ Cancer Registry.

Cases: All women who died of breast cancer during 2002-2012 with a diagnosis during 2002-2010.

Controls: Age (+/-1 year) and year of diagnosis, matched controls (up to three controls per each case) that were alive on the date of death of the case to which they were being matched

Results

258 women who died of breast cancer and 652 matched controls were identified. Proportion of Maori women among cases was higher compared to controls (17.4% vs. 13.3%). Compared to controls (59.2%) a higher proportion of cases (84.5%) were diagnosed symptomatically. 61% of cases had advanced cancers (stage III and IV) compared to only 14.2% for controls. 50.7% cases were grade-3 cancers compared to 17.5% controls. Significantly higher ($p<0.05$) proportion of cases were ER/PR negative (27.3% vs. 9.6%) and HER-2 positive compared to controls (30.1% vs. 14.8%). Among cases, compared to NZ Europeans, Maori women had advanced staged ($p<0.01$), lower grade ($p=0.02$), more ER/PR negative ($p=0.26$) and more HER-2 positive ($p<0.01$) cancers. Multivariate analysis identified tumour stage, grade and ER/PR status as tumour factors significantly associated with mortality from breast cancer among Waikato women.

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Conclusions

Advanced stage, higher grade, ER/PR negativity and HER-2 positivity were found to be significantly associated with mortality from breast cancer. Higher proportion of advanced staged, ER/PR negative and HER-2 positive cancers are likely contributors to mortality inequity seen among Maori women.

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DEVELOPMENT OF A REALISTIC MODEL FOR TEACHING BREAST EXAMINATION

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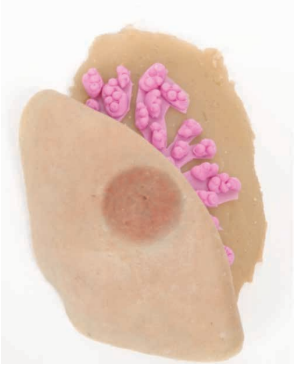
Background and purpose

Breast cancer mortality can be significantly reduced by early detection, however many medical students and doctors report that they feel they could improve their skills in clinical breast examination (CBE). There are more medical students and fewer opportunities for them to practice on patients. Realistic simulation models can help address this need. Training programs including silicone breast simulators can improve the rate of detection of lumps in patients. (Saslow CA Cancer 2004) Despite this, medical students and trainees typically have low performance scores for breast examination. This indicates that current simulation models are not sufficient to provide the training required for CBE. Most patient simulators lack complexity, are not shaped and do not feel like real people. In this paper we show the process for developing realistic breast examination simulators.

Method

This paper shows the development of a complex, multi-layered breast model. Through the testing of various materials it shows the systematic building of a life-like look and feel model, including the realistic, anatomically correct layering of ribs, soft adipose tissue, nodularity and complex placement of tumors.



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USE OF BLUE DYE IN SENTINEL LYMPH NODE BIOPSY: TIME TO REEVALUATE

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Background and Purpose

Sentinel node biopsy (SNB) using both blue dye and radioisotope is the recommended approach for axillary staging in patients with early breast cancer. SNB is associated with a learning curve and blue dye may have been useful adjunct to radioisotope when SNB was a relatively new technique[1]. Blue dye is associated with adverse effects such as hypersensitivity reactions including anaphylaxis, long-term skin discolouration and interference with carbon tracking. The aim of this pilot study was to reevaluate the need for blue dye in SNB.

Methods

Consecutive patients with early breast cancer from May 2011 to May 2012 underwent SNB using the standardised combination of ^{99m}Technetium-labelled radioisotope and patent B blue dye or ^{99m}Technetium alone. The primary endpoint was demonstration of at least one lymph node on histology, regardless of pathological status.

Results

Eighty five patients underwent 87 SNB procedures. Forty nine procedures were performed using blue dye and radioisotope and 38 procedures with radioisotope alone. Overall sentinel node identification rate was 99%. The mean sentinel lymph nodes removed in the combination technique and radioisotope alone was 2.6 and 1.8 respectively (p=0.002). Sentinel nodes were demonstrated histologically in 98% (48 of 49) patients using the combination technique and 100% (38 of 38) patients using radioisotope alone. There was no significant difference in the proportion of patients with nodal disease in both groups (adjusted OR = 1.39, 95% CI 0.46 – 4.21, p=0.58).

Conclusions

SNB using radioisotope alone appears comparable to the combination technique. The use of blue dye warrants reevaluation in view of increasing surgeon experience and advancements in gamma probe since the advent of SNB.

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Notes

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AUDIT OF FINE NEEDLE ASPIRATION CYTOLOGY OF BREAST VERSUS HISTOPATHOLOGICAL OUTCOME IN A BUSY PUBLIC HOSPITAL SETTING: VALUABLE TOOL OR AN ANACHRONISM?

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Background and purpose
Fine needle aspiration (FNA) cytology remains a valuable tool in the initial investigation of breast pathology. The minimally invasive nature of this technique lends itself well to outpatient and inpatient settings. Audit of the clinical outcome is important in determining the reliability of this technique in this era of increasingly invasive biopsy techniques.

Methods and Results
439 consecutive FNAs of breast lesions were performed over a 2 year period (Jan 2010 – Dec 2011) and reported by one of four histo/cytopathologists in the Department of Surgical Pathology, Flinders Medical Centre, two of whom have a specialised interest in breast pathology. The FNA diagnoses were correlated with an audit of subsequent histopathology results (core biopsy or surgical excision in 185 patients) or clinical follow up. 00 FNAs (22.8%) yielded a diagnosis of malignancy. There were no false positive FNA diagnoses. The false negative rate was 0.67% and inadequate rate 15.9%. Complete sensitivity of FNA was 91.28%. Positive and negative predictive rates of the various benign, atypical and suspicious categories will be presented.

Conclusion
This audit indicates that FNA remains an accurate tool for the diagnosis of benign and malignant breast disease with a high concordance with the histopathological outcome.

CLOSURE OF THE AXILLARY FASCIAL SPACE AVOIDS THE NEED FOR DRAINAGE IN AXILLARY DISSECTION

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Background
Axillary drainage is routinely employed after axillary lymphadenectomy to reduce the rate of seroma formation in these patients. This unit adopted a new technique for axillary dissection that allows closure without the use of an axillary drain.

Methods
A standard axillary clearance was modified to a single linear incision of the axillary fascia and predominantly blunt dissection of the axillary tissues, followed by watertight closure of the fascia without the use of a drain. Axillary clearances performed using this technique between January 2010 and December 2011, were monitored for the development of seroma.

Results
41 patients underwent axillary dissection using this technique. The mean number of lymph nodes excised per patient was 13.46 (6-15). 2/41 (4.88%) patients developed a seroma in the postoperative period.

Conclusion
Axillary surgery can be done without axillary drainage when the axillary fascia can be securely closed at the end of the procedure.

Session 7: Managing the Extremes – interactive case presentations

BORDERLINE AND ATYPICAL LESION MANAGEMENT
HIGH RISK DISEASE MANAGEMENT

Panel: Pathologist, Surgeons, Medical Oncologist, Radiation Oncologist, Cardiologist

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Session 8: Beyond Primary Treatment

WHAT'S NEW IN ADJUVANT HORMONAL THERAPY?

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Adjuvant endocrine therapy remains pivotal in the systemic approach following primary surgery for breast cancer. At present there are no data showing that neoadjuvant endocrine therapy is or is not equally efficacious or safe as adjuvant therapy. Therefore outside of an experimental setting, or in the very elderly in whom surgery is not planned, a neoadjuvant endocrine approach should not be considered.

Five years of adjuvant tamoxifen therapy has been standard for many years for premenopausal women with results that reduce breast cancer recurrence rates by 40%, and improve overall survival rates by about 25% in ER positive women[1]. We are well aware that compliance with adjuvant tamoxifen is less than optimal, probably related to vasomotor side effects and concern regarding other real but relatively infrequent side effects such as deep venous thrombosis (DVT) and endometrial cancer. Indeed it is clear that the use of five years of tamoxifen is accompanied by an increased rate of the development of endometrial cancer, but these cancers are still rare and with appropriate attention to any spotting or bleeding, are almost always caught at a very early stage and can be treated for cure. There are now new and exciting data showing that ten years of tamoxifen in the pre- and postmenopausal setting combined seems clearly superior to five. These data have come from the ATLAS[2] and aTToM[3] studies, which have recently been updated, presented[2-3], and published[2] and/or submitted for publication[3]. Meta analysis of the two studies together shows definite reduction in disease-free survival (DFS) and also improvement in overall survival (OS) when ten years is compared to five. However, there is almost a doubling of rate of endometrial cancer, when ten is compared to five years of tamoxifen, and this will remain something that must be carefully attended to as tamoxifen is used for longer time periods.

The aromatase inhibitors (AIs) have been shown in many studies to be superior to tamoxifen for postmenopausal women; in the ATAC[4] and BIG 1-98 trials[5], for women that are randomized from very shortly after the time of diagnosis to receive an AI versus tamoxifen, and in the International Exemestane Study (IES)[6] when women are randomized after two years of tamoxifen to receive three years of exemestane versus continuing on tamoxifen[7]. Meta analysis of these trials show improved DFS, DDFS and marginally improved OS[8] when patients were given an AI rather than tamoxifen either immediately after surgery or after two years of tamoxifen. Side effects of the AIs are also problematic and include musculoskeletal syndromes which can be very difficult to tolerate for a proportion of patients, increased risk of osteopenia and osteoporosis, and vasomotor symptoms similar to those seen with tamoxifen. The AIs have also been shown to be helpful when given after five years of tamoxifen[9] where they clearly improve local, distant and overall disease-free survival. It is also shown that adding an AI, two to three years after completing five years of tamoxifen is additionally helpful[10] as tested in patients who were in the control arm of the MA.17 trial once the results were released. These patients gained a benefit even though they began treatment with an AI a number of years after they completed tamoxifen therapy.

Issues have been raised about the efficacy of the aromatase inhibitors in overweight women, but to date information from ATAC[11], BIG 1-98[12] and TEAM[13] all demonstrate that the differential benefit (if any) of the AIs is not different amongst women of different BMI. However, the Austrian Breast Cancer Study Group (ABCSG) Trial[14] in which premenopausal women were all given an LHRH agonist and then randomized to tamoxifen versus an AI showed both different results (tamoxifen better than the AI) and a differential effect between women of different BMIs. This smaller ABCSG study is,

however, the outlier and involved premenopausal women all made postmenopausal by the LHRH agonist. At the moment it does not seem clear that women of different weights should be given AIs or tamoxifen differentially.

It should also be noted that in the adjuvant setting, beginning with an AI and switching to tamoxifen after two years seems, at least early in follow-up, similar in efficacy to continuing on an AI. With this in mind, patients who cannot tolerate an AI should certainly be diverted to tamoxifen. It would appear evident that being on some type of endocrine therapy, either an AI or tamoxifen, is superior to being on none in this setting.

Management of the side effects of both tamoxifen and the AIs including vasomotor symptoms, as well as musculoskeletal symptoms, osteopenia, and osteoporosis remain important in order to help patients continue their medications throughout the optimal time periods.

At this point, tamoxifen is most effective when given over ten years. Five years of tamoxifen, followed by five years of an AI is clearly more effective than five years of tamoxifen alone. For postmenopausal women five years of an AI appears more effective than five years of tamoxifen. Of course the AI can only be given to patients who are postmenopausal, and this must be clearly delineated before attempting this approach. Now that the optimal lengths of endocrine therapy for many patients with hormone positive breast cancer are out to ten years, one wonders whether women in the postmenopausal setting who have completed five years of an AI should also have additional therapy. While there are no data at present addressing this matter, a number of randomized studies exploring ten versus five years of an AI have completed accrual and we await results. Theoretically, one could additionally add five years of tamoxifen after an AI, as this would seem as a reasonable approach, although not data driven.

Drugs such as the mTOR inhibitors which may add to the effectiveness of hormones have been explored in the metastatic setting and are already approved and being fairly widely used for this purpose. The BOLERO-3 study showed that the mTOR inhibitor everolimus when added to exemestane, gave increased progression-free survival which was quite dramatic[15]. Although drugs such as everolimus do have side effects including pneumonitis, mucositis, and fatigue, this drug and others of its class are being explored in the adjuvant setting. In particular, adjuvant studies are planned in which everolimus will be used together with an AI in high-risk women with endocrine positive breast cancer.

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BREASTS, BONES AND BISPHOSPHATES

Richard De Boer

Among patients with advanced breast cancer, approximately 70% develop bone metastases[1], which lead to bone destruction, mediated by increased osteoclast activity. Clinical consequences include: skeletal-related events (SREs) such as pathological fracture, spinal cord compression, or radiation or surgery to bone, hypercalcaemia of malignancy, and pain[2].

Intravenous bisphosphonates, predominantly zoledronic acid (ZA), have been commonly used to delay or prevent SREs; however, SREs may still occur[3]. Bisphosphonates work by decreasing the number and activation of osteoclasts, and in so doing, shutting down the vicious cycle of bone metastases in which various products of cancer cells (e.g. IL-11, PTHrP) stimulate osteoclasts to break down bone which in turn releases factors that encourage tumour cell growth (e.g. TGF-beta, IGF-1). Bisphosphonates have an established safety profile characterized by manageable adverse events, such as transient flu-like symptoms after initial infusions. Osteonecrosis of the jaw (ONJ) is an uncommon event (~1%). Renal toxicity can also occur and monitoring renal function is recommended. Despite now long term use of bisphosphonates in this setting, the optimal duration of use remains to be established. Trials such as BISMARK and ZOOM have attempted to answer this important practical clinical question[4].

The latest development in the management of bone metastases has been the development of denosumab. Denosumab is a fully human monoclonal antibody, administered subcutaneously, that targets the key regulator of cancer-induced bone destruction, receptor activator nuclear factor B ligand (RANKL), resulting in inhibition of osteoclast formation, function and survival. In a randomised, head-to-head trial in patients with breast cancer and bone metastases, denosumab was superior to ZA in preventing first and multiple SREs[5]. This has led to the approval and widespread use of denosumab in patients with bone metastases from breast cancer. Denosumab has a somewhat different toxicity profile to the bisphosphonates with little impact on renal function and less acute phase reactions, but there have been increased reports of hypocalcaemia, and the ONJ may be a more frequent event, reflecting the more targeted and potent effect of denosumab on osteoclasts[6-7]. It is now strongly recommended that patients commencing anti-osteoclast agents have their vitamin D and calcium levels checked and are commenced on adequate and appropriate supplements of vitamin D and calcium.

In addition to their established roles for treating bone metastases, there are strong preclinical and recent clinical data indicating that bisphosphonates also have antitumour activity. The ABCSG-12 study (N = 1,803) evaluated the efficacy of combining Zoledronic acid (4 mg q 6 mo) with endocrine therapy in premenopausal women with early breast cancer (EBC). At 84-month median follow-up, ZA significantly improved DFS by 28% and OS by 37% (P = 0.011 and 0.033 respectively)[8]. Similarly, the ZO-FAST study, looking at ZA as a way of preventing bone loss in patients using aromatase inhibitors (AI), found improvements in disease free survival as a secondary endpoint[9]. Unfortunately, the large AZURE trial did not find an overall survival impact for ZA in the adjuvant setting. There was however an intriguing subgroup analysis suggesting a positive effect in the post-menopausal subgroup. Further support for this hypothesis is awaited. Denosumab is now being studied in the adjuvant in the DCARE study which has recently completed its recruitment of over 4000 high risk early breast cancer patients and is now in follow up. The primary endpoint of the ZOFAST study was the prevention of aromatase-inhibitor induced bone loss. Initial work on the ATAC and BIG 1-98 adjuvant endocrine studies confirmed that use of AI's resulted in accelerated bone mineral density loss and increased fracture rates. A series of trials, looking at the 3 different AI's, and utilizing different bisphosphonates, were carried out and have all shown that the bisphosphonates can successfully prevent this bone loss. A similar effect was shown with the use of denosumab in this setting[10]. Thus, management of bone health has become an important area in the management of the patient with early stage breast cancer.

Notes

Notes

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ADDRESSING NEEDS OF CANCER SURVIVORS - WHAT, WHO AND HOW

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Survivors of breast cancer represent approximately a quarter of cancer survivors in Australia and with improved cancer outcomes, their numbers will steadily increase. While most of them will enjoy excellent quality of life long term, some will experience physical or emotional problems, related to cancer diagnosis and/or cancer treatment. These problems may require ongoing management and some could be prevented. Many of undesirable consequences of cancer treatment include chronic conditions like obesity, cardiovascular illness and osteoporosis, which require comprehensive approach to management including lifestyle interventions. Cancer clinicians often have limited skills in managing these and run the risk of not recognising their importance in the environment focussed mainly on detection of cancer recurrence.

The key elements of effective survivorship care include prevention of late effects of treatment, palliation of symptoms and health promotion. The evidence supporting these after breast cancer is better established than for many other cancers. What remains unclear however is who should be delivering survivorship care and what is the optimal (ie cost effective) model for such care delivery. Most importantly, the challenge is not to turn survivorship into a disease but rather to ensure that the focus is on health and not illness and that the unique skills of the patient as the expert in her health are recognised and harnessed.

MRI GUIDED VACUUM ASSISTED BIOPSIES – THE RBWH EXPERIENCE

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Background

Many breast lesions can usually be detected using mammography and ultrasound given the advancements made in these imaging modalities. However, few lesions can only be demonstrated by magnetic resonance imaging (MRI) and in such cases MRI-guided vacuum-assisted breast biopsy (VABB) becomes an essential diagnostic technique in obtaining specimens for pathological diagnosis.

Method

We performed a retrospective study covering a period of 18 months to review the MRI VABB of suspicious breast lesions at the Royal Brisbane Hospital, the first public hospital in Queensland, Australia to offer this diagnostic procedure. We evaluated the MRI findings that led to biopsy and correlated the radiological BIRADS score with the pathological outcome.

Patients and results

Of 11 women (median age 47 years), MRI Guided vacuum assisted biopsies were successfully conducted in 10 women for suspicious breast lesions detected and visible only on MRI. Of the 10 cases, 1 revealed ductal carcinoma in situ (DCIS), 1 was reported as atypical lobular hyperplasia and the remaining 8 had benign histology on pathology. One case was cancelled as the patient opted to have short-term follow-up MR imaging instead of the biopsy.

Conclusion

Our preliminary experience shows that MRI-guided vacuum assisted biopsy holds promise of being a fast and safe alternative to surgical biopsy for lesions detected and visible only on MRI.

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COMPARISON OF QUALITY OF LIFE FOLLOWING MASTECTOMY AND IMMEDIATE RECONSTRUCTION VERSUS MASTECTOMY ALONE IN AN ONCOPLASTIC BREAST UNIT

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Background and purpose

In modern practice immediate reconstruction is routinely discussed if appropriate with women requiring mastectomy for breast cancer treatment. We aim to determine if there is a difference in Quality of Life (QoL) outcomes between patients who had immediate reconstruction versus those who underwent mastectomy alone.

Notes

Methods

Data was collected retrospectively for patients who underwent mastectomy from February 2006 until February 2012. There were 81 reconstruction cases, consisting of 55 expander implants (EIR), 14 TRAM and 12 LD flaps. The mastectomy alone group was best matched according to age, disease stage and adjuvant treatments. QoL was evaluated using QLC-C30 and QLC-BR23 questionnaires (1) and visual assessment of reconstruction was scored by patients using a linear scale.

Results

We had 117 responses (72% response rate), which consisted of 55 reconstruction cases and 62 mastectomy alone cases. When analysing the groups there were no differences in QoL in either global scores or sub-scores (body image or sexual function). Those less than 2 years from surgery had significantly higher scores relating to breast symptoms but no significant differences were seen between the groups. Overall women were satisfied with their reconstruction based on visual assessment scores but numbers in TRAM and LD group were too small to make any comparison.

Conclusions

QoL has been found to be similar in both groups of patients. Good patient selection is crucial in the reconstruction group, but for women who underwent mastectomy without reconstruction, a similar QoL can be achieved.

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THE SAFETY AND EFFICACY OF THE SEQUENCE OF TREATMENTS FOR LOCALLY ADVANCED BREAST CANCER PATIENTS UNDERGOING MASTECTOMY AND IMMEDIATE BREAST RECONSTRUCTION

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Background and purpose

Adjuvant radiotherapy decreases local recurrence rates and improves survival in patients with locally advanced breast cancer (LABC)[1]. The usual sequence of treatments is chemotherapy and surgery, followed by adjuvant radiotherapy. Postoperative radiotherapy will compromise aesthetic outcomes in cases of Immediate Breast Reconstruction (IBR)[2]. The aim of this study was to determine the safety and efficacy of mastectomy and IBR after neoadjuvant chemo-radiotherapy.

Methods

Operative databases and casenotes were reviewed for all patients who had undergone IBR following neoadjuvant chemo-radiotherapy. Safety and efficacy were analysed in terms of reconstructive flap complications and overall survival.

Results

15 patients underwent mastectomy, axillary node clearance and autologous flap reconstruction in the study period 1998-2013. Median age at diagnosis was 48 years (range 33-65). Median period of follow-up was 35.5 months (range 6-175).

There were two early reconstruction complications – one infected tissue expander and one donor site wound breakdown. No patients have had locoregional recurrence. Four patients died – three from metastatic breast cancer. One patient is alive with distant metastases.

Conclusion

Autologous flap IBR is a safe and viable option in patients who have undergone neoadjuvant chemo-radiotherapy; further expanding breast surgery choices for women with LABC.

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IDENTIFICATION OF THE SENTINEL LYMPH NODE IN THE SNAC-1 TRIAL

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Background

A combination of scintigraphy and a lymphotropic dye (patent blue dye) is the recommended technique to detect the Sentinel Lymph Node (SLN) in early breast cancer. Reports of allergic reactions to patent blue dye have questioned its safety. This study determined the effect of clinical factors on SLN identification in the SNAC trial and the contribution of blue dye to the outcomes.

Methods

1088 women were registered[1]. Lymphatic mapping was performed using preoperative lymphoscintigraphy (LSG) and the gamma probe (GP) combined with peritumoural injection of patent blue dye (BD) (971 patients) or BD alone (106 patients). SLNs were identified in 1024 women (94%). SLNs were visualised by LSG in 779 (81.4%), and were identified by GP in 879 (91.8%). The BD identified SLNs in 890 out of 1073 (82%). BD detected the SLNs in 141 of 178 women with negative LSG mapping and in 44 of 79 women with no hot SLNs detected intraoperatively. Age, BMI and tumour presentation (screen detected vs. symptomatic) were significantly related to the identification of the SLN. For BD, primary tumour location was significantly related to identification rate.

Conclusion

The combined technique resulted in a high identification rate. BD contributed to the identification of the SLNs in patients where LSG and the gamma probe failed to identify the sentinel node. Special attention to the techniques is needed in particular groups of patients such as those with high BMI, screen detected primary tumours and tumour located in the inner quadrants.

Reference

1 Gill G. Sentinel-Lymph-Node-Based Management or Routine Axillary Clearance? One-Year Outcomes of Sentinel Node Biopsy Versus Axillary Clearance (SNAC): A Randomized Controlled Surgical Trial. *Ann Surg Oncol.* 2009; 16:266-75.

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FACTORS PREDICTING THE NODAL INVOLVEMENT IN EARLY BREAST CANCER

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Background

The nodal status is an important prognostic factor in early breast cancer. This study assessed association between clinicopathological factors and involvement of Sentinel Lymph Node (SLN) and Non Sentinel Lymph Node (NSLN) in the SNAC 1 trial. Accurate statistical models can assist surgical counselling and potentially avoid axillary surgery in selected cases.

Method

This is a retrospective analysis of 1088 patients. Lymphoscintigraphy, blue dye injection and gamma probe were used for SLN mapping and retrieved nodes were examined with H&E and immunohistochemistry. Validations of the Memorial Sloan–Kettering Cancer Center (MSKCC) and Coombs's equations to predict the status of SLN were performed and the Area Under Curve (AUC) was calculated.

Results

Positive SLNs were detected in 291 out of 1024 patients. 162(55.7%) patients had macrometastases, whereas micrometastases and isolated tumour cells were identified in 100 and 29 women respectively. Univariate analysis revealed that the involvement of SLNs was correlated with age, palpability, primary tumour site, Peritumoural Vascular Invasion (PVI), extensive intraductal component and tumour grade. Multivariate analysis demonstrated that the PVI status ($p<0.001$), tumour size ($p<0.001$), tumour site ($p<0.05$) were significant predictors of the SLN status. The AUCs of the (MSKCC) and Coombs's equations were 0.723 (95% CI 0.688–0.758) and 0.693 (95% CI 0.659–0.728) respectively.

Conclusion

Primary tumour characteristics were significant predictors of SLN involvement. The validation of existing models revealed that those models are imperfect for clinical use. Creation of a nomogram with high predictive performance based on the analysis of local patients' data may yield more accurate outcomes.

Reference

1 Gill G. Sentinel-Lymph-Node-Based Management or Routine Axillary Clearance? One-Year Outcomes of Sentinel Node Biopsy Versus Axillary Clearance (SNAC): A Randomized Controlled Surgical Trial. *Ann Surg Oncol*. 2009; 16:266-75.

TREATMENT DELAY FOR MAORI WOMEN WITH BREAST CANCER IN NEW ZEALAND

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Background

Delays in diagnosis and treatment of breast cancer are associated with lower survival rates [1]. Indigenous Maori women have 60% higher overall and 32% higher stage adjusted breast cancer mortality compared to European women in New Zealand (NZ)[2]. We sought to evaluate factors associated with delays of >31 and >90 days for surgical treatment of breast cancer among NZ women with newly diagnosed breast cancer.

Methods

A retrospective analysis of prospectively collected data included in the Waikato Breast Cancer Register from 01/01/2005 through 31/12/2010 was performed.

Results

1449 (out of 1510, 96%) breast cancers diagnosed within Waikato, over the study period were included.

Out of women undergoing primary surgery (n=1264), 59.6% and 98.2% underwent surgery within 31 and 90 days of diagnosis respectively.

Compared with NZ European women (mean 30.4 days), significantly longer delays for surgical treatment were observed among Maori (mean 36.9, $p<0.001$) and Pacific Island women (mean 42.8, $p=0.005$). Compared with NZ European women, higher proportions of Maori and Pacific Island women (statistically non-significant) experienced delays longer than 31 days (40.2% vs. 47.8% and 52.1%, $P>0.05$) and 90 days (1.6% vs. 2.7% and 4.3%, $p>0.05$).

Multivariate analysis identified public sector treatment (OR 5.93 and 8.14), DCIS (OR 1.53 and 3.17), mastectomy as treatment (OR 1.75 and 6.60) and earlier year of diagnosis (1.21 and 1.03) as factors significantly associated with delays longer than 31 and 90 days.

Conclusions

A high proportion of women not initiating surgical treatment of breast cancer within the stipulated guideline limit of 31 days and significantly longer delays experienced by ethnic minority women were highlighted in this study. Urgent steps are needed to improve performance and to shorten treatment delays in public sector to minimize delays overall, and to reduce ethnic inequities in breast cancer treatment in NZ.

References

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TEMPORARY TISSUE EXPANDERS AND POST-MASTECTOMY RADIATION TREATMENT: A LITERATURE REVIEW

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Background and purpose
Post-mastectomy radiation treatment (PMRT) is increasing in frequency, in light of strengthening evidence that there is a benefit in patients with 1-3 positive lymph nodes. Staged breast reconstruction involves the use of tissue expanders in women undergoing mastectomy who are likely to require PMRT. This has raised uncertainties regarding the impact of the expanders on radiation dosimetry, tumour control, cosmetic outcome, and the quality of the reconstruction. The purpose of this literature review is to assess the available evidence regarding patients undergoing post-mastectomy irradiation with tissue expanders in situ.

Methods
The medline database was searched for articles related to tissue expanders and breast radiation treatment which were published from 1946 until February 2013. Titles, abstracts, and subsequently articles were reviewed according to their relevance.

Results
The initial medline search yielded 9980 results. Review of the titles resulted in 56 articles that were deemed relevant. On review of these abstracts, 18 articles were excluded. 38 of the articles were reviewed in detail. 30 articles reported on complications, risk factors for complications, and aesthetic outcome. 5 articles assessed radiation dosimetric implications, and 3 articles reported primarily on oncological outcome.

Conclusions
The majority of articles reported on complication rates and patient satisfaction, with a paucity of articles on the technical aspects of radiation dosimetry. Overall, most articles supported the use of tissue expanders in the setting of PMRT, but acknowledged higher rates of complications and the need for identification of patients at higher risk of reconstruction failure. Cosmesis was, in general, suboptimal but despite this patient satisfaction was acceptable in most articles. More trials are needed to better understand implications for the delivery of radiation treatment and the optimal protocol for tissue expanders in the setting of PMRT.

SILICONE INJECTION AND BREAST CANCER: A SYSTEMATIC REVIEW OF THE LITERATURE

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Introduction
Silicone injections are a rare method of breast augmentation. Despite this, patients particularly from Asian Countries, present to clinics worldwide. We present a systematic review of the literature pertaining to cases of silicone injections and associated breast cancer.

Methods
Exclusion criteria were silicone patients where prosthesis rather than direct injection was performed.

Two authors (SW and JR) independently searched the Medline, Pubmed, Embase and Cochrane Library databases. The key word "breast cancer" and "silicone injections" was used in combination with the Boolean operators AND, OR and NOT.

Results
31 cases documented time from injection to diagnosis of cancer. The range was from 1 to 42 years with mean age from diagnosis being 16 years.

The mean age for diagnosis of Breast cancer in the setting of silicone injections was 52 years.

Lymph nodal involvement was present in 58%. Isolated breast disease was present in 32%, while 10% of cases had distant metastasis (liver, lung, bone).

Ductal carcinoma was the commonest malignancy noted at diagnosis (71%). 10% of cases were associated with squamous cell carcinoma. 19% were associated with other specific types of breast cancer. These included mucinous (1/31), micropapillary (1/31), atypical medullary (2/31) and angiosarcoma (1/31). Interestingly no cases were associated with lobular carcinoma of the breast.

The surgical management of the breast was by mastectomy (90%) and wide local excision (10%). In 48% of cases the axilla was dissected (level 2/3). In 29% sentinel node biopsy was performed. In 22% of cases the axillary nodes were not assessed (19%) or not reported (3%).

Conclusion
This review demonstrates that cases of silicone injection related breast cancer often present late with a higher incidence of nodal involvement than non silicone injection related breast cancer. This likely reflects difficulty with diagnosis in the setting of silicone injected breasts.

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PRESERVATION OR DIVISION OF THE INTERCOSTOBRACHIAL NERVE IN AXILLARY DISSECTION FOR BREAST CANCER: META-ANALYSIS OF RANDOMISED CONTROLLED TRIALS

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Purpose

Management of the ICBN during axillary dissection is controversial and the division of ICBN is often trivialised.The effect of dividing the ICBN, and its association with sensory disturbance, is unclear. A systemic review and meta-analysis was performed to evaluate the effect of preserving the ICBN during axillary dissection.

Methods

A systemic literature review and meta-analysis was performed according to the PRISMA and Cochrane Collaboration guidelines. Two authors (SW and SH) independently searched Medline, Pubmed, Embase, Cochrane Database of Systemic Reviews and the Cochrane Controlled Trials Register from 1950 to December 2012 for studies comparing preservation or division of the ICBN in axillary dissection for breast cancer. The primary outcome of this meta-analysis was sensory disturbance, defined as objectively assessed change in sensation in the distribution of the ICBN after axillary dissection. The nature of sensory disturbance was assessed as a secondary outcome, categorised into two types: "hypersensitivity" and "hyposensitivity".

Results

Three RCTs and four non-RCTs were reviewed. A meta-analysis demonstrated that the incidence of sensory disturbance was significantly lower with preservation of ICBN compared to division of the ICBN with Mantel-Haenzel combined odds ratio 0.31 (0.17-0.57, 95% CI). There was relatively low level of heterogeneity (I^2 = 19%, χ^2 =2.48, df = 2).

The sensory disturbance was more likely to be hyposensitivity when compared to hypersensitivity (p <0.0001). No difference on number of lymph nodes dissected or operating time was noted.

Conclusion

This meta-analysis demonstrates that division of the ICBN is associated with higher risk of sensory disturbance, and that the nature of this sensory disturbance is more likely to be hyposensitivity, attributable to reduced nerve function.

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