Australasian Society for Breast Disease

ASBD UPDATE

IMPORTANT DATES

14 October 2021 7.00pm AEDST
2021 ASBD Annual General Meeting – online

2022 13-15 October
Australasian International Breast Congress, Brisbane

2023 14-16 September
ASBD 13th Scientific Meeting, Adelaide Convention Centre, Adelaide

Dedicated to promoting knowledge in the areas of prevention, diagnosis and management of breast disease

Edition No. 20 | September 2021

CONTENTS

PRESIDENT'S REPORT

Greetings to you all from a Sydney in lockdown. The COVID pandemic has proven to be long lasting and highlighting the importance of community, perseverance and resilience.

As you would know by now, we have made the decision to postpone until October 2022 the AIBC conference which was supposed to be held in Brisbane in October this year. For a while we hoped interstate travel would have been possible by now, allowing the majority of delegates to attend in person with international speakers participating virtually in a hybrid model. However, as events have evolved, the only viable option for a conference this year would have been to hold a totally virtual conference. With a program covering several days including interactive workshops and multiple networking opportunities, we thought that a wholly virtual conference would not do justice to the very exciting planned program. So, make sure to put 13-15 October 2022 in your calendar now! By then, there is even a possibility that some international speakers may be able to attend in person.

Some of the high-quality industry sponsored symposia that were planned to be held as breakfast or lunch sessions, may now instead be delivered as evening time webinars and I would strongly encourage you to attend these as they become available. Details will be advised via monthly ASBD emails and at www.asbd.org.au .

Take a look at the Online Education page of the ASBD website for online courses about lymphoedema and fundamentals in breast pathology. Additional courses on fundamentals of other aspects of breast disease management, such as oncoplastic breast surgery and radiation oncology, will be announced as they are added to the series later this year. We are aiming to make the Online Education Series a major feature of ASBD, and where possible hope to include these courses as a complimentary feature of ASBD membership. Please let us know if you have topics or ideas for educational resources you would like to see made available to ASBD members.

Keep strong, keep calm and we'll get through these challenging times.

A/Prof Elisabeth Elder

TELL US WHAT YOU THINK

We want to hear from you!

ASBD wants to remain relevant to its members' needs. If you have any articles to submit, feedback or suggestions on meetings, membership or other issues please take a few moments to email Kerry at: kerrye@asbd.org.au

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DCISionRT Test Update

Dr Yvonne Zissiadis, Radiation Oncologist, Genesiscare, Hollywood Private Hospital

GenesisCare recently announced a program allowing Australian women with biopsy proven Ductal carcinoma in situ (DCIS) access to a new predictive and prognostic test which will aid clinicians and patients in making more informed and personalised treatment decisions.

Surgery is the backbone of treatment for DCIS. For most women, breast-conserving surgery is the treatment of choice, though mastectomy is appropriate for a small proportion of patients. Clinical trials have provided level [1] evidence that the addition of postoperative radiation therapy to the breast will further reduce the risk of both invasive cancer and DCIS by approximately 50%[1]. The challenge is that there are varying risks of recurrence in different sub-groups of DCIS, and predicting an individual's risk of recurrence can be tricky.

Ideally clinicians have strived to select those patients with a high risk of recurrence who will obtain a significant absolute benefit from the addition of radiation therapy. In the past, clinicians have relied on clinical and pathological factors such as size of lesion, palpability, margins, patient age and grade to make treatment recommendations for women with a diagnosis of DCIS. [2,3] Decision aids such as the Van Nuys Prognostic Index [4] and the MSKCC prognostic Index [5] were developed using clinicopathological factors to guide clinicians and patients in their decision-making. Neither of these tools used molecular information.

The DCISionRT test uses [7] immunohistochemical markers to calculate a protein expression signature and combines this with clinicopathologic factors to generate a recurrence score from 0-10.[6] In addition, the test predicts 10-year recurrence rates for ipsilateral breast events (invasive + DCIS) and 10 year recurrence rates for ipsilateral invasive cancer recurrence. The recurrence rates are calculated for surgery alone as well as surgery + radiation therapy hence providing clinicians and patients information as to whether there will be a benefit from the addition of radiation therapy.

International validation studies have been completed in over 3500 women. Interestingly the studies have shown that initial treatment decisions have been changed in 30-50% of cases once the results of the DCISionRT test are available. For example, among women whose DCIS was initially thought to have a low risk of recurrence or progression, 2 in 5 had their risk reclassified to elevated risk when assessed using DCISionRT, revealing a potential need for radiation therapy post-surgery.[7]

Furthermore, women under 50 with DCIS are generally considered to have an elevated risk of recurrence and radiation therapy is commonly recommended for this age group.[7] When using DCISionRT, however, almost 1 in 2 women under 50 were classified with a low risk of DCIS recurrence or progression, indicating that surgery alone may be appropriate.

As part of this access program, a Registry Study is being performed. It is a collaboration between Genesiscare and Professor Bruce Mann's RMH team who recently presented their experience with DCISionRT testing in 183 women from Melbourne at the Surgical Oncological Society Meeting 2021. This Registry Study will assess the 5 and 10 year outcomes as well as the impact of the DCISionRT test on treatment decisions for Australian women.

DCISionRT is now available to women with DCIS in Australia. For more information on DCIS and DCISionRT head to: https://www.genesiscare.com/au/treatment/cancer/dcisionrt/

References:

1. Early Breast Cancer Trialists' Collaborative, Group, C. Correa, P. McGale, et al. 2010. "Overview of the randomized trials of radiotherapy in ductal carcinoma in situ of the breast." J Natl Cancer Inst Monogr 2010(41):162-177
2. McCormick et al, J Clin Oncol 2015; 33:709-715
3. Solin et al. JCO 2015;33:3938
4. Silverstein, M. J. 2003. "The University of Southern California/Van nuys prognostic index for ductal carcinoma in situ of the breast." Am J Surg. 186:337-343.
5. MSKCC, Memorial Sloan Kettering Cancer Center. 2014. "Breast Cancer Nomogram: Ductal Carcinoma Recurrence."
6. Kerlikowske et al. JNCI, 2010
7. Bremer TM, et al. Clin Cancer Res. July 2018:clincanres.0842.2018. doi:10.1158/1078-0432.CCR-18-0842

ASBD Online Learning

ASBD continues to grow its online learning portfolio with the aim of providing quality online CPD accredited educational opportunities for all disciplines with an interest in breast cancer diagnosis and management.

Currently the ALERT Lymphoedema Modules from Macquarie University are available and the Pathology Fundamentals course is in the final testing phase. Both these courses are FREE to members. The Pathology Fundamentals course is based on the lectures presented in the live Pathology Fundamentals webinar held late in 2020.

ASBD is planning to use this model to develop other courses. The next webinar and course in development is a Surgery 101 course. Oncology 101, and Genetics 101 are also in the planning phase for delivery later in 2021 or early 2022.

The theory component of the Applied Breast Ultrasound for Clinicians course is also available online and is a pre-requisite to attending the half-day practical component of the RACS and ASUM accredited course.

All online courses can be accessed at: https://asbd.org.au/education/online-course-registration.

WHAT WE LEARNT FROM ASCO 2021

Dr Sanjeev Kumar, Medical Oncologist, Chris O'Brien Lifehouse and the Kinghorn Cancer Centre

I think we can all agree that watching ASCO 2021 from the confines of our own home environment wasn't nearly as much fun as maximising your step count through the endless corridors of McCormick Place in Chicago. Without the promise of a cheeky post-conference cocktail with colleagues in a piano bar and a deep pan pizza, presented abstracts still retained their high quality and provided us with some practice-changing developments for our breast cancer patients.

Highlights in the ***early breast cancer*** space included a plenary session by Andrew Tutt presenting early interim analyses from the double blind, phase 3 OlympiA study in patients with early, high risk, ER+ and triple-negative breast cancer (TNBC) harbouring germline BRCA1 and 2 mutations. **OlympiA** revealed that 12 months of adjuvant olaparib conferred significantly reduced risks of both local and distant recurrence compared to placebo, with an immature trend towards improved overall survival at 3 years.

While we may need to wait for mature overall survival and longer-term haematological safety data, these findings are practice-changing, and have already been incorporated into an expedited ASCO guideline update.

Additionally, given that 82% of patients had TNBC, this study highlights the importance of genetic testing in this population, and offers a more targeted alternative to adjuvant capecitabine in gBRCA1/2 patients with residual disease after neoadjuvant chemotherapy.

Ingrid Mayer then presented data from the ECOG-ACRIN study, **EA1131**, asking whether platinum chemotherapy can improve invasive disease-free survival compared to adjuvant capecitabine in patients with residual disease after neoadjuvant chemotherapy. This study recruited a high risk population with bulky, residual disease (to allow PAM50 analysis to occur), and was unable to demonstrate non-inferiority or superiority of adjuvant platinum, which we know can augment response in the neoadjuvant setting. Given the lower dose and shorter duration of capecitabine in the control arm of this study, EA1131 simply confirms that capecitabine remains the current, preferred post-neoadjuvant therapy for early TNBC with residual disease after neoadjuvant chemotherapy.

Sibylle Loibl from the German Breast Group also presented updated results from the **GeparNUEVO** study in early TNBC. This phase 2 study combined the checkpoint inhibitor durvalumab with neoadjuvant chemotherapy and had previously confirmed a significantly improved pathological complete response (pCR) rate with this combination. Bucking the trend of both the Keynote-522 and Impassion031 studies, GeparNuevo avoided administration of adjuvant immunotherapy, but still confirmed significantly improved longer term outcomes in patients with early triple-negative breast cancer (TNBC).

In contrast, Jennifer Litton presented data from the **NEOTALA** study, confirming impressive pCR rates with 24 weeks of single agent, neoadjuvant talazoparib (comparable to multi-agent chemotherapy). In this carefully selected cohort of patients with TNBC harbouring gBRCA1/2 mutations, this further highlights the potential to tailor treatment based on the findings of genetic testing.

In the metastatic space, the updated survival outcomes from the **PALOMA-3** and **MONALEESA-3** trials were presented by Massimo Cristofanilli and Dennis Slamon in the oral abstract session, together assessing the combination of a cyclin-dependent kinase 4/6 (CDK4/6) inhibitor (Palbociclib or Ribociclib) with fulvestrant in patients with ER+, HER2 negative breast cancer. Both studies confirmed a prolonged overall survival benefit with the combination compared to fulvestrant therapy alone, and both presented interesting subset analyses, including second PFS (PFS2) data in MONALEESA-3, that can serve to allay some of our fears that patients may experience rapid disease progression on cessation of CDK4/6i therapy.

While it was disappointing to see negative results presented by local luminary Geoff Lindeman from the **Veronica** study, confirming no role for the BCL-2 inhibitor Venetoclax in combination with fulvestrant following progression on CDK4/6i therapy, some truly exciting findings highlighting a promising new compound were presented in the setting of metastatic triple negative breast cancer. Further data from the phase 3 ASCENT trial confirmed the impressive superiority of the antibody-drug conjugate Sacituzumab govitecan compared to standard chemotherapy, irrespective of patient age, in often heavily pre-treated participants with metastatic TNBC.

ASBD MEMBERS ONLY DINNER AT AIBC - POSTPONED!

Due to the postponement of the AIBC, the ASBD Member's Only Dinner has also been postponed. In 2022 the ASBD will celebrate our 25th Anniversary at the member's dinner. The new date for the private 25th Anniversary Dinner for ASBD members is Thursday 13th October 2022 at The Rooftop, Level 12, Rydges South Bank, Brisbane, adjacent to the conference venue.

Come along, enjoy a fun night and catch up in person with friends and colleagues.

Registrations already received for the 2021 dinner will be rolled over to the 2022 dinner and honoured even if the fee for the 2022 dinner increases. If you would prefer a refund please contact **Kerry Eyles**.

The fee for the 2022 dinner will be finalised and promoted early in 2022.

Autologous fat grafting – the latest addition to oncoplastic breast surgery item numbers

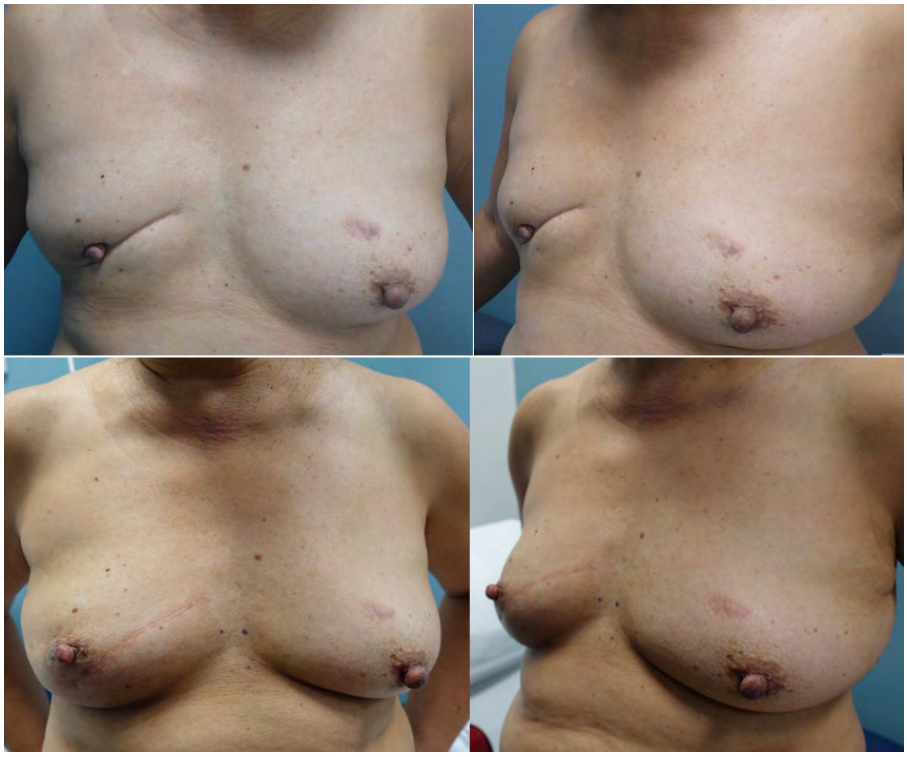
A/Prof Elisabeth Elder, Breast Surgeon, Westmead Breast Cancer Institute and Lakeview Private Hospital

From 1 November 2021, Autologous Fat Grafting (AFG), also called lipofilling or lipomodelling, will be funded through the MBS scheme. This change will make this potentially very useful technique available to a wider group of patients both in the public and private system. AFG is used to correct or prevent defects after breast conserving surgery, smooth the contours over breast reconstruction or rejuvenate irradiated skin prior to reconstruction. It may also reduce pain arising from scarred tissue. Occasionally it may also be used for a whole breast reconstruction. The new MBS item number is only applicable after treatment or prevention of breast cancer or developmental disorders, not for cosmetic purposes.

AFG involves harvesting of fat usually from the abdomen or the thighs, preparation of the fat by various methods of centrifugation and/or purification, and then re-injection of the fat into the affected breast area. The prepared fat needs to be injected in small strips, like 'spaghetti' so that it can integrate properly with the surrounding tissue, and to avoid oversaturation. The survival rate, or take rate, of the fat is about 50-70% and often the procedure needs to be repeated at least once after a minimum of three months to achieve optimal results. The new MBS item allows up to five sessions. The fat resorption long term seems to be minimal, leading to long term stable results.

The procedure can be done in day surgery and typically takes 30-60 minutes. The main issue in recovery is potential bruising from the donor site. The complication rate is low, but oil cysts and areas of fat necrosis may develop over time which can be seen on breast imaging.

Fat has a very high content of adipocyte-derived stem cells which has a regenerative potential and also an extensive secretory profile of pro- and anti-inflammatory cytokines and growth factors. AFG has been shown to increase angiogenesis as well as lymphangiogenesis, suppress local inflammatory responses and reduce fibrogenesis. This means that AFG may not only add volume, but can also rejuvenate the recipient tissue and improve skin quality and may to some degree reverse radiation induced damaged such as fibrosis, microvascular damage and chronic inflammation.



Before and after 5 sessions of AFG to the right breast, in a woman who had developed a defect of the right lower pole after breast conserving surgery and radiotherapy 10 years earlier.

Because of the regenerative properties of AFG, there have been theoretical concerns about an increase breast cancer risk which were backed by some early experimental data. However, this has not been shown to translate into a clinically significant risk, and several long-term well-designed studies have now shown that there is no increase in local recurrence rate after AFG.

The purpose of all of this is, of course, to provide women with as good a result as possible from their surgery, not just from an oncological point of view but also from an aesthetic and quality of life perspective. Many studies have shown how poor cosmetic outcomes after breast surgery may lead to negative body image, which in turn is associated with anxiety/depression and other psychosocial issues. AFG can provide a cost-effective alternative to more complex surgical procedures or, in some cases, to long term pain medication.

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ASBD Conference Plans – Save the Dates!

2022 13-15 October, Australasian International Breast Congress, Brisbane

2023 14-16 September, ASBD 13th Scientific Meeting, Adelaide Convention Centre, Adelaide

Roadmap for Optimising Screening

Amanda Tattam, Cancer Council Australia

Our knowledge about breast cancer detection, risk factors, and medical imaging technology has advanced enormously over the past 20 years.

Yet, the system for screening women aged over 50 has remained essentially unchanged since the mid-1990s. Most Australian women are offered biennial screening with mammography unless they are in a high-risk category.

Cancer Council Australia is undertaking a large Australian Government funded project to investigate how to potentially personalise breast cancer screening for all women by tailoring screening protocols according to different risk factors.

The "Roadmap for Optimising Screening in Australia" - Breast (ROSA)* project was established in 2018. It is led by Associate Professor Carolyn Nickson from the Daffodil Centre (a joint venture between Cancer Council NSW and the University of Sydney) and the University of Melbourne. The ROSA project team is assembling the best available evidence through systematic and scoping reviews, epidemiological studies and Australian modelling evaluations of the costs, benefits and harms of different approaches to risk-based breast screening. Stakeholder consultation to find the best way forward is also an important part of the project.

Associate Professor Carolyn Nickson from the Daffodil Centre

ROSA is supported by an independent, multidisciplinary expert advisory group (EAG) comprising breast cancer specialists, radiologists, health services managers and researchers. Professor Bruce Mann, University of Melbourne and Director of Breast Services at Royal Women's and Royal Melbourne Hospitals and Paul Vardon, QLD Health Director of Cancer Screening are co-chairs of the EAG.

Professor Christobel Saunders AO from the University of Western Australia is also on the group.

They support a nationally consistent approach to BreastScreen offering tailored screening for women with different levels of risk.

"While BreastScreen has contributed enormously to improved outcomes for those diagnosed with breast cancer, there is more we can do," says Professor Mann.

"We need to reduce the number of women diagnosed with later-stage cancer so that that treatment can be more effective. ROSA offers our best opportunity to do this."

Professor Saunders, who is a consultant surgeon for Fiona Stanley Hospital and St John of God Hospital Subiaco, believes modelling data generated by the project can contribute to refining approaches to personalised risk-based screening. "Clearly BreastScreen offers a fantastic service and outcomes to Australian women and has done over many years, but if we can use the information and data generated by screening programs to improve BreastScreen outcomes, and tailor services more to the individual and her personal risk, this would be a great achievement."

As Associate Professor Nickson explains, "ROSA's goal is to identify the best possible breast screening services for Australian women at all levels of breast cancer risk. The project is assessing the quality of available breast cancer risk tools and the role of breast density in both breast cancer risk and screening accuracy."

The ROSA project is answering key questions such as:

1. **Which screening technologies and intervals should be offered to different risk groups?**
2. **How and when should risk be assessed, and which health professionals should be involved?**
3. **Which age groups should be included in risk-based, personalised screening?**
4. **How would risk-based screening relate to other services such as primary care and family cancer centres?**

ROSA is guided by a five-year Roadmap that includes monitoring emerging technologies and innovations such as new breast imaging methods, new approaches to risk assessment, and the use of Artificial Intelligence (AI) algorithms to optimally combine information at the time of screening with clinical histories.

"Our goal is to identify and recommend solutions that suit the Australian health setting and population, using a nationally coordinated and flexible approach that can continue to adapt to new evidence as it emerges. We also want to map out how screening and clinical health services could work together as smoothly as possible if more risk-based screening protocols are recommended."

Further information is available on the Cancer Council Australia website.To keep up to date, contact ROSA Project via email: rosabreast@nswcc.org.au

*Prior to 2021, the ROSA project was known as Optimising Early Detection of Breast Cancer in Australia (OEDBCA).

Robots for learning in the Metastatic Breast Cancer Nurse Training Program

Jenny Gilchrist, Chief Clinical Leader – Metastatic, The McGrath Foundation

The Metastatic Breast Cancer Nurse Training Program (MBCNTP) is a joint collaboration between McGrath Foundation, Monash Health, Monash University and Southern Melbourne Integrated Cancer Service offering an individualised, experiential learning approach to improve nursing knowledge, skills and confidence in the area of metastatic breast cancer nursing.

In 2021-2022 the MBCNTP will be run as a pilot, with Monash University conducting research around the impact and acceptability of the training program, including the use of telepresence robots to facilitate remote learning. The MBCNTP will be conducted at the Monash Cancer Centre in Melbourne, facilitated by Metastatic Breast Cancer Nurse Practitioner Monash Health / McGrath Education Clinical Lead Gillian Kruss.

Eight nurses from across Australia will have the opportunity to participate in the pilot - either in-person or via a telepresence robot. The MBCNTP was originally planned to be delivered in-person with nurses to travel to Melbourne to attend, however ongoing COVID-19 travel and lockdown restrictions delayed commencement of the program. This prompted the McGrath Foundation to seek an innovative solution that would allow nurses to participate without having to travel or even leave their own homes. The telepresence robot nicknamed 'Rosie' looks like an 'iPad on a Segway' and can be operated remotely by the participating nurse using any hand-held device. Through the robot they can 'shadow' the nurse practitioner and see, hear and interact with patients and clinicians – just as if they were there in the hospital. Robot training sessions are held prior to commencement of the education program with each nurse to ensure they are comfortable controlling the robot and to practice navigating around the hospital.

Recognising that breast care nurses bring varying knowledge and experience to their roles, the MBCNTP offers an individualised approach to learning – each training program will be designed from a curriculum of 20 modules according to the nurse's responses to a baseline learning needs assessment and interview.

The MBCNTP involves three components:

Prepare – Online learning component – Nurses will work through individualised online coursework to prepare them for their 3-day practicum. Approximately 20 hours learning time.

Explore – 3-day Practicum – Nurses will attend a 3-day practicum at the Monash Cancer Centre in-person OR remotely via a telepresence robot. During this time the paired nurses will have the opportunity to observe and engage in a nurse-led MBC MDTM and dedicated MBC clinic along with other clinical experiences according to their learning needs, such as attending a menopause or familial cancer clinic or sitting in on medical or radiation oncology consultations.

Apply – Bi-monthly clinical supervision – Following completion of the 3-day practicum, nurses will return to their workplaces with continued support to integrate their learning into practice via 6 x 1-hour clinical supervision sessions over 12 months. Clinical supervision will be provided by experienced metastatic breast cancer nurses trained in clinical supervision.

McGrath Foundation's Chief Clinical Lead - Education, Gillian Kruss and the telepresence robot nicknamed 'Rosie'

Expressions of interest were received and accepted from eight dedicated Metastatic McGrath Breast Care Nurses, one of whom has already undergone the program. The feedback thus far has been excellent, with nurses describing the experience as intensive but very beneficial.

ASBD 2021 AGM

Due to the ongoing COVID-19 pandemic the 2021 Annual General Meeting will be a virtual meeting and will be held online on **Thursday 14th October 2021 at 7.00pm AEDST.** Instructions on how to access the virtual AGM will be advised soon to all members.

To indicate your intention to attend and ensure you get login instructions **email Kerry Eyles**

If you are interested in joining the ASBD Board of Directors, please **email Kerry Eyles** for more information.

THE LATEST RESOURCES FROM RESEARCH REVIEW

RESEARCH REVIEW™
Australia's Leader in Specialist Publications

RECENT REVIEWS

Breast Cancer Research Review Issue 38 – Dr Hilary Martin

- Tool to individualise prognosis and predict chemotherapy benefit in early breast cancer
- Mindfulness-based intervention in breast cancer
- Gene signature to aid treatment decisions in early breast cancer

Oncology Practice Review Issue 15

- COVID-19 vaccines in cancer patients
- USANZ framework to address gender equity
- COVID-19 resources

ASCO 2021 Focus on Breast Cancer

ANZGOG Annual Scientific Meeting 2021

EDUCATIONAL SERIES

Cancer immunotherapy adverse reactions in the ED - Dr George Plunkett

Opioid medications in Australia: A review of the harms – Dr Malcolm Hogg

PRODUCT REVIEWS

3D Mammography – Dr Geraldine Goss

INDUSTRY RESOURCES

Choose below from educational resources that include topical videos with international experts.

Managing common side effects of abemaciclib, Dr Alistair Ring, Medical Oncologist, Royal Marsden Hospital, London

A case study in endocrine-resistant MBC with liver metastasis, Dr Giuseppe Curigliano, European Institute of Oncology, IRCCS, and University of Milano, Italy

A case in MBC with endocrine sensitivity, Prof. Sherko Kümmel, Director, Interdisciplinary Brest Unit, Kliniken Essen-Mitte (KEM), Germany

ICCR datasets for Breast (June 2021)

International Collaboration on Cancer Reporting latest datasets:

Invasive carcinoma of the breast

Ductal carcinoma in situ, variants of lobular carcinoma in situ and low-grade lesions

Surgically removed lymph nodes for breast tumours

AIBC Registration Update

NEW DATE: 13-15 October 2022, Brisbane Convention Centre

REGISTRATIONS

Registrations including workshop registrations already made will be transferred to the 2022 dates. If you would prefer to receive a refund, please contact the registration department no later than September 8th 2021 by replying to the email you received from IMPACT Events regarding your registration.

If you registered for the Virtual Congress we encourage you to upgrade to a full in-person registration before the new early fee deadline.

IMPORTANT DATES

EARLY BIRD DEADLINE
Wednesday 13th July 2022

CALL FOR ABSTRACTS
Wednesday 6th 2022

A DARKER SHADE OF PINK

The story of the Advanced Breast Cancer Group by group therapists Mary O'Brien and Pia Hirsch. *"Our hope is that the book will encourage more health professionals and breast cancer services to invest in developing professionally led group services to complement individual support that is available."*

The book describes the story of 21 years of supporting women living with metastatic breast cancer. It is a pragmatic guide about establishing and running this kind of group as well as a collection of funny, sad, and creative stories and experiences told by Mary, Pia and the women who have been a part of the ABCG throughout the last 21 years.

"For any person who has ever loved someone who has advanced cancer and struggled to know what to say – this book is for you.

For any health professional who is uncertain about how far to explore the emotional dimensions of the experience of advanced cancer – this book is for you.

For anyone who is interested in establishing a support group – this book is for you. It is warm and engaging and demonstrates the power of shared humanity even in the darkest of places and is likely to provide hope and comfort for those who have advanced cancer."

Professor Jane Turner,
University of Queensland

MORE INFO/ORDER

CASE PRESENTATION
An unusual Triple Negative Breast Cancer

Nirmala Pathmanathan (Director, Westmead Breast Cancer Institute and Specialist Breast Pathologist Douglass Hanly Moir Pathology)

DG is a 58-year-old woman who presented with a self-detected right breast lump. She has no relevant past medical history and is on no regular medications. On examination a firm, mobile mass was felt in the central breast in the upper outer quadrant of the breast adjacent to the areola. There was no axillary lymphadenopathy. On ultrasound a well-defined mass was seen 23mm x 18mm x 14mm. On mammogram a mass lesion was seen with some some spicular extensions.

A core biopsy was performed and reported as "salivary gland type tumour", with differential diagnosis including adenoid cystic carcinoma.

A wide local excision and sentinel node biopsy were performed.

Macroscopic Findings: a partly well circumscribed tan tumour was seen in the breast tissue

Microscopic findings: The tumour showed cribriform and tubular growth patterns and much of the lesions showed a pushing and circumscribed edge. Both true lumina (containing mucin) and pseudolumina (containing basement membrane like material) were seen. The luminal cells were positive for CK8/18, CK7 and CD117 (c-Kit). The basal cells were positive with basal cytokeratins (CK5/6, CK14) and myoepithelial markers (P63, SMMHC). Both ER and PR as well as HER2 were negative. The surgical margins were clear of the tumour and the sentinel node was negative.

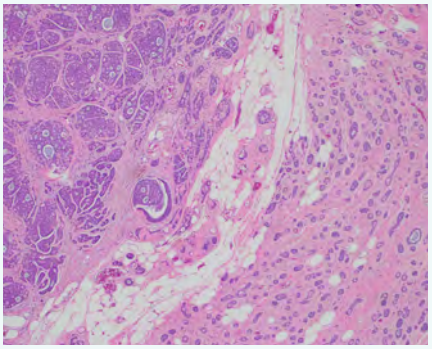


Fig. 1

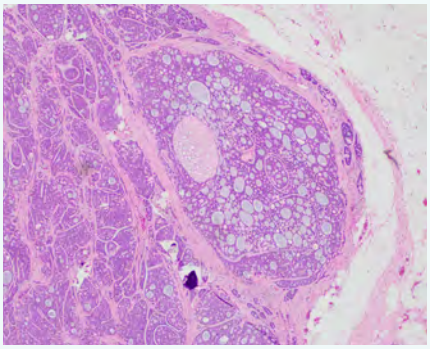


Fig. 2

Low power view at X40 Magnification showing cribriform and tubular growth (Fig. 1) and circumscription (Fig. 2)

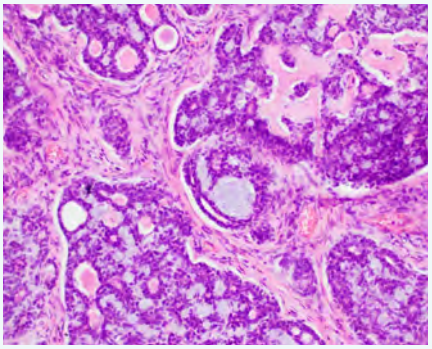


Fig. 3

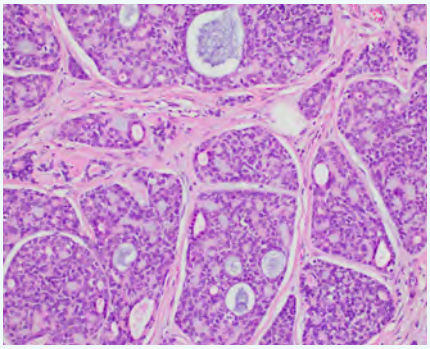
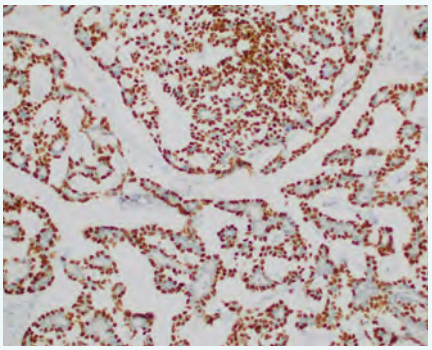
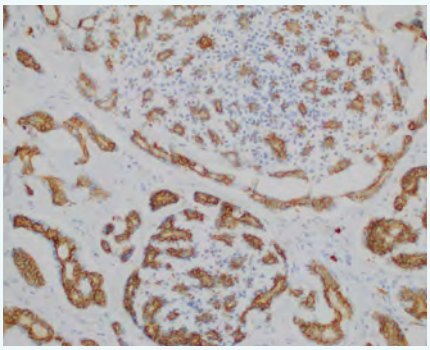


Fig. 4

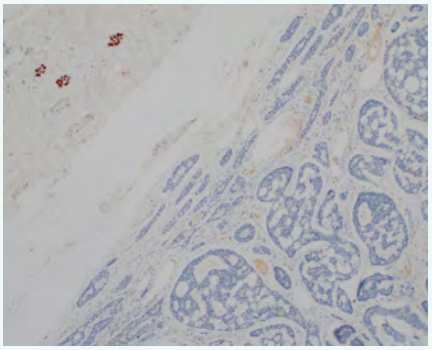
Basophilic mucin in true lumina (Fig. 3) and pink basement membrane material in pseudolumina (Fig. 4)



P63 positive basal cells (Fig. 5)



cKit positive luminal cells (Fig. 6)



ER negative with positive internal control in normal breast ducts (Fig. 7)

Discussion

Clinical and Imaging findings

Primary adenoid cystic carcinoma (ACC) of the breast is rare, accounting for less than 1% of breast malignancies. ACCs are more prevalent in the salivary glands and upper respiratory tract. They occur in patients aged between 38-81 years according to various published case reports but there is a preponderance in post-menopausal women. The tumours are often central in location and present as a palpable mass. On imaging the tumours appear as asymmetric densities or irregular masses mammographically, and well defined, irregular or hypoechoic masses. In most cases the findings on imaging are non-specific and a histologic diagnosis is needed for confirmation of malignancy.

Morphology and Immunophenotype

ACCs are characterised histologically dual cell populations of luminal and basal cells, which are arranged in characteristic growth patterns. In addition there is an abundance of basement membrane-like material. Three architectural patterns are described; tubular-trabecular, cribriform and solid-basaloid. The tumours display true lumina and pseudolumina. The true lumina contain PAS positive mucin and are lined my epithelial cells, whereas the pseudo lumina contain basement membrane material and are lined by myoepithelial/basal cells. The luminal cells display rounded nuclei and eosinophilic cytoplasm and are positive for CK8/18, CK7, CD117 (c-Kit) and MYB. The basal cells have more oval shaped nuclei with scant cytoplasm and are positive with basal cytokeratins (CK5, CK5/6, CK14, CK17), myoepithelial markers (P63, S-100, SMA, SMMHC). Perineural infiltration is uncommon.

These tumours are triple negative (ER/PR and HER2 negative), and on gene expression profiling these tumours align with a basal-like phenotype. However in contrast with the other triple negative and basal-like tumours which are characterised by an aggressive clinical course, ACCs exhibit a low grade clinical course and more indolent behaviour. This is corroborated by usually low levels of Ki67 expression.

The solid-basaloid variant displays a predominant solid growth with increased atypia and higher mitotic rates. Necrosis and perineural invasion are seen in this variant.

ACCs have been associated with microglandular adenosis (MGA) and there are some case studies that have shown a progressions from MGA to atypical MGA to ACC.

Molecular and Genetic Features

Molecular subtype analyses mostly place ACC with other basal-like phenotypes, but unlike medullary and metaplastic members of this group, displayed considerably less genetic instability, lower copy number alterations and infrequent aneuploidy. This illustrates the heterogeneity that exists within the basal group. ACC frequently shows MYB-NFIB fusion gene, MYBL1 rearrangements or MYB amplification. Downstream signals of these alterations may be candidates for potential therapeutic targets.

Differential Diagnosis

ACC should be distinguished from tubular and cribriform carcinomas, and this may be problematic particularly on core biopsies. Tubular/cribriform carcinomas usually have only a luminal cell type and are mostly strong ER/PR positive. CD117(c-Kit) and P63 are also negative. Collagenous spherulosis is a benign condition characterised by spherules of collagen bound by small cells. No PAS positive mucin is seen in these lesions in contrast to ACC and c-Kit is also negative. Solid variants of ACC can be distinguished from neuroendocrine tumours on the basis of immunohistochemistry.

Clinical Course

In the salivary gland where these tumours are more prevalent, the tumours are graded on the basis of the proportion of the solid component (no solid growth considered grade 1, less than or equal to 30%, grade 2, and >30% grade 3). Grade 2 and 3 primary breast ACCs using this schema tend to present with larger tumours and were more likely to recur. Nottingham grading is still the recommended grading system for these tumours. The few cases that are in the literature hat have metastasised, these were all at least grade 2. Solid-basal variants of ACC with greater degrees of atypia and mitotic activity are also associated with a more aggressive clinical course.

The 10 year survival rate according to meta-analyses is 90-100% and lymph node and distant metastases are rare. When metastases do occur these are to visceral organs.

Management

In view of the usual indolent clinical course and good prognosis, ACC is usually cured following breast conservation surgery where surgical clearance is achievable. Positive margins are often seen and should be re-excised to avoid recurrences. A study with a large patient cohort found that radiotherapy was of considerable benefit in overall as well as disease specific survival. The utility of chemotherapy is less well defined and variably used mostly in high grade lesions or those with axillary lymph node involvement.

Even following local recurrence or distant metastases, a prolonged clinical course is still usual. Long term follow up is recommended given this long clinical course.

Conclusion

ACC is a rare type of triple negative breast cancer, with very few cases/series reported in the literature. Accurate identification of ACC is important as this type of triple negative breast cancer is characterised by an indolent clinical course and is unlikely to warrant or even respond to chemotherapy, unlike the other members of the basal/triple negative group.

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