BreastScreen WA

Breast Cancer Prevention, Screening and Diagnosis Clinical Research Symposium Report

Overview of Presentations and Discussion

Symposium of Friday 3rd May 2013

Wollaston Conference Centre

Government of Western Australia
Department of Health
WA Cancer and Palliative Care Network

BreastScreen WA
WA's only accredited screening service

Telephone: 13 20 50

Contents

Welcome - commentary

Welcome:

Dr Amanda Frazer

Opening comments:

- One in eight Australian women will develop breast cancer in their lifetime.
- The Western Australian public have been very generous over the years supporting fundraising efforts to promote breast cancer research. There is a perception that Western Australia has in recent years not attracted funding grants back to the State for breast cancer research proportional to the States research potential and fundraising efforts.
- The high standard of medical service delivery in Western Australia in respect to breast cancer diagnosis is nationally recognised. It would be good to see Western Australia equally recognised as a national leader in breast cancer diagnosis research.
- The purpose of today's seminar is to bring the WA Research Community together to share information about data resources available in Western Australia and to show case research and innovation that is already occurring.
- Today is an opportunity for potential and emerging breast cancer researchers to network and hopefully develop research propositions and collaborations that will improve outcomes for all Australian women in respect to breast cancer detection and survival.

Objectives and agenda

Objectives:

- To inform researchers of current resources available
- To showcase current WA breast cancer research projects
- To formulate plans and ideas for future research projects
- To explore possible collaborations and partnerships in the field of breast cancer research
- To facilitate networking and liaison among people interested in breast cancer research

Agenda:

- Current resources
- Current research in WA
- Small group session
    - Priorities for research and collaboration
    - Where to from here?

Facilitator: Janelle Marr

StepBeyond Business Advisors

Contents

Part 1: Current Resources

Agenda	Focus Topic	Presenter
Part 1 - Current Resources	**1. WA Cancer Registry**	Dr Tim Threlfall, Principal Medical Officer/ Manager, Health Department of WA, Performance Activity and Quality, Data Integrity
	2. Health Linkage	A/Prof Angela Ives, Cancer and Palliative Care Research and Evaluation Unit (CaPCREU), University of Western Australia
	3. Breast Screen Data	Dr Liz Wylie, Medical Director, BreastScreen WA
	4. Current Breast Cancer Research Funding and Biobanks	Christobel Saunders, Winthrop Professor, Deputy Head of School, School of Surgery, University of Western Australia
Wrap up	**Current Resources in WA – gaps, discussion themes**	Facilitator: Janelle Marr Chair: Christobel Saunders

Current resources:
1. WA Cancer Registry – Dr Tim Threlfall

- Dr Tim Threlfall, Principal Medical Officer / Manage, Health Department of WA, Performance Activity & Quality, Data Integrity, Contact: tim.threlfall@health.wa.gov.au

Summary:

- Provided an overview of the range of statistical information on breast cancer available in the WA Cancer Registry database including the following themes:
  - WACR update on breast cancers based on 2011 data
  - Most common cancer in women
  - Now grossly outnumbered by prostate cancers in men BUT almost as many deaths
  - Relative prominence highest in middle age (incidence) but worse in the young (mortality)
  - There are a lot of cases apart from the "first ever" cancers usually reported
  - Histological diagnosis in almost 97% of cases
  - Tumour size well-reported
  - Gaps in information about nodes
  - Are positive nodes where you look for them?
  - Personal history affects tumour size

Current resources:
2. Health Linkage – A/Prof Angela Ives

- A/Prof Angela Ives - Cancer and Palliative Care Research and Evaluation Unit (CaPCREU)
  The University of Western Australia, Contact: angela.ives@uwa.edu.au

Summary:

- Provided a summary on data linkage – a technique for creating links within and between data sources for information that is thought to relate to the same person, family, place or event.
- Data linkage is a technique for creating links within and between data sources for information that is thought to relate to the same person, family, place or event. By creating links for the same person with medical information in different datasets, the data can be extracted in a de-identified version for audit and research to ensure patient privacy.
- The use of data linkage in WA was first proposed in 1970 and construction of the WA Data Linkage System (WADLS) commenced in 1995 with infrastructure funding from the Lotteries Commission of WA. Since its inception the WADLS has undergone substantial growth and change and today brings together more than 30 million patient records from the WA.
- The WADLS is run by Data Linkage WA and is located within the Department of Health, Perth. The WADLS includes eight core data sets: birth registry, death registry, electoral roll, emergency department data, hospital mortality database (inpatient registrations), cancer registry, midwives notifications and mental health data. Currently linkage is available to more than 30 datasets and other datasets can be linked on an ad hoc basis. Data is available in some datasets from 1966 but generally data is available on people from the early 1980s on.

(continued over page)

Current resources:
2. Health Linkage – A/Prof Angela Ives

(continued)

- The core datasets themselves are stored at the Department of Health WA but not within the WADLS. The WADLS acts more like a library catalogue. The WADLS function is to maintain a master linkage key for each individual so that if data on someone is requested the core datasets can be interrogated and data on that person obtained from the custodians of the specific datasets.
- Data linkage is being used in many more countries and even within Australia systems are being developed in other states and territories. At a national level the Population Health Research Network was created to develop a national data linkage system in Australia. Pilot projects are underway around Australia.
- For cancer audit and research some data is currently not easily available for linkage eg Outpatient and Radiotherapy data. Plans are being developed so that this data can be linked.
- Data Linkage Website: http://www.datalinkage-wa.org/
- Population Health Research Network Website: http://www.phrn.org.au/

Current resources:
3. Breast Screen Data – Dr Liz Wylie

- Dr Liz Wylie, Medical Director, BreastScreen WA, Contact: liz.wylie@health.wa.gov.au

Summary:

- BreastScreen Australia's services regularly undergo data audits to ensure that data is collected in a comprehensive, secure, and consistent manner.
- Dr Wylie outlined the strict Department of Health research governance guidelines and operational directives to which Breast Screen WA must adhere to ensure compliance, particularly in respect to Human Ethics Research Committee approval, formal data applications, and client data confidentiality.
- BreastScreen Australia does not receive State or Federal funding to undertake research. BreastScreen has been disappointed in the past that researchers have submitted research proposals to potential funders' dependant on the use of BreastScreen data, or access to BreastScreen clients without appropriately collaborating with the program, at the initial steps of proposal development.
- BreastScreen Australia wants to encourage researchers to address and funders to support BreastScreen priority research themes and questions.
- The BreastScreen Australia Evaluation released in September 2009 made 19 recommendations:
- Recommendation 15 of the evaluation noted that very little research had been published using BreastScreen Australia data.

(continued over page)

Current resources:
3. Breast Screen Data – Dr Liz Wylie

(continued)

- The BreastScreen evaluation report recommended that BreastScreen Australia performance data be used to inform policy development; monitor and evaluate program performance; and enable strategic research.
- BreastScreen Australia service performance is measured against 177 National Accreditation Standards.
- BreastScreen Australia data is standardised across the country through the use of a data dictionary.
- BreastScreen Australia services' regularly undergo data audits to ensure that data is collected in a comprehensive, secure, and consistent manner.
- Research undertaken utilising Department of Health data must comply, with the Departments research governance, policy and procedures operational directive, particularly in respect to Human Ethics Research Committee approval, formal data applications, and client data confidentiality.
- Each women screened in the program consents at each screening episode to her de-identified data being used for research.
- BreastScreen Australia has developed in 2012 a "research framework" to ensure the Program communicates its research priorities in the fields of clinical, behavioural and service systems to the research community in a systematic way.

Current resources:
4. Current Breast Cancer Research Funding and Biobanks – Dr Christobel Saunders

- Christobel Saunders, Winthrop Professor, Deputy head of School, School of Surgery, University of Western Australia, Contact: christobel.saunders@uwa.edu.au

Summary:

- Provided a summary on the funding of cancer research in Australia and an overview of biobanks. Information of the continuum through the pyramid of research; sources of funding; use of competitive funding; breakdown by disease type; who is funding research; hot topics in research; and biobanks.
- Topics in research include:
  1. Identify molecular signatures to select patients who could be spared chemotherapy
  2. Identify molecular features which indicate the optimal chemotherapy
  3. Determine the factors in DCIS leading to progression
  4. Determine the role of stem cells in breast cancer
  5. Basal: Identify response/resistance mechanisms and thereby therapy targets
  6. Develop computer system that will integrate all the information so far gathered about breast cancer
  7. Identifying which low risk patients require NO adjuvant therapy
  8. Determine if other growth factor pathways are important targets for therapy
  9. Investigate which gene mutations in a cancer lead to metastases
  10. Identify targets that can be exploited for therapeutic gain to overcome endocrine resistance

Current resources:
4. Current Breast Cancer Research Funding and Biobanks – Dr Christobel Saunders

Continued:

Use of Biobanks:

- Clinical trials – provides translational arm e.g. looking for SNPs that influence risk or response to intervention
- In-vivo experiments eg. locally advanced breast cancer in patients undergo neo-adjuvant chemotherapy – core biopsy and surgical specimen – FFPE and frozen tissue collected and access to archival tissue

What do we have in WA?

- SJOG; Linked to ABCTB in NSW; PathWest; TMA collections; DNA bank

Practical thoughts for collecting and curating clinical specimens:

- ETHICS
- Make it routine for radiologists, surgeons and pathologists
- Clearly identify what tissue and what data needs to be collected.
- Then put foolproof systems in place that DO NOT ADD ANY BURDEN to clinicians
- Regularly update follow up data for recurrence and death - Death and cancer registries; Hospital based cancer registries; Health linkage; PBAC etc data; ? From patient or GP

What data to collect?

- Conventional pathology phenotype –IHC; Molecular phenotypes; Normal like; Luminal A; Luminal B; HER2 positive; Basal like; Claudin-low; Patient details; Treatment details

Current resources: Group discussion items

Summary of key points:

- Statistical unit record level data requires – free service (appropriate person contact Tim)
  - Type/Location; Sex; Dx age; Dx address; Dx date; Size, noder
- Other data linkages:
  - Appropriate team Data Services Branch (has link to Ethics Committee website, Tim can provide this information also)
  - Consider what specific data sets, costs associated with request, protocols and literature reviews
- Data pre-2006 relatively reliable and accurate
- Follow up reports (gaps in service currently)

Contents

Part 2: Current Research

Agenda	Focus Topic	Presenter
Part 2 - Current Research	**1. Translational Research Portfolio**	A/Prof Andrew Redfern, Professor of Medical Oncology, Royal Perth Hospital and Translational Cancer researcher, University of Western Australia
	2. New Diagnostic Tools	Dr Robert McLaughlin, Optical + Biomedical Engineering Laboratory, University of Western Australia
	3. C.E.S.M. Study	Dr Donna Taylor, Consultant Radiologist, Department of Diagnostic and Interventional Radiology, Royal Perth Hospital
	4. New Localisation Tools	Dr Anita Bourke, Radiologist, Sir Charles Gairdner Hospital
	5. Circulating Tumour Cells	Dr Vineeta Singh, Consultant Surgeon, Armadale Health Service
	6. Breast Screening: Pre/Post Evaluation of new CA Screening Leaflet	Dr Toni Musiello, PhD, Research role at University of Western Australia and Clinical Psychologist Registrar, AHPRA

Part 2: Current Research *(continued)*

Agenda	Focus Topic	Presenter
Part 2 - Current Research	**7. Breast Cancer Research for Indigenous Women**	Dr Shaouli Shahid, Assistant Research Professor (NHMRC-funded Research Fellow), Combined Universities Centre for Rural Health, University of Western Australia
	8. Genetic Research: ICON project	Dr Nicholas Pachter, Clinical Geneticist, Familial Cancer Program, Genetic Services of Western Australia
	9. Breast Density	Dr Jennifer Stone, National Breast Cancer Foundation Research Fellow, Centre for Molecular, Environmental, Genetic and Analytic (MEGA) Epidemiology, University of Melbourne
	10. Breast Density Interventions	Dr Hilary Martin, Registrar, Department of Medicine, Royal Perth Hospital
	11. Assessment of Ki67 Proliferative Activity in Breast Carcinoma	W/Prof Jennet Harvey, Winthrop Professor, School of Pathology and Laboratory Medicine, University of Western Australia

Current research:
1. Translational Research Portfolio – A/Prof Andrew Redfern

- A/Prof Andrew Redfern, Professor of Medical Oncology at Royal Perth Hospital and Translational Cancer Researcher with University of Western Australia, Contact: andrew.redfern@optusnet.com.au

Summary:

- Provided an overview of a spectrum of ongoing translational projects from prevention of initial breast cancer occurrence to treatment resistance in metastatic disease. New breast cancer cases were at a record high by latest figures for WA and targeted preventative strategies will be explored inclusive of a potential initiative to tailor screening protocols to mammographic density and other factors. Further to this, indigenous outcomes across Australia are significantly inferior to the general population, even when corrected for tumour stage, remoteness and socioeconomic disadvantage.
- A proposition for an exploration of tumour biology and other risk elements was presented. For those diagnosed with early cancer a significant proportion will have both adjuvant endocrine and chemotherapy but the optimum schedule of the two remains unknown. A pilot randomised controlled trial (RCT) was outlined to address this question although with plans for a translational strategy looking at the balance of apoptosis to proliferation.
- For those then entering the survivorship arena there has been a significant body of work on the role of vitamin D levels in recurrence prevention. An initial tumour demographic analysis of a prospective case series of WA patients with assayed vitamin D levels will be presented. Finally some work on effector proteins of breast cancer treatment resistance will be discussed along with plans to validate promising biomarkers in this arena through construction of a substantial TMA library plus retrospective usage of material from completed RCTs.

Current research:
2. New Diagnostic Tools – Dr Robert McLaughlin

- Dr Robert McLaughlin, Optical + Biomedical Engineering Laboratory, University of Western Australia, Contact: robert.mclaughlin@uwa.edu.au

Summary:

- Provided an overview of work in developing a new generation of high resolution, optical imaging probes to assess breast cancer.
- Using extremely small optics, we have managed to create scanning probes that are encased within a hypodermic needle and can be inserted deep into tissue during scanning.
- Smallest probes have an outer diameter of only 310 microns – one third of a millimeter. These probes acquire images with near infrared light, using a technology called optical coherence tomography (OCT).
- Dr McLaughlin presented initial results with breast cancer tissue, and work to extend these probes into multi-modality imaging, capable of simultaneously acquiring OCT and fluorescence images.
- Dr McLaughlin also described recent work using optical techniques to perform a new type of high resolution elastography imaging.

Current research:
3. C.E.S.M. Study – Dr Donna Taylor

- Dr Donna Taylor, Consultant Radiologist in the Department of Diagnostic and Interventional Radiology at Royal Perth Hospital, Contact: donna.taylor@health.wa.gov.au

Summary:

- Provided an overview of a validation study to assess the effectiveness of Contrast Enhanced Spectral Mammography (CESM) in comparison with Contrast Enhanced Magnetic Resonance Imaging (CEMRI) as a tool for local staging of breast cancer (The “CESM V” study).

Background and purpose:

- Contrast enhanced MRI (CEMRI) is the most sensitive imaging modality for breast cancer diagnosis. Barriers to its use include cost, accessibility and patient contraindications. Using a similar principle to CEMRI, contrast enhanced spectral mammography (CESM) can delineate malignant lesions by showing areas of abnormal contrast uptake associated with tumour neoangiogenesis and "leaky" vessels.
- Equipment used in CESM delivers low energy and high energy XRay exposures in quick succession. An intravenous injection of non-ionic iodinated contrast is followed by dual-energy views of both breasts. A recombination algorithm suppresses background tissue revealing areas of contrast enhancement.
- Studies support diagnostic accuracy of CESM for breast cancer detection as superior to mammography and ultrasound combined. CESM can detect known primary tumours at a rate comparable to MR imaging. Sensitivity is slightly inferior and specificity slightly superior in assessing extent of malignant disease.

(continued over page)

Current research:
3. C.E.S.M. Study – Dr Donna Taylor

Continued

Aims:

- Compare the accuracy of CESM and CEMRI in preoperative staging of the breast in women with proven breast cancer based on conventional imaging (mammography +/- ultrasound).
- Quantify the accuracy of each test in detecting additional foci of cancer and ability to measure the size of the index cancer(s). Determine presence or absence of incremental improvement in malignant lesion detection by adding CESM vs MRI findings to those of conventional imaging with mammography +/- ultrasound.

Protocol:

- Sixty participants from the RPH Breast Clinic will undergo CESM and CEMRI examinations, double read by two independent sets of radiologists (blinded to CEMRI findings and vice versa). Readers will document: (1) technical adequacy; (2) size, location, morphology and degree of enhancement of the primary index lesion(s); (3) any additional lesions; (4) distance between lesions
- Findings that could modify patient treatment will be confirmed with biopsy using ultrasound, stereotactic or MRI guidance. Imaging lesions will be correlated with histopathology where possible. Participants in whom CE MRI or CESM have shown additional lesions not surgically removed will have follow-up CEMRI at 12 months. All participants to undergo bilateral mammography 12months post treatment.

Outcome measure/accuracy measures:

- Detection of additional lesions (classified as benign or suspicious, determination of TP, FP, TN, FN), size of index lesion(s). Other variables: procedure times, interpretation times and participant satisfaction survey.

Current research:
4. New Localisation Tools – Dr Anita Bourke

- Dr Anita Bourke, Radiologist, Sir Charles Gairdner Hospital, Contact: anita.bourke@health.wa.gov.au

Summary:

- Provided an overview of a Radioguided Occult Lesion Localization of breast cancers using 125Iodine Seeds (ROLLIS) and linked studies.
- Background: Mammographic screening has resulted in >50% breast cancers being diagnosed whilst impalpable, and 74% are now treated with breast conserving surgery.
- Current image guided lesion localization/excision, using hookwire localization (HWL) performed the same day as surgery, is associated with high re-excision rates (30%) - a significant burden for the woman and the health care system.
- A technique inserting a low activity radioactive 125I seed into the lesion using imaging guidance (ROLLIS) reduces re-excision rates, can be performed quickly and easily in advance of surgery and may result in improved cosmesis. A Western Australian multidisciplinary collaboration, the ROLLIS Working Group, have pioneered this technique in Australia.

Aims:

- A multicentre pilot study (RPH and SCGH) and extended pilot study were performed to familiarise our Multidisciplinary Breast Care Teams (MBCT) including Radiologists, Radiographers, Surgeons, Pathologists, Theatre nurses, Physicists with this new technique.

(continued over page)

Current research:
4. New Localisation Tools – Dr Anita Bourke

(continued)

Methods:

- Pilot Study: 20 participants with biopsy proven impalpable invasive cancer scheduled for breast conserving surgery underwent image guided lesion localisation with insertion of both a low activity (3 MBq) 125I seed and a hookwire for back-up.
- Where indicated, sentinel node localisation was performed using 99mTc colloid. Both sentinel node and lesion were removed using a gamma probe. Specimen radiography confirmed lesion excision and seed location.

Results:

- MBCT were trained. Developed seed tracking/handling protocols were successful. All lesions and seeds were successfully removed. Radiologists and surgeons preferred ROLLIS over HWL. Pathologists reported no difficulty with seed removal.
- Extended pilot almost concluded. RCT is about to commence. Other linked studies include Re-excision Audit, OCT, Cosmesis, Breast Volume, spatial resolution of I125seed radiation, Specimen Radiography and microCT.

Current research:
5. Circulating Tumour Cells – Dr Vineeta Singh

- Dr Vineeta Singh, Consultant Surgeon, Armadale Health Service, Contact: vineeta.singh@health.wa.gov.au

Summary:

- Provided an overview of research into the effect of surgical resection of primary tumour on Circulating Tumour Cell (CTC) number in Early Breast Cancer. The detection of CTC in the blood and cancer specific markers in plasma DNA will be valuable methodologies for monitoring response to therapy and early prediction of response. Breast cancer cells undergo dynamic reversible phenotype transformation between epithelial and mesenchymal states during metastatic progression.

Background:

- At present we do not understand the metastatic potential the CTCs. We propose to investigate how extensive cell shedding is, how many of these cells persist in the circulation, and any association between persistence of circulating cells and outcome (disease-free and overall survival). Effects of systemic treatment on CTCs have been widely studied but there are no significant studies about effect of removal of primary tumour on CTCs in breast cancer patients.

Hypothesis:

- Removal of primary tumour in breast cancer reduces or eliminates the CTCs in peripheral blood of early breast cancer patients
- Persistent or recurrence of CTCs may predict future metastatic disease.

(continued over page)

Current research:
5. Circulating Tumour Cells – Dr Vineeta Singh

Continued

Aims:

- To measure CTC numbers in the peripheral blood of breast cancer patients undergoing resection for breast cancer immediately pre- and post-operatively, and at post-operative follow up at ten days as a surrogate for number of 'viable' CTC after surgery but before start of systemic therapy .
- To study if persistence or recurrence of CTCs can be a prognostic maker for future metastatic disease.

Expected outcome:

- To observe if removal of primary reduces the number of CTCs in peripheral blood.
- To establish CTCs as a predictive tool for development of future metastatic disease.

Current research:
6. Breast Screening: Pre/Post Evaluation of new CA Screening Leaflet – Dr Toni Musiello

- Dr Toni Musiello, Researcher at University of Western Australia and Clinical Psychologist Registrar, Contact: toni.musiello@uwa.edu.au

Summary:

- Dr Musiello's main research area is in Psycho-Oncology and current research interests include decision making in breast cancer in relation to contralateral prophylactic mastectomy; routine screening of oncology patients for pscyho-social distress; mammography screening for breast cancer; gestational breast cancer; the psychosocial needs of adolescents and young adults with cancer; and the use of mindfulness based cognitive therapy for cancer patients and their carers.
- The scientific community continue to argue about the benefits of breast screening. It's stated that for every 2000 women attending routine screening for 10 years, one will be prevented from dying of breast cancer. Conversely many will be labelled with "cancer", and undergo treatment for it, when they may not have a condition which is in fact life threatening, and many more will have "false alarms". For a woman invited to attend mammography screening these outcomes may prove confusing and counterintuitive.
- In order to enable an informed decision, women need to be given information on both the benefits and harms of attending screening. To date information on harms is not easily accessible to women nor presented in easy to understand formats. Breast screening services focus on the benefits but find it difficult to explain the potential harmful consequences of screening. ***(continued over the page)***

Current research:
6. Breast Screening: Pre/Post Evaluation of new CA Screening Leaflet – Dr Toni Musiello

Continued

- This study aims to compare women who are invited to attend routine mammography screening. Half of these women will receive the standard screening information leaflet, and the other half will receive a leaflet detailing both the benefits and harms of screening.
- These groups will then be compared on their anxiety, emotional, social and physical well-being and on their routine mammography screening attendance rates.
    - Mammography screening - Regardless of the actual figures, it's clear that mammography breast screening has both benefits (your death can be prevented from breast cancer) & harms (false positives/ false negatives & over-diagnosis); and women should be making an informed choice to attend or not attend screening.
    - Making the choice - assessing the impact of informed decision making on psychological wellbeing, anxiety and screening uptake in women invited for mammography
    - Main outcomes - Decision making; Psychological well – being (anxiety); and Screening Uptake

Current research:
7. Breast Cancer Research for Indigenous Women – Dr Shaouli Shahid

- Dr Shaouli Shahid, Assistant Research Professor (NHMRC-funded Research Fellow), Combined Universities Centre for Rural Health, University of Western Australia, Contact: shaouli.shahid@uwa.edu.au

Summary:

- Provided an overview of a breast cancer research for Indigenous Women. Aboriginal and Torres Strait Islander (hereafter respectfully referred to as Indigenous) Australians compared with non-Indigenous people have a higher occurrence of preventable cancers and are less likely to access cancer screening.
- They are more likely to be diagnosed with cancer at a more advanced stage, have poorer uptake and lower compliance with treatment and to have lower five-year survival rates. Over the last 30 years, biomedicine has delivered steady improvements in cancer outcomes across a range of cancer types - yet improvements in cancer survival have not been seen for the Indigenous Australian population.
- This highlights that advances in medical treatments alone will be insufficient to minimise the disparity in cancer outcomes for Indigenous people. Research that focuses attention on the social context of how screening programs and cancer care is delivered is needed.
- Several research projects have been carried out in different jurisdictions in Australia over the last decade. In Western Australia 2005-2012, in-depth qualitative research has been undertaken, interviewing Aboriginal patients, families and cancer service providers to investigate and explore Aboriginal Australians' beliefs, understanding and perceptions around cancer, their experiences with cancer services and understand Aboriginal decision-making around screening and treatment.

(continued over page)

Current research:
7. Breast Cancer Research for Indigenous Women – Dr Shaouli Shahid

***Continued*:**

- Recently, a coordinated, collaborative, Indigenous-led national Centre for Research Excellence program entitled DISCOVER-TT (Discovering Indigenous Strategies to improve Cancer Outcomes Via Engagement, Research Translation and Training) has been funded by the NHMRC.
- This brings together key researchers, practitioners, and consumer advocacy groups from across Australia and actively promotes the translation of research knowledge into Australian public health policy and practice.
- It will train a new generation of researchers in Indigenous cancer related health services research. Several research projects under the umbrella of DISCOVER-TT will be carried out by the Combined Universities Centre for Rural Health (CUCRH) in University of Western Australia.
- A student Masters project is underway to quantify the number of Aboriginal women participating in breast cancer screening, assessment and treatment in WA between 2001 and 2010 inclusive and to determine how knowledge, attitudes and cultural factors impact on Aboriginal women attending screening and for those who are called to assessment after breast screening.

Current research:
8. Genetic Research: ICON project – Dr Nicholas Pachter

- Dr Nicholas Pachter, Clinical Geneticist, Familial Cancer Program, Genetic Services of Western Australia and Clinical Senior Lecturer in the Department of Medicine University of Western Australia, Contact: nicholas.pachter@health.wa.gov.au

Summary:

- Dr Pachter runs the Familial Cancer Program at GSWA, where patients with or at risk of Familial Cancer disorders are assessed, counselled and tested if indicated.
- Provided an overview of his research interests in the inherited basis of breast cancer, and colorectal cancer, in his role as Chief Investigator for the Inherited Cancer Connect Partnership (ICon), a multidisciplinary group of clinicians and scientists who are focused on improving the outcomes of people with rare inherited cancer syndromes.

Aims:

- To improve the outcomes of people with inherited cancer syndromes
- To formalise the links between clinics and between clinics and researchers
- To set a national translational research agenda and the means to deliver it by integrating clinic and research activities (harness the research potential of the FCCs!)

Priority areas:

- Develop a national infrastructure to connect the inherited cancer community; Develop a national approach to identify people at risk of heritable cancers; Improve the accuracy of inherited cancer risk predictions; and Improve cancer risk management of people with hereditary cancer syndromes

Current research:
9. Breast Density – Dr Jennifer Stone

- Dr Jennifer Stone, National Breast Cancer Foundation Research Fellow, Centre for Molecular, Environmental, Genetic and Analytic (MEGA) Epidemiology, The University of Melbourne, Contact: stonej@unimelb.edu.au

Summary:

- Provided an overview of research investigating not only the genetic and environmental determinants of mammographic density, but also its use in a clinical setting to optimise breast screening programs.
- Mammographic density is a strong and highly heritable breast cancer risk factor. Women with extensive mammographic density are 4-6 times more likely to develop breast cancer than women of the same age with little or no mammographic density.
- Determinants - Approximately 60% of the large variation of mammographic density in women is due to genetic factors. Potentially Modifiable: Age, BMI, number of live births, hormone therapy use, tamoxifen

Research opportunities:

- The Busselton Health Study - Currently has over 2600 women with genome wide scan data available. Of these, almost 1800 were over the age of 40 at the time of data collection (1994/5) and currently, almost all are of mammogram age.
- The Ark - an open-source web-based data management tool for medical research.
- Mammographic density in Indigenous populations

(continued over page)

Current research:
9. Breast Density – Dr Jennifer Stone

Continued

The Ark:

- Data is time-consuming to obtain and good data is invaluable
- Data should be managed with state-of-the-art techniques
- Formerly known as WAGER, The Ark was developed at UWA in 2004 to combine and manage data from ~50 studies.
  - To encourage collaboration with other researchers and policy makers
  - To encourage the exchange of ideas and data
- Currently, the Ark uses state-of-the-art security measures to provide a web-based data management solution with local support from the development team at UWA and no licensing costs.

Current research:
10. Breast Density Interventions – Dr Hilary Martin

- Dr Hilary Martin, Registrar Department of Medicine, Royal Perth Hospital,
  Contact: hilary.martin@health.wa.gov.au

Summary:

- Provided an overview of a project that aims to correlate changes in mammographic density measurement with outcome in hormone receptor positive breast cancer, treated with antiestrogen therapy. The longer term goal is to utilise MBD changes to tailor treatment.

Background:

- Two thirds of early breast cancer patients in WA receive antiestrogen therapy (AE) to reduce the risk of cancer recurrence. High mammographic breast density (MBD) has been shown to be a strong predictor for development of breast cancer. The IBIS 1 prevention study comparing tamoxifen with placebo showed individuals who experienced a fall in MBD of at least 10% had a reduction in their risk of development of breast cancer, whereas those who did not have a reduction in breast density derived no benefit. This has lead to the hypothesis that changes in breast density could be used as a marker of response to endocrine therapy in patients with early breast cancer receiving adjuvant antioestrogen therapy.

Aims:

- This project aims to correlate changes in mammographic density measurement with outcome in hormone receptor positive breast cancer treated with antiestrogen therapy. The longer term goal is to utilise MBD changes to tailor treatment.

(continued over page)

Current research:
10. Breast Density Interventions – Dr Hilary Martin

Continued

Methods:

- From the Royal Perth Hospital (RPH) Breast Clinic database 1942 patients have been identified who have had localised breast cancer treated with antiestrogen therapy between 1994-2011.
- Additional demographic, case management and endocrine data will be obtained from the RPH medical records, electronic databases. Mortality information will be requested from the State Cancer Registry.
- Eligible patients are required to have a baseline contralateral mammogram available and a further contralateral mammogram for comparison following 9-24 months of hormonal therapy. Change in density will be assessed between the baseline contralateral breast mammogram and the follow up mammogram using Cumulus software.
- Tissue microarrays will be made from retrospectively collected tissue to study further potential markers of AE resistance including, initially, Ki67 and Bcl-2 and their ratios as well as a panel of estrogen receptor co-regulators.

(continued over page)

Current research:
10. Breast Density Interventions – Dr Hilary Martin

Continued

Initial demographic data:

- Of 1942 potentially eligible patients, 413 premenopausal (21%), 140 perimenopausal (7.2%), 1333 postmenopausal at diagnosis (68.6%). Status was uncertain for 31 patients who were <50 and had had a hysterectomy and unknown for 26 patients.
- 1162 (59.8%) commenced tamoxifen as initial therapy, 4 zoladex alone (0.002%), 207 (10.7%) letrozole, 354 (18.2%) anastrazole, 2 with examestane (0.001%), 61 (3.1%) tamoxifen plus zoladex, 140 (7.2%) were treated through a clinical trial, 5 (0.003%) received another form of treatment, and treatment was unknown for the remaining 7 (0.004%) patients.
- Cuzick J, Warwick J, Pinney E, Duffy SW, Cawthorn S, Howell A, Forbes JF, Warren RML Tamoxifen-Induced Reduction in Mammographic Density and Breast Cancer Risk Reduction: A Nested Case-Control Study J Natl Cancer Inst 2011;103(9):744-752

Current research:
11. Assessment of Ki67 Proliferative Activity in Breast Carcinoma – W/Prof Jennet Harvey

- W/Prof Jennet Harvey, Withrop Professor, School of Pathology and Laboratory Medicine, University of Western Australia, Contact: jennet.harvey@uwa.edu.au

Summary:

- Provided an outline of the results of the comparison study undertaken to compare rapid semi-quantitative assessment of Ki67 Labelling index with assessment by automated digital image analysis.
- Proliferative activity is well established as a prognostic parameter in breast carcinoma and various methods of assessment have been proposed, including simple counting of mitotic figures in a defined area, as used in standard assessment of histological grade.
- Markers of proliferative activity are also central to a number of recently implemented molecular prognostic tools such as Oncotype Dx (1), however to date no histological, immunohistochemical or molecular assessment of proliferation is included in the WHO classification of carcinoma of the breast or in ASCO guidelines.
- Ki-67 is a cell proliferation-associated antigen that is expressed in all stages of the cell cycle except G0 and use of a Ki-67 labelling index has been found to be a prognostic marker in breast cancer in several studies, including a publication from the St Gallen International Expert Consensus, which reviewed evidence for the inclusion of Ki-67 labelling index as a predictive parameter in selection of appropriate systemic treatment in certain subsets of cases (1,2).

(continued over page)

Current research:
11. Assessment of Ki67 Proliferative Activity in Breast Carcinoma – W/Prof Jennet Harvey

Continued

- Although considered a particularly robust antibody, Ki-67 nuclear reactivity on most occasions being easily demonstrated and assessed in formalin-fixed paraffin-embedded tissue using routine immuno-histochemical techniques, measurement procedures and the definition of what constitutes low/intermediate/high Ki-labelling index vary widely.
- Guidelines from the International Ki67 in Breast Cancer Working Group included a recommendation that 'interpreting pathologists score at least 1000 cells and that 500 cells be accepted as the absolute minimum' (3).
- Adoption of such a recommendation would impose a significant burden on a pathologist in busy routine practice and is likely to make widespread adoption of this methodology impractical. Our experience suggests that rapid semi-quantitative assessment and automated image analysis are potential practical alternative methods of assessing Ki-67 proliferative activity.
- There is evidence that formal manual and automated assessment are highly correlated and the latter might be considered the de facto 'gold standard (4,5). In this study we compared rapid semi-quantitative assessment of Ki-67 Labelling index with assessment by automated digital image analysis.
- Results indicate that rapid semi-quantitative manual assessment by the method we have used shows only a fair correlation with automated assessment and is unlikely to be sufficiently robust for clinical application. In contrast there is good correlation between automated assessment of single and double stained sections, suggesting that the latter may be unnecessary for valid automated assessment.

Contents

Contents – Part 3: Facilitated discussion

Agenda	Focus Topic	Presenter
Part 3 – Prompts for discussion	**Key themes from presentations**	Facilitator: Janelle Marr • Priorities for Research and Collaboration – specific research questions (and resource considerations) • BreastScreen Australia – research themes and questions
Discussion	**Small group discussion**	Outputs of small group discussion around research and collaboration priorities
Additional	**Post Symposium input**	Canine mammory neoplasia – Murdoch University
Wrap up	**Closing considerations**	Facilitator: Janelle Marr

Priorities for Research and Collaboration: Specific research questions

1. Prevention – targeting high risk for screening
2. Prevention interventions and tailoring these
3. Lifestyle research
4. Improving breast cancer services
5. New diagnostic/ localisation technologies
6. Prognostic predictive markers
7. Decision making in screening and treatment
8. Improving indigenous outcomes
9. Genetics – linking to other areas of research (e.g. imaging, prevention, psycho-oncology)
10. Mammographic density – how it predicts risk of breast cancer and response to treatment

Also consider resources:

- How can we facilitate, enhance and promote breast cancer research in WA? What do we need?
- What resources are available (e.g. data linkages, funds, infrastructure support)?
- Any other burning issues and challenges we need to address?

BreastScreen Australia
Research themes and questions

Service system:

- Epidemiology of breast cancer
- Technical efficiency, allocative efficiency and cost effectiveness of screening
- Program eligibility rules including: age, re-screening intervals; inclusion of symptomatic women; eligibility based on risk (including breast density and individualised risk assessment)
- Access to modalities of treatment (surgery, radiotherapy, chemotherapy, psychosocial supports)
- Factors that influence access and equity
- The impact of service delivery models on outcomes
- Service system capacity and planning (including workforce)
- Use and outcomes of non-BSA screening

Clinical:

- Risks and benefits of screening and early intervention
- Morbidity associated with screening and recall
- Risks and benefits of biopsy and imaging techniques
- Effectiveness of screening (cancer detection and recall rates, interval cancer rates, rescreening rates, tumour size and survival rates)
- Optimal management of 'borderline' lesions
- Models of management of lesions detected by screening (surgery, radiotherapy, chemotherapy) and their impact on outcomes
- Use and impact of new technologies (imaging, pathology)

Behavioural:

- Factors that influence participation including influence of general practitioners and other stakeholders
- Participation of special groups (e.g. ATSI, CALD, rural) and women who under-screen
- Women's experience of screening and the management of detected lesions
- Awareness-raising including the role of social marketing
- Consent, choice and health literacy
- Optimal methods of recall

Discussion – key themes (1)

#	Research Questions	Key discussion points
Q1	**Prevention – Targeting high risk for screening**	**Group 1:** ▪ Target Biomarkers for inherited breast cancers ▪ Molecular profiling - GP education and referral ▪ More integration of markets re breast density
		Group 2: ▪ Tomosynthesis - for Dense Breast for screening
		Group 3: ▪ Targeting high risk population - Risk Adjusted Screening; Risk Adjusted Prevention ▪ 1st Mammography (All) (collection of more detailed history, e.g. predictors, blood test, family history and psychological component) ▪ Risk Adjusted Model for Screening - High Risk (mammo + US or CESM) more intense screening - Do less for low risk (less screening e.g. every 4 years) - 'normal' risk' - normal (normal screening) ▪ Risk Adjusted Prevention: Healthways Grant - 25,000 Half have prevention - Vitamin D, BMI, exercise, aspirin, drugs (metformin, tamoxifam) and Half none

Discussion – key themes (2)

#	Research Questions	Key discussion points
Q3	**Lifestyle factors**	▪ Chemotherapy & HT - Research into weight gain. Difficult to determine cause / extents. Exercise Physiologist ▪ Vit D Deficiency - Ensure all B/C patients have blds taken. Educate patients as well ▪ Stress Area - ECU looking at stress areas? ▪ Breast Cancer Research Collaborative in WA
Q4	**Improving breast cancer services**	▪ Improving access to screening mammography - units at shopping centres. ▪ Screening age range correct for our population in Western Australia. Age extension. ▪ Publicise women over 69 can have free mammography - awareness they are still at risk. ▪ Targeted screening over 70 | density and risk factors | via GPs ▪ Fridge magnet - health promotion. ▪ Alternative screening + questions. Blood Test. ▪ High risk screening - remove 50 yr cut-off for MRI ▪ Renaming pathologies "indolent IAE origin" to over Dx and over Rx - minimally invasive Rx? ▪ Targeted research which ones - invasive poor Px | which ones can we leave? Watch

Discussion – key themes (3)

#	Research Questions	Key discussion points

Q5	**New diagnostic/ localisation technology**	<u>Broad</u>
		▪ Clinical
		▪ Radiological
		▪ Pathoogy - HRT/Immunohistochmistry/CISH.SISH.FISH/
		▪ Molecular - *New molecular profiles for targeted therapies*
		  ▪ *Translational research*
		  ▪ N*eed more next generation sequencing*
		  ▪ *Equipment/expertise (bioinformatics "geeks")*
		  ▪ Embedding within clinical trials
		▪ New biochemical markers in blood

Q6	**Prognostic predictive markers**	▪ "Smart Screening" ▪ Affordable prognostic markers ▪ Histopathological markers replace genetic testing (on cotype Dx)

Discussion – key themes (4)

#	Research Questions	Key discussion points
Q7	**Decision making in screening and treatment**	Group 1: ▪ Screening high risk and breast density to be screened more often. ▪ Better understand genomwide snps
		Group 2: ▪ Early breast cancer is currative - screening benefits ▪ 55% Breast Screen - ? % private. ▪ Ý Screening Uptake ▪ High risk - Family risk. ▪ Interval cancers (20%) ▪ Best use of evolving technologies ▪ Role of MRI in breast screening ▪ Indigenous women ▪ Age for screening ▪ Tension between GPs and BreastScreen ▪ Test for need for oncology treatment (28% don't need) Oncotype Dx

Discussion – key themes (5)

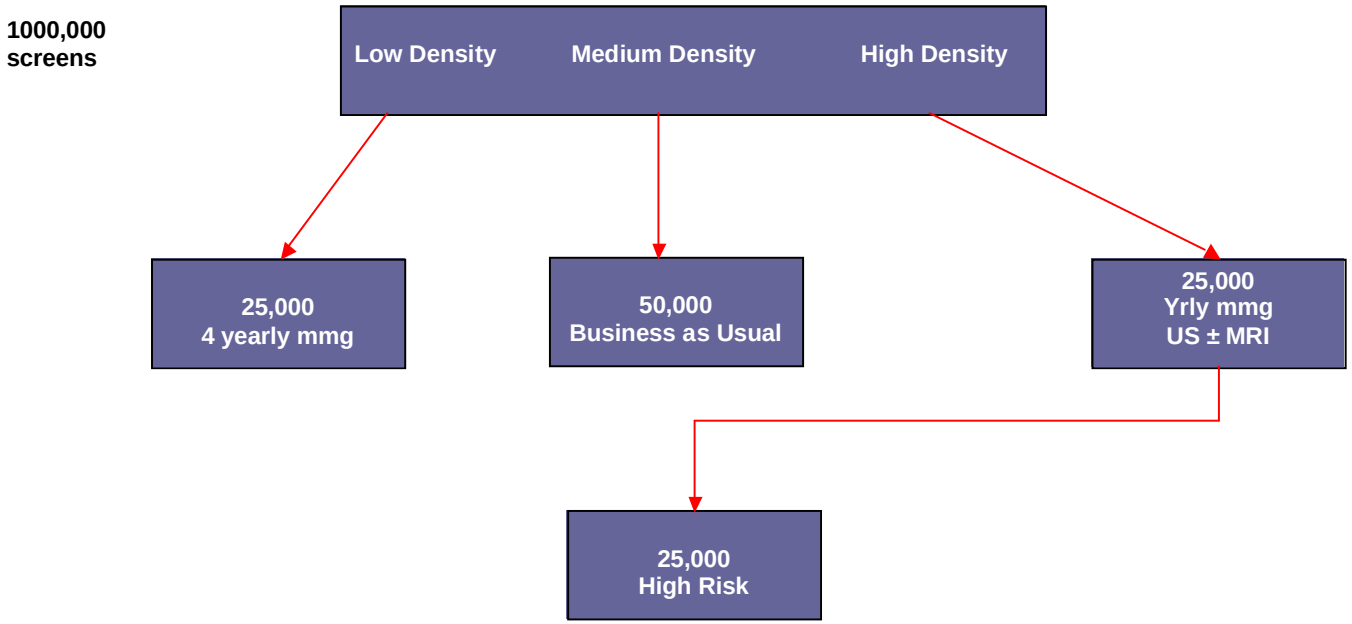
#	Research Questions	Key discussion points
Q8	**Improving indigenous outcomes**	Group 1: ▪ Screening / Community Interventions ▪ More aggressive tumours ▪ Prevention ▪ Ratio to Cervical / Breast Cancer ▪ Questionnaire
		Group 2: ▪ Educating country health workers ▪ Look at BSWA data to answer questions on indigenous mammograms
Q9	**Database for high risk women**	▪ Is there a database for high risk women - can we have a registry?
Q10	**Mammographic density – screening**	▪ Recommendation for FU - GP / Patients ▪ Dense Breast? Normal MMG ▪ Tomosynthesis. for screening

Discussion – key themes (6)

#	Research Questions	Key discussion points
	Neo adjuvant therapy	▪ Patient selection? Database set-ups? - central source, Imaging tools development. ▪ Risk Factors ▪ Demographics ▪ Treatment ▪ Follow-up ▪ Standard Definitions | Coding (Build on data that already exists!)
	Resources and other	Resources: ▪ Centralised body for research support ▪ Health Department support for academic positions ▪ Create academic positions to foster research ▪ Centralised body for research questions in WA ▪ Use the data we've already collected Research Questons: ▪ Optimising testing specific to the patient - better allocation of resources. ▪ Who to screen, how often, what testing to perform.

Discussion – key themes (7)

R.A.S.C.A.L.



Questions:

- **Vitamin D con**
- **BMI**
- **Folate Hx**
- **Exercise levels**
- **Melfamin**
- **Aspirin**

Canine mammary neoplasia

Additional input post Symposium – Murdoch University

Canine mammary neoplasia - model for breast cancer?

- heterogeneous genetic background (unlike rodent models)
- BRCA-1 & BRCA-2 associated with mammary neoplasia in dogs, & reduced expression with progression
  Rivera et al 2009
- Breed-related incidence parallels familial breast cancer
  Egenvall et al 2005
- WHO classification, follows human system where possible
- similarities with human breast tumours
  Rivera & Von Euler 2011
  Klopfleisch et al, 2011
  Pinho et al, 2012
- Various types, often mixed ep/myoep
- 50% are malignant
- large, long-lived species
- easy serum, urine, tissue harvest, sequential biopsy
- breed-structure & genetic bottlenecks may assist studies
  Karlsson & Lindblad-Toh 2008
- Canine genome sequenced
  Lindblad-Toh et al., 2005
- 20-30% overexpress HER-2, increased survival, polymorphism
  Martin de las Mulas *et al.*, 2003
  Hsu et al , 2009
- Affymetrix Canine Genome 2.0 Array allows gene profiling
- Canine GWAS possible
  Karlsson *et al* 2007
- spontaneous
- highest incidence all domestic spp. 0.2% prevalence
  Zachary *et al.*, 2012
- 30% metastatic gene profile similarities
  Klopfleisch *et al.*, 2010a
- Biological relevance & ethical advantages
- Can recruit cases from veterinary practice
- Excellent surgical facilities & veterinary specialists at Murdoch University
- Proof of principle studies? Mouse-to-human intermediate stage?
- BMP2, LTBP4, and DERL1 discriminate benign & malignant tumours
  Klopfleisch *et al.*, 2010c
- Altered INSR expression in neoplasia
  Klopfleisch *et al.*, 2010b

Closing considerations

Closing comments:

- Lyn Fritchy – occupational and lifestyle research (unable to attend, research of interest)
- John Emery Erco project – rural project (unable to attend, interesting project)
- Murdoch veterinary science research (see attached slide canine mammary neoplasia)
- ECU – exercise interventions (interesting project)
- NBCF Conference – community forum (attendance encouraged)
- Busselton study (interesting longitudinal research)
- ICON project (noted again from presentations)




Information stalls

BreastScreen WA

Cancer Council WA

Breast Cancer Care WA