ORIGINAL ARTICLE

ANZJSurg.com

Breast cancer screening in women at high risk of hereditary breast cancer: an Australian experience

Ian Bennett,*† Saam Tourani,† Linda Cockburn,* Jane Reasbeck,* Neels Grobbelaar,‡ Sonia Dann,* Penny Patrikios* and Jane Brazier*

*BreastScreen Queensland, North Brisbane Service, Brisbane, Queensland, Australia
†Department of Surgery, Princess Alexandra Hospital, The University of Queensland, Brisbane, Queensland, Australia and
‡Queensland X-Rays, Greenslopes Private Hospital, Brisbane, Queensland, Australia

Key words
familial breast cancer, multimodality screening.

Correspondence
Professor Ian Bennett, Princess Alexandra Hospital, 199 Ipswich Road, Woolloongabba, Brisbane, QLD 4102, Australia.
Email: iancben@bigpond.com

I. Bennett MBBS, FRACS, FACS, CCPU; **S. Tourani** MD,FRACS, PhD; **L. Cockburn** MBBS, FRANZCR; **J. Reasbeck** MBBS (LOND), DDR, FRANZCR; **N. Grobbelaar** MBChB, FCRAD, FRANZCR (Sydney); **S. Dann** RN; **P. Patrikios** MMBS; **J. Brazier** MBBS.

Accepted for publication 3 September 2020.

doi: 10.1111/ans.16320

Abstract

Background: While population-based breast screening is a well-documented health strategy worldwide, very few centres offer breast-screening programmes specifically targeted at women at high risk of hereditary breast cancer. We present our experience with multimodality breast screening in a high-risk population.

Methods: The outcomes from a familial breast cancer clinic at the North Brisbane BreastScreen Queensland Service providing a multimodality screening programme for high-risk women were reviewed from the prospectively maintained database between 2011 and 2018.

Results: Over the 8 years of study period, a total of 6686 annual screening rounds were performed for 823 asymptomatic women at high risk of hereditary breast cancer. As a result, 40 cancers were diagnosed including 25 invasive ductal cancers, three invasive lobular cancers, two invasive cancers with mixed ductal and lobular features and 10 ductal carcinomas *in situ*. Ultrasound and mammography detected 72.5% (29/40) and 55% (22/40) of the cancers, respectively. A total of 3672 magnetic resonance imaging studies were performed. Ten (25%) cancers were initially only seen on magnetic resonance imaging including seven invasive ductal cancers, one invasive lobular cancer and two high-grade ductal carcinomas *in situ*. The cancer detection rate for first-round screening was 13.3 cancers per 1000 women screened, with 4.9 cancers per 1000 women detected on subsequent-round screening. One interval cancer occurred in the study period.

Conclusion: Multimodality breast screening of younger women at high risk of hereditary breast cancer is effective with the yield substantially exceeding the results from established breast screening programmes in older women. Co-location of this service within BreastScreen Australia efficiently shares resources.

Introduction

Hereditary or familial breast cancer accounts for 5–10% of new breast cancer diagnoses and 25% of breast cancers in women younger than 30 years old. Over the past 20 years, our understanding and knowledge of hereditary breast cancer predisposition genes have dramatically expanded, and gene mutation testing has now become more readily available and more cost affordable. Additionally, the identification of women at high risk of familial breast cancer has been made more definable with the use of various clinical assessment tools and decision-making paradigms including the Gail[1], Tyrer-Cuzick (IBIS models)[2], BRCAPRO[3] and the breast and ovarian analysis of disease incidence and carrier estimation algorithm[4]. In Australia, the National Breast and Ovarian Cancer Centre (NBOCC) developed a risk classification system assigning women into one of three risk categories based on the family pedigree, with category 2 including women at moderately increased risk and category 3 representing women at highest risk (Table S1).[5] The Cancer Australia Familial Risk Assessment Breast and Ovarian Cancer tool represents an online computer-formatted version of this same classification system.[6]

However, in Australia the management of women at high risk of familial breast cancer has seen a varied approach depending on the availability of state-based or regional facilities, with the absence of a uniform national approach to this issue, particularly in regard to the provision of appropriate breast screening protocols tailored to

match the increased risk. Yet, with increasing population awareness of familial breast cancer risk, and the increasing availability of assessment tools to define risk, there is an expanding demand for services to counsel and to provide management strategies for such women.

The Familial Breast Cancer Screening Clinic (FBCSC) at Chermside, Queensland, was established in 1999 to provide a regular multimodality screening programme for women at increased risk of familial breast cancer, as well as serving as a referral hub networking with local genetic counselling services and regional surgical services for those women requiring prophylactic surgeries. The clinic is co-located with the North Brisbane BreastScreen Queensland service. In 2010, we reported on the favourable outcomes of our first 10 years' experience in providing this screening service, which at that time included only mammography and ultrasound screening[7]. Since 2011, our screening protocol has expanded with the utility of breast magnetic resonance imaging (MRI) being added to our multimodality screening protocol. The purpose of this paper is to present an update on our experience in offering this service.

Methods

Asymptomatic women identified as being at a high risk of familial breast cancer are eligible to attend the clinic. The clinic operates on a referral basis and women are referred to the clinic from general practitioners, specialists, geneticists and Genetic Health Queensland. Additionally, internal referrals are received of women identified at high risk whilst attending the North Brisbane BreastScreen Queensland service, a population-based screening programme, within which the FBCSC is conveniently co-located. The FBCSC is staffed by a multidisciplinary team consisting of nurse counsellors, specialist medical officers, specialist sonographers, radiologists and surgeons and has a working relationship with Genetic Health Queensland. Once a referral is received, a breast care nurse will conduct a phone interview with the client to assess her familial breast cancer risk and ascertain her eligibility to attend the FBCSC.

Since our original report in 2010, our selection criteria have changed. Although initially women at both moderate and high risk of familial breast cancer were invited to attend the clinic, from 2011 the service has been limited to only women aged between 30 and 60 in the high-risk group to better manage the workload capacity, largely due to the popularity of the clinic. Women are eligible to attend the clinic if they are identified as falling into the NBOCC high-risk category 3 on the basis of their family pedigree or if they have a proven predisposing gene mutation, for example BRCA1, BRCA2, PALB2, PTEN, STK11 *etc*. Asymptomatic women between the ages of 30 and 60 years are invited to attend the clinic. Women who have been previously diagnosed and treated for breast cancer or who have an external current breast cancer diagnosis requiring treatment are excluded from the clinic. These eligibility criteria for triage into the clinic are similar to those outlined in the NCCN guidelines and the recommendations of the American Cancer Society.[8,9]

The screening methods utilized in the clinic include clinical breast examination (CBE) by a breast care nurse, breast ultrasound, mammography, and since 2011 breast MRI for women <50 years of age who fulfil the eligibility criteria for a Medicare rebate[10], which is very similar to the criteria associated with NBOCC risk class 3. Our screening protocols for new and returning clients are outlined in Table 1. Screening is performed on an annual basis for all women and the protocol takes into account the woman's age and breast density, with ultrasound in particular being offered for women with high breast density (Breast Imaging-Reporting and Database System C and D). Mammographic screening includes the use of tomography, and in women aged 30–39 years, following the initial screen, mammography is performed as a single view screen on subsequent years to minimize radiation exposure in this younger age group.

Table 1 First and subsequent round screening protocols

Age	Screening methods
First round screening protocol	
30–49	• Clinical breast examination • Mammography (MLO + CC view) • Baseline bilateral ultrasound • MRI if Medicare eligible
50–59	• Clinical breast examination • Mammography (MLO + CC view) • Baseline bilateral ultrasound
Subsequent rounds screening protocol (annual)	
30–39	• Clinical breast examination • Mammography (MLO view) • Ultrasound if high breast density (C or D) • MRI if Medicare eligible
40–49	• Clinical breast examination • Mammography (MLO + CC view) • Ultrasound if high breast density (C or D) • MRI if Medicare eligible
50–59	• Clinical breast examination • Mammography (MLO + CC view) • Bilateral ultrasound if high breast density (C or D)

CC, craniocaudal; MLO, mediolateral oblique; MRI, magnetic resonance imaging.

Table 2 Details of 40 detected cancers

Age of patients	
Mean age	44 (range 32-58)
Histological type	
IDC	25
ILC	3
Mixed	2
DCIS	10
Histological grade of invasive cancer	
Grade 1	12
Grade 2	10
Grade 3	8
Histological size	
Total (invasive + *in situ*): mean 21 mm (range 4–77 mm)	
Invasive: mean 15 (range 1–47)	
Invasive cancer ≤15 mm 17/30 (56%)	
Axillary lymph nodal involvement	7/30 (23%)
First or subsequent round detection	
First round	11
Subsequent rounds	28
Interval cancer	1

DCIS, ductal carcinomas *in situ*; IDC, invasive ductal cancers; ILC, invasive lobular cancer.

All the screening modality examinations are concluded in a single visit, except for the breast MRI examinations that are performed at an off-site collaborative radiology service, Queensland X-Rays, and within 3 months of the screening mammogram. Women were recalled for further assessment if any abnormality was detected on their MRI, which often included targeted

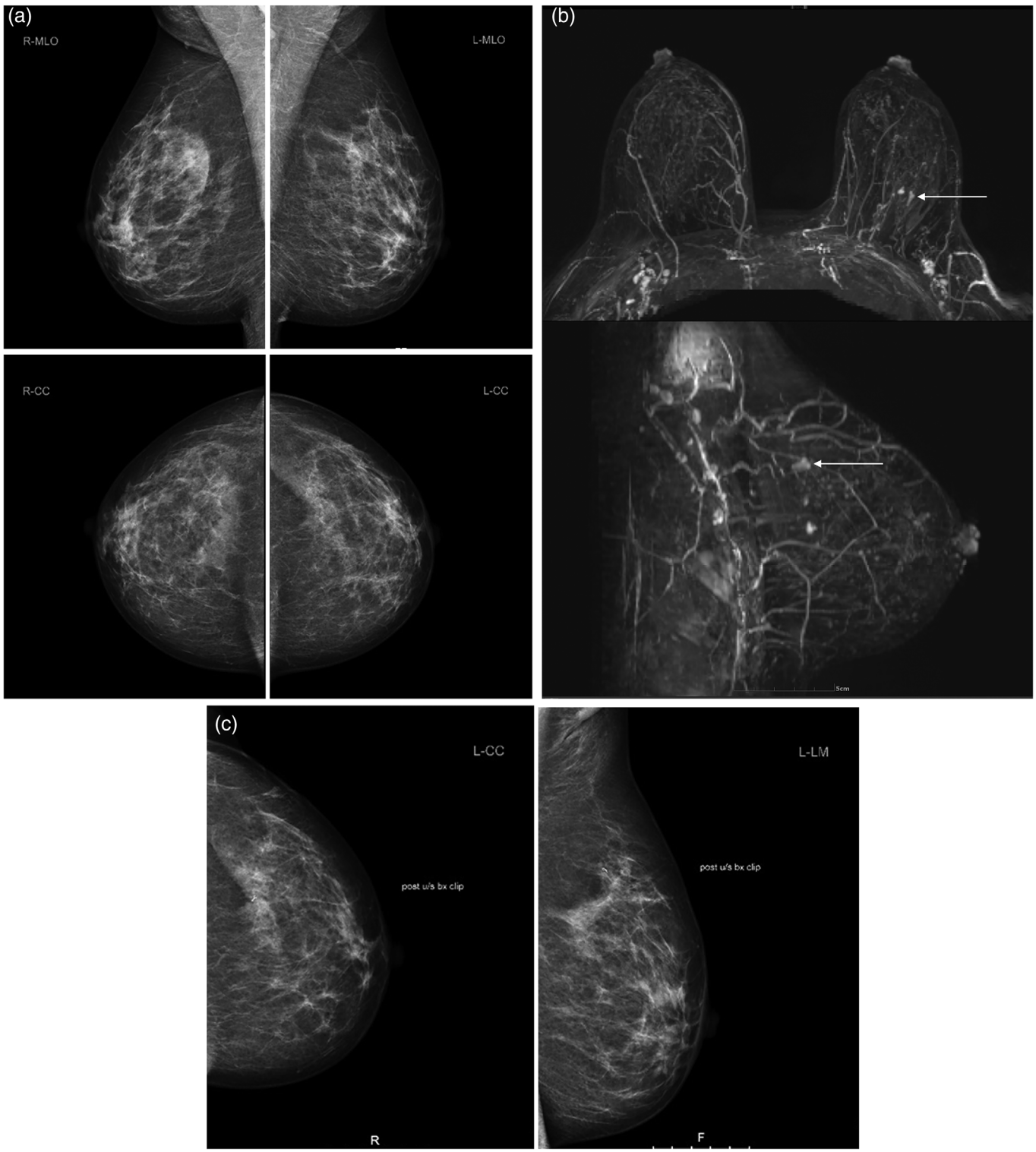

Fig. 1. (a) Normal appearing screening mammogram images of 48 year old female subsequently demonstrated to have a malignancy in the left breast at 12/4. (b) Non-contrast magnetic resonance images of left breast demonstrating a small focus of enhancement consistent with a 7 mm ovoid mass-like area seen in the breast at 12 o'clock 4 cm above the level of the nipple. The margins are slightly irregular on the sagittal images. Core biopsy under second-look ultrasound demonstrated invasive carcinoma NST. (c) Left mammogram following the ultrasound core biopsy with placement of marker clip.

ultrasound ± percutaneous biopsy, or occasionally a repeat MRI at 6-month interval.

All women who attend the FBCSC are initially counselled by a specialist Breast Surgeon to discuss their risk based on their family pedigree. A pedigree chart is prepared in advance by the breast care nurse and made available to the clinician to facilitate this consultation. The results of any genetic testing if available are noted and where possible confirmation of those results are obtained from the relevant genetic testing service. The patient's lifetime risk of breast cancer is discussed based on her familial risk categorization or any gene-testing results that might be available. Management options are discussed with the patient, including an outline of the screening protocol offered by this service. In addition, other options are discussed with the patient, including prophylactic surgery (both mastectomy and oophorectomy), chemoprevention with tamoxifen and risk-reducing lifestyle modifications. Referral to Genetic Health Queensland, the public genetic counselling service, is offered for all women at high risk of breast cancer for genetic counselling and testing. A checklist of discussion points is included in the patient chart to facilitate the conduct and documentation of this consult.

For the purpose of this manuscript, the records of all women attending the FBCSC from 2011 to 2018 inclusive were accessed from the prospectively maintained computer database using the TrakGene software (TrakGene Pty Ltd.; Clinical Genetics Information Management Solution, Adelaide). Cancer detection rates, the detection modality, histology and the rate of interval cancers were extracted.

Results

Over the 8-year period of the study, a total of 6686 screening rounds were performed in a total of 823 women at high risk of hereditary breast cancer. Of these, 39 women had a proven pathogenic gene mutation: 14 BRCA1 mutations, 18 BRCA2 mutations, one client with both BRCA1 and BRCA2 mutation, three CDH1 mutations and three STK11 mutations.

A total of 40 cancers in 40 women were diagnosed over the 8-year study period, including 30 invasive cancers (25 invasive ductal cancers (IDC), three ILC, two mixed ILC and IDC) and 10 ductal carcinomas *in situ* (Table 2). The mean total size of the cancers was 21 mm (range 4-77 mm), and the mean size of invasive cancers was 15 mm (range 1-47 mm). The majority (56%) of invasive cancers were less than 15 mm. Of the 30 invasive cancers, a greater proportion were of higher grade (grade 2 or 3) (18, 60%). About a one-third of the cancers (n = 13, 32%) were noted to have a clinical abnormality on breast examination, which did not necessarily correspond with the site of the malignancy. Axillary nodal metastasis was seen in seven invasive cancers (23%).

Of the 40 detected malignancies, 22 (55%) were visible mammographically and 29 (72.5%) were visible on ultrasound. A total of 3672 MRI studies were performed. There were 25 cancer patients in this series who underwent MRI screening, and MRI detected 20 (80%) of these cancers. Out of the 40 malignancies, 10 (25%) were initially only seen on MRI including seven IDC, one ILC and two high-grade ductal carcinomas *in situ*. Of the five (5/25) malignancies not seen on MRI, two were ultrasound only visible, one was mammographically only visible and two were visible on both ultrasound and mammography.

Abnormalities detected on MRI lead to further investigations including 128 MRI studies with 6-month interval examinations, 256 targeted ultrasound studies, and 93 biopsies. Figure 1 demonstrates a case in which the malignancy was not seen on mammography, but was essentially only screen-detected on MRI, and only seen on a second-look ultrasound under which a core biopsy was performed.

Nine of the 40 breast cancer cases occurred in women with proven gene mutations, of which there were two BRCA1 mutations, six BRCA2 mutations and one STKII mutation (Peutz-Jeghers syndrome) (Table S2). Seven of the nine cases demonstrated high-grade (2, 3) features and two were triple negative tumours, malignant characteristics known to be associated with gene mutation status. Of these nine mutation-associated cancers, five were MRI visible, four were mammographically visible and eight were ultrasound visible.

Of the 40 cancers detected over the study period, 11 cancers were detected on first-round screening and 29 cancers were detected on subsequent rounds. There were 823 first-round screens performed and 5863 subsequent-round screening events. The cancer detection rate for first-round screening was 13.3 cancers per 1000 women screened, and with 4.9 cancers per 1000 women detected on subsequent rounds. There was one interval cancer patient. The patient with the interval cancer was a 37-year-old BRCA2 carrier who had been attending annual screening since 2008. Her last normal screening mammogram and CBE were performed in February 2018. Her MRI scan was delayed due to her plans for overseas travel. She then presented in June 2018 with a new 13 mm lump. Her core biopsy showed a G3 ILC, strongly oestrogen and progesterone receptor positive, and HER2 negative. She underwent a wide local excision and sentinel node biopsy with the final pathology showing T2N0 disease.

Discussion

The FBCSC is the first public clinic of its kind in Australia providing a tailored multimodality breast screening surveillance programme, in addition to acting as an initial triage and counselling service with referral pathways to local genetic and surgical services within the regional network. Its co-location with BreastScreen Queensland at the North Brisbane Service provides logistical and economical advantages, with the FBCSC being able to have access to and share the expertise of radiology, medical and nursing staff who have pre-existing and long-term experience in breast screening. Additionally, there are cost savings in being able to utilize the imaging and biopsy equipment and computer programmes already available and designed for breast screening purposes. Consultation with new patients, which is undertaken by the surgical specialists, is facilitated by the prior prepared detailed family pedigree documented by the breast care nurses and by the use of a formulated checklist used by the counselling surgeon. Breast imaging is performed with mammography and ultrasound on the same visit as the initial consultation. Following the initial consultation with a new client, referrals to gynaecological oncology services for ovarian risk

assessment and management, breast surgical services for risk-reducing surgery, and to Genetic Health Queensland for consideration of gene mutation testing are initiated where appropriate and as desired by the client. Subsequent-round screening events are managed by the nursing staff and the radiology team.

Overall in this series, the 40 breast cancers were diagnosed as a result of 6686 screening episodes. This represents an overall cancer detection rate of 5.98 cancers per 1000 women screened, and with a cancer detection rate of 13.3 per 1000 women screened for first-round screening and 4.9 per 1000 women screened for subsequent-round screening. BreastScreen Australia determines national accreditation standards for cancer detection for population screening of five cancers per 1000 women screened or greater for first-round screening, and 3.5 cancers or greater per 1000 women screened for subsequent-round screening.[11] The BreastScreen Australia upper threshold for interval cancer rate occurrence is 7.5 per 10 000 screens up to 12 months after completion of a negative screening episode. In this current series, only one interval cancer in 6686 screens (1.5 interval cancers per 10 000 screens) was observed, and as previously noted this was due to the delay in MRI screening secondary to her personal circumstances. The cancer screening detection rates and the interval cancer rate in this current series from the FBCSC are therefore very acceptable and exceed the screening guidelines as outlined in the BreastScreen Australia National Accreditation Standards. Other parameters reflecting an acceptable performance by the FBCSC include an overall small mean tumour diameter of 15 mm for invasive cancers, with 56% of invasive cancers being 15 mm or smaller, and a low overall incidence of lymph node metastasis (17.5% overall, 23% invasive cancers). Based on the recommendation by Tabar, at least 50% of invasive cancers need to be 15 mm or less in diameter in order achieve mortality reduction through screening.[12] The finding of a higher proportion of invasive carcinomas demonstrating higher grades of malignancy is in keeping with well-documented tendency of hereditary breast cancers to be more aggressive.[13]

These current results are improved over the outcomes reported in our previous study[7] when MRI was not utilized and which demonstrated a mean cancer size of 16 mm, nodal involvement at 24.5% and a first-round screening cancer detection rate of 8.3 cancers per 1000 women screened.

There have been quite a number of reports validating the role of MRI screening in high-risk women who generally have been demonstrated to have increased breast density and are usually of a younger age cohort and in whom the sensitivity of mammography is greatly reduced.[14–17] Whilst these studies in MRI screening have demonstrated substantially better sensitivity for MRI over mammography, MRI has been shown to have a lower specificity resulting in higher rates of false positives and higher recall rates. In the current series, the sensitivity of MRI was 80% compared to 55% for mammography. However, of a total of 3672 MRI studies performed, 477 further investigations were triggered including 128 6-month interval MRI's, 256 targeted ultrasound studies and 93 needle biopsies. On the other hand, 10 (25%) out of the 40 cancers were only initially visible on MRI and would have otherwise been missed if MRI had not been used. Indeed our only interval cancer in this series was in a patient who failed to have her MRI performed as scheduled. However, only three biopsies in this series had to be performed under MRI guidance, as even amongst those lesions that were initially only seen on MRI, second-look ultrasounds enabled detection and intervention.

Ultrasound has proven to be a very useful tool in this setting of high-risk women, both as a screening tool and as a second-look procedure following the detection of an abnormality on MRI. In the current series, 72.5% (29/40) cancers were visible on ultrasound. There have been a number of reports indicating that breast ultrasound screening has been associated with an increased cancer detection rate over and above mammographic screening; however, the use of ultrasound screening has not been widely accepted due to the length of time taken to perform an examination and the fact that it is operator dependent.[18,19] As the technology continues to improve, there may be a role for automated breast ultrasound in the screening setting.[20]

This study is subject to the usual limitations and biases associated with this type of retrospective study; however, the results of this report are comparable with other relevant similar studies in the literature[14,15,16] but provide further knowledge specifically in relation to the outcomes within an Australian clinical setting.

The management of women at high risk of familial breast cancer requires that the advice offered to each woman be tailored to their individual circumstances, such as age, parity and personal and social preferences. In particular, the management of these women requires the coordination of genetic health services, screening services and surgical and gynaecological specialists. The model offered at the Chermside FBCSC has proven to be very successful with the screening service based in BreastScreen Queensland acting as an important entry point to the network, and additionally acting as a referral hub to regional genetic counselling and surgical services. The breast screening protocol offered by the FBCSC is a tailored programme appropriate to the increased risk of this population of women. There is indeed an important role for breast screening amongst these high-risk women, even for women with proven genetic mutations, as many of these women are of a younger child-bearing age and do not wish to contemplate undergoing bilateral mastectomies until the conclusion of their family planning. For this group of women, prophylactic mastectomies even if ultimately desired, often would not be seriously considered until the age of late 30s or early 40s. Multimodality breast screening therefore represents a very valid interim approach until that time. Indeed previous Australian data have shown that even amongst women with proven genetic mutations, the uptake of prophylactic mastectomies historically has been remarkably low (21%) with conservative management and screening being preferred[21].

Conclusion

The current report demonstrates that a tailored multimodality breast screening programme including MRI for women at high risk of familial breast cancer offers a valid, efficient and effective means of management, with cancer detection rates and interval cancer rates at more than acceptable standards when compared to national screening programmes. The co-location of this breast screening programme for high-risk women within BreastScreen Services has

proven to be a practical and efficient use of services already available on-site and could serve as a model for the selective establishment of other similar clinics within BreastScreen Australia based on population demographics. Such a service also provides a multidisciplinary network for the management of these high-risk women by linking in with other specialist genetic and surgical groups.

Author Contributions

Ian Bennett: Conceptualization; data curation; methodology; project administration; supervision; validation; writing-review and editing. **Saam Tourani:** Data curation; formal analysis; writing-original draft. **Linda Cockburn:** Project administration; supervision; validation. **Jane Reasbeck:** Project administration; supervision; validation. **Neels Grobbelaar:** Data curation; investigation; supervision; validation; writing-review and editing. **Sonia Dann:** Data curation; formal analysis; software. **Penny Patrikios:** Data curation; resources; validation. **Jane Brazier:** Data curation; methodology; project administration; resources; supervision.

Conflicts of interest

None declared.

References

1. Gail MH, Brinton LA, Byar DP *et al*. Projecting individualized probabilities of developing breast-cancer for white females who are being examined annually. *J. Natl. Cancer Inst.* 1989; **81**: 1879–86.
2. Tyrer J, Duffy SW, Cuzick J. A breast cancer prediction model incorporating familial and personal risk factors. *Stat. Med.* 2004; **23**: 1111–30.
3. Berry DA, Parmigiani G, Sanchez J, Schildkraut J, Winer E. Probability of carrying a mutation of breast-ovarian cancer gene BRCA1 based on family history. *J. Natl. Cancer Inst.* 1997; **89**: 227–38.
4. Antoniou AC, Pharoah PPD, Smith P, Easton DF. The BOADICEA model of genetic susceptibility to breast and ovarian cancer. *Br. J. Cancer* 2004; **91**: 1580–90.
5. NHMRC National Breast & Ovarian Cancer Centre, South Australia. Advice about familial aspects of breast cancer and ovarian cancer: a guide for health professionals. 2010. [Cited 1 June 2020.] Available from URL: https://canceraustralia.gov.au/publications-and-resources/cancer-australia-publications/advice-about-familial-aspects-breast-cancer-and-epithelial-ovarian-cancer
6. Cancer Australia. Familial Risk Assessment – Breast and Ovarian Cancer (FRA-BOC). On-line Tool. 2011. [Cited 1 June 2020.]. Available from URL: https://canceraustralia.gov.au/clinical-best-practice/gynaecological-cancers/familial-risk-assessment-FRA-BOC
7. Bennett IC, Muller J, Cockburn L *et al*. Outcomes of multimodality breast screening for women at increased risk of familial breast cancer. *World J. Surg.* 2010; **34**: 979–86.
8. Daly M, Pilarski R, Berry M *et al*. NCCN guidelines insights: genetic/familial high-risk assessment: breast and ovarian. Version 2.2017. *J. Natl. Compr. Canc. Netw.* 2017; **15**: 9–20.
9. Saslow D, Boetes C, Burke W *et al*. American Cancer Society guidelines for breast screening with MRI as an adjunct to mammography. *CA Cancer J. Clin.* 2007; **57**: 75–89.
10. Department of Health, A. G. Medicare Benefit Schedule, item 63464. [Cited 1 June 2020.]. Available from URL: http://www9.health.gov.au/mbs/fullDisplay.cfm?type=item&qt=ItemID&q=63464
11. BreastScreen Australia National Accreditation Standards. Developed by National Quality Management Committee of BreastScreen Australia. Revisions endorsed by Australian Screening Advisory Committee, 2004.
12. Tabar L, Fagerberg G, Chen HH *et al*. Efficacy of breast-cancer screening by age – new results from the swedish 2-county trial. *Cancer* 1995; **75**: 2507–17.
13. Eerola H, Heikkila P, Tamminen A, Aittomaki K, Blomqvist C, Nevanlinna H. Histopathological features of breast tumours in BRCA1, BRCA2 and mutation-negative breast cancer families. *Breast Cancer Res.* 2005; **7**: R93–100.
14. Kriege M, Brekelmans CTM, Boetes C *et al*. Efficacy of MRI and mammography for breast-cancer screening in women with a familial or genetic predisposition. *N. Engl. J. Med.* 2004; **351**: 427–37.
15. Warner E, Plewes DB, Hill KA *et al*. Surveillance of BRCA1 and BRCA2 mutation carriers with magnetic resonance imaging, ultrasound, mammography, and clinical breast examination. *JAMA* 2004; **292**: 1317–25.
16. Leach MO, Boggis CRM, Dixon AK *et al*. Screening with magnetic resonance imaging and mammography of a UK population at high familial risk of breast cancer: a prospective multicentre cohort study (MARIBS). *Lancet* 2005; **365**: 1769–78.
17. Kuhl CK, Schrading S, Leutner CC *et al*. Mammography, breast ultrasound, and magnetic resonance imaging for surveillance of women at high familial risk for breast cancer. *J. Clin. Oncol.* 2005; **23**: 8469–76.
18. Brem R, Lenihan M, Lieberman J *et al*. Screening breast ultrasound: past, present and future. *AJR Am. J. Roentgenol.* 2015; **204**: 234–40.
19. Geisel J, Raghu M, Hooley R. The role of ultrasound in breast cancer screening:the case for and against ultrasound. *Semin. Ultrasound CT MR* 2018; **39**: 25–34.
20. van Zelst JCM, Mann RM. Automated three-dimensional breast US for screening: technique, artifacts, and lesion characterization. *Radiographics* 2018; **38**: 663–83.
21. Collins IM, Milne RL, Weideman PC *et al*. Preventing breast and ovarian cancers in high-risk BRCA1 and BRCA2 mutation carriers. *Med. J. Aust.* 2013; **199**: 680–3.

Supporting information

Additional Supporting Information may be found in the online version of this article at the publisher's web-site:

Table S1. Australian NHMRC National Breast and Ovarian Cancer Centre risk classification for familial breast cancer.
Table S2. Outcomes for cancer patients with gene mutations.