Breast Density Research at BreastScreen SA

Information for medical professionals

BreastScreen SA is conducting a 6-month research study into reporting individual breast density for women as part of its regular breast cancer screening program. The research will evaluate women's response to being informed about their individual breast density and ultimately help to shape future breast care recommendations for women in South Australia.

Key points

- Breast density can be measured through screening mammography using Volpara software and requires no additional time or radiation.
- Higher breast density can increase the risk of breast cancer and reduce the visibility of breast cancers on screening mammography.
- BreastScreen SA does not currently recommend supplemental imaging for asymptomatic women with high breast density who have no other risk factors for breast cancer.

Background

Breast cancer is the most common cancer and the second leading cause of cancer deaths in Australian women. Every day around 55 Australian women are diagnosed with breast cancer, and 1 in 7 women will develop breast cancer by age 85.[1]

Established in 1989, BreastScreen SA is the accredited South Australian component of BreastScreen Australia – a population-based breast cancer screening program that provides free, two-yearly screening mammograms to asymptomatic women, primarily aged 50 to 74 years. Asymptomatic women aged 40 to 49 and over 75 are also eligible. The program screens around 100,000 women each year and aims to detect breast cancer at an early stage, when there is a greater chance of simpler and more successful treatment. The highly effective public health initiative has been found to reduce deaths from breast cancer by up to 41% for South Australian women who screen regularly. [2]

BreastScreen SA adopts world best practice for radiology reading. Every screening mammogram is independently read by two radiologists, with any discordance arbitrated by a third radiologist. There is a small cohort of Australian women who are diagnosed with breast cancer within the 24 months after their regular screening mammogram. Known as interval cancers, they are typically more advanced and symptomatic at the time of diagnosis and often associated with poorer outcomes. BreastScreen SA closely monitors interval cancer rates.

What is the research?

BreastScreen SA is conducting research into the reporting of individual breast density as part of regular breast cancer screening. The 6-month study will run across 3 BreastScreen SA screening clinics – Arndale, Hyde Park and one mobile screening unit.

The research will use Volpara, an automated software program, to produce a volumetric measurement of breast tissue from a woman's mammogram data. There is no additional time or radiation required, and there will be no difference to the woman's screening experience.

Women participating in the research will receive their breast density category as part of their regular screening results and they will be invited to complete an online survey. The survey aims to capture qualitative feedback about how women respond to being told their individual breast density. Breast density results will also be provided to each participant's nominated doctor, and some women may wish to discuss their result with their doctor. As well as providing written information, BreastScreen SA research staff are also available to discuss any questions or concerns about breast density.

BreastScreen Australia does not currently report on breast density across all states and territories, but recognises that breast density may have a future role in determining the frequency and method of an individual's breast cancer screening.[3] BreastScreen Australia supports research, greater discussion and

public awareness of breast density and endorses BreastScreen SA's model of care.

BreastScreen SA believes every woman has a right to know her breast density as it represents a factor contributing to the individual risk of developing breast cancer. However, breast density is not yet widely understood. The research will evaluate women's feedback after being informed of their breast density category, recognising this as critical to improved client care and future national screening guidelines based on risk stratification.

What is breast density?

Mammographic breast density, or breast density, refers to the appearance and volume of fibroglandular breast tissue relative to breast fat on a mammogram. Breast density is a mammographic finding and has no association with the look and feel of the breast on clinical examination.

Breast density can only be measured from a mammogram but there are several methods, including:

- a radiologist analysing an image to make a subjective estimate of density
- a commercially available computer software program providing a volumetric measurement.

Clinical assessment of breast density is commonly classified into four categories using the Breast Imaging Reporting and Data System (BI-RADS), American College of Radiology (ACR) 5th edition.[9]

BI-RADS:

- **a**: breasts are almost entirely fatty.
- **b**: breasts have scattered areas of fibroglandular tissue.
- **c**: breasts are heterogeneously dense. The mix of non-dense and dense tissue may hide small cancers.
- **d**: breasts are extremely dense, reducing the visibility of cancers on a mammogram.

Women with **BI-RADS c** or **d** classification are regarded as having high breast density.

For a small number of women (3 to 5%), breast density will not be measured as their screening may be incomplete or inadequate views obtained due to physical limitations in the positioning of the breast. In some situations, the software may also be unable to provide an accurate measurement. Where this occurs, a repeat screening will not be offered due to the additional unnecessary radiation, based on the 'as low as reasonably achievable' (ALARA) principle. These women will still be included in the research.

Dense breasts are common – approximately 50% of women, aged 40 to 74 years, have high breast density.[9] Breast density usually reduces with age as most women undergo involution to a fatty, low density pattern as they pass through menopause.[8] A small number of women maintain a high breast density pattern after menopause. In addition to this, post-menopausal women who take hormone replacement therapy (HRT) typically have increased breast density.[16]

What is the significance of breast density?

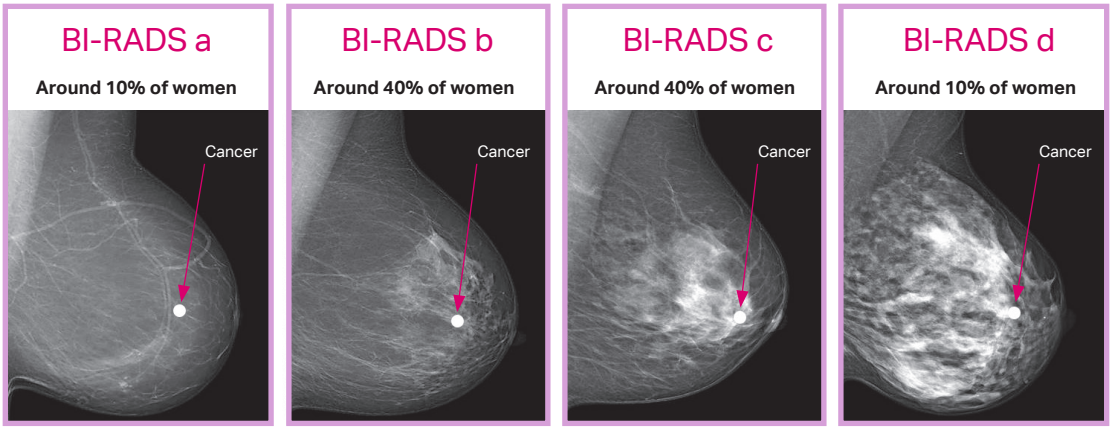
On a mammogram, breast fat appears grey and the fibroglandular tissue (stromal and epithelial elements) appears white. The higher the ratio of fibroglandular tissue to fat, the higher the breast density and the more white the mammogram appears.[4, 5]

- Increased breast density is associated with an increased risk of breast cancer.[5]
- Increased breast density lowers the accuracy or 'sensitivity' of mammography for breast cancer detection due to a masking effect.[8] As cancers are typically white in appearance on a mammogram, they may be camouflaged by dense tissue, reducing the sensitivity of mammography for the detection of breast cancer.[6, 7]
- Higher interval cancer rates are seen in women with higher breast density.[10]

Breast density and cancer risk

High breast density is a recognised risk factor for the development of breast cancer.

Although women with high breast density have an increased risk of breast cancer, it is important to put this into context and recognise that there are a number of lifestyle, environmental and genetic risk factors, including some modifiable factors.



Being female is the biggest risk factor, while age remains the strongest predictor when determining the risk for breast cancer, with more than 75% of breast cancers occurring in women over the age of 50 years. [13] [14]

We also know that 2-5% of all breast cancers occur in women carrying a gene mutation BRCA 1 or 2.[15] The genes occur in 1 in 400 Australian women (0.2%).

About 10% of women with breast cancer have a previously diagnosed family member. It is important to note that most women who get breast cancer do not have a family history of the disease. [22]

Many breast cancers are hormone driven, having receptors for oestrogen and progesterone, and many of the influencing factors for breast cancer relate to these hormone levels. This increased hormone exposure may occur over a lifetime – such as early menarche, late menopause, nulliparity, combined oral contraceptive pill (COCP), HRT and obesity in post-menopausal women.

Risk factors include:

- Previous breast biopsy showing atypia (ADH, ALH) or lobular carcinoma in situ (LCIS)
- Elevated BMI
- Alcohol consumption
- Smoking
- HRT
- COCP
- Personal history of breast cancer
- Early menarche, late menopause

There are a multiple websites that discuss the risk factors for breast cancer.[23, 24, 25]

High breast density and supplemental imaging

There are currently no randomised controlled studies that show supplemental imaging (such as MRI, ultrasound or tomosynthesis) saves additional lives in asymptomatic women with high breast density who have no other risk factors for breast cancer.

In some circumstances, supplemental imaging is of benefit for women with other significant risk factors.

- Women with BRCA 1 or 2 gene mutations are recommended to undergo annual breast MRI from the age of 30 to 50 years.
- Women with a strong family history of breast cancer are recommended to undergo annual screening mammograms . Breast Screen SA's definition of a strong family history is a:
  - a first-degree relative diagnosed with breast cancer before the age of 50
  - a first-degree relative with cancer in both breasts (diagnosed at any age)
  - 2 or more first-degree relatives with breast cancer (diagnosed at any age)

Please note: clients are eligible to screen at BreastScreen SA from the age of 40 years.

- Women with previous biopsy results showing a premalignant disease are recommended to undergo annual screening mammograms.

There is some early emerging evidence from international studies that supplemental imaging of women with high breast density may detect additional cancers. [17] [18] [19] However, there has not been sufficient follow-up to show evidence of improved survival benefits from either altering the frequency of mammographic screening or from supplemental imaging with ultrasound or MRI.

A Dutch screening program has trialled combining biennial mammography with breast MRI for women with BI-RADS d breast density.[26] While Round 1 results showed higher rates of breast cancer detected (16.5 per 1000 screens), there was a considerable increase in false positives. Round 2 results showed a lower cancer detection rate (5.9 per 1000 screens), with a significant reduction in false positive results.

While supplemental imaging may detect additional cancers, the incremental and relative benefits of these technologies need to be balanced against the potential harms. The success of a population-based breast cancer screening program depends on the balance between early diagnosis and the potential harm caused by heightened anxiety and false positive results. False positives can be as high as 8.1% with ultrasound, in women recalled for further examination.[17] Unnecessary needle biopsies and the potential for overdiagnosis also remain an important consideration.

Without further research-based evidence, breast density needs to be put into the context of other risk factors when deciding whether supplementary imaging is required.

BreastScreen SA is therefore recommending that women do not alter from current screening protocols based on their breast density. All risk factors should be taken into consideration when determining whether more frequent mammographic screening or alternative imaging is appropriate.

Health professionals may consider using a risk assessment tool such as iPrevent www.petermac.org/iprevent

It is important to recognise that regardless of an individual's breast density, mammography is still the best breast cancer screening test in a population-based screening program for asymptomatic women, aged 50 to 74 years.

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