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The Challenge of Breast Density— Options for Management and Breast Cancer Screening

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Breast density is now well established as an independent risk factor for breast cancer.¹ Dense breast tissue, as measured on mammography, also has a masking effect, making breast cancer more difficult to detect. It reduces the sensitivity of mammography and increases the likelihood of an interval cancer (malignancy presenting with symptoms between screening rounds).¹

While the risk and the diagnostic challenges associated with dense breast tissue are understood, the way it should be managed remains less clear. There is increasing pressure from consumer groups for women to be notified of their breast density. These community groups, representing women at risk of breast cancer, or with a history of breast cancer, have lobbied strongly, and across most of the United States notification is now mandated by legislation. This means that every woman with dense breasts must be sent a letter by her radiologist informing her of her breast density.

However, evidence-based risk management guidelines are lacking, leading to confusion and anxiety. This Commentary will discuss the breast cancer risk associated with breast density and the options for cancer screening. On the basis of this, it will propose recommendations for the assessment and management of women with dense breasts. Options include the use of supplemental screening with tomosynthesis, ultrasound and/or MRI or varying the screening interval.

What is breast density?

Breast density is a measurement of the proportion of stroma and epithelium (which appears opaque/

white on a mammogram) relative to fatty tissue (which appears lucent/black on a mammogram). Density is a mammographic measurement. High mammographic density may be associated with clinical density (i.e. breasts that feel lumpy to palpation); however, there is a poor correlation between density measured by clinical examination and imaging.² The American College of Radiology (ACR) BiRADS system is a widely accepted method for classifying density into four categories, A (almost entirely fatty) to D (extremely dense,) as can be seen in Table 1.³ Categorisation can be made by visual estimation or using programs to calculate density from digital mammography images (automated measurement). Measurements can be difficult to reproduce and may vary between observers and time intervals.⁴ There is no universally accepted method for density estimation.

Breast density is determined by several factors. Young women (20's and 30's) tend to have very dense breast tissue and there is a trend for density to decrease with increasing age, breast feeding and post-menopausal status. Obesity is associated with lower breast density.⁵

Table 1. Categories of Breast Density³

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| a. The breasts are almost entirely fatty |
| b. There are scattered areas of fibroglandular density |
| c. The breasts are heterogeneously dense, which may obscure small masses |
| d. The breasts are extremely dense, which lowers the sensitivity of mammography |

What is the risk of breast cancer in dense breasts?

Although the estimates vary, women with high breast density (>75%) have a risk of developing cancer 4.7 times higher than women of the same age with density <10%, or a risk 2.3 higher for women with a density of <25% compared to density 75%.⁵ As a comparison, the risk ratio associated with two first-degree relatives with breast cancer is estimated at 3.8, a single first-degree relative with breast

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cancer younger than 50 years at 2.7, previous benign breast biopsy 1.9, a second-degree relative with breast cancer 1.7 and nulliparity 1.3.⁶

The prevalence of mammographic density in the screening population has been reported at 43% in a cohort aged 40-74, (with dense tissue defined as being in the highest two (of four) categories of density, i.e. Category C or D); 57% for women aged 40-44 decreasing to 28% for women aged >85.⁵

How can breast density be managed?

There are no treatments currently recommended to reduce density. Incidental reduction in density has been observed in women with breast cancer after withdrawal of hormone replacement therapy and during treatment with tamoxifen. A reduction is also seen in pre-menopausal women with BRCA mutations undergoing risk reducing salpingo-oophorectomy.

There is uncertainty about whether density-guided supplemental screening improves health outcomes. Population screening programs in the UK and Australia have not recommended any change to screening on the basis of breast density and do not routinely notify women of their density.^{7,8}

The most important initial management strategy for women with dense breasts is education and support. Women should be given explanation of what mammographic density is, what their individual risk may be and reassurance that dense breasts are common, and that density will usually naturally reduce with age. Density can be explained as a risk factor for breast cancer that can be managed but not changed, similar to having a family history in

close relatives. The decreased accuracy of mammography in dense breasts can be explained and there are several options to manage this:

- (1) following age-related population mammographic screening recommendations without any additional interventions;
- (2) screening with mammography more frequently (annually rather than biennially);
- (3) considering breast tomosynthesis (3-D mammography) in place of standard (2-D) mammography if 2-D is the usual as in many screening programs;
- (4) screening with mammography (tomosynthesis or standard 2-D) combined with supplemental screening modalities, such as screening ultrasound and/or MRI.

What supplemental screening is available?

Supplemental imaging for women with dense breasts and normal mammography can increase the cancer detection rate, but there is limited evidence on whether this improves health outcomes beyond that from mammography alone. There are also potential harms to this approach as with all breast cancer screening, including false-positive examinations, potential overdiagnosis and additional cost. Therefore, careful discussion is required in order to formulate a strategy that is acceptable to the woman (Table 2).

1. Breast tomosynthesis

Digital 2-D mammography is the standard form of mammography and that used for screening in the Australian and UK screening programs and

Table 2. Managing breast density – individualised breast cancer screening

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|--|---|
| 1. Assess traditional breast cancer risk factors | <ul style="list-style-type: none"> • Risk factors should be assessed at the age of 40. • Consider potentially significant risk factors such as family history or personal history of breast cancer, previous atypical breast biopsy (lesions such as atypical ductal hyperplasia or lobular neoplasia). • Include lesser risk factors such as nulliparity, elevated age at first birth and lifestyle factors (alcohol intake, physical activity and BMI) |
| 2. Assess breast density | <ul style="list-style-type: none"> • The first screening mammogram at age 40 should include an assessment of mammographic density at baseline and this information can be used for planning. • If density is BI-RADS category C or D, this carries an increased risk of cancer and masking. |
| 3. Patient education and support | <ul style="list-style-type: none"> • Discuss the risk factors, how breast density fits in with the other risk factors |
| 4. Discuss screening interval | <ul style="list-style-type: none"> • Consider mammographic screening more frequently than every two years, or • Consider 2-yearly mammography with supplemental screening |
| 5. Discuss supplemental breast cancer screening | <ul style="list-style-type: none"> • If increased breast density exists with other risk factors, consider supplemental screening, which may include breast tomosynthesis, ultrasound and/or MRI. • Consider issues of local availability and patient acceptability. • Include information about supplemental screening: cancer detection is increased; however, the trade-offs are higher recall rate, biopsy rate and risk of overdiagnosis. |
| 6. Continually re-assess the plan | <ul style="list-style-type: none"> • Breast density changes over time and tends to decrease with age. • After menopause, breast density will usually decrease as a gradual process and supplemental imaging may not be needed in the long-term, should the density category reduce. • It is expected that evidence-based guidelines for managing breast density will become available in the next few years and advice to patients can be updated accordingly. |



tomosynthesis is used for work-up of abnormalities only. Breast tomosynthesis (3-D mammography) is a newer imaging technology. The patient experience is similar; however, tomosynthesis will acquire a series (a 'stack') of images rather than a single image. In the screening setting, 3-D mammography is able to detect more cancers than 2-D mammography, but with higher expense, longer reporting time, higher radiation dose and a possible increase in recall rate in settings with a low background recall rate. There is also concern that the additional cancers identified with tomosynthesis may represent overdiagnosis of indolent cancers rather than detection of additional clinically significant cancers.⁹ For women with dense breast tissue, the incremental cancer detection rate is higher than for women with non-dense tissue so 3-D mammography appears to have advantages in this sub-group.^{10,11}

2. Ultrasound

Supplemental ultrasound following negative mammography has been shown to increase the number of cancers detected (4.2 per 1000) in women with dense breasts. However, significant numbers of false positives are found. The biopsy rate was five times higher when ultrasound was added¹², and the positive predictive value from combined mammogram and ultrasound was only half of that for ultrasound alone (22% vs 11%) in a key study.¹³

Supplemental whole-breast ultrasound is usually by hand-held ultrasound. Automated technology is also being evaluated, which appears to have a benefit of being less operator-dependent and requiring less physician time.¹⁴

3. Magnetic resonance imaging

There is little available evidence on which to form recommendations about the use of MRI in women with dense breast tissue as their only risk factor. However, a recent large-scale randomised controlled trial demonstrated that the use of supplemental MRI in women with extremely dense breast tissue (Category D) and normal results on mammography resulted in the diagnosis of significantly fewer interval cancers than mammography alone. In that study, there was an increased risk of false positives and it is unknown whether the additional cancers detected were clinically significant.¹⁵ The cost of MRI is also a challenge in many settings. Abbreviated MRI protocols are being evaluated and these have the potential to be more acceptable to women and to be available at a lower cost.¹⁶

4. Screening interval

There is no evidence to inform the ideal screening interval for women with dense breasts. Currently, some screening programs that recommend biennial or triennial mammography may recommend annual mammography for women above population risk of

breast cancer based on their family history. As the risk of cancer related to dense breasts is similar to this, it may be reasonable to recommend annual screening; however, this has not been specifically studied and it not routinely available in the UK or Australia.

Should women be notified of their breast density?

As it is a risk factor for breast cancer, the case for density notification is strong. There is a powerful ethical argument for density to be disclosed to patients and this is being demanded by women around the world. However, in the US, notification legislation has not been accompanied by clinical guidelines or by support and educational materials for general practitioners and patients. This has led to anxiety among women and confusion about what to do with the information. There is also an increase in supplemental screening without compelling evidence to support it and with the potential for increasing anxiety further with false positive examinations and overdiagnosis.¹⁷ With density notification likely to become routine in many countries, it is important that support and education is in place for women and their doctors.

Proposed individualised screening recommendations

Breast cancer screening is likely to become more tailored, with assessment of all risk factors, including density, and development of an appropriate personalised screening regimen for the patient. The current 'one-size-fits-all' approach to population screening requires review.

On the current evidence, it is difficult to justify definitive recommendations for additional screening based on breast density alone. However, when breast density exists in combination with other risk factors such as multiple affected relatives and/or previous atypical breast biopsy, supplemental screening can be discussed (Table 2).

In conclusion, an appropriate screening regimen can be developed in consultation with the well-informed patient after detailed assessment of risk factors. There may be no change to general population screening recommendations for women with dense breasts and no other risk factors. For others, supplemental imaging with tomosynthesis, ultrasound and/or MRI can be considered. All of these options can increase the cancer detection rate but have trade-offs such as higher false positive and biopsy rate, risk of overdiagnosis and higher cost.

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Conflicts of Interest

None.



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