Breast density in screening mammography

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BREAST DENSITY is frequently reported in screening mammograms, which can result in discussions between patients and their general practitioners (GPs) regarding its significance in cancer detection. In the US, mammographic breast density notification has become mandatory in 38 states since initial legislation was passed in 2009.[1] Subsequently, in 2023, the US Food and Drug Administration updated mammography regulations requiring the compulsory notification of breast density to patients and referring practitioners. Currently, BreastScreen Australia does not report breast density, except in Western Australia, and does not recommend supplemental imaging in this group of patients. International counterparts in the US and Europe recommend mandatory reporting of breast density with some speciality groups, such as the European Society of Breast Imaging (EUSOBI), recommending interval supplementary screening breast magnetic resonance imaging (MRI).[2–4] In the context of this conflicting landscape, GPs are placed in a quagmire where patients, aware of their breast density, could enquire about supplemental screening that might or might not be warranted.[5] Here, we provide an update to GPs regarding breast density and cancer risk while providing an evidence-based framework for approaching the consultation.

Breast density refers to an increase in radio-opaque structures (glandular and fibrous tissue) compared with radiolucent elements (fat) of the breast.[6] There is no gold standard for the measurement of breast density. Nevertheless, the American College of Radiology Breast Imaging-Reporting and Data System (BI-RADS) A–D classification scale is commonly used, with A being almost entirely fatty and D being extremely dense.[6] Approximately 43% of women aged 40–74 years have heterogeneous or extremely dense breasts, with the proportion increasing with decreasing age (26% for those aged 70–74 years vs 57% for those aged 40–44 years).[7]

Increased breast density can mask cancer. The reduced sensitivity is well established in both the screen-film and digital mammography eras.[8,9] For example, the sensitivity of screen-film mammography is 62.2% in extremely dense breasts, compared with 88.2% in almost entirely fatty breasts.[8] Similarly, the sensitivity of digital mammography is 61.5% for dense breasts (BI-RADS C/D) compared with 86.6% for non-dense breasts (BI-RADS A/B).[9]

Increased breast density is also an independent risk factor for breast cancer.[10] McCormack and Dos Santos Silva's landmark review of 240,000 patients identified that the relative risk (RR) of developing cancer increases with increasing percentage density (50–74%, RR 2.9; >75%, RR 4.6).[10] Breast density measured both pre- and postmenopausally was a marker of breast cancer risk with no lower threshold where the relationship between density and increased risk ceased to exist.[10]

Supplemental testing can include digital breast tomosynthesis (DBT), ultrasound and/or MRI. Although the interval cancer detection rate is reduced, there is currently no evidence that supplemental imaging reduces mortality where increased density is the only risk factor.[11] The potential harms of supplemental imaging include cost, higher false positives and unnecessary biopsy rates. Harms of breast MRI include the risk of nephrogenic systemic fibrosis in women with comorbid kidney disease. Further, supplemental DBT more than doubles the radiation exposure at each screening examination.[11] Recent studies have focused on the use of supplemental MRI due to its advantages of increased sensitivity and minimisation of ionising radiation exposure. The 2018 Dense Tissue and Early Breast Neoplasm (DENSE) trial confirmed that although MRI reduced the rate of interval cancers, there was a high false-positive rate (74%) with unknown survival benefit.[12] Supplementary ultrasound in addition to mammography has been recently compared to mammography alone for patients with dense breasts in the only large-scale randomised controlled trial to date, the Japan Strategic Anti-cancer Randomised (J-START) trial.[13] In that trial, although the addition of ultrasound increased sensitivity (93.2% vs 70.6%), it resulted in a decreased specificity (85.4% vs 91.7%) and higher recall (15.2% vs 8.7%) and biopsy rate (6.2% vs 2.3%) compared with mammography alone.[13] So what should Australian GPs consider when patients present to discuss their breast density? It would be important to discuss that high breast density is common, representing almost half of the population, and to note that density is a known risk factor for breast cancer and can mask cancer detection.

However, if breast density is the only risk factor present, supplementary imaging is currently not recommended due to the high false-positive rate with associated invasive tests and unknown overall survival benefit. An evidence-based approach might include the use of a validated risk calculator such as the Tyrer–Cuzick/International Breast Cancer Intervention Study (IBIS) model (Box 1), which incorporates breast density, also supported by the American Cancer Society.[14,15] The calculator provides an estimated lifetime risk of breast cancer: if the risk is <15%, no supplemental testing needs to be offered; if the risk is >20%, supplemental MRI might be offered by way of referral to a specialist breast clinic; where the risk is between 15% and 20%, there is inconclusive data on the role of supplemental imaging and referral to a specialist breast clinic might be considered (Table 1). The recent results from secondary analysis of J-START might also result in ultrasound being considered as an adjunct for women at average risk.[13] Providing an individualised risk assessment might be used by the GP during the consultation to assist in shared decision making, as well as to facilitate greater patient understanding of their personalised risk of breast cancer that takes into account breast density.

Box 1. Inputs required for the Tyrer–Cuzick/International Breast Cancer Intervention Study (IBIS) model V8[15]

- Age
- Weight
- Age of first period
- Has the woman given birth to one or more children?
- Has the woman gone through menopause?
- Hormone replacement therapy usage?
- Breast density
- *BRCA* gene (if known)
- Ovarian cancer
- Previous breast biopsy results (if known)
- Family history (breast cancer, ovarian cancer, *BRCA* gene)

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Table 1. American Cancer Society guidelines for supplementary breast magnetic resonance imaging screening according to calculated lifetime risk[14]

Recommend annual MRI screening	Lifetime risk >20%
Insufficient evidence to recommend for or against MRI screening	Lifetime risk 15–20%
Recommend against MRI screening	Lifetime risk <15%

MRI, magnetic resonance imaging.