Mammographic / Breast Density

Facts and Issues

Clinical Oncology Society of Australia

Target Audience

This document is targeted towards the Professional Groups represented by COSA, and other health professionals, to help ensure they are well informed of the current issues surrounding high breast density in Australia.

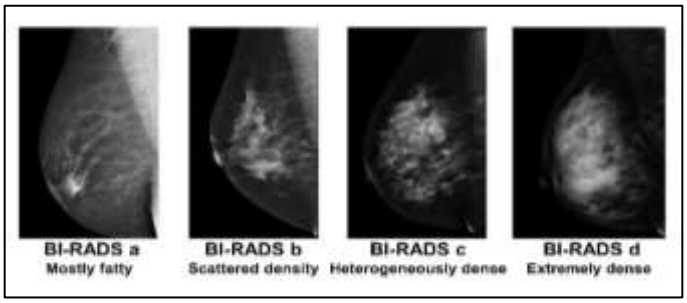
Key Points

The following key points are highlighted by the document:

- The benefits of continued mammography screening irrespective of density score.
- The importance of considering mammographic density-associated risk in the context of overall risk of an individual women, due to other factors.
- The complexities of providing breast density information and supplementary screening, which require careful explanation, and still may cause anxiety.
- The need for further research and important ongoing studies and clinical trials

What is breast density?

Figure 1



Breast density, also known as mammographic density, refers to white regions on a mammogram. The white regions contain predominantly fibroglandular tissue, whereas the darker regions are predominantly adipose tissue. The American College of Radiology [1] describe four categories of density in the BI-RADS Atlas corresponding to 'Mostly fatty' (BI-RADS-a), 'Scattered density' (BI-RADS-b, 'Heterogeneously dense' (BI-RADS-c) and 'Extremely dense' (BI-RADS-d) (Figure 1 image courtesy of *inforMD*, [2, 3]. These categories represent 13%; 40%; 35% and 5% of USA women aged 40-74 years [4], although these proportions vary from country to country. The BI-RADS-c and -d categories are often combined as 'dense breasts'.

How is high breast density detected?

A mammogram is required to assess breast density. Breast density bears no relation to how breasts look or feel and cannot be assessed by a physical exam.

What causes a woman's breast density?

Environmental and genetic factors are involved in determining a woman's breast density, which is established during puberty as the breasts develop and declines gradually with age, particularly after menopause. Hormone replacement therapy increases breast density, and anti-estrogen therapy for breast cancer treatment or prevention may reduce it. Effects of fertility treatments or the contraceptive pill on breast density are not clear.

How does high breast density affect detection of breast cancer?

Breast cancers appear white on a mammogram, as does the dense tissue. In women with BI-RADS-a or-b, the sensitivity for a screening program to detect breast cancer is high (~90%), but drops to ~84% for women with BI-RADS-c and to ~64% for BI-RADS-d [(5)]. This is due to masking of some of the mammography features that identify cancers, contributing to a higher rate of interval cancers (those that appear within 1-2 years of a clear mammogram) in women with dense breasts.

How does high breast density affect risk of breast cancer?

High breast density is a known risk factor for breast cancer. BI-RADS-a have ~ half of the risk of women with BI-RADS b, while those with BI-RADS-c and-d have 1.6-fold and 2.6-fold higher risks, respectively, than women with BI-RADS-b [(6)]. Breast density should be considered in the context of other known breast cancer risk factors e.g. age, BMI, long-term alcohol consumption, family history, known genetic status, age at menarche, number of childbirths and breastfeeding, as well as use of exogenous hormones, i.e. composite risk estimate [(7)].

What to tell women about their breast density?

Most important is that even for women with dense breasts, mammography remains the best screening modality for breast cancer. No matter her breast density, a woman is better off being screened in an audited, double read screening program such as BreastScreen than not undergoing screening for breast cancer. There is great variability in Australia on how women are informed about breast density, which is a concern for both patients and providers. The current position statement of BreastScreen Australia (BSA; 2020) does NOT recommend recording breast density or notifying women of their breast density, other than currently in WA, where breast density has been reported on for over a decade [(8)]. This is primarily due to the lack of evidence-based research indicating a benefit to women by informing them of their breast density, possible harms from supplemental screening (see below), and the lack of clear evidence and clear pathways to balance benefit versus harm from altering current recommended screening intervals and methods of screening. There remain some uncertainties around the measurement accuracy and the clinical management of women with dense breasts, and revising recommendations will also result in significant cost implications both for women and the health system. The guidelines of the Royal Australian and New Zealand College of Radiologists (RANZCR, 2018) recommend that breast density be listed in the mammogram report; this does not apply to the BreastScreen programs in

Australia or New Zealand, where a formal report is not issued [9]. Breast Cancer Network Australia (BCNA) provides information on mammographic density designed specifically for women in the community [10], as does and the Information Forum on Mammographic Density (inforMD; [11]), and Pink Hope [12]. Uniformity on this issue is an important goal.

What are the issues associated with Supplementary Screening?

No randomised controlled trials evaluating supplemental screening tests in women with dense breasts have sufficient follow up to determine a survival benefit. No studies have yet evaluated adjunct breast MRI screening in women of average risk with dense breasts. Research demonstrates that supplementary breast ultrasound in women with dense breasts increases cancer detection by 40%, but has a high false positive biopsy rate (>90%) [13], and to be applied as a recommendation would need further evaluation. There are trials ongoing overseas to test the detection benefits of supplementary screening tests. WISDOM and MyPEBS are based on composite breast cancer risk, including breast density, whereas J-START is population-based. The DENSE trial of supplemental MRI screening in women with extremely dense breast tissue and normal results on mammography recently reported the diagnosis of many more cancers during the initial screening round, and significantly fewer interval cancers than mammography alone during a 2-year screening period [14].

What else to tell younger women about their breast density?

Breast cancer is relatively uncommon in younger women but they are encouraged to report any abnormalities. Although breast density is generally higher overall in younger women (<40 years old), breast cancer risk still varies across the density quartiles, and associations appear even stronger in younger women. Mammography screening in women aged <45 is controversial, due to radiation exposure and low absolute risk. Mammography can be used diagnostically at any age if the woman has a symptom suggestive of breast cancer. High breast density may ultimately alter the age at which a woman should start screening, so younger women with high breast density should monitor screening recommendations, which may evolve to include them.

What about women who want to know their breast density?

There are currently no clinical guidelines for breast screening or managing cancer risk for women with dense breasts, due to imprecision in measurement and insufficient evidence to guide best practice. Indefinite biomedical information can cause anxiety in patients and uncertainty for health professionals required to provide clinical advice. However, if women wish to be informed about their breast density, the only option available is to refer them to a private radiology provider who offers breast density measurement but at the patient's expense (Medicare rebate for private radiology is only available for women with symptoms or a family history, not screening). The most common method is the subjective BI-RADS classification a-d (see figure 1). Some private clinics offer quantitative measures of density, such as Volpara and Quantra, which can improve the reproducibility of assessment.

Western Australia

Currently, BreastScreen Western Australia is the only Australian screening program to notify women if they have dense breasts (BIRADS categories c & d) by dichotomous assessment and have been doing so for over 10 years. The information they communicate to women with dense breasts is largely focussed on reassurances that dense breasts are common, explaining the lowered sensitivity of the mammogram to detect cancer, and directing women to their GP for a breast check and advice. A survey of notification effects in WA showed an increase in screening intention [15].

Tomosynthesis and other new methodologies?

Tomosynthesis (3D mammography) has a higher cancer detection rate but is not yet proven to show a survival benefit as a screening modality in women with dense breasts. Without studies demonstrating a survival benefit, the concern is that some of the cancers detected by other screening modalities could result in diagnosis of clinically unimportant cancers (over-diagnosis). Although MRI is regarded as the most sensitive supplemental screening technology, it is not widely implemented in its current form due to cost. More accessible forms of MRI that are quicker and less expensive (e.g. Accelerated MRI) are being investigated.

Breast density notification in the USA and Canada

Non-uniform breast density notification laws in 38 American States to date have led to a fragmented approach to measuring breast density, notification and management strategies. Unlike Australia, the US has no organised national mammography screening program, so evidence and observations from the US is of limited relevance to Australia in relation to health policy. However, Canada does have a population-based breast screening program, and British Columbia adopted the policy of notifying all women of their BI-RADS density category in 2018. They provide fully funded ultrasound to women with dense breasts with a doctor's referral. A number of other Canadian provinces are now in the process of similar policy change.

What is in the pipeline about Breast density?

BreastScreen Australia commissioned an extensive *literature review on breast density* [16] and the Australian Government Department of Health has funded the Optimising Early Detection of Breast Cancer in Australia project at Cancer Council Australia to explore risk-based adjustments to breast cancer screening in Australia, including breast density [17]. Ongoing studies are refining breast density measurement associations with both risk and masking of breast cancer (e.g. brightness [18], deep learning [19]). As evidence is collected and reviewed, decision analytic models will be needed to evaluate the cost-effectiveness and budget implications of any emerging or potential tailored breast cancer screening tools, the balance of benefits and harms, and best ways to assess breast density with reference to other breast cancer risk factors, to inform reimbursement decisions and implementation strategies. While this important work evolves, COSA will work with its members in oncology, allies, and stakeholders, to encourage consistency in clinical practice and advice to Australian women.

Useful Links

Royal Australia College of General Practitioners: https://www.racgp.org.au/clinical-resources/clinical-guidelines/key-racgp-guidelines/view-all-racgp-guidelines/guidelines-for-preventive-activities-in-general-pr/early-detection-of-cancers/breast-cancer

American Cancer Society: https://www.cancer.org/cancer/breast-cancer/screening-tests-and-early-detection/mammograms/breast-density-and-your-mammogram-report.html

Health Link British Columbia, Canada: https://www.healthlinkbc.ca/health-topics/abp2024#abp2025

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Approval

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