

Ultrasound as a secondary screening tool in mammographically dense breasts

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Abstract It is well known that breast screening is a part of our society and is designed to reduce the mortality and morbidity from breast cancer. Mammography is the imaging modality of choice in a breast-screening environment. Both the detection rate of mammography in a screening environment and the sensitivity of mammography in symptomatic women are known to be greater than that of ultrasound. However, after a review of literature both of these are said to increase when the two imaging modalities are combined. This paper will present that mammography has limitations in breast imaging, especially in women with dense breasts and that ultrasound can have a benefit as a secondary screening tool in these women. It will be shown that although ultrasound also has its limitations, these can be minimised with the implementation of effective education and imaging protocols.

The paper will conclude that although further research into ultrasound as screening tool is required, its use as a complement to mammography can only be of benefit to the general population.

Introduction

Although mammography is known to be the most effective form of breast screening, it has limitations. In particular, it is known to have limitations in high-risk patients especially those with mammographically dense breasts because of the radiographically occult nature of such breasts. It will be presented that although ultrasound also has its limitations, it can have a viable role in the secondary screening of dense breasts. The purpose of screening will be defined and the limitations of mammography will be described with particular relevance to breast density. The benefits and limitations of ultrasound as a screening tool will be evaluated after review of current literature and it will be shown that the limitations of ultrasound can be minimised to achieve the best possible outcome for the general population.

The results of breast screening

Breast screening is where asymptomatic women are imaged for the early detection of breast cancer with the aim of reducing the morbidity and mortality of breast cancer.

It is widely accepted that the primary method of breast screening is mammography and that the use of ultrasound is the most effective adjunct to mammography in helping to distinguish benign from malignant disease.^{1,2,3,5} Mammography has a screening detection rate of between 0.20 per cent and 0.70 per cent which is partly dependent on patient age.⁵

BreastScreen Victoria, however, reports in its 2001 Annual Statistical Report,¹² that screening mammography detects a higher average of 0.73 per cent of cancers. The 40-49-year-old age group, which is more likely to have dense breasts, is reported as having a 0.38 per cent detection rate. Ultrasound, as a primary screening tool, is reported to detect approximately 0.30 per cent of breast cancers.^{2,3,4,6}

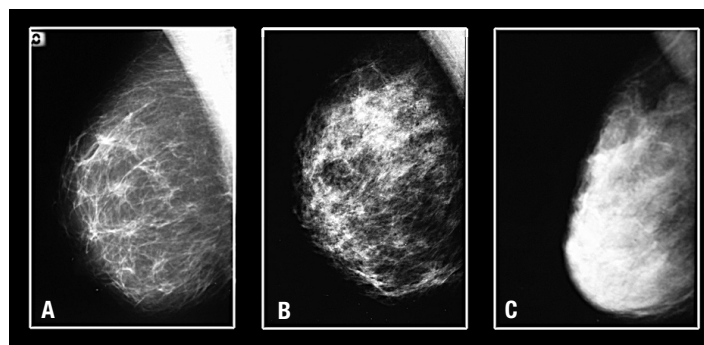


Figure 1 mediolateral oblique views of three different breast densities. Ranging from scattered fibroglandular densities in (A) to a heterogeneously dense breast (B) to being an extremely dense breast (C).

Mammography has its limitations and the use of ultrasound as a secondary screening tool, especially in high risk patients, must be considered.^{3,4,5} The sensitivity of an imaging modality is defined as the percentage of cancers detected among all cancers detected with any modality.¹³ Mammography in symptomatic patients is reported to have a sensitivity of up to 98 per cent in women with fatty breasts. However, in women with very dense breasts it is reported to diminish to a low of only 48 per cent, with an average of 78 per cent. The sensitivity of ultrasound in women with dense breasts is around 75 per cent. The use of ultrasound combined with mammography in these women can increase the sensitivity to 97 per cent.¹³ Therefore, it is clear that ultrasound can play a role in the secondary screening of dense breasts.

What is a dense breast?

The interpretation of the density of a breast is very subjective. Some studies rate the denseness of the breast according to the Breast Imaging Reporting and Data System (BIRADS) as set by

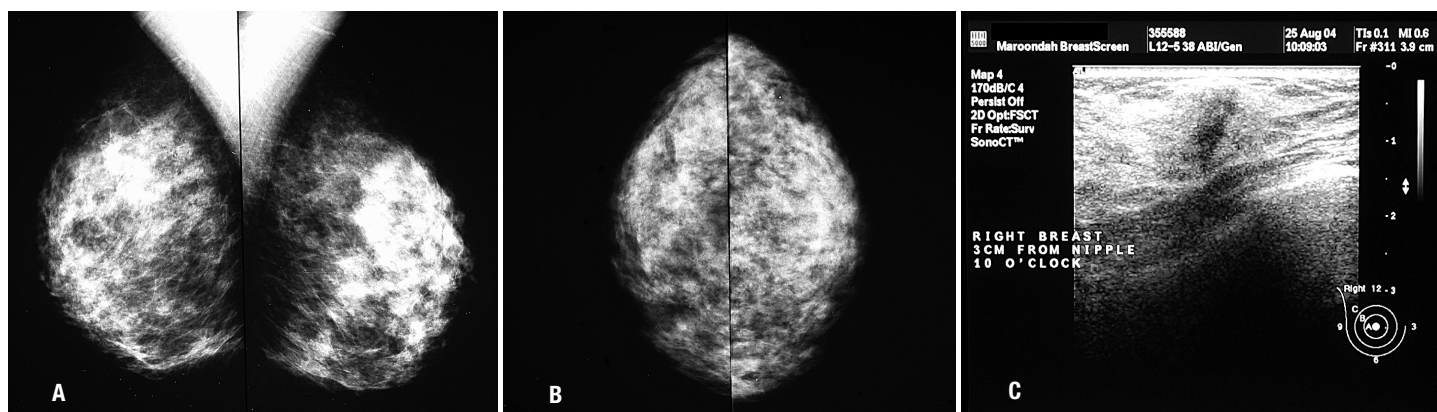


Figure 2 mediolateral (A) and craniocaudal (B) views of a 52-year-old woman with heterogeneously dense breasts. The mammogram was normal while an ultrasound (C) revealed an invasive ductal carcinoma in the right breast at 10 o'clock. The carcinoma is hypoechoic in a hyperechoic background.

the American College of Radiologists.

Kolb *et al.*⁶ define the BIRADS classification of breast density as being:

- 4 – being an extremely dense breast;
- 3 – an heterogeneously dense breast;
- 2 – scattered fibroglandular densities in the breast and;
- 1 – a breast that is almost entirely fat.

Other studies simply rate the density of the breast into three categories, being dense, mixed and fatty breast.^{7,9} The density of the breast is graded by visual means only. It is clear that the definition of a dense breast needs to be defined objectively in order to carry out studies on the sensitivity of ultrasound in dense breasts. Figure 1 shows varying breast densities.

It is understood that, with the introduction of digital mammography and computer aided detection (CAD), the denseness of a breast will be able to be defined more objectively, however, the use of digital mammography may also reduce the effect of breast density on the sensitivity of mammography.⁶ It is reported that the different definitions of breast density in varying studies may be the cause for varying results and, as breast parenchyma density can vary in the same patient, the difficulty of definition will always be there.

The limitations of mammography

Mammography is based on the contrast differences between fatty and glandular tissue. The glandular areas in the breast show as areas of increased density. However, mammographically, breast cancers can also show as areas of increased density. Therefore, in dense breasts, cancers may be radiographically occult. Although the biological basis is unclear, it is suggested that the denseness of the breast contributes to breast cancer risk,⁴ and in understanding this failure of mammography in imaging dense breasts other imaging modalities need to be considered.⁹

A study by the Wesley Breast Clinic⁷ suggested that the number of mammographically occult cancers per 1000 mammograms was almost twice as many in dense breasts as in average density breasts, which is why ultrasound must be considered as a secondary screening tool. Mammography also has limitations related to patient age, the use of hormone replacement therapy and the location of a lesion in the breast,⁴ these all affect the sensitivity of mammography.

With much publicity today about the effectiveness of breast imaging and the increased knowledge of our patients, it is of concern that mammography alone cannot always satisfy and reassure the patient who is at high risk of breast cancer.²

Ultrasound as a breast-imaging tool

Ultrasound in breast imaging is a very useful adjunct to mammography as it can help to classify the nature of lesions seen in the breast. Stavros *et al.*¹¹ showed in their landmark study that sonography improves the specificity of diagnoses of breast lesions, both benign and malignant. It is the most common complement to mammography and can often be necessary for complete evaluation of the breast.

Ultrasound is the recommended adjunct for mammographically dense breasts as fibroglandular tissue appears hyperechoic and breast cancers usually present as hypoechoic. Therefore, it is thought that cancers can be well visualised in this background.^{4,6} See Figures 2 and 3.

Ultrasound has fewer limitations when it comes to patient age and positioning. Unlike mammography, the location of a lesion in the breast is of decreased significance with ultrasound usually providing easy access for guiding needle core biopsies and localisations.

As an imaging tool, ultrasound has limitations that make it unsuitable for use as a primary screening modality. Ultrasound cannot detect microcalcifications and is operator dependent. It is reported as not being cost effective as a screening modality if performed by radiologists.³

Stavros³ also reports a medico legal disincentive for performing whole breast ultrasound in the United States. He states that:

'A radiologist can be held liable only for a missed cancer that lies in the part of the breast that was examined sonographically. He or she cannot be held liable for a missed cancer that lies in a part of the breast that was not examined sonographically. Thus, certain American radiologists have tended to avoid scanning areas other than the immediate area of clinical or mammographic concern.'³

Ultrasound, however, needs further investigation if it is to be used as a secondary screening tool.

There are no hard data on the effectiveness of sonographic screening. Ultrasound needs to be explored further as a secondary screening tool with newer high resolution equipment and improved scan technique.^{2,3}

Madjar² conducted a small pilot study on asymptomatic women that showed that ultrasound was a feasible option for secondary screening. He also showed that operator skill can be transferred with effective education and training, thus partly overcoming the issue of operator dependence. Madjar also believes the extra cost of ultrasound is justified in high risk patients, as does Stavros.³ Stavros reports the cost of cancer found by ultrasound is similar

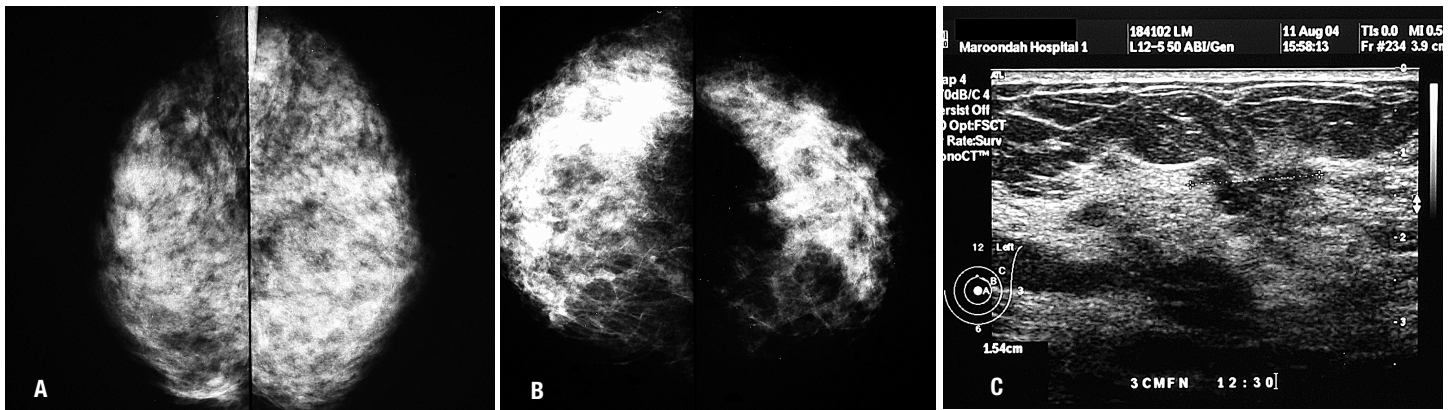


Figure 3 Mediolateral (A) and craniocaudal (B) views of a 48-year-old woman with dense breasts. The mammogram was normal while the ultrasound revealed a tubular carcinoma with invasive components in the left breast at the 12.30 position. There were no clinical indications.

to the cost of cancer found at screening mammography and that ultrasound is viable when the mammogram is negative in a high risk patient.

Crystal *et al.*⁴ also reports the effectiveness of ultrasound as a secondary screening tool. Their study shows a 0.46 per cent cancer detection rate for screening ultrasound. They believe that ultrasound is not cost effective for all patients but has the potential to be beneficial for patients with dense breasts. Their study achieved a high rate because of the high number of patients with dense breasts. It is believed that if there had been more patients with less fatty breasts the detection rate would not have been as high with ultrasound and would, therefore, not be as cost effective. The study by Crystal *et al.* also used modern high resolution equipment as they recognised the need for this. However, Crystal *et al.* recognise the need for further studies in this area to reproduce their results and to look at the cost effectiveness of ultrasound. Of course the cost of ultrasound as a screening modality will vary between countries depending on different regulations. The true benefit from ultrasound 'cannot be determined other than by performance of a randomised control trial (RCT) using death as the end point'.⁴ A RCT is actually unlikely in today's times as women are better informed and, therefore, there is more likely to be less compliance resulting in contamination. It is known that women who volunteer for a trial but who are assigned to the control group are likely to seek information outside the trial and will therefore, receive the examination anyway. This contamination would likely affect the difference in mortality between groups.⁵

Kolb *et al.*⁶ found a 0.30 per cent detection rate for screening ultrasound alone. They found that the size and stage of cancers detected was not statistically different to those detected by screening mammography. They agree that, because of the limitations of mammography, a secondary screening method needs to be investigated as finding cancers by mammography is just as beneficial as finding them by ultrasound. Again, it is thought that more studies using high resolution equipment need to be performed to assess whether the benefits of the increased detection outweigh the increased costs and time associated with secondary screening.

Minimising the limitations of ultrasound

The main concern for ultrasound is the fact that it is so operator dependent. However, it can also be argued that mammography is operator dependent as well. The introduction of guidelines for a screening program including comprehensive training and accreditation for mammographers has helped to overcome this problem. It has already been stated that Madjar² demonstrated in

his study that good ultrasound technique can be learned and transferred. There is no reason why, with the availability of dedicated breast ultrasound training programs, that the effect of operator dependence can be minimised in a controlled screening environment. Standards for ultrasound examinations of the breast are already set by various bodies such as the Australian Society for Ultrasound in Medicine and the International Breast Ultrasound School to ensure a systematic approach to the imaging process.

Previous studies report an increased cost of ultrasound screening because of a radiologist performing the scan.^{3,4,6} These are overseas studies. The author believes that, with the quality of sonography in Australia, in conjunction with continued education standards as set by the Australasian Sonographers Accreditation Registry, there is no reason why feasible studies cannot be undertaken with sonographers rather than sonologists in this country. This would reduce the previously noted high cost of secondary screening ultrasound. The time taken for screening ultrasound and the increased anxiety level of patients undertaking an extra test has been reported as a negative aspect in ultrasound screening. However, the time for a screening ultrasound examination has been reported as between 4–15 min with an average of only 7 min.⁴ Also, if the screening ultrasound is performed immediately following the mammogram, thus negating the need for a recall, time is saved and the effect of adverse psychological consequences from a recall is reduced.⁴

Conclusion

It has been shown that screening mammography has its limitations especially in high-risk patients such as those with dense breasts. Because of these limitations, it is generally agreed that a secondary screening option needs to be considered. We need to improve our ability to detect breast cancers in mammographically dense breast to satisfy the expectations of the general population. Ultrasound, although it has its own limitations, is a viable option as a secondary screening tool as it has been shown to improve cancer detection rates in this high-risk group. It is known, though, that more research needs to be carried out to prove its effectiveness and to reproduce the encouraging results already obtained.

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