



This statement is to provide clarity for health professionals to assist women to make informed decisions. The BreastScreen Aotearoa programme aims to maximise benefits and minimise harms in the screening environment.

Position

The National Screening Unit (NSU) does not support the use of ultrasound as a primary screening tool or the routine use of ultrasound as an adjunct screening tool in the BreastScreen Aotearoa (BSA) programme, as presently there is insufficient evidence to do so.

Screening for breast cancer

Breast screening programmes aim to detect tumours at an early stage, resulting in fewer people dying from breast cancer. When well women are invited to participate in New Zealand's national screening programme, BSA, it is on the understanding that the benefits of participation will outweigh the harms. This approach is in line with international standards for screening. It is vital, therefore, that any screening test is assessed through well-conducted medical research, ideally randomised controlled trials (RCTs) or meta-analyses of RCTs.^{1,2}

BSA recommends a screening mammogram every two years for eligible women aged 45 to 69 years. Mammography is the only screening test that has been shown to reduce death rates from breast cancer, based on the results of RCTs and meta-analyses.^{3,4}

Breast ultrasound

In screening programmes, ultrasound has been used for many years in assessment clinics to look at areas of interest detected by mammogram or clinical examination, such as a mass seen on a mammogram, or a palpable lump. Ultrasound

is helpful in these circumstances, in both characterising the area of concern and guiding a biopsy (tissue sample) of the area. Ultrasound is safe and widely available, though ultrasound of the breast should be performed by clinicians with specialised training in this area.

In some international literature, ultrasound screening has been suggested as an adjunct to mammography, especially in the surveillance of women with dense breast tissue who may be at higher risk of developing breast cancer.

Recent literature on screening ultrasound

In 2006, a large single centre study was published⁵ looking at the role of ultrasound in detecting mammographically occult breast cancer in women with dense breast tissue. In the study, ultrasound found breast cancers not detected on mammograms at a rate of 2.3 cancers per 1000 women screened. However, the patients were self-referred and not representative of a screening population. The study was also a consecutive series and not randomised in any way.

The authors of this study published further in 2008,⁶ showing a cancer detection rate from ultrasound alone of 4 cancers per 1000 women screened, again with consecutive self-referred women. Five percent of the women who had ultrasound required needle or surgical biopsy, of which eight percent were confirmed with cancer, meaning that the rate of false positive examinations was high.

In the United States, ACRIN 666, a large multi-centre randomised controlled trial of screening ultrasound in the USA, was published in 2008.⁷ The authors looked at combined screening with ultrasound and mammography, compared to mammography alone, in women at 'high risk'⁸ of breast cancer who also had dense breast tissue. The trial found that in this selected 'high risk' group of women,⁹ ultrasound in addition to

mammography detected an additional 4.2 cancers per 1000 women screened. However, it had an increased number of false positive examinations, with less than 10 percent of the biopsies prompted by the ultrasound examination showing cancer.

In 2012, results of a clinical trial on the detection of breast cancer in women with increased breast cancer risk were published.¹⁰ The trial compared mammography screening with the addition of annual ultrasound or MRI. The study found that supplemental screening ultrasound detected an additional 3.7 cancers per 1000 women screened. Rates of biopsy for findings seen only on ultrasound remained substantial, representing five percent of women, with only 7.4 percent of those women found to have cancer. Participants in this study were from a selected population with an expected higher rate of breast cancer, and were not representative of a general screening population.

Authors of a systematic review of six cohort studies of ultrasonography over the period 2000 to 2008¹¹ noted an increased biopsy rate after ultrasound of women at intermediate risk of breast cancer. The review also noted the lower positive predictive value of biopsies indicated on ultrasound, which was about one third of those indicated by mammogram.

In 2013, a Cochrane review¹² sought to assess the comparative effectiveness and safety of breast screening for women at average risk¹³ of breast cancer aged between 40 and 75 years. The aim was to review mammography alone versus mammography in combination with breast ultrasound. For efficacy, this study considered RCTs, prospective studies and controlled non-randomised studies with a low risk of bias. The review sought a study size of at least 500 participants. This review did not identify any studies that met its criteria for study type or quality. It concluded that presently there is no methodologically sound evidence available justifying the routine use of ultrasound as an adjunct screening tool in women at average risk of breast cancer.

Considerations regarding screening ultrasound

Screening ultrasound has been shown to be more sensitive but less specific than mammography as a screening tool. Ultrasound identifies more lesions than mammography, which can result in a higher rate of biopsies. The proportion of biopsies that identify cancer is significantly lower than for mammographically indicated biopsies.

Recall for a biopsy means repeat visits for additional tests. Needle biopsy is a safe procedure, but can be stressful and occasionally painful. BSA aims to maximise benefits and minimise harms in the screening environment. A test with a high number of false positive outcomes is not well suited to the screening environment.

Additionally, some cancers may be missed with ultrasound. In particular, ultrasound does not usually show the micro-calcifications which are commonly associated with ductal carcinoma in situ, which means that a mammogram is still required.

For these reasons, ultrasound is utilised in BSA as an additional assessment tool, not as an alternative to mammography.

Conclusion

The NSU does not support the use of ultrasound as a primary or adjunct screening tool in the BSA programme, as presently there is insufficient evidence to do so.

If any health providers are offering screening ultrasound to women, it is important that the women are informed that ultrasound does not replace a screening mammogram. Women should also be informed of the increased risk of a false positive examination and the risk that some lesions may not be detected with ultrasound.

The NSU will continue to monitor emerging research and new technologies.

- 1 National Health Committee. 2003. *Screening to Improve Health in New Zealand: Criteria to assess screening programmes*. Wellington: National Advisory Committee on Health and Disability (Health Committee).
- 2 Muir Gray JA. 1997. *Evidence Based Healthcare*. (1st ed). Edinburgh: Churchill Livingstone.
- 3 International Agency for Research on Cancer (IARC). 2002. *Breast Cancer Screening*. 1st ed. Lyon, France: IARC Press.
- 4 Breast Cancer Screening: A summary of the evidence for the US Preventive Services Task Force. 2002. *Annals of Internal Medicine* 137:347–360.
- 5 Corsetti V et al. 2006. Role of ultrasonography in detecting mammographically occult breast carcinoma in women with dense breasts. *Radiol Med (Torino)* 111 (3):440–448.
- 6 Corsetti et al. 2008. Breast screening with ultrasound in women with mammography negative dense breasts: Evidence in incremental cancer detection and false positives and associated costs. *European Journal of Cancer* 44 (4):539–544.
- 7 Berg W et al. 2008. Combined screening with Ultrasound and mammography vs mammography alone in women at elevated risk of breast cancer. *Journal of the American Medical Association* Vol.299, No.18 2151–2163.
- 8 The women were considered at high risk because of a personal history of breast cancer, a previous biopsy showing a high risk lesion on pathology, a gene mutation, previous chest irradiation or a high risk score on various risk models.
- 9 A high risk group was chosen for the trial because it was thought that combined screening would be more cost effective in this group, in whom the expected prevalence of disease is higher than for a general population.
- 10 Berg W et al. 2012. Detection of breast cancer with addition of annual ultrasound or a single screening MRI to mammography in women with elevated breast cancer risk. *Journal of the American Medical Association* Vol. 307(13) 1394–1404.
- 11 Nothacker, M. et al. 2009. Early detection of breast cancer: Benefits and risks of supplemental breast ultrasound in asymptomatic with mammographically dense breast tissue. A systematic review. *BMC Cancer* 9:335.
- 12 Gartlehner, GK et al. 2013. Mammography in combination with breast ultrasonography versus mammography for breast cancer screening in women at average risk. *Cochrane Database of Systematic Reviews*.
- 13 Average risk is defined as those who have a lifetime risk of less than 15 percent or who have dense breasts without any additional risk factors for breast cancer.