Update on Screening Breast Ultrasonography

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KEYWORDS

• Screening breast ultrasonography • Breast cancer screening • Dense breast tissue
• Cancer detection rate • Positive predictive value

KEY POINTS

- Handheld screening breast ultrasonography has been shown across multiple studies of patients with dense fibroglandular tissue and/or increased risk of breast cancer to have an average breast cancer detection rate of 3.7 additional cancers detected per 1000 women screened.
- The additional cancers detected by screening breast ultrasonography are at the cost of a low positive predictive value of biopsy (averaging 9.5% across multiple studies) leading to many unnecessary biopsies and at the cost of detection of many Breast Imaging Reporting and Data System 3 probably benign findings that require additional short-interval follow-up.
- As part of widespread implementation of screening breast ultrasonography, appropriate training courses, accreditation criteria, and guidelines should be developed to ensure safe and efficacious use of breast ultrasonography as a screening tool.

Screening mammography is the only modality that has been proved to reduce mortality from breast cancer; however, mammography has limitations and therefore other modalities are being investigated as possible screening tools for breast cancer. Breast ultrasonography and magnetic resonance (MR) imaging are the primary modalities that have been investigated and this article focuses on breast ultrasonography as a screening tool. This article discusses the current recommendations for screening breast ultrasonography, presents a review of the literature, and discusses problems associated with the implementation of screening breast ultrasonography and the political and economic factors influencing the use of screening breast ultrasonography.

CURRENT RECOMMENDATIONS FOR SCREENING BREAST ULTRASONOGRAPHY

The American College of Radiology (ACR) and Society of Breast Imaging currently recommend that screening breast ultrasonography be used, in addition to mammography, in women with a high risk of developing breast cancer who cannot have MR imaging. Breast ultrasonography is considered a possible screening supplement option for women with dense breast tissue who are at an intermediate risk of developing breast cancer.[1,2] High risk is defined as one or more of the following: breast cancer susceptibility genes 1 or 2 (BRCA1 or BRCA2) mutation carrier or untested first-degree relative of a BRCA mutation carrier; history of chest wall radiation between the ages of 10 and 30 years; women with a genetic syndrome that increases the risk of breast cancer; and lifetime risk of breast cancer of 20% or more. Intermediate risk of breast cancer is defined as having a 15% to 20% lifetime risk of breast cancer; this includes risk associated with a personal history of breast or ovarian cancer, and prior breast biopsy diagnosis of lobular neoplasia or atypical ductal hyperplasia.[1,2]

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Dense breast tissue is considered a possible indication for screening breast ultrasonography because mammography is less sensitive in detecting breast cancer in dense breast tissue, breast cancer is more likely to develop in areas of denser breast tissue, and having dense breast tissue is a risk factor for breast cancer.[3–6] Breast tissue density is categorized by the Breast Imaging Reporting and Data System (BI-RADS) into 1 of 4 categories based on the composition of glandular tissue seen mammographically: (1) almost entirely fat (<25% glandular), (2) scattered fibroglandular densities (approximately 25%–50% glandular), (3) heterogeneously dense (approximately 51%–75% glandular), and (4) extremely dense (>75% glandular).[7] Although the forthcoming fifth edition of BI-RADS[8] will eliminate the percentage-based subcategorization of breast densities, most published work on ultrasonography screening in women with dense breast tissue defines dense breast tissue as breast tissue with more than 50% glandular tissue (categories 3 and 4) and, unless otherwise stated, this definition applies throughout this article as well.

REVIEW OF THE LITERATURE ON SCREENING WHOLE-BREAST ULTRASONOGRAPHY

Handheld Screening Whole-Breast Ultrasonography

A summary of studies evaluating whole-breast ultrasonography as a screening tool is presented in **Table 1**. Initial small-scale, single-institution, observational studies of supplemental handheld screening breast ultrasonography showed promising results for screening breast ultrasonography using a handheld device as a supplement to screening mammography.[9–14] Berg[15] summarized these results, which included 42,838 examinations from 6 different studies performed between 1995 and 2004. Supplemental screening breast ultrasonography performed in these studies had a mean cancer detection rate of an additional 3.5 cancers per 1000 women screened that were not detected by screening mammography; however, the range was wide (from 2.7 to 9.0 cancers per 1000 women screened).[15,16] Of the cancers seen only by ultrasonography, 94% were invasive and 70% of the invasive cancers were 1 cm or smaller in size.[15] Three of the studies detailed staging and, in total, 36 (90%) of 40 cancers identified only by ultrasonography were stage 0 or I.[15] Also, as predicted, ultrasonography was superior to mammography at detecting cancers in mammographically denser breasts. Women with fatty breast density were excluded from all of these studies, but a disproportionate number (90%) of the cancers detected only by ultrasonography were in women with dense breasts.[15] These studies also suggested that supplemental ultrasonography was most appropriate in women at increased risk of developing breast cancer. Women at higher risk for breast cancer were 2 to 3 times more likely to have a cancer identified by ultrasonography that was not seen mammographically.[15] The biopsy rate for ultrasonography-only findings in these studies averaged 3.1% and the positive predictive value (PPV) for biopsies (core biopsy or fine-needle aspiration) performed for suspicious findings seen only by ultrasonography was 11.4% with a range of 6.6% to 18%.[15,16] The low PPV for biopsies has caused concern, and many consider this as an unacceptably high percentage of false-positives, with many unnecessary biopsies having been performed as a result.

Although these initial studies showed promise for screening breast ultrasonography as a possible breast cancer screening tool, they were all single-institution studies with varying study designs and several important limitations. One limitation is that the studies were nonblinded; the ultrasonography interpretation was not done independently from the mammography interpretation, with potential bias and leading to screening recalls (targeted ultrasonography evaluations). In addition, these studies only reported prevalence and not rate of incidence; therefore it was not known whether annual screening ultrasonography would provide any additional benefit compared with the initial screening ultrasonography. Follow-up data were incomplete, incremental cancer rates were not reported, and standardized BI-RADS reporting was not uniformly applied. The ability to generalize these studies to current radiology practice is limited because of the single-institution observational nature, variability in interpretive and reporting criteria, and the use of film-screen mammography during these study periods.

The results from these single-institution studies, showing that screening breast ultrasonography is able to detect small, invasive but early stage, mammographically occult breast cancers, was encouraging and in response several larger, prospective, multi-institution studies have been developed. At this point, some questions remained; primarily whether earlier detection of these small invasive cancers can be measured in mortality reduction and whether the results of the studies can be generalized not only across institutions but also among the individuals performing the handheld ultrasonography examinations. A randomized controlled trial (RCT) would have been ideal before implementing ultrasonography