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Incorporating Imaging Into the Locoregional Management of Breast Cancer

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Although some breast cancers present as palpable masses or with other clinical findings, many are detected at screening. Most screening is currently done with digital mammography, but high-risk patients or those with dense breast tissue may undergo additional screening examinations with magnetic resonance imaging or ultrasound. Additionally, digital breast tomosynthesis, contrast-enhanced mammography, and molecular breast imaging are newer technologies available at some sites. Optimal usage of breast imaging technologies remains controversial, both in screening and diagnostic settings following a new diagnosis of breast cancer. This article will review well established and newer, alternative breast imaging technologies as well as recent data regarding their role in optimizing patient care.
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Introduction

Although screening mammography has been used routinely in the United States since the 1990s and prospective studies[1-3] have shown an associated decrease in breast cancer mortality, there is persistent controversy regarding how frequently to screen women and at what ages. The U.S. Preventive Services Task Force recommendations released in 2009 advocated only biennial screening starting at the age of 50 years.[4] This recommendation was met with significant opposition from patients, as well as physician professional societies, and ultimately resulted in an amendment to the Patient Protection and Affordable Care Act to insure screening mammography would be covered by insurers. The recently released draft[5] of the 2015 update to the U.S. Preventive Services Task Force recommendations remains largely unchanged, garnering renewed opposition, and fueling the controversy. Despite or perhaps because of the controversy surrounding mammography, multiple other techniques are emerging as adjuncts to mammography.

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Supplemental Screening

Although mammography is the only screening modality that has demonstrated a mortality reduction for breast cancer, it is less effective in women with dense breasts. Mammography has a sensitivity of 98% in women with fatty breasts, but sensitivity in women with dense breasts ranges from 30%-69% and is particularly low in young women or women at increased risk.[6-8] As 43% of women of screening age have dense breasts on mammography,[9] there has been considerable interest and debate about supplemental screening. Understanding the risks and benefits of supplemental screening is particularly relevant today, as increasing numbers of states are passing breast density legislation that requires women be informed about their breast density and possible benefits of supplemental screening if they have dense breasts. As of January 15, 2015, 21 states have passed some form of breast density legislation,[10] despite the lack of consensus from the medical community about whether the risk-benefit ratio of additional screening is justified.

Although supplemental screening tests such as ultrasound (US) and magnetic resonance imaging (MRI) increases cancer detection rate, they do so at the cost of decreased specificity and a resultant increase in false positive examinations. MRI has the highest sensitivity, is not limited by breast density, and does not use ionizing radiation. In studies of high-risk women, MRI has a higher sensitivity than mammography (71%-77% vs 36%-40%) but a lower specificity (71%-77% vs 81%-95%).[11-13] As the sensitivity of the 2 combined is over

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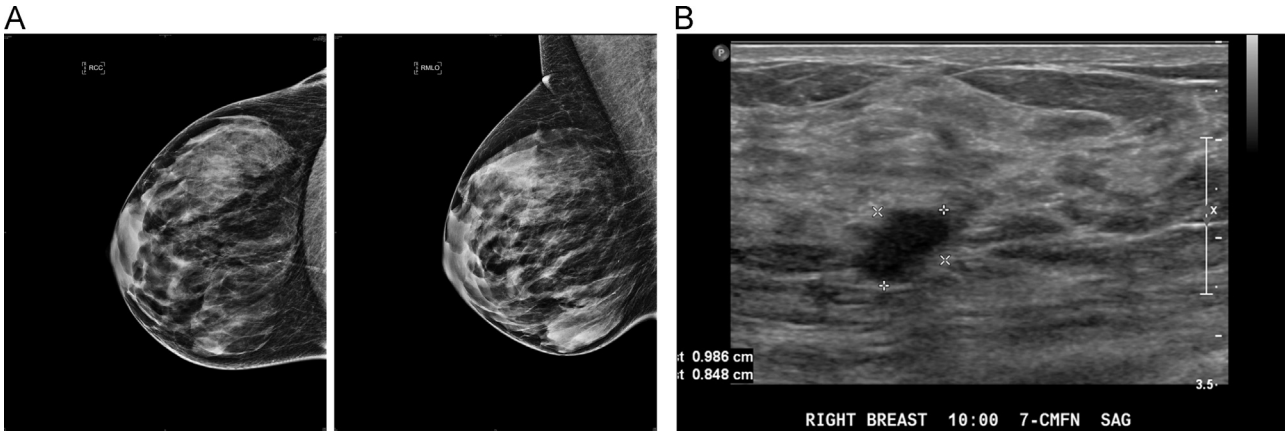

Figure 1 (A) Craniocaudal and mediolateral oblique screening mammogram with DBT showed heterogeneously dense breast tissue but was negative. (B) Screening US identified an ill-defined hypoechoic solid mass in the right breast at 10-o'clock position. US-guided biopsy confirmed invasive ductal carcinoma.

90%, screening MRI is recommended as an adjunct to mammography in high-risk women. For example, the American Cancer Society recommends annual screening MRI in patients who are BRCA positive, who have had radiation to the chest between the ages of 10-30, or whose lifetime risk of breast cancer is greater or equal to 20%.[14] MRI outperforms US for high-risk screening and if MRI is performed, US is not indicated.[15] The use of MRI as an adjunct screening modality in women of average risk is limited by cost, access, and exclusion criteria such as claustrophobia and pacemakers, in addition to concerns about increasing false positives.

As US is available at the time of mammography, does not use ionizing radiation, is much easier to tolerate, and less costly than MRI, there has been a great deal of interest and investigation on using US as a supplementary screening tool for women with dense breasts on mammography (Fig. 1). The cancer detection rate for screening mammography averages 4.3 per 1000 examinations.[16] The use of US as a supplement to mammography detects an additional 3-4 cancers per 1000 examinations.[17,18] For comparison, MRI detects an additional 11-18 cancers per 1000 examinations, depending upon patient risk factors.[19] In addition to being less sensitive than MRI, US suffers from poor specificity, even when patients have had prior US screening (ie, incidence screening). In the ACRIN 6666 trial, 5% of women had a biopsy prompted by screening US and only 7.4% of those were positive for cancer.[19] In addition to increasing the number of unnecessary biopsies, screening US leads to an increase in 6-month follow-up recommendations. Screening mammography has a 2% BI-RADS 3 rate (recommendation for 6-month follow-up) compared with 20% BI-RADS 3 rate in screening US.[18,20] Currently, there are no accepted guidelines for when to use US in women with dense breasts as a supplement to screening mammography. Current recommendation from the American College of Radiology is that screening US is an option in women with intermediate risks, but the risks and benefits of supplementary screening need to be considered on an individual basis.[12]

New Breast Imaging Modalities

Digital Breast Tomosynthesis

Of the newer breast imaging technologies, digital breast tomosynthesis (DBT) is probably the most widely available. Since Food and Drug Administration (FDA) approval in 2011, use of DBT has increased[21] and this trend will likely continue, as an approved Current Procedural Terminology code for billing just became available in 2015. From the patient's perspective, there is little difference between a standard digital mammogram and DBT. In DBT, numerous images of the breast are obtained in an arc during both craniocaudal and mediolateral oblique positions as the x-ray tube moves over the breast (details vary by manufacturer). Images are then reconstructed into 1-mm slices for interpretation. This pseudo–3-dimensional (3D) look at the breast tissue minimizes artifacts from overlapping tissue, allowing improved visualization of mass margins and increased conspicuity of subtle findings such as architectural distortion.[22,23,2] DBT was initially performed in addition to routine 2D digital mammography, resulting in approximately twice the radiation dose to the breast, although still within Mammography Quality Standards Act limits. However, with the FDA approval of C-view (Hologic; Bedford, MA), a synthetic 2D mammogram image created from the DBT data, routine acquisition of additional 2D mammogram images will likely cease, thus bringing the radiation dose back down to digital mammography levels.

Numerous studies have shown that using DBT results in a substantial decrease in screening recall rates ranging from 15%-40%.[24-32] Given recent criticisms of screening mammography for the "harms" of false positive re-calls,[4,33-36] a decrease in such re-calls is welcomed. When patients are re-called, many more can proceed directly to US without additional mammographic views.[24,37] Multireader studies[25,38] have shown increased diagnostic accuracy with DBT, and several studies have shown increased cancer detection rates (Fig. 2).[27,28,39] Despite the increased reading time[28,30,40] for DBT, an economic modeling study[41] in commercially insured patients demonstrated economic favorability of DBT screening.