Digital Breast Tomosynthesis

Description

Digital breast tomosynthesis uses modified digital mammography equipment to obtain additional radiographic data that are used to reconstruct cross-sectional “slices” of breast tissue. Tomosynthesis may improve the accuracy of digital mammography by reducing problems caused by overlapping tissue. Tomosynthesis involves some additional imaging time and radiation exposure, although a recently improved modification may change this.

Background

Conventional mammography produces two-dimensional (2D) images of the breast. Overlapping tissue on a 2D image can mask suspicious lesions or make benign tissue appear suspicious, particularly in women with dense breast tissue. As a result, women may be recalled for additional mammographic spot views. Inaccurate results may lead to unnecessary biopsies and emotional stress, or to a potential delay in diagnosis. The spot views are often used to evaluate microcalcifications, opacities or architectural distortions or to distinguish masses from overlapping tissue, as well as to view possible findings close to the chest wall or in the retro-areolar area behind the nipple. (1) The National Cancer Institute (NCI) reports that approximately 20% of cancers are missed at mammography screening. (2) Average recall rates are approximately 10%, with an average cancer detection rate of 4.7 per 1,000 screening mammography examinations (3). The Mammography Quality Standards Act audit guidelines anticipate 2-10 cancers detected per 1,000 screening mammograms (4). Interval cancers, which are detected between screenings, tend to have poorer prognoses. (5)

Digital breast tomosynthesis was developed to improve the accuracy of mammography by capturing three-dimensional (3D) images of the breast, further clarifying areas of overlapping tissue. Developers proposed that its use would result in increased sensitivity and specificity, as well as fewer recalls due to inconclusive results (6). Digital breast tomosynthesis produces a 3D image by taking multiple low-dose images per view along an arc over the breast. During breast tomosynthesis the compressed breast remains stationary while the x-ray tube moves approximately 1 degree for each image in a 15-50 degree arc, acquiring 11-49 images (7). These images are projected as cross-sectional “slices” of the breast, with each slice typically 1 mm thick. Adding breast tomosynthesis takes about 10 seconds per
view. In one study in a research setting, the mean time to interpret the results was 1.22 (SD=1.15) minutes for digital mammography and 2.39 (SD=1.65) for combined digital mammography and breast tomosynthesis (8).

With conventional 2D mammography, breast compression helps decrease tissue overlap and improve visibility. By reducing problems with overlapping tissue, compression with breast tomosynthesis may be reduced by up to 50%. This change could result in improved patient satisfaction (7).

A machine equipped with breast tomosynthesis can perform 2D digital mammography, 3D digital mammography, or a combination of both 2D and 3D mammography during a single compression. The radiation exposure from tomosynthesis is roughly equivalent to a mammogram. Therefore, adding tomosynthesis to mammography doubles the radiation dose, although it still is below the maximum allowable dose established in the US Mammography Quality Standards Act.

Studies typically compare one- or more commonly, two-view breast tomosynthesis alone or combined with standard 2D mammography to standard 2D mammography alone. The assessment focuses on two-view tomosynthesis. According to the FDA Radiological Devices Panel, which reviewed this new modality: “2D [full-field digital mammography] plus a single [digital breast tomosynthesis] view (3D MLO) could be another exam option, but the full 2-view [digital breast tomosynthesis] protocol (MLO and CC) would be recommended.” (9)

In May 2013, the FDA approved new tomosynthesis software that will permit creation of a 2D image (called C view) from the tomosynthesis images. (10) As a result, the 2D mammography may become unnecessary, thereby lowering the radiation dose. In other words, only the tomosynthesis procedure will be needed and both 2D and 3D images will be created from them. It is too early to gauge how traditional mammography plus tomosynthesis compares to the C view plus 3D images. The study submitted to the FDA was a noninferiority trial that compared the combined C view and 3D reconstruction to digital tomosynthesis alone, so it does not provide information on the comparison of greater interest.

**Regulatory Status**

The Selenia® Dimensions® 3D System manufactured by Hologic, Inc. achieved U.S. Food and Drug Administration approval on February 11, 2011 through the premarket application (PMA) approval process. It is currently the only tomosynthesis system with FDA approval on the market. This system is a software and hardware upgrade of the Selenia Dimensions 2D full-field digital mammography system, which the FDA approved in 2008. Facilities using a digital breast tomosynthesis system must apply to the FDA for a certificate extension covering the use of the breast tomosynthesis portion of the unit. The Mammography Quality Standards Act requires the interpreting physicians, radiologic technologists, and medical physicists to complete 8 hours of digital breast tomosynthesis training, and mandates a detailed mammography equipment evaluation prior to use. In May 2013, the FDA also approved Hologic’s C-View 2D imaging software. This software is used to create 2D images from the tomosynthesis results, rather than performing a separate mammogram.
Several other manufacturers are working towards FDA approval of their digital breast tomosynthesis systems. GE Healthcare is seeking FDA premarket approval (PMA) for breast tomosynthesis, specifically as an add-on option for the Senographe™ Essential mammography device. The U.S. Food and Drug Administration (FDA) has agreed to a modular PMA submission, which means that GE Healthcare will submit the request in different sections. The first of 4 sections was submitted in November 2011. Three completed trials sponsored by GE are listed at online site clinicaltrials.gov. They focus on the use of breast tomosynthesis in routine screening (NCT00535678), in women undergoing diagnostic mammography (NCT00535327), and in women referred for breast biopsy (NCT00535184). The results do not appear to have been published to date.

Related Policies

6.01.18 Scintimammography/Breast-Specific Gamma Imaging/Molecular Breast Imaging
6.01.29 Magnetic Resonance Imaging (MRI) of the Breast
6.01.52 Positron Emission Mammography (PEM)

Policy

*This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims

Digital breast tomosynthesis is considered not medically necessary in the screening or diagnosis of breast cancer.

Rationale

Literature Review

Using information from a 2013 TEC Assessment (11), the primary outcomes to be examined include the number of cancers detected and the number of unnecessary recalls and biopsies. Improvement in sensitivity and specificity of testing is an intermediate outcome that will impact the ultimate health outcomes, but is not by itself sufficient to establish that outcomes are improved. If the sensitivity of breast cancer detection is improved by tomosynthesis, then the number of cases detected will increase. If the specificity of cancer detection is improved, then the number of recalls and biopsies for patients without cancer will decreased. If tomosynthesis is performed during screening, the number of unnecessary recalls may decline, with the attendant anxiety and inconvenience for the patient. If tomosynthesis is performed as part of the diagnostic workup, after a woman is recalled for questionable findings during screening, then a lower false positive rate could prevent unnecessary biopsies. Screening. Four studies addressed the use of mammography with or without digital breast tomosynthesis for screening. The strongest evidence for using mammography and breast tomosynthesis for screening women for breast cancer comes from the interim results of a large trial in Norway. (12) The sample consisted of 12,621 women with 121 screening-detected cancers who underwent routine screening. The cancer detection rate was 6.1 per 1000 screenings for mammography alone and 8.0 per 1000 screenings for mammography plus DBT. After adjusting for reader differences, the ratio of cancer detection rates for mammography versus mammography plus breast tomosynthesis was 1.27 (98.5% CI: 1.06 to 1.53; p=0.001). The authors note that they did not
ascertain any improvement in detecting ductal carcinoma in situ (DCIS) by adding breast tomosynthesis; the additional cancers detected were largely invasive. The false-positive rate was 61.1 per 1,000 screenings for mammography alone and 53.1 per 1,000 screenings for mammography plus breast tomosynthesis. A reduction in the false-positive rate would decrease the number of women recalled after screening for additional imaging or biopsy. In Norway, as in much of Europe, women are screened every other year, and 2 readers independently interpret the images, which differs from usual practice in the US. After adjusting for differences across readers, the ratio of false positive rates for mammography alone versus mammography plus breast tomosynthesis was 0.85 (98.5% CI: 0.76 to 0.96; p<0.001). The authors note that for this interim analysis, only limited data were available about interval cancers so they could not estimate “conventional absolute sensitivity and specificity.” Additional information will be available when the trial is completed.

The second study examined comparative cancer detection for traditional mammography with or without breast tomosynthesis in a general Italian, asymptomatic screening population of 7,292 women. (13) The reference standard was pathology for women undergoing biopsies; women with negative results on both mammography and breast tomosynthesis were not followed up, so neither the sensitivity nor specificity could be calculated. Mammography plus breast tomosynthesis revealed all 59 cancers, while 20 of them were missed by traditional mammography (p<0.0001). The incremental cancer detection of using both modalities was 2.7 cancers per 1,000 screens (95% CI: 1.7 to 4.2). There were 395 false-positive results: 181 were false-positive using either mammography or both imaging modalities together; an additional 141 occurred using mammography only and 73 occurred using mammography and breast tomosynthesis combined (p<0.0001). In preplanned analyses, the researcher found that the combined results of mammography and DBT yielded more cancers in both age groups (<60 versus >60 years) and breast density categories (1, least dense, and 2 versus 3 and 4, most dense).

Another study compared the results of mammography alone versus breast tomosynthesis plus mammography among 997 subjects with mixed indications: 780 were women undergoing routine screening, and 217 were women scheduled for biopsy. (14) Two retrospective reader studies were conducted. Some of these results were included in the submission to the U.S. Food and Drug Administration for premarket application approval of Hologic, Inc.’s Selenia Dimensions tomosynthesis system. Readers were trained in interpreting tomosynthesis images, and the training was augmented between the first and second reader studies to emphasize how to read certain lesions which were often misinterpreted in the first reader study. In both reader studies, the area under the receiver operating characteristic curve for mammography plus breast tomosynthesis was greater than for mammography alone; the difference for the second study was 6.8% (95% CI: 4.1% to 9.5%, p<0.001). For noncancer cases, adding breast tomosynthesis to mammography changed the mean recall rate across readers for study 2 from 48.8% (95% CI: 28.2% to 69.1%; SD=12.3%) to 30.1% (95% CI: 19.8% to 41.3%; SD=7.6%) for the combined modalities. Almost all of the improvement among readers was attributable to noncalcification cases, including masses, asymmetries, and architectural distortions.

All of these studies had a medium risk of bias using the QUADAS-2 (Quality Assessment of Diagnostic Accuracy Studies; www.quadas.org) tool, except for the fourth screening study, which had a high risk of bias. (8, 15, 16) One of the three related articles on this study reported that the recall rate among noncancer cases was 0.42 (95% CI: 0.38 to 0.45) for digital mammography alone and 0.28 (95% CI:
0.25 to 0.31) for digital mammography plus breast tomosynthesis (p<0.0001). The analogous rates for cancer cases were 0.88 (95% CI: 0.84 to 0.91) for digital mammography alone and 0.93 (95% CI: 0.90 to 0.96) for digital mammography plus breast tomosynthesis. The sensitivity of digital mammography alone was 60% and increased to 72% when breast tomosynthesis was added (p=0.034, but the authors note the small number of positive findings). These articles did not describe the sample, the time between digital mammography and breast tomosynthesis, or how the reference standard was verified. These studies provide some evidence that adding breast tomosynthesis to mammography may increase the accuracy (and possibly the sensitivity) of screening while reducing the number of women who are recalled unnecessarily. Two of the studies took place in a routine screening environment and did not have adequate follow-up of women with negative screening results; the larger study provided interim results. The other two studies were retrospective reviews of cases; the sample for one had a mixed indications, while it is unclear for the other study.

Diagnosis: Six studies address the use of breast tomosynthesis in the diagnostic setting, i.e., if there are suspicious findings on screening mammography or if the woman is symptomatic. The studies vary considerably in the types of suspicious mammographic findings (e.g., calcifications versus noncalcifications); the patient population; and the comparators to breast tomosynthesis, e.g., two-view mammography, mammographic spot views, ultrasound. One study had a medium risk of bias; the remainder, a high risk of bias using the QUADAS-2 tool.

In a study of 158 women consecutively recalled after screening mammography, breast tomosynthesis was evaluated as a possible triage tool to reduce the number of false positive results. (17) The results of the diagnostic assessment (including ultrasound and needle biopsy where performed) were used as the reference standard. Breast tomosynthesis eliminated 102 of the 158 recalls, all of which were unnecessary (i.e., false-positive results on mammography). No cancers were missed on breast tomosynthesis. The performance of breast tomosynthesis did not vary by breast density or age group, but the reduction in recalls was greater for asymmetric densities and distortions, and nodular opacities with regular margins. The authors note that the decline in recall rates following the use of breast tomosynthesis was higher in this study than in blinded comparisons of digital mammography and breast tomosynthesis.

Another study compared the performance of mammographic spot views versus tomosynthesis among 52 consecutive recalled women with a BI-RADS rating on initial screening of 0 (which means “Need Additional Imaging Evaluation and/or Prior Mammograms for Comparison”). (1) Women with calcifications were excluded. The study was designed as a noninferiority analysis for areas under the receiver operating characteristic (ROC) curve, sensitivity, and specificity, with a noninferiority margin of delta=0.05, so that if breast tomosynthesis were noninferior to mammographic spot views, breast tomosynthesis could be performed right after screening mammography to avoid a recall. The sensitivity and specificity were extremely high for both modalities, and there was no statistically significant difference between them.

A third study compared diagnostic mammography to breast tomosynthesis among women with abnormalities on screening mammography with no calcifications in a “simulated clinical setting.” (4) The breast tomosynthesis rating was based on both readers’ ratings and their confidence that no additional studies were needed, as well as ultrasound results in some cases. The reference standard was either
the results of the entire clinical workup, including biopsy if performed, or follow-up for women not undergoing biopsy (86.1% of entire sample). There was not a statistically significant difference between diagnostic mammography and breast tomosynthesis in sensitivity or specificity.

Two of the these three studies found no difference in sensitivity and specificity between breast tomosynthesis and a clinical workup that consisted of diagnostic mammographic images or a more comprehensive diagnostic work-up. The third study examined the use of breast tomosynthesis to triage women recalled after screening and substantially reduced the recall rate.

Another study evaluated 738 women with 759 lesions recalled after screening with film mammography. In this unblinded study, the incremental value of breast tomosynthesis added to film and digital mammography was assessed. (18) The reference standard consisted of pathology results or follow-up for 18 to 36 months. Adding breast tomosynthesis to film and digital mammography results increased the area under the ROC curve from 0.895 (0.871-0.919) to 0.967 (0.957-0.977) (p=0.001). The complete sensitivity (counting ratings of 3-5 as positive) increased from 39.7% for digital mammography to 58.3% when breast tomosynthesis was added; no confidence intervals or p values were reported. The specificity increased from 51% to 74.2% when breast tomosynthesis was added to digital mammography. The difference in areas under the ROC curve after the addition of breast tomosynthesis was statistically significant for soft-tissue lesions, but not for microcalcifications.

One study compared diagnostic mammography images to dual-view breast tomosynthesis in 217 lesions (72 [33%] malignant) among 182 women. (19) In this retrospective study, women who had undergone diagnostic mammography and breast tomosynthesis were included. The sample included women with clinical symptoms such as a palpable lump, or findings on mammograms, ultrasound, or MRI. Women with only calcifications were excluded. The area under the ROC curve for diagnostic mammography was 0.83 (95% CI: 0.77 to 0.83; range across readers = 0.74-0.87), while for tomosynthesis it was 0.87 (95% CI: 0.82 to 0.92; range across readers = 0.80-0.92; p<0.001). The authors of the Norse trial also wrote another article on their initial experience with digital breast tomosynthesis in a clinical setting. (20)

This mixed set of articles provides evidence of either a similar diagnostic performance between breast tomosynthesis and other approaches or an advantage for breast tomosynthesis. The mixed patient populations, differences in references standard, use of different imaging tests to compare to breast tomosynthesis, and variations in follow-up make it difficult to draw a conclusion from these studies.

Clinical Trials

Digital breast tomosynthesis continues to be an active field of investigation. According to clinicaltrials.gov (http://clinicaltrials.gov/ct2/results?term=breast+tomosynthesis), as of May 18, 2013, there were 15 trials on breast tomosynthesis enrolling subjects and 7 that were active but not recruiting. All but 2 of the studies had sample sizes larger than 100, and 6 studies were larger than 1,000—e.g., studies had estimated sample sizes of 10,000 (NCT01569802); 15,000 (NCT01091545); and 25,000 (the study whose interim analysis is reported by Skaane et al; NCT01248546) (12). A study comparing screening recall rates for digital mammography versus breast tomosynthesis is being conducted by the American College of Radiology Imaging Network (ACRIN) and has a sample size of 550.
Several studies have also been conducted using different breast tomosynthesis equipment, including one using the Siemens Inspiration Digital Breast Tomosynthesis system (NCT01373671) and three completed studies sponsored by GE Healthcare that have not yet been published (NCT NCT00535184, NCT NCT00535327, NCT00535678).

**Practice Guidelines and Position Statements**

The American College of Radiology does not include digital breast tomosynthesis in its Appropriateness Criteria for breast imaging (http://www.acr.org/Quality-Safety/Appropriateness-Criteria/Diagnostic/Breast-Imaging). However, in a joint news release with the Society of Breast Imaging following the release of the interim analysis by Skaane et al. (12), discussed below, the organizations stated that “While the study results are promising, they do not provide adequate information to define the role of tomosynthesis in clinical practice.” (21) They also noted that while cancer detection was greater with tomosynthesis, it is not known whether the incremental benefit would be the same during a second round of screening. Furthermore, they note “[h]ow the technology will affect screening accuracy among women of different ages, risk profiles and parenchymal density is uncertain. In addition, how this technology would affect reader performance among U.S. radiologists with varying practice patterns and expertise is also uncertain. Other questions include whether computer aided detection will provide any further benefit, and if reconstructed images (presumably 2D) can be used, in lieu of standard full field digital images, to reduce radiation dose.”

In its practice bulletin on breast cancer screening, the American College of Obstetricians and Gynecologists notes that digital breast tomosynthesis on one of several screening techniques that were considered but not recommended for routine screening. (22) According to the National Comprehensive Cancer Network, “Early studies show promise for tomosynthesis mammography. Currently, there is insufficient evidence to recommend routine use for screening or diagnosis at this time.” (23)

**Summary**

There are unanswered questions about the number of images needed as well as concerns about radiation dose and time for interpretation. There are no studies currently published that provide adequate information about outcomes (sensitivity, specificity, accuracy, recall rate) when DBT is used in clinical practice. This contrasts to other breast imaging technologies such as computer aided detection (CAD) and full-field digital mammography (FFDM) where large clinical studies have demonstrated effectiveness in clinical care; therefore the use of digital breast tomosynthesis in generating images for screening or diagnosis of breast cancer is considered **not medically necessary.**

**References**


11. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Use of Digital Breast Tomosynthesis with Mammography for Breast Cancer Screening or Diagnosis. TEC Assessments 2013; Volume 28, Tab TBA.


Policy History

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<td>September 2012</td>
<td>New Policy</td>
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Keywords

3D Mammography  
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This policy was approved by the FEP Pharmacy and Medical Policy Committee on September 20, 2013 and is effective November 1, 2013.

Signature on file

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