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 typically involves additional imaging time and radiation exposure, although recent improvements may change this.

**Policy**

Digital breast tomosynthesis is considered **investigational** in the screening or diagnosis of breast cancer.

**Policy Guidelines**

At this time, there are no specific CPT codes for this testing. The testing would be reported with the appropriate breast mammography code (77055-77057 or G0202-G0206) along with an unlisted code (e.g., 76499) for the additional views.

**Benefit Application**

Benefit determinations should be based on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

Some state or federal mandates (e.g., Federal Employee Program (FEP)) prohibit Plans from denying Food and Drug Administration (FDA) - approved technologies as
investigational. In these instances, plans may have to consider the coverage eligibility of FDA-approved technologies on the basis of medical necessity alone.

**Rationale**

**Background**

Conventional mammography produces 2-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. Spot views often are used to evaluate microcalcifications, opacities, or architectural distortions; to distinguish masses from overlapping tissue; and to view possible findings close to the chest wall or in the retro-areolar area behind the nipple. (1) The National Cancer Institute 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 1000 screening mammography examinations. (3) The Mammography Quality Standards Act audit guidelines anticipate 2 to 10 cancers detected per 1000 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 3-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° for each image in a 15° to 50° arc, acquiring 11 to 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 1 study in a research setting, mean time for interpretation of results was 1.22 (1.15) minutes for digital mammography and 2.39 (1.65) minutes 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. Radiation exposure from tomosynthesis is roughly equivalent to mammography. Therefore, adding tomosynthesis to mammography doubles the radiation dose, although it still is below the maximum allowable dose established in the U.S. Mammography Quality Standards Act.

Studies typically compare 1-view (i.e., mediolateral oblique [MLO] view), or more commonly, 2-view (MLO plus cranio-caudal view) breast tomosynthesis alone or combined with standard 2D mammography to standard 2D mammography alone. A 2014 TEC Assessment focused on 2-view tomosynthesis. (9) The FDA Radiological Devices Panel, which reviewed this new modality in 2011, recommended that 2-view breast
tomoynthesis is preferable to 1-view tomosynthesis (both used in combination with full-field digital mammography).

In May 2013, the U.S. Food and Drug Administration (FDA) approved new tomosynthesis software that permits creation of 2D images (called C view) from images obtained during tomosynthesis. As a result, 2D mammography may become unnecessary, thereby lowering radiation dose. In other words, only the tomosynthesis procedure will be needed, and both 2D and 3D images will be created. It is too early to gauge how traditional mammography plus tomosynthesis compares with C view plus tomosynthesis.

**FDA Status**

The Selenia® Dimensions® 3D System manufactured by Hologic Inc. (Bedford, MA), received FDA approval on February 11, 2011, through the premarket application (PMA) approval process (PMA P080003). Currently, it is the only commercially available tomosynthesis system with FDA approval. This system is a software and hardware upgrade of the Selenia® Dimensions 2D full-field digital mammography system, which FDA approved in 2008. Facilities using a digital breast tomosynthesis system must apply to FDA for a certificate extension covering use of the breast tomosynthesis portion of the unit. The Mammography Quality Standards Act requires interpreting physicians, radiologic technologists, and medical physicists to complete 8 hours of digital breast tomosynthesis training, and mandates a detailed mammography equipment evaluation before use. In May 2013, FDA also approved Hologic's C-View 2D imaging software. This software is used to create 2D images from the tomosynthesis results, rather than perform a separate mammogram.

Several other manufacturers are working toward FDA approval of their digital breast tomosynthesis systems. GE Healthcare is seeking FDA approval for breast tomosynthesis, specifically as an add-on option for the Senographe™ Essential mammography device. 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 diagnostic mammography (NCT00535327), and for breast biopsy (NCT00535184). Results do not appear to have been published to date.

**Literature Review**

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 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 decrease. If tomosynthesis is performed during screening, the number of unnecessary recalls may decline, along with 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**

The 2014 TEC Assessment identified 4 studies that addressed the use of mammography with or without digital breast tomosynthesis for screening. These studies are summarized next.
The strongest evidence for using mammography and breast tomosynthesis for screening women for breast cancer comes from interim results of a large 2013 trial in Norway.(12,13) The sample comprised 12,621 women with 121 cancers detected on routine screening. Cancer detection rate was 6.1 per 1000 screenings for mammography alone and 8.0 per 1000 screenings for mammography plus digital breast tomosynthesis. Cancers missed by digital breast tomosynthesis were missed due to reading errors, either detection or interpretation.(14) After adjusting for reader differences, the ratio of cancer detection rates for mammography plus breast tomosynthesis versus mammography alone was 1.27 (98.5% confidence interval [CI], 1.06 to 1.53; p=0.001). The authors did not ascertain any improvement in detecting ductal carcinoma in situ by adding breast tomosynthesis, i.e., additional cancers detected were mostly invasive. The false-positive rate was 61.1 per 1000 screenings for mammography alone and 53.1 per 1000 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 U.S. After adjusting for differences across readers, the ratio of false-positive rates for mammography plus breast tomosynthesis versus mammography alone was 0.85 (98.5% CI, 0.76 to 0.96; p<0.001). For this interim analysis, only limited data were available about interval cancers so “conventional absolute sensitivity and specificity” could not be estimated. Additional information will be available when the trial (NCT01248546) is completed (estimated study completion date, September 2015).

The second study (STORM) examined comparative cancer detection for traditional mammography with or without breast tomosynthesis in a general Italian, asymptomatic screening population of 7292 women. (15) 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 sensitivity nor specificity could be calculated. Mammography plus breast tomosynthesis revealed all 59 cancers; 20 (34%) were missed by traditional mammography (p<0.001). Incremental cancer detection by using both modalities was 2.7 cancers per 1000 screens (95% confidence interval [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<0.001). In preplanned analyses, combined results of mammography and digital breast tomosynthesis yielded more cancers in both age groups (<60 vs ≥60 years) and breast density categories (1 [least dense] and 2 vs 3 and 4 [most dense]).

Another study compared results of mammography alone versus breast tomosynthesis plus mammography among 997 patients with mixed indications: 780 women were undergoing routine screening, and 217 were scheduled for biopsy. (16) Two retrospective reader studies were conducted. Some of these results were included in the submission to the U.S. Food and Drug Administration (FDA) for premarketing application (PMA) approval of Hologic’s Selenia® Dimensions tomosynthesis system. Readers were trained in interpreting tomosynthesis images, and training was augmented between the first and second reader studies to emphasize how to read certain lesions that were often misinterpreted in the first reader study. In both reader studies, the area under the receiver operating characteristic curve (ROC) 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% (SD=12.3% 95% CI, 28.2% to 69.1%) to 30.1% (SD=7.6% 95% CI, 19.8% to 41.3%) 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 Quality Assessment of Diagnostic Accuracy Studies (QUADAS)-2 tool (available online at: www.quadas.org), except for the fourth screening study, which had a high risk of bias. (8, 17, 18) One of 3 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<0.001). 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. Sensitivity of digital mammography alone was 60% and increased to 72% when breast tomosynthesis was added (p=0.034, but authors noted 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.

Several studies assessing digital breast tomosynthesis for breast cancer screening have been published subsequent to the TEC Assessment. These studies are summarized in Table 1. Studies by Friedewald et al (19) and Rose et al (20) were retrospective; all others were prospective. Studies consistently showed improved breast cancer detection rates (sensitivity) with addition of tomosynthesis to digital mammography. Improvements were not always statistically significant or statistical significance was not reported. Reduction in noncancer recall rate was observed in 2 studies, but reduction in noncancer biopsy rate was observed in only 1 of 2 studies. The smallest study (21) reported the largest improvements in performance with the addition of tomosynthesis. Performance of breast tomosynthesis did not vary by breast density or age group in 4 studies that examined these variables. (15,20,22,23) The largest study by Friedewald et al reported no difference in DCIS detection rates between screening methods (1.4/1000 examinations [95% CI, 1.2 to 1.6] for both methods). (19)

Table 1 includes a study by Skaane et al (2014) of 2D images reconstructed from digital tomosynthesis (C view or synthesized 2D mammography). (24) In another study of C view tomosynthesis (N=236), Zuley et al (2014) compared diagnostic accuracy of synthesized 2D mammography and digital mammography, both alone and in combination with 3D breast tomosynthesis. (25) Area under ROC was 0.894 and 0.889 for synthesized and digital mammography, respectively; with the addition of 3D tomosynthesis, values increased to 0.916 and 0.939, respectively. In the second half of the Skaane et al (2014) study (after improvements to 2D image processing were made), there was no statistical difference in cancer detection rates, positive predictive values (PPV), and false-positive rates (noncancer recall rates) between synthesized and digital mammography (both in combination with tomosynthesis). Mean glandular radiation dose for a single mammographic view was 45% less in the synthesized mammography group compared with the digital mammography group (mean, 1.58 mGy vs 3.53 mGy, respectively).

**Table 1. Studies of Digital Breast Tomosynthesis for Breast Cancer Screening**

<table>
<thead>
<tr>
<th>Study</th>
<th>Noncancer Recall Rate, %</th>
<th>Noncancer Biopsy Rate, %</th>
<th>CDR/1000</th>
<th>PPV, %</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Digital Mammography vs Digital Mammography + Tomosynthesis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bemardi (2014) (15,26-28) (STORM), N=7292</td>
<td>2.8</td>
<td>NR</td>
<td>5.3</td>
<td>NR</td>
</tr>
<tr>
<td>DM</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DM + DBT</td>
<td>2.2</td>
<td>NR</td>
<td>8.1</td>
<td>NR</td>
</tr>
<tr>
<td>Destounis (2014) (21), N=1048</td>
<td>6.9</td>
<td>1.9</td>
<td>3.8</td>
<td>16.7</td>
</tr>
</tbody>
</table>
Medical Policy

Section Summary

These studies provided some evidence that adding breast tomosynthesis to mammography may increase accuracy (and possibly sensitivity) of screening while reducing the number of women who are recalled unnecessarily. However, the available studies have methodologic limitations. Several studies did not have adequate follow-up of women with negative screening results; 1 larger study provided interim results. Other studies were retrospective case reviews; patients had mixed or unclear indications for screening. More recently, prospective and large retrospective studies have reported cancer detection rates with reduced false recall rates. This evidence is from nonrandomized designs with a lack of long-term follow-up to assess false negative results. Therefore, performance of digital breast tomosynthesis in the screening setting cannot be determined with certainty. Two studies of synthesized 2D mammography showed comparable diagnostic performance with digital mammography and lower radiation exposure. Replication of these findings is warranted.

Diagnosis

Lei et al (2014) conducted a systematic review with meta-analysis of 7 studies (total number of patients, 2014; total number of lesions, 2666) that compared digital breast tomosynthesis with digital mammography in patients with Breast Imaging-Reporting and Data System (BI-RADS) 2 or higher breast lesions. (29) All studies were rated high quality using the QUADAS tool. As shown in Table 2, compared with histologic diagnosis, performance of both imaging modalities was approximately similar; PPVs were low (57% for breast tomosynthesis and 50% for digital mammography), and negative predictive values (NPV) were high. Statistical heterogeneity in these analyses was considerable ($I^2=90\%$). Studies used both 1-view ($n=4$) and 2-view ($n=3$) breast tomosynthesis. Pooled sensitivity and specificity for only 1-view breast tomosynthesis studies were 81% and 77%.
respectively; for 2-view studies, pooled sensitivity and specificity were 97% and 79% respectively. (30)

**Table 2. Side-by-Side Comparison of Digital Breast Tomosynthesis and Digital Mammography Diagnostic Performance Compared with Histologic Diagnosis: Pooled Results (29)**

<table>
<thead>
<tr>
<th></th>
<th>Digital Breast Tomosynthesis, Pooled Estimate (95% CI)</th>
<th>Digital Mammography, Pooled Estimate (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sensitivity</strong></td>
<td>90% (87 to 92)</td>
<td>89% (86 to 91)</td>
</tr>
<tr>
<td><strong>Specificity</strong></td>
<td>79% (77 to 81)</td>
<td>72% (70 to 74)</td>
</tr>
<tr>
<td><strong>PPV</strong></td>
<td>57% (53 to 61)</td>
<td>50% (46 to 53)</td>
</tr>
<tr>
<td><strong>NPV</strong></td>
<td>96% (95 to 97)</td>
<td>95% (94 to 97)</td>
</tr>
<tr>
<td><strong>DOR</strong></td>
<td>26.04 (8.70 to 77.95)</td>
<td>16.24 (5.61 to 47.04)</td>
</tr>
<tr>
<td><strong>LR+</strong></td>
<td>3.50 (2.31 to 5.30)</td>
<td>2.83 (1.77 to 4.52)</td>
</tr>
<tr>
<td><strong>LR–</strong></td>
<td>0.15 (0.06 to 0.36)</td>
<td>0.18 (0.09 to 0.38)</td>
</tr>
<tr>
<td><strong>AUC</strong></td>
<td>0.867</td>
<td>0.856</td>
</tr>
</tbody>
</table>

AUC: area under the summary receiver operating characteristic curve; CI: confidence interval; DOR: diagnostic odds ratio (ratio of the odds of positivity in cases to the odds of positivity in controls = [LR+] ÷ [LR–]); LR+: positive likelihood ratio (ratio of the probability of positivity in cases to the probability of positivity in controls = sensitivity ÷ [1-specificity]); LR–: negative likelihood ratio (ratio of the probability of a negative result in cases to the probability of a negative result in controls = [1-sensitivity] ÷ specificity); NPV: negative predictive value; PPV: positive predictive value.

* Calculated by author.

The 2014 TEC Assessment identified 6 studies that addressed the use of breast tomosynthesis in the diagnostic setting, i.e., when there are suspicious findings on screening mammography or when the woman is symptomatic. Studies vary considerably in types of suspicious mammographic findings (e.g., calcifications vs noncalcifications); patient sample; and comparators to breast tomosynthesis (e.g., 2-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. These studies are summarized next.

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. (31) Results of diagnostic assessment (including ultrasound and needle biopsy when performed) were used as the reference standard. Breast tomosynthesis eliminated 102 (65%) of 158 recalls, all of which were unnecessary (i.e., false-positive results on mammography). No cancers were missed on breast tomosynthesis. Performance of breast tomosynthesis did not vary by breast density or age group, but reduction in recalls was greater for asymmetric densities and distortions, and nodular opacities with regular margins. As noted by the authors, the observed decline in recall rates after breast tomosynthesis exceeded that observed 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 of area under the ROC curve, sensitivity, and specificity, with a noninferiority margin of delta of 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. 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) 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 results of the entire clinical workup, including biopsy if performed, or follow-up for women not undergoing biopsy (86% of the entire sample). There was no statistically significant difference between diagnostic mammography and breast tomosynthesis in sensitivity or specificity.

Two of these 3 studies found no difference in sensitivity and specificity between breast tomosynthesis and a clinical workup comprising 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. This unblinded study assessed the incremental value of breast tomosynthesis added to film and digital mammography. (32) The reference standard comprised pathology results or follow-up for 18 to 36 months. The addition of breast tomosynthesis to film and digital mammography increased the area under the ROC curve from 0.895 (95% CI, 0.871 to 0.919) to 0.967 (95% CI, 0.957 to 0.977; p=0.001). Complete sensitivity (i.e., counting ratings of 3-5 as positive) increased from 39.7% for digital mammography to 58.3% when breast tomosynthesis was added; confidence intervals or p values were not reported. 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 with dual-view breast tomosynthesis in 217 lesions (72 [33%] malignant) among 182 women. (33) This retrospective study included women who had undergone diagnostic mammography and breast tomosynthesis. The sample included women with clinical symptoms such as a palpable lump, or findings on mammography, ultrasound, or magnetic resonance imaging (MRI). Women with only calcifications were excluded. Area under the ROC curve was 0.83 (95% CI, 0.77 to 0.83; range across readers 0.74-0.87) for diagnostic mammography, and 0.87 (95% CI, 0.82 to 0.92; range across readers, 0.80-0.92) for tomosynthesis (p<0.001).

Authors of the Norse screening trial wrote about their initial experience with digital breast tomosynthesis in a clinical setting. (34)

Several studies assessing diagnostic digital breast tomosynthesis have been published subsequent to the TEC Assessment. These studies are summarized in Table 3. These studies reported that addition of tomosynthesis to digital mammography increased diagnostic accuracy overall, with improvements in true positive rates (sensitivity) exceeding improvements in true negative rates (specificity). However, PPV remained low (»50%). Differences in test performance between studies (i.e., between Rafferty 2014(35) and Thibault 2013(36)) are likely due to the difference in technologies studied (2-view digital mammography plus 1-view tomosynthesis vs 1-view digital mammography plus 1-view tomosynthesis, respectively), but also to differences in sample size (310 vs 130, respectively), setting (U.S. vs Europe, respectively), number of readers (15 vs 7, respectively), training (150 cases vs 20 cases, respectively).
### Table 3. Studies of Diagnostic Digital Breast Tomosynthesis

<table>
<thead>
<tr>
<th>Study</th>
<th>AUC</th>
<th>Sensitivity, %</th>
<th>Specificity, %</th>
<th>PPV, %</th>
<th>NPV, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rafferty (2014)(35), N=310</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>DM</td>
<td>0.828</td>
<td>63</td>
<td>86</td>
<td>47</td>
<td>92</td>
</tr>
<tr>
<td>DM + 1-view DBT</td>
<td>0.864a</td>
<td>71a</td>
<td>86</td>
<td>50</td>
<td>94</td>
</tr>
<tr>
<td>DM + 2-view DBT</td>
<td>0.895a</td>
<td>79a</td>
<td>85</td>
<td>50</td>
<td>95</td>
</tr>
<tr>
<td>Gennaro (2013)(37), N=463</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DM</td>
<td>NR</td>
<td>76</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>1-view (CC) DM + 1-view DBT</td>
<td>NR</td>
<td>79</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Thibault (2013)(36), N=130</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DM</td>
<td>0.756</td>
<td>73</td>
<td>53</td>
<td>53</td>
<td>74</td>
</tr>
<tr>
<td>1-view (CC) DM + 1-view DBT</td>
<td>0.780</td>
<td>68</td>
<td>64</td>
<td>58</td>
<td>73</td>
</tr>
<tr>
<td>DM + 1-view DBT + US</td>
<td>0.763</td>
<td>81</td>
<td>52</td>
<td>55</td>
<td>79</td>
</tr>
</tbody>
</table>

Note: One-view DBT is MLO unless noted otherwise.

AUC: area under the receiver operating characteristic curve; CC: craniocaudal; DBT: digital breast tomosynthesis; DM: digital mammography (2-view unless noted otherwise); MLO: mediolateral-oblique; NPV: negative predictive value; NR: not reported; PPV: positive predictive value; US, ultrasound.

* Statistically significant difference from DM.

** Statistically significant difference from 1-view DBT.

### Section Summary

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. Mixed patient populations, differences in references standard, use of different imaging tests to compare with breast tomosynthesis, and variations in follow-up make it difficult to draw conclusions from these studies.

### Summary

#### Screening

The Norse and Italian screening studies published in 2013 provide the strongest evidence available to date on the use of mammography plus digital breast tomosynthesis versus mammography alone for screening women for breast cancer. This evidence suggests that use of mammography plus breast tomosynthesis may modestly increase the number of cancers detected, with a large decrease in the number of women who undergo unnecessary recalls or biopsies. For example, in interim analysis of the Norse screening trial, the ratio of cancer detection rates per 1000 screens for mammography plus breast tomosynthesis versus mammography alone was 1.27 (98.5% CI, 1.06 to 1.53; p=0.001). The ratio of false-positive rates for mammography plus breast tomosynthesis versus mammography alone was 0.85 (98.5% CI, 0.76 to 0.96; p<0.001). Even if adding breast tomosynthesis simply maintained the same sensitivity as mammography, a decline in the false-positive rate would reduce the substantial number of unnecessary diagnostic work-ups in the U.S. and spare women the psychological stress these engender.

Additional studies generally have supported these findings, with no observed differences in test performance across subgroups defined by age or breast density. However, all studies were nonrandomized. Lack of long-term follow-up prevents assessment of false negative results and full assessment of test performance. Further, overall impacts on health outcomes are unknown. Long-term effects of additional radiation exposure also are unknown. For these reasons, digital breast tomosynthesis is considered investigational. A trial that randomizes women to digital mammography with or without tomosynthesis, or
performs both screening methods in the same woman, is required to demonstrate that improvements in screening are due to tomosynthesis and not to confounding variables, e.g., patient characteristics or radiologist experience in tomosynthesis interpretation.

The configuration of mammography and breast tomosynthesis used in these studies roughly doubled the radiation dose of mammography alone, but exposure was still lower than the guideline established in the Mammography Standards and Quality Act. On May 20, 2013, FDA approved new tomosynthesis software from Hologic that creates a 2D image from tomosynthesis images (C view), obviating the need for a separate mammogram. This approach reduces the radiation dose of the combination. Two studies reported comparable performance with digital mammography plus breast tomosynthesis, which reduces radiation exposure. Results warrant replication.

Diagnosis

The potential of digital breast tomosynthesis, as an addition to diagnostic mammography (such as spot views), is primarily to reduce the number of women who undergo biopsy by screening out some fraction of women who have false-positive results. The body of evidence on breast tomosynthesis to evaluate women who are recalled for a diagnostic workup after a suspicious finding on screening mammography is weaker than that on adding breast tomosynthesis to mammography for screening. Confounding this analysis is the fact that diagnostic mammography is not the only imaging modality used during the diagnostic workup. US is also commonly used and less often, MRI. As a result, study designs are more complicated in terms of how they incorporate ultrasound into the comparison between diagnostic mammography and breast tomosynthesis. A different research design is needed to assess the incremental value of tomosynthesis compared with currently-used diagnostic tests. Additionally, some studies focused on 1 type of finding, e.g., masses versus calcification. These studies do not provide data on the accuracy of breast tomosynthesis for the full range of findings.

Ongoing Research

Digital breast tomosynthesis continues to be an active field of investigation. A search of online site, clinicaltrials.gov, identified 17 active studies of digital breast tomosynthesis. All but 2 studies had sample sizes larger than 100, and 6 studies were larger than 1000 (e.g., 15,000 [NCT01091545] and 25,000 [NCT01248546, the study whose interim analysis was reported by Skaane et al (2013) (12)]. A large study with target enrollment of 12,000 was suspended due to funding unavailability (NCT01593384).

Several studies have assessed different breast tomosynthesis equipment, including a study of the Siemens Inspiration Digital Breast Tomosynthesis system (NCT01373671) and 3 completed studies sponsored by GE Healthcare that have not yet been published (NCT NCT00535184, NCT NCT00535327, NCT00535678).

Practice Guidelines and Position Statements

American College of Radiology

ACR does not include digital breast tomosynthesis in its Appropriateness Criteria for screening (38) or diagnostic (39) breast imaging. However, in a joint news release with the Society of Breast Imaging after release of the Norse study interim analysis by Skaane et al (2013)(12), the organizations stated, “While the study results are promising, they do not provide adequate information to define the role of tomosynthesis in clinical practice.”(40) They also noted that while cancer detection was greater with tomosynthesis, it is unknown whether incremental health benefits would be the same during a second round of screening. Furthermore, they noted “[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.”

American College of Obstetricians and Gynecologists

In its 2011 practice bulletin on breast cancer screening, ACOG noted that digital breast tomosynthesis is 1 of several screening techniques that were considered but not recommended for routine screening. (41)

National Comprehensive Cancer Network

According to the National Comprehensive Cancer Network, “Early studies show promise for tomosynthesis mammography. Two large trials showing a combined use of digital mammography and tomosynthesis resulted in improved cancer detection and decreased call back rates; of note, this is double the dose of radiation and is a factor in recommending this modality. Definitive studies are still pending.”(42)

U.S. Preventive Services Task Force

In 2009, USPSTF updated its recommendations for breast cancer screening using film mammography and using methods other than film mammography. (43) USPSTF recommends mammography and digital mammography but does not include digital tomosynthesis. However, the Department of Health and Human Services, in implementing the Affordable Care Act, utilizes USPSTF 2002 recommendations on breast cancer screening. (44) These recommendations do not include digital breast tomosynthesis. USPSTF is in the process of updating its recommendations for breast cancer screening. (45)

Medicare National Coverage

There is no national coverage determination (NCD). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.

References


### Documentation Required for Clinical Review

- No records required

### Coding

This Policy relates only to the services or supplies described herein. Benefits may vary according to benefit design; therefore, contract language should be reviewed before applying the terms of the Policy. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement.

#### IE

The following services are considered investigational and therefore not covered for any indication.

<table>
<thead>
<tr>
<th>Type</th>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td>76499</td>
<td>Unlisted diagnostic radiographic procedure [when specified as digital breast tomosynthesis]</td>
</tr>
<tr>
<td>ICD9 Procedure</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>ICD-10-PCS</td>
<td>BH00ZZZ, BH01ZZZ, BH02ZZZ</td>
<td>Imaging, breast, plain radiography, code by location (right, left or bilateral)</td>
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</table>
### Definitions of Decision Determinations

**Medically Necessary:** A treatment, procedure or drug is medically necessary only when it has been established as safe and effective for the particular symptoms or diagnosis, is not investigational or experimental, is not being provided primarily for the convenience of the patient or the provider, and is provided at the most appropriate level to treat the condition.

**Investigational/Experimental:** A treatment, procedure or drug is investigational when it has not been recognized as safe and effective for use in treating the particular condition in accordance with generally accepted professional medical standards. This includes services where approval by the federal or state governmental is required prior to use, but has not yet been granted.

**Split Evaluation:** Blue Shield of California / Blue Shield of California Life & Health Insurance Company (Blue Shield) policy review can result in a Split Evaluation, where a treatment, procedure or drug will be considered to be investigational for certain indications or conditions, but will be deemed safe and effective for other indications or conditions, and therefore potentially medically necessary in those instances.

### Prior Authorization Requirements

This service (or procedure) is considered **medically necessary** in certain instances and **investigational** in others (refer to policy for details).

For instances when the indication is **medically necessary**, clinical evidence is required to determine **medical necessity**.

For instances when the indication is **investigational**, you may submit additional information to the Prior Authorization Department.
Within five days before the actual date of service, the Provider MUST confirm with Blue Shield that the member's health plan coverage is still in effect. Blue Shield reserves the right to revoke an authorization prior to services being rendered based on cancellation of the member's eligibility. Final determination of benefits will be made after review of the claim for limitations or exclusions.

Questions regarding the applicability of this policy should also be directed to the Prior Authorization Department. Please call 1-800-541-6652 or visit the Provider Portal www.blueshieldca.com/provider.

The materials provided to you are guidelines used by this plan to authorize, modify, or deny care for persons with similar illness or conditions. Specific care and treatment may vary depending on individual need and the benefits covered under your contract. These Policies are subject to change as new information becomes available.