Breast Tomosynthesis
The Use of Breast Tomosynthesis in a Clinical Setting
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Introduction

Since the United States (U.S.) Food and Drug Administration’s (FDA) approval of the first commercial systems in 2000, digital mammography has become an accepted standard of care in breast cancer screening and diagnosis and has paved the way for the newest groundbreaking technology in this arena – breast tomosynthesis, also referred to as tomosynthesis, or simply “tomo.”

Breast tomosynthesis is a screening and diagnostic modality that acquires images of a breast at multiple angles during a short scan. The individual images are then reconstructed into a series of thin, high-resolution slices typically 1 mm thick, which can be displayed individually or in a dynamic cine mode. A tomosynthesis dataset greatly reduces detection challenges associated with overlapping structures in the breast, which is the primary drawback of conventional 2D analog and digital mammography.

This technology has been available in Europe and other countries recognizing the CE mark since 2008. In February 2011, the Hologic Selenia® Dimensions® 3D mammography™ system was the first commercial system approved by the FDA. The system is approved for use in the same clinical indications as 2D mammography, including breast cancer screening, diagnosis, and intervention. With the Hologic 3D mammography™ system, a combined examination of 3D and 2D imaging, known as combo mode, takes only seconds longer than a conventional two dimensional digital mammogram. In clinical use, Hologic 3D mammography offers significant benefits, including increased cancer detection, decreased callback rates, help in localizing structures in the breast, and improved lesion and margin visibility. In 2013 the FDA approved a new mode for the Hologic 3D mammography system, whereby C-View® software generates the 2D image from the 3D dataset directly, avoiding the need for a separate 2D exposure and essentially halving the radiation dose associated with the combo mode procedure.

This white paper provides detailed information about the performance of Hologic 3D mammography technology now that it has been evaluated in large-scale screening trials and is in routine clinical use. It also looks at the performance of 3D mammography in different breast composition and lesion types, discusses several issues to consider when introducing this technology into clinical practice, and provides a summary of some of the advanced applications for this modality.

Superiority of Hologic 3D Mammography to 2D

The performance of 3D mammography has been evaluated in a number of venues, including the clinical trials in support of the FDA submissions, and more recently, in Europe in large screening trials and in U.S. sites that monitored performance before and after the introduction of 3D mammography into routine clinical practice. Hologic 3D mammography has been shown to be superior to 2D mammography.

Hologic conducted a large multi-center clinical trial comparing the performance of combo mode to that of 2D digital mammography alone in support of its FDA submission. The two reader studies for this trial found that the addition of tomo to digital mammography both significantly increased diagnostic accuracy and significantly reduced recall rates for non-cancer cases. These results were consistent with those of an independent reader study in which University of Pittsburgh researchers found a 7% improvement in the area under the receiver operating characteristics (ROC) curve for 2D plus tomo compared to 2D alone. The FDA advisory panel considered all three reader studies and voted that Hologic’s clinical data demonstrated both the effectiveness and safety of 3D mammography.

Improved Sensitivity and Reduced Recalls

The performance of 3D mammography has been evaluated in a large screening trial from Oslo, Norway. Results have been presented from the first three months and the first year of the two-year trial. In the one-year evaluation of 12,631 screening examinations, in which participants were imaged with both 2D and 3D mammography, the researchers reported that the detection rate for invasive cancers increased 40%, the overall cancer detection rate increased 27% and the false positive rates decreased by 15% for examinations employing 2D and 3D mammography compared to 2D mammography alone. These results were seen across all breast densities.

The results of the Oslo trial are summarized below:

- Invasive cancer detection increased 40%.
- Cancer detection increased 27%.
- False positives decreased 15%.

Another large population-based screening trial conducted in Italy involved over 7,000 women and reported a 51% increase in cancer detection with the use of tomosynthesis.
The performance of 3D mammography in routine screening practice has also been evaluated in observational studies, in which the changes in performance measures with and without the use of tomosynthesis in clinical practice were reported. The largest of these (Friedewald, et al. 2014) reported on the performance of tomosynthesis in 13 sites in the United States, and found that the introduction of 3D mammography increased the invasive cancer detection rate by 41% while reducing the recall rate by 15%, as well as observing an increase in the positive predictive value for both recalls and biopsies. The other studies reported single-institution results, but with similarly positive results, showing an overall average cancer detection rate increase of 22% and an average recall rate reduction of 28%. The Rose study specifically called out the invasive cancer detection rate, which showed an increase of 54% with the use of 2D and 3D mammography.

Greater Performance Using Two-view Tomosynthesis

All of the previously referenced clinical studies used two-view mammography for both 2D and 3D imaging. As part of the study submitted to the FDA, another arm was investigated: single-view tomosynthesis (MLO) imaging in combination with two-view (CC and MLO) 2D imaging. In this study, the performance of 2D imaging plus tomo MLO showed that the tomo MLO-only arm performed better than 2D imaging alone, but not as well as 2D plus both tomo views.

These results are consistent with other studies, illustrating that MLO-only tomosynthesis is likely to be inferior to two-view tomo. These study results are explored in greater detail in the discussion of one-view versus two-view tomosynthesis later in this paper.

Performance in Different Breast Compositions and Lesion Types

The expanding library of clinical trial results on the use of tomosynthesis makes it possible to evaluate its performance in different breast compositions and lesion types such as calcifications, masses and distortions, invasive and noninvasive cancers, and fatty and dense breast tissue. There are also some study results demonstrating how the use of tomosynthesis may affect the management of symptomatic patients.

Performance in Calcifications, Masses and Distortions

The clinical trial data presented as part of Hologic’s FDA submission has been analyzed by separating the image sets into calcification and non-calcification cases. Rafferty et al. found that 2D plus 3D offered a very significant increase in performance relative to 2D imaging for cases involving masses and distortions. For cases involving microcalcifications, there was a small, but not statistically significant, improvement in the ROC performance with the addition of 3D imaging.

Performance in Invasive and Noninvasive Cancers

From the FDA studies it could be predicted that the majority of additional cancers found by 3D mammography will be mass lesions and not calcification-only cancers because of the much greater improvement in the ROC curve performance in the reader studies for non-calcifications than for cases involving calcifications. Thus, it is to be expected that the gain in sensitivity using 3D mammography can be primarily attributable to invasive cancers. Recent results reporting the performance of 3D mammography in screening are showing exactly this. Skaane reported a 40% increase in the detection of invasive cancers using 3D mammography, with no increase in the detection of ductal carcinoma in situ (DCIS). Similarly, Rose reported a 53% increase in invasive cancer detection using 3D mammography, and as with Skaane, no increase in the detection of noninvasive cancers. Ciatto also showed an increase in cancer detection of about 50% and no increase in the detection of in-situ cancers.

The study by Skaane showed improvements in cancer detection in both fatty and dense breast categories.

INCREASED CANCER DETECTION: The 3D reconstructed slice shown on the right reveals a definitive spiculated mass that is only faintly revealed in the 2D image shown on the left. (Diagnosis: Invasive ductal carcinoma)
This represents one of the key benefits of 3D mammography – the potential for earlier detection of invasive cancers – exactly the cancers that will advance to become life-threatening if not detected in time for effective treatment. These tomo-only cancers represent cancers that were missed in 2D imaging and would not have been found until a successive screening round one or more years out or when the mass became palpable, had the tomo scan not been performed.

**Performance in Fatty and Dense Breasts**

The addition of 3D imaging has been shown to improve the performance of mammography in both fatty and dense breasts. Because denser breasts have more structure noise (fibroglanular tissue) than fatty breasts, it was expected that 3D mammography would provide improved performance in the denser breasts; however, clinical data shows that 3D mammography helps in both fatty and dense breast groups.³

This was reported in the paper by Haas et al.⁷ This study looked at the performance of 3D mammography in 13,000 women undergoing breast cancer screening. They found that the addition of 3D imaging reduced recall rates for all breast density groups, with statistically significant reductions in recall rates for scattered fibroglanular (reduction of 25%), heterogeneously dense (reduction of 39%) and extremely dense breasts (reduction of 57%).

Other researchers have reported similar trends. Rafferty studied the performance of 3D mammography in women with dense breasts and found an increase in the recall rate for cancer cases and a reduction in the recall rate for non-cancer cases.¹² In a separate study, Rafferty found that 2D plus tomo was significantly better than 2D mammography alone in ROC performance for both fatty and dense breasts.¹³ While there was a gain in the area under the ROC curve in both breast density types, the gain was 2-3 times higher in dense breasts than it was in fatty breasts. Rafferty also reported large recall rate reductions in both fatty and dense breast types.

Philpotts et al. reported on tomosynthesis visualization of breast cancers as a function of mammography density.¹⁴ They found that 3D mammography was particularly beneficial for visualizing non-calcified breast cancers in scattered and heterogeneously dense breasts, with about 70% of cancers in these density categories seen only or better with tomosynthesis. Patients with fatty and extremely dense breasts had cancers seen equally well using tomosynthesis and 2D mammography.

In terms of the detection of invasive lobular carcinoma (ILC), Gandini et al. has reported that the detection of ILC was significantly higher using tomosynthesis
than digital mammography, especially in dense breasts. Radiologists were twice as likely to miss an ILC in dense breasts using digital mammography than when using tomosynthesis.

These results are as expected. Fatty breasts often have sufficient parenchyma that tomosynthesis would be expected to offer some advantages. However, the even larger improvement in performance in denser breasts using tomosynthesis illustrates that the technology is doing what is expected from the physics principles – reducing superimposed parenchyma.

Performance Compared to Ultrasound

Of great interest is understanding the relative performance of ultrasound compared to tomosynthesis in breast cancer screening. 3D mammography, like ultrasound, has a superior performance in dense breasts relative to 2D mammography. However, unlike ultrasound, in which the recall rate of 2D and ultrasound was 4 times that of 2D mammography alone as was seen in the ACRIN 6666 trial, 3D mammography improves sensitivity without increasing the recall rate. Further clinical research will be needed to identify the respective roles of 3D mammography and ultrasound, particularly in screening women, but it is clear that 3D mammography can offer improved cancer detection while simultaneously reducing false positives.

Some recent studies have compared the relative performance of tomosynthesis and ultrasound. Aguillar looked at whole breast handheld physician-performed ultrasound following breast tomosynthesis and concluded that adding the ultrasound exam had little impact in cancer detection and a low positive predictive value. Similar to Chung concluded that in dense breasts, tomosynthesis showed better diagnostic performance and a reduced benign biopsy rate than breast ultrasound.

Performance in the Evaluation of Symptomatic Patients

The use of 3D mammography in diagnostic assessment offers the opportunity for both
improved performance and a reduction in the number of X-ray images needed, with a resultant reduction in both dose and exam time.

Zuley et al. found that two-view tomo significantly improved diagnostic accuracy for non-calcified lesions compared to supplemental mammographic views. All 8 radiologists participating in the study showed improved performance. Because the number of diagnostic views in the evaluation of masses or focal asymmetries can average three or more, there is a clear opportunity to reduce radiation exposure through the use of 3D mammography in diagnostic evaluations.

Butler et al. had similar conclusions, and reported that 3D mammography results in decreased number of images required for diagnostic cases. They further concluded that this expedites the workup and yields better patient throughput.

Other researchers such as Svahn have also shown that the combined diagnostic performance of digital mammography and tomosynthesis is superior to either digital mammography or tomosynthesis alone.

Several studies have shown that 3D mammography is superior to 2D mammography in predicting tumor size, demonstrating margins, extents of lesions, and in staging:

- Rafferty et al. reported that 3D mammography was significantly better than 2D mammography in detecting cancers, particularly those exhibiting architectural distortion, and in characterizing cancer morphology.
- Moon et al. showed that adding tomosynthesis to digital mammography increased cancer detection and diagnostic performance in diagnostic workup.
- Michell et al. showed that 3D mammography is superior to 2D mammography in predicting the histological tumor size because 3D mammography demonstrates the margins and extents of the mammographic lesions more clearly.
- His study concluded that this modality provided critical information for prospective treatment planning by the multi-disciplinary team.
- Fornvik et al. found 3D mammography superior to 2D digital mammography in the assessment of breast tumor size and stage.
- Meacock et al. found that 3D mammography was more accurate than 2D in tumor size measurement.
- Tagliafico et al. found that 3D mammography could replace spot compression views, lowering both radiation dose and offering the potential to reduce biopsies on non-malignant lesions.

Clinical Considerations in Implementing Breast Tomosynthesis

Clinical research has shown the benefits of 3D mammography in screening and diagnostic indications, as well as in a range of breast compositions and tissue types. However, there are a number of clinical
considerations to be evaluated when determining how to introduce this technology to a clinical practice. What configuration of 2D and tomo views ensures the earliest possible detection of breast cancers and reduction of unnecessary recalls? How will these choices affect patient dose? How should patients be managed in a mixed environment?

These considerations are discussed in more detail below.

One-view Versus Two-view Tomosynthesis

The relative performance of one-view versus two-view 2D mammography is well understood. Screening using two views offers an increase in cancer detection and a reduction in recall rates compared to single-view mammography; the paper by Wald et al. estimates the sensitivity gain is 24% and recall rate reduction is 15%.29 Equivalently, single-view tomosynthesis (either CC or MLO) is a lower-dose procedure compared to two-view tomosynthesis, but it has been demonstrated to have poorer clinical performance. There is considerable evidence that two-view tomo has increased sensitivity relative to one-view tomo. This has been illustrated in the reader study reported by Rafferty in which the clinical performance of two-view 2D combined with two-view tomo imaging, with the single-view tomo providing only half the performance gain of two-view tomo.20

Other data supports this finding:

- Rafferty et al. found that 12% of lesions were better seen on the tomo MLO image, 15% better seen on tomo CC and 9% of lesions were visible only on tomo CC.31
- Beck et al. found that only about half of the lesions were equally well seen on both the MLO and CC view, with 34% of cancers better or only seen on the CC view,32 while 7% of lesions were only seen on one view. The authors emphasized the importance of including the CC view in 3D mammography and concluded that obtaining both views is necessary to ensure that a cancer will be optimally visualized, and the greatest potential benefit from tomosynthesis will be derived.
- Similar results were reported by Baker et al., who found 8% of lesions were visible only on the tomo CC view and 1.4% only on the tomo MLO.33

These results are also consistent with evaluations in which studies comparing the ROC performance of two tomo views demonstrate superior performance over two-view digital mammography (Michell), but studies comparing one-view tomo to two-view digital mammography have poorer performance and do not show superiority (Gennaro, Wallis).14,15,16

No published study using single-view tomo has demonstrated an increase in both sensitivity and specificity compared to 2D digital mammography.

In addition to the likely loss of sensitivity that occurs if only one tomo view is taken, there are some clinical challenges that arise with single-view tomo imaging. Neither the CC nor the MLO view always captures all the breast tissue, so both views in some form are preferred.

Mixing technologies, such as combining a tomo MLO view and a 2D mammography CC image, might address the tissue coverage, but creates its own set of issues. It might be difficult, for example, to correlate a suspicious lesion seen in 2D CC with the same lesion in the tomo MLO, or vice versa. The approach of a tomo MLO and a 2D CC is likely inferior in clinical performance to performing tomo imaging in both the MLO and CC view – and offers no dose advantage. The reason for this is clear. Just as some cancers in the MLO view are better appreciated in tomo imaging than in a 2D MLO image, some cancers in the CC view are better appreciated in tomo imaging than in a 2D CC image. Indeed, the recent publication of a clinical trial in support of tomosynthesis approval for GE Healthcare showed no superiority of single-view tomosynthesis compared to 2D mammography.17

Recall Rate Reduction by Breast Density

In the study by Haas, et al., the addition of 3D mammography decreased recalls across all breast densities, with significant reductions in denser breasts.

VALUE IN FATTY BREASTS: While the 2D mammogram reveals the 12:00 o’clock mass, the 3D images more accurately characterizes this mass as spiculated (invasive ductal carcinoma).
The presentation by Zuley et al., which looked at the visibility of cancers in the CC and the MLO tomo views, concluded that the tomo CC view depicted “substantially more cancers” than the tomo MLO view.\textsuperscript{38} Given this body of evidence, if only one tomo view is to be acquired, the MLO tomo view appears to be the wrong one if maximizing cancer detection is the clinical goal.\textsuperscript{39}

An even more challenging situation is when the exam consists solely of a tomo MLO. It could be difficult to see asymmetries with only one view, and comparison to 2D prior images would also be challenging. The best clinical performance will likely be seen in protocols that acquire both tomo CC and MLO image sets.

Performing two views uses more radiation dose than one view. However, these doses are commonly accepted in conventional mammography, in which two-view mammography is performed to improve the cancer detection rate. Likewise, two-view tomo is associated with higher sensitivity along with reduction in recall rates, as compared to single-view tomo, in which sensitivity will suffer.

An alternative approach to acquiring two tomo views, given a fixed radiation dose, would be to acquire only one tomo view, but double the dose for that view. This certainly would lower noise and may result in a superior image due to the increased photon statistics. However, better clinical performance has been seen for two-view tomo than for higher dose single-view tomo. The Gennaro 2009 study showed that the use of single-view tomo at 2x dose achieved inferior performance, compared to digital mammography, whereas Michell, who used two tomo views at approximately 1x dose each, achieved superior performance.\textsuperscript{33,35}

**Benefits of Having Both Tomo and 2D Images in All Views**

There are several reasons why acquiring both a 2D and tomo image together are useful, especially in screening. It is well known that comparison of current images with prior images is standard mammography practice and critical to perceiving subtle changes that may be associated with a cancer. Obtaining a 2D exam along with the tomo exam allows direct comparison of current 2D images with prior 2D images.

The 2D exam is also useful for the rapid detection of calcifications and perception of their distribution. Segmental and clustered calcifications are more easily and quickly appreciated with 2D because they can traverse multiple tomo slices.

The tomosynthesis portion of the 2D plus tomo exam is also critical in optimizing performance. The tomosynthesis image reduces structure overlap, minimizing recalls for overlapped structures and better demonstrates masses and architectural distortions.

Because of the value of having both 2D and 3D views, the original Hologic FDA trials looked at the performance of 3D imaging when used in combination with 2D mammography. The trial demonstrated superior performance with the addition of tomo, but at the cost of additional radiation...
dose to the patient due to the essentially double exposures of both tomo and 2D. Using Hologic C-View software, it is possible to generate a 2D image directly from the 3D dataset, obviating the need for 2D exposures, and providing the clinical benefit of both 2D and tomo at essentially the same radiation dose as a 2D exam alone. Additional information about this process is provided in the following section.

Both the 2D and tomo images in an exam are valuable. In conclusion:

- The 2D image is useful for comparison to priors.
- The 2D image allows for quick reading of microcalcifications.
- The tomo image reduces structure overlap and better demonstrates masses.
- Using both 2D and tomo in both the CC and MLO views maximizes clinical performance.
- Using C-View software allows the generation of the 2D images with no additional radiation beyond the tomo exposures.

Patient Selection and Management

Most breast imaging centers have multiple digital mammography systems, and it may not be economically feasible to immediately replace every 2D system with tomo-capable units. It is likely that many facilities will implement tomosynthesis mammography in phases, beginning with one or two systems initially, similar to the pattern seen in the transition from analog to digital mammography. During this implementation phase, facilities will need to develop criteria for determining which patients will receive tomo exams, as well as processes to ensure efficient patient management in a mixed environment.

Determining which patients should receive tomo exams is not a straightforward issue, and there is not a single solution that will fit every situation. Each facility must consider what is known about the benefits of tomosynthesis and make decisions based on their unique requirements and implementation strategy. Some potential considerations are outlined below.

Use for Screening or Diagnostic Imaging

3D mammography has shown value in a diagnostic evaluation of a symptomatic breast. It also can be used as a screening tool to improve sensitivity and reduce recalls. Therefore, either or both indications are acceptable uses of the technology. Since diagnostic procedures often take longer than screening exams, more women per day can be accommodated on machines dedicated to screening use. This might be a consideration in situations where a limited number of tomo-capable systems are available.

Use for Women with Dense Breasts

3D mammography has been shown to have value in both fatty and dense breasts, but it has a greater impact for women with dense breasts. Therefore, if a practice does not have enough systems to screen all women, it is reasonable to reserve 3D mammography for women with dense breasts. However, as 3D mammography offers a benefit in both fatty and dense breasts, the eventual goal should be to screen all women using tomosynthesis imaging.

Reducing Patient Dose in 3D Mammography

One area in which extensive research and development efforts have been focused is the creation of a 2D image generated from a 3D dataset. This method provides a 2D image for use during image review, but does not require an X-ray exposure to generate the 2D image, as it is created directly from the 3D slices. In November 2011, Hologic announced the commercial
The lesion is easily seen on the 3D CC slice 21, but not on the 2D CC, even in retrospect.

No lesion is apparent on the standard 2D screening views, above.

The lesion cannot be seen on the 3D MLO slices, shown here at every 10 mm.

The lesion is easily seen on the 3D CC slice 21, but not on the 2D CC, even in retrospect.
release and CE mark of its C-View synthesized 2D image reconstruction algorithm that eliminates the need for a conventional 2D mammogram as a component of a tomosynthesis screening procedure. C-View technology became available in the U.S. in 2013.

This approach provides the advantage of reducing the number of exposures, leading to shorter exam times, increased patient comfort due to reduced time under compression and reduced patient dose. This software allows screening with 3D mammography at the same dose as conventional digital mammography.40

The performance of the generated 2D image has been evaluated in the clinical trial in support of the C-View software FDA submission. The clinical trial demonstrated that:

• 3D mammography with C-View 2D images is superior to 2D alone for all breast types.
• 3D mammography with C-View 2D images is superior to 2D alone in reducing recall rates.

Wallace et al. studied the performance of C-View 2D images in a reader study, and using ROC analysis, they concluded that generated 2D mammograms with tomosynthesis allowed similar interpretive performance to standard digital mammography in combination with tomosynthesis, and therefore, may be an acceptable alternative for screening.4 Zuley et al. studied the performance of C-View 2D images in a reader study, and concluded that generated 2D alone or in combination with tomosynthesis, is comparable in performance to standard 2D mammography alone or in combination with tomosynthesis, and may eliminate the need for acquired 2D images as part of a routine clinical study.42

The performance of C-View software in screening has perhaps been most extensively measured in the Skaane screening trial. Using tomosynthesis plus C-View 2D images, Skaane reported an increase in cancer detection compared to 2D imaging. A direct comparison between the performance of tomosynthesis with digital mammography to the performance of tomosynthesis with C-View 2D images found comparable results regarding positive predictive values and cancer detection rates.43

In the Oslo trial, tomosynthesis with C-View 2D images showed comparable cancer detection and positive predictive value as tomo with digital mammography.

Reading Time

Breast tomosynthesis involves the generation of considerably more images than standard 2D digital mammography, as each single 2D digital image is now replaced with perhaps 50 or more slices. As a result, the time to perform the evaluation of these images has been a topic of interest. Initial results indicated that the reading time approximately doubled from 49 seconds to 92 seconds for a 4-view bilateral exam.3 As readers gain experience, it now appears that the increase in reading time using 3D mammography is shrinking. The group from Oslo reports that after reading 2,000 examinations, the 3D mammography reading time dropped 40% from initial values.
and is now ~60 seconds. They conclude that 3D mammography interpretation time is acceptable for high-volume screening. Other researchers report that the reading time for 3D mammography is about 50% longer than for 2D mammography.

**Advances in Hologic 3D Mammography**

The growing adoption of 3D mammography in clinical use creates an opportunity for technological evolutions that may be useful in streamlining workflow, improving diagnostic accuracy and expanding clinical applications. Some of the recent advances and ongoing efforts in these areas are discussed in the following sections.

**3D Guided Biopsy**

The ultimate diagnosis of a breast cancer lesion is made using biopsy tissue sampling. The ability for 3D mammography to identify lesions not readily visible with 2D digital mammography or ultrasound has created a problem – how can a biopsy be performed if a lesion cannot be located using standard biopsy imaging methods? Many lesions found with 3D mammography can in retrospect be located and biopsied using ultrasound or stereotactic guidance. But subtle lesions sometimes can only be identified using 3D imaging. This requires that biopsy systems employ imaging and localization using 3D. The Hologic 3D mammography system offers an interventional add-on device that utilizes 3D imaging for lesion identification and targeting. Using this device, a single tomo scan is performed, the lesion is targeted and the x,y,z location of the lesion calculated directly from the 3D image. Advantages of this procedure compared to stereotactic biopsy include improved visibility of lesions that are occult in 2D imaging, faster lesion targeting, fewer X-ray exposures, and reduced patient procedure time. Even without the add-on biopsy device, there is a method whereby lesions can be targeted under tomosynthesis guidance. An open surgical biopsy can be performed as long as the system supports tomosynthesis-guided needle localizations. The ability to perform tomosynthesis imaging using a biopsy paddle and fast tomosynthesis reconstructions may facilitate biopsies using tomosynthesis.

**Contrast-enhanced Breast Imaging**

Contrast-enhanced breast imaging is a procedure that images the distribution of an iodinated contrast agent using either 2D or 3D X-ray imaging technologies. This technology is in its early evaluation stage, but may offer some advantages relative to contrast breast MRI in terms of reduced cost, comparable care to patients for whom MRI is contraindicated, and access to patients in areas where MRI systems are not available. Contrast-enhanced breast imaging combines functional information from the distribution of the contrast agent and morphological information from the X-ray images. Hologic has received FDA...
approval and CE mark for a dual modality system, which is capable of imaging the functional 2D contrast uptake and the morphological 3D image in rapid sequence, and combining these two image sets into a single fused study. In the fused study, the 2D contrast image can identify potential lesions based on their physiological state that causes increased contrast agent uptake. The standard 3D image can then be overlaid on the 2D contrast image and provide morphological information on the lesion, such as improved visibility of associated spiculations.

**Conclusions**

Breast tomosynthesis is an exciting technology that is revolutionizing breast imaging. It has demonstrated value in both screening and diagnostic evaluations. The improvements in clinical performance, compared to 2D mammography, are significant. Multiple peer-reviewed clinical publications report that the use of two-view tomo in screening offers both improved cancer detection rates and reduced callback rates compared to 2D alone.

Clinical studies using the Hologic 3D mammography system have demonstrated superior performance in the detection of masses and architectural distortions and equivalent or slightly better performance in the detection of microcalcifications in using 2D plus tomo imaging compared to 2D alone. Acquisition of both the CC and MLO views in 2D and tomo provided statistically significant superior performance compared to 2D alone; however, use of only the MLO tomo with both the 2D CC and MLO tomo views also provided better performance compared to 2D alone – just not as good as acquiring both CC and MLO tomo views. Finally, it was demonstrated that the addition of 3D imaging to conventional 2D imaging provides improved performance in both fatty and dense breasts, compared to 2D alone, with the performance gain in dense breasts higher than in fatty breasts.

With the use of the C-View generated 2D image, cancer detection and other clinical benefits of 3D mammography are available at comparable radiation dose to standard 2D digital imaging and at about half the dose of 2D plus 3D imaging.

There is a growing body of evidence that 3D mammography has the potential to reduce the number of exposures needed for diagnostic imaging and provide other diagnostic benefits, including enhanced performance in assessing tumor size and stage and more clearly demonstrating margins and extent of lesions.

Important new applications involving 3D mammography include contrast-enhanced imaging for patients when access to breast MRI is limited or contraindicated, and methods of biopsying lesions under 3D image guidance.

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**Glossary**

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
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<tbody>
<tr>
<td>2D</td>
<td>Conventional digital mammography. Also known as FFDM.</td>
</tr>
<tr>
<td>3D</td>
<td>A technology involving limited angle tomography acquisition and reconstruction. Also referred to as digital breast tomosynthesis, DBT, 3D tomosynthesis, tomosynthesis and tomo.</td>
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<tr>
<td>Callback rate</td>
<td>Same as recall rate. The percentage of women recalled from screening for further assessment. In mammography screening, the majority of recalled cases are false positives.</td>
</tr>
<tr>
<td>Combo mode</td>
<td>An imaging mode whereby both a 3D and 2D digital mammography image set are acquired in one breast compression.</td>
</tr>
<tr>
<td>C-View™</td>
<td>2D image generated from the 3D reconstructions.</td>
</tr>
<tr>
<td>Recall rate</td>
<td>The percentage of women recalled from screening for further assessment. In mammography screening, the majority of recalled cases are false positives.</td>
</tr>
<tr>
<td>ROC</td>
<td>Receiver Operating Characteristics</td>
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<tr>
<td>Sensitivity</td>
<td>The measure of how many cancers are detected.</td>
</tr>
<tr>
<td>Specificity</td>
<td>The measure of how many non-cancers are correctly identified.</td>
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<tr>
<td>Synthesized or generated 2D</td>
<td>A method of creating a 2D image from a reconstruction of a 3D dataset. See C-View.</td>
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