American Society of Breast Disease Statement on Digital Breast Tomosynthesis

Introduction
The widespread implementation of screening mammography has decreased the mortality of breast cancer by as much as 50% [1]. Despite recent controversies regarding the benefits of screening mammography, and the age at which screening mammography should begin, mammography remains the most widely utilized tool for early detection of breast cancer. However, it is also evident that mammography remains an imperfect tool. A standard two-view analog or digital mammogram does not detect all cancers. In fact, the sensitivity of mammography decreases as the density of breast tissue increases. Holland et al. found that 76% of missed cancers occurred in dense breasts [2]. One of the reasons for the limited sensitivity is the “structural noise” that is created by the overlap of normal breast tissue. This resultant “structural noise” makes it more difficult for a radiologist to perceive a cancer that is obscured by the normal breast tissue. Also, normal structures superimposed on each other in a conventional 2 view mammogram may produce a false positive ‘finding’.

The growing use of full field digital mammography has led to significant improvement of sensitivity in women with dense breast tissue secondary to improved contrast sensitivity [3]. Unfortunately, digital mammography is still limited by the overlapping breast tissue. However, digital breast tomosynthesis (DBT), often referred to as three-dimensional (3D) mammography eliminates the overlapping tissue problem.

DBT is a system that produces a series of images with multiple low-dose tomographic images acquired in an arch. These images are reconstructed and allow for visualization of the breast in multiple contiguous slices. This novel technology reveals the internal architecture of the breast. The potential benefits of DBT include a reduction in the tissue overlap leading to increase sensitivity and specificity of breast cancer detection. It may also improve the characterizations of different lesion types. Early clinical studies suggest that DBT reduces screening recall rates, improves screening sensitivity and improves diagnostic accuracy [4-13]. DBT does not have its own CPT code. In addition, solutions for workflow issues regarding the display and storage of these images continues to evolve in a positive direction.

DBT Technique
The Selenia Dimensions System (Hologic, Bedford, MA, USA) approved in the U.S. in February 2011, remains the only DBT system that is currently approved by the FDA. Therefore, the technique described in this section is based upon the Hologic system. During the acquisition of a conventional mammogram, the x-ray tube is positioned in a stationary fashion above the compressed breast and a full-dose exposure is obtained. In contrast, during a DBT acquisition, the compressed breast remains stationary, but the x-ray tube rotates through a small arc acquiring a series of low-dose projection images of the breast from multiple angles. The projection images are reconstructed into a series of 1 mm slice thickness [14]. The acquisition time for a single-view DBT with the Hologic system is 4 seconds. However, the acquisition time with other manufacturer systems can be up to 25 seconds depending on the manufacturer specifications, angular range, and number of projections taken [15].
Total Radiation Dose
The total radiation dose of DBT is the cumulative sum of the doses for all projections. For single view FFDM combined with a single view DBT, the mean gland dose (MGD) for a 5 cm thick 50% glandular breast is 2.50 mGy, less than the Mammography Quality Standards Act (MQSA) and European protocol limits for two-view screening mammography [14,16]. Hologic received FDA approval to market a “no increase in dose” DBT software option called C-View. The C-View software generates the FFDM image set from the 3D image set, eliminating the need for conventional 2D images. This reduces the dose to the same level as the conventional FFDM.

Limitations of Current Imaging Techniques
Three imaging tools are commonly utilized for early detection of breast cancer: conventional analog or digital mammography, breast ultrasound and breast MRI. These 3 imaging technologies have limitations that may be addressed by DBT. The main shortcoming of conventional mammography is its decreased sensitivity; the overall sensitivity is approximately 70% [3]. Published studies show the sensitivity of mammography in women with extremely dense breast tissue is 30% compared with 80% for women with very little dense tissue [18]. The decreased sensitivity in women with dense breast tissue is of particular concern in young women who often have dense breast tissue [15,18]. In addition, conventional screening mammography has a poor specificity with recall rates up to 10% for negative or benign findings [3,19]. These false-positive findings often lead to unnecessary follow-up studies and/or biopsies. These additional tests lead to additional cost and anxiety for the patients.

Breast ultrasound has been widely utilized to characterize an indeterminate finding seen on mammography and to evaluate a palpable abnormality. Recent literature shows that ultrasound may also increase the detection of breast cancers in women with dense breast tissue and in high-risk women [20,21]. A 2011 study found that approximately 90% of women with breast cancer detected only on ultrasound had a mammographic density of 50% or higher [22]. However, the specificity of breast ultrasound is even lower than mammography. The positive predictive value (PPV) for biopsy of lesions detected on sonography is reported to be as low as 5%-10% [20-22].

Breast MRI utilizes the ability of MRI to distinguish between different tissue types and the injection of contrast to identify mammographically, and often, sonographically occult breast cancers. Multiple studies show that breast MRI has a very high sensitivity (77-91%) and has consistently been shown to be greater than that of mammography (32.6-50%) [23-25]. The American Cancer Society recommends a screening MRI in addition to screening mammography in women at high-risk for breast cancer [26]. The bulk of the large prospective studies evaluating MRI sensitivity and specificity in the literature have been performed on this high-risk population. In these studies, MRI specificity (81-97.2% across studies) is consistently lower than for mammography [23-26]. In addition, breast MRI is an expensive tool that isn’t widely available. Further, women with metal implants and individuals who are claustrophobic cannot undergo a breast MRI exam.

Given these limitations, multiple groups have been exploring the ability of DBT to address some of these limitations.

Advantages and Disadvantages of Digital Breast Tomosynthesis
DBT’s advantage over digital mammography is that a series of images are generated through the breast rather than a composite image of the breast in 2 projections. DBT allows the radiologists to scroll through these images and to visualize the breast tissue in layers. These cross-sectional images may allow better visualization of cancers by reducing tissue overlap and the masking effect of tissue density. This improved visualization may also lead to reduced recall rates because findings could be confidently attributed to superimposition of normal breast tissue. It is important to note that the FDA has not approved for DBT to be a ‘stand-alone’ modality. All published studies
evaluate the added benefit of DBT to conventional mammography. The exact imaging protocol varies between all the institutions and is a limitation in comparing the diagnostic performance of the published literature.

**Improvement in Performance of Diagnostic Mammography**

A systematic review of the literature (Pubmed search from 2000 – 2012) identified approximately 20 studies that evaluated the diagnostic accuracy of DBT [27]. Studies were excluded if they were phantom studies, had a small sample size (< 50 pts) or were limited to specific lesions types (egg calcifications only) [27]. Most of the studies were focused on reader studies of cases that were recalled for diagnostic imaging after conventional screening mammography. The following is a summary of the common findings in these studies:


[2] The addition of DBT significantly improves the diagnostic accuracy of conventional mammography [11,12,27,30,32-34]. Most of this improvement was attributed to a reduction of false-positive findings, especially in the evaluation of architectural distortion and asymmetries detected on screening mammography.

- For e.g., architectural distortion, a secondary finding of breast cancer, is the most commonly missed finding in a false-negative mammogram [14,35]. DBT can enhance the detection of subtle architectural distortion. However, pseudo-architectural distortion, due to the summation of multiple linear structures in the breasts can be attributed to overlapping tissue on mammography [14].
- Michell et al. performed one of the largest diagnostic DBT studies [32]. They evaluated the benefit of DBT in the evaluation of findings detected at screening mammography. They concluded that the addition of DBT led to significantly increased reader accuracy. The shift in the ROC curve was not simply due to the reader having ‘another look’ at the mammographic exam. In fact, the ROC analysis suggests that DBT helped the readers to better discriminate between benign and malignant lesions [27,32].
- DBT can enhance the evaluation of the margins of a mass because it eliminates the overlapping breast tissue. Recently, Zuley et al. compared DBT to supplemental diagnostic mammographic views for the evaluation of noncalcified breast lesions [36]. The study utilized eight radiologists who retrospectively reviewed 217 lesions (72 cancers and 145 benign lesions) [36]. The authors concluded that tomosynthesis significantly improves diagnostic accuracy for noncalcified lesions in comparison to supplemental views. Noroozian et al. concluded that mammographic spot compression views may not be necessary for mass characterization when performing DBT because of its ability to facilitate the analysis of the margins of a lesion [37].
- DBT can also facilitate a more accurate three dimensional localization of lesion. This ability is especially helpful in women who have multiple masses and multiple clusters of calcifications on mammography [14,34].
- Several studies show that DBT has a lower sensitivity for the detection of calcifications compared with digital mammography [38-39]. This limitation is based on the inability of multiple cross sectional images to depict the distribution of calcifications, i.e., a true cluster of calcifications is only detected on a volumetric summation image, such as those produced with conventional imaging. A slab, where multiple slices are combined to produce a composite image may address this limitation [14,27,38-39].

To summarize, the use of DBT in screening mammography may result in an expedited or abridged subsequent diagnostic work up.
Breast Cancer Screens with Tomosynthesis: Increased Detection Rates and Reduction in Recall Rates

The above studies showed that DBT has a higher diagnostic accuracy in the evaluation of masses, asymmetries and architectural distortion. This improvement should lead to a decrease in the false-positive recalls from screening mammography [40-42]. This hypothesis was corroborated in a recent study by Rafferty et al. compared the radiologists' diagnostic accuracy and recall rates for DBT combined with digital mammography versus digital mammography alone [43]. They performed two reader studies in a total of 27 radiologists. All readers reported increased diagnostic accuracy with addition of tomosynthesis. Recall rates for noncancer cases for all readers significantly decreased with addition of DBT (range, 6%-67%; P < .001 for 25 readers, P < .03 for all readers).

In the screening setting, DBT is being evaluated to determine if this new technology could improve the detection of cancers in cases where overlapping breast tissue exists [44]. The addition of DBT could potentially allow for detection of breast cancers at earlier stages when they are most treatable. The utility of DBT in a screening setting is still being explored. Several large studies that investigate the role of combined DBT and 2D screening mammography are underway. These screening trials include the Malmo Trial, the UK TOMMY trial and the Yale Trial. Preliminary data from these trials suggest that DBT combined with 2D screening mammography substantially improves the cancer detection rate [31,45].

Recently, the Italian trial, Screening with Tomosynthesis OR standard Mammography (STORM) published their results in Lancet [46]. The STORM trial was a prospective comparative study that investigated the effect of integrated 2D and 3D mammography in population breast-cancer screening in 7292 women. The cancer detection rates were 5.3 cancers per 1000 screens (95% CI 3.8-7.3) for 2D only, and 8.1 cancers per 1000 screens (6.2-10.4) for integrated 2D and 3D screening. The incremental cancer detection rate attributable to integrated 2D and 3D mammography was 2.7 cancers per 1000 screens (1.7-4.2). There was a simultaneous 17% recall rate reduction when DBT was performed in addition to conventional screening mammography.

The Oslo screening trial is a prospective study of 12,631 subjects who underwent digital mammography alone and combined with DBT [47]. In this study, Skaane et al reported the detection rates, for invasive and in situ cancers, were 6.1 per 1000 examinations for mammography alone and 8.0 per 1000 examinations for mammography plus DBT. They concluded that DBT plus digital mammography provided a 27% increase in cancer detection rates, with 40% increase in invasive cancer detection. There was a significant 38% drop in recall rates - from 8.7% to 5.5% (P<0.001).

The findings in a recent study by Rose et al. are consistent with the STORM and the Oslo Tomosynthesis Screening Trial [48]. They reported an 11% decrease in biopsy rates -- from 15.2 to 13.5 per 1,000 screenings (P=0.59), a 35% increase in cancer detection rates -- from 4.0 to 5.4 per 1,000 screenings (P=0.18), and a 53% increase in the invasive cancer detection rate -- from 2.8 to 4.3 per 1,000 screening examinations (P=0.07).

The results from Haas et al. are also consistent with the above studies. In this study from Yale, a total of 13,158 patients presented for screening mammography; 6,100 received DBT. The cancer detection rate increased by 9.5% with the addition of DBT to 2D DM. The overall recall rate was 8.4% for patients in the DBT and 12.0% for those in the conventional mammography group (P < .01). There was a 30% reduction in the overall recall rate (8.4% compared to 12%). Lower recall rates were seen for all breast density and patient age groups, with significant differences (P < .05) found for scattered fibroglandular, heterogeneously dense, and extremely dense breasts and for patients younger than 40 years, those aged 40–49 years, those aged 50–59 years, and those aged 60–69 years. These findings persisted when multivariate logistic regression was used to control for differences in age, breast density, and elevated risk of breast cancer. This larger reduction in recall rates in women with mammographically dense breast tissue confirms Skaane et al.’s initial study [31].
Implementation of DBT

DBT is an exciting new technology that may alter the way we perform screening and diagnostic mammography. However, several issues must be addressed to allow wider access to DBT. DBT equipment costs more than that for 2D digital mammography and currently is not reimbursed at a higher rate. No temporary (G) or permanent (CPT) billing code has been assigned to DBT [49]. Some centers will perform the combined 2D/3D mammography at no additional cost to the patient. For example, at the Hoag Breast Care Center in California and the University of Pittsburgh, a miscellaneous code 76499 is attached to the DBT study; allowing them to receive a higher reimbursement and track their data[49]. Other facilities such as the Ellen de Paredes Breast Imaging Center in Richmond, Virginia allow patients to pay an additional out-of-pocket fee for tomosynthesis and provide the extra service at no extra charge for lower income women.

Cost is another issue that needs to be resolved. However, the cost of implementing DBT not only includes the system itself but the expense of digital storage capacity. DBT studies are large data set studies, with approximately 500 GB per four view study [49]. Also, workflow issues need to be resolved. The interpretation time for DBT is almost twice as long as conventional digital mammography [4,12,50]. Skaane et al. reported that the mean interpretation time was doubled; 45 seconds for mammography alone and 91 seconds for mammography plus tomosynthesis (P < .001) [47]. Also DBT can only be evaluated on vendor specific workstations.

CONCLUSIONS

- DBT is an advanced imaging technology for breast cancer screening and diagnosis. The DBT technology produces cross-sectional images by using multiple, low-dose acquisitions with total radiation exposure and breast compression similar to that used for conventional 2D digital mammography.

- The addition of DBT to conventional DM improves the accuracy of diagnostic mammographic interpretation. This improvement in diagnostic accuracy can be achieved by enhanced detection of lesion, improvement in the analysis of the margins of a lesion and precise localization of a lesion. DBT with DM has a higher sensitivity than DM alone. Published studies showed an increase cancer detection rate of 27 - 30% at screening.

- Single center studies have shown that DBT and DM has increased specificity compared to DM alone. Multiple studies noted reduction in the recall rates of screening mammography with the addition of DBT. Recent studies suggest that young women with dense mammographic breast tissue may benefit the most from DBT and may have the greatest reduction in the recall rates.

- The three largest published DBT screening studies demonstrate a 40-50% increase in cancer detection rates.

References


