



Digital Breast Tomosynthesis for Screening and Diagnostic Imaging

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Digital breast tomosynthesis (DBT), which was FDA approved in 2011, is rapidly emerging as the new standard of care for x-ray imaging of the breast. Multiple studies have shown that when DBT is coupled with conventional 2D mammography, improvements in both sensitivity and specificity are achieved for screening and diagnostic breast imaging. A derivative of digital mammography, DBT is a form of limited angle tomography; it consists of multiple low-dose x-ray exposures which are acquired along a limited arc creating data which are reconstructed into a series of thin images or “slices” or “planes” of the breast.^{1,2} The ability to scroll thru the stack of reconstructed “layers of the breast” minimizes the impact of overlapping tissue that can mask lesions making them difficult to detect in conventional 2D mammography.³ The “quasi” three-dimensional format of the reconstructed DBT images also allows better localization of lesions and improves the conspicuity of both benign and malignant lesion margins. Details of acquisition of tomosynthesis imaging data and reconstruction vary by vendor and thus far, there has been no direct comparison of vendor-specific imaging in a clinical trial.

In breast cancer screening, DBT outcome data have repeatedly demonstrated a reduction in false positive recalls as well as an increase in breast cancer detection when DBT is combined with conventional 2D mammography (Table 1). In most series, the incorporation of DBT imaging in screening is associated with an increase in the detection of invasive breast cancers often without a significant change in the detection of ductal carcinoma in situ (DCIS).^{4,7,8} This combination of improvements in specificity and sensitivity directly addresses the criticism of 2D mammographic screening – too many false positives and too few cancers detected. In addition, the preferential increase in detection of invasive cancers (rather than DCIS) may address the concern that screening mammography may detect some indolent breast cancers (e.g. low grade DCIS) that may not otherwise become clinically evident over a woman’s lifetime.

When DBT screening outcomes are analyzed by breast density, studies show that the majority of women benefit from the incorporation of DBT.^{8,14} Even women with less dense breasts (i.e., fatty or scattered densities) have been shown to benefit from the incorporation of DBT, perhaps due to breast parenchymal complexity on the 2D mammogram rather than just the degree of optical density or areas of masking dense breast tissue. In women with dense breasts, the improvement in outcomes with DBT appears to be achieved mostly in women with heterogeneously dense breasts.¹⁴ While numbers are small for the sub-analysis of women with extremely dense breasts, there is a suggestion that tomosynthesis improves outcomes but not to the same extent as in the other 3 categories of lower breast density.¹⁴ Interim results from the first year of a prospective, multicenter Italian study comparing handheld physician-performed screening ultrasound with combination digital mammography (DM) and DBT in women with dense breasts and negative conventional DM screening demonstrated that screening ultrasound found significantly more additional cancers than did DBT,



suggesting that supplemental screening (in addition to DBT) will continue to have a role in some women with dense breasts.¹⁵ Further study of this important issue is ongoing.

Much of the early data published on DBT screening have been in women at the first, prevalence round of DBT screening (with or without prior DM screening) and often without follow-up data to assess false negative and/or interval cancer rates. A recent, single site study of the first 3 consecutive years after complete conversion to DBT screening has shown a small prevalence effect in improved cancer detection at the first round of DBT compared to that at a second round of screening.¹² At the second round of screening (the first incident round), the cancer detection rate was very similar to the site's historic DM levels. At the third round of DBT screening (second incident screening round), the cancer detection rate was higher than seen at the first DBT screening round, perhaps due to continued learning of the DBT readers. (Although incident cancer detection rates are expected to be lower, cancers may be smaller in size due to earlier detection. However, there are no data to support this hypothesis at this time.) Importantly, the recall rate dropped with each consecutive DBT screening round.¹² Early data on false negative rates have also been promising with a trend to a reduction in interval cancers with DBT screening compared to DM alone screening.^{4, 12, 13}

Combination DM/DBT screening incurs a higher radiation dose (however, still within MQSA guidelines) than screening with DM alone. Recently, the FDA has approved the use of a reconstructed "synthetic", 2D-like image (s2D) to replace the 2D dose portion of a DBT study thereby reducing the overall x-ray dose by up to 45%, or 1.2 fold that of standard DM.⁴ However, there are few reported clinical studies comparing DBT using only synthetic images versus 2D mammography.¹⁶⁻¹⁹ These studies will be important to assess if the improvement noted when DBT is combined with 2D can be maintained with s2D/DBT. Early data on the clinical implementation of s2D/DBT screening have shown that the combination is non-inferior to DM/DBT with similar or even lower recall rates and similar cancer detection rates.¹⁹

While most literature to date on digital breast tomosynthesis focuses on screening, DBT is also being recognized as beneficial in the diagnostic setting. The impact of DBT on diagnostic imaging has been assessed in several ways. First, some facilities implementing DBT with a limited number of units, may choose to utilize DBT only for diagnostic patients. Such diagnostic exams will then include patients recalled after 2D mammography along with those seen for other diagnostic reasons. Early reader studies evaluating one or two-view DBT compared with conventional 2D diagnostic images found DBT was equivalent or superior.²⁰⁻²² Studies comparing conventional (2D) spot compression views found DBT comparable or superior in characterizing noncalcified lesions for diagnostic purposes.²³⁻²⁵ Non-calcified lesions can often be assessed without obtaining multiple additional 2D views making diagnostic evaluations more efficient when DBT is used. Ultrasound should still be performed to fully characterize palpable abnormalities and to further evaluate masses seen on tomosynthesis. Magnification views are usually still needed to fully characterize the morphology and extent of any suspicious calcification.

For patients who have already undergone DBT screening and are recalled for further evaluation of a finding, an abbreviated diagnostic workup may be possible. Due to the ability of DBT to both better localize and



characterize lesions, many patients recalled from DBT screening may go directly to targeted diagnostic ultrasound for further evaluation rather than having multiple additional mammographic views previously needed for 3D localization (i.e., mediolateral or rolled views) or margin characterization (i.e., spot compression views).²⁶ In addition, many asymptomatic patients in the diagnostic pool, e.g. women undergoing surveillance years after a diagnosis of breast cancer, are adequately served by standard DBT imaging alone. Indeed, in many centers, such women can be returned to screening using DBT. The reduction in additional diagnostic imaging in this population also increases the throughput of patients and can improve the efficiency of a breast center.²⁷

Beyond the reduction in screening recalls and improved efficiency of diagnostic workup of imaging findings, the use of DBT has been found to reduce the proportion of BI-RADS 3 cases by up to 50% when compared with 2D mammography.⁹ DBT allows for more definitively benign or suspicious characterizations and fewer 'Probably Benign' assessments, with a concomitant shift to a greater proportion of patients receiving BI-RADS 1 and 2 assessments, and thus returned to screening. Over time, this decrease in category 3 patients results in progressive shrinking of the number of patients undergoing diagnostic follow-up. With this decrease, changes in departmental workflow and resources can be anticipated.²⁸

Additionally, due to DBT's superior lesion assessment, the positive predictive value (PPV3) of diagnostic biopsy performed has also been observed to increase. A more than 50% increase in PPV over 2D mammography has been observed.²⁸ This results in fewer biopsies, improved efficiency, and thus saves costs, resources, and patient inconvenience and anxiety. For malignancy, the improved definition of shape and margins can result in improved assessment of lesion size along with the improved detection of multifocal and multicentric disease.

While concern has been raised over the fact that the interpretation of combination DM/DBT studies takes approximately two times that of DM-only cases, the dramatic improvement in screening outcomes and diagnostic mammography workflow can partially counter this effect. Implementation of DBT imaging has resulted in changes in the workflow in breast imaging departments due to expedited work-ups, increased throughput of patients which allow the potential for additional patient centered service with online reading and the immediate delivery of both screening and diagnostic imaging results. It is important to note, however, that when implementing large volume DBT imaging, a radiology department should anticipate significantly increased storage requirement for the large DBT data files. Recent advances have been made to not only standardize the storage format across vendors but to also improve the data compression techniques for the DBT data to reduce storage demands.

In summary, DBT imaging has had a dramatic impact on the delivery of screening and diagnostic breast imaging in just the 5 years since FDA approval. The innovative technology should no longer be considered as "investigational" but rather viewed as the new, "better mammogram". In addition, the tomosynthesis platform continues to evolve with continued improvements in image quality, x-ray dose reduction and the development of navigational tools to help improve reading efficiency. As with any newly implemented technology, longer



term DBT outcomes and evolving data from ongoing trials will help to further clarify the role of DBT imaging in optimizing patient outcomes in both screening and diagnostic breast imaging.



Table 1. Comparison of outcomes in screening with digital mammography combined with tomosynthesis (DBT) compared to digital mammography alone (DM).

Reference	Study Type, Age of Patients and additional Comments	Number of Screening Examinations	Recall Rate	Change in Cancer detection rate/1000 women screened from DM to DBT screening (absolute change as well as percent change)
Skaane (Radiology 2013)	Prospective single site, multiple arms with multiple independent reads of same patients. Age: 50-69 years old Comments: Patients underwent both DM and DBT. Each arm interpreted by different radiologist with arbitration for positive studies, some patients included were symptomatic (i.e., lumps, discharge)	12,631 women	DM: 6.1% DBT: 5.3% (15% decrease)	DM: 6.1 DBT: 8.0 (increase of 1.9 cancers per 1000 screened; 31% increase)
Ciatto (Lancet 2013)	Prospective study at 2 sites. Age: 48 years and over	7292 women	DM: 5.0% DBT: 4.3%	DM: 5.3 DBT: 8.1



	Comments: Patients underwent both DM and DBT. Consecutive reads of DM then DM plus DBT also double reading and so difficult to assess for false negative DM rate		(17.2% decrease in conditional recall)	(increase of 2.8 cancers per 1000 screened; 53% increase)
Haas (Radiology 2013)	Observational study at network sites. Age: all patients presenting for screening Comments: Potential for bias since concurrent DM screening. No follow-up data for false negatives	DM: 7058 DBT: 6100	DM: 12.0% DBT: 8.4% (30% decrease)	DM: 5.2 DBT: 5.7 (increase of 0.5 cancers per 1000 screened; 9.6% increase)
Rose* (AJR 2013)	Observational study at single site. Age: all patients presenting for screening Comments: Potential for bias since concurrent DM screening. No follow-up data for false negatives	DM: 13,856 DBT: 9,499	DM: 8.7% DBT: 5.5% (37% decrease)	DM: 4.0 DBT: 5.4 (increase of 1.4 cancers per 1000 screened; 35% increase)
Greenberg* (AJR 2014)	Observational study at network sites. Age: all patients presenting for screening Comments: Potential for bias since concurrent DM screening. No follow-up	DM: 38,674 DBT: 20,943	DM: DBT: (16.1%	DM: 4.9 DBT: 6.3 (increase of 1.4 cancers per 1000 screened; 28.6%



	data for false negatives		decrease)	increase)
Friedewald* (JAMA 2014)	Observational, 13 U.S. sites combine MQSA outcome data. Age: all patients presenting for screening Comments: Potential for bias since concurrent DM screening. Also used historic DM for comparison. No patient level data or follow-up data for false negatives	DM: 281,187 DBT: 173,663	DM: 10.7% DBT: 9.1% (15% decrease)	DM: 4.2 DBT: 5.4 (increase of 1.2 cancers per 1000 screening; 29% increase)
McCarthy* (JNCI 2014)	Observational study at single site. Age: all patients presenting for screening Comments: Complete conversion to DBT with historic DM comparison. No follow-up data for false negatives.	DM: 10,729 DBT: 15,571	DM: 10.4% DBT: 8.8% (15% decrease)	DM: 4.6 DBT: 5.8 (increase of 1.2 cancers per 1000 screened; 26% increase)
Lorenco (Radiology)	Observational study at single site. Age: all patients presenting for screening	DM: 12,577 DBT: 12,921	DM: 9.3% DBT: 6.4%	DM: 5.4 DBT: 4.6



2015)	Comments: Complete conversion to DBT with historic DM comparison. No follow-up data for false negatives		(31% decrease)	(*cancer detection decreased by 0.8 cancers per 1000 screened; 17% decrease)
Durand* (Radiology 2015)	Observational study at network sites. Age: all patients presenting for screening Comments: Potential for bias since concurrent DM screening. No follow-up data for false negatives	DM: 9,364 DBT: 8,591	DM: 12.3% DBT: 7.8% (36.6% decrease)	DM: 5.7 DBT: 5.9 (increase of 0.2 cancers per 1000 screened; 3.5% increase)
Conant* (BCR&T 2016)	Observational, multi-site. Patient level data with follow-up for false negative assessment. Age: all patients presenting for screening Comments: Potential for bias since concurrent DM screening.	DM: 142,882 DBT: 55,998	DM: 10.4% DBT: 8.7% (16% decrease; however, when adjusted for patient level factors, recall reduction was	DM: 4.4 DBT: 5.9 (increase of 1.5 cancers per 1000 screened; 34% increase). Also trend in decreased false negatives; 0.06 to 0.46/1000 for DM vs. DBT,



			21%)	n.s.)
Range			Range of 9-37% decrease in recall	Range from a reduction of 0.2 to an increase of 2.8 cancers per 1000 screened Or, a 17% decrease to 53% increase in overall cancer detection rate

*Trials which contain a degree of overlap of patient populations also reported in Friedewald et al⁷



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