Original Article

Impact of Addition of Digital Breast Tomosynthesis to Digital Mammography in Lesion Characterization in Breast Cancer Patients

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Abstract

Context: Digital breast tomosynthesis (DBT) is a new development in mammography technology which reduces the effect of overlapping tissue. **Aims:** The aim is to interrogate whether addition of DBT to digital mammography (DM) helps in better characterization of mammographic abnormalities in breast cancer patients in general and in different breast compositions. **Settings and Design:** Retrospective, analytical cross-sectional study. **Subjects and Methods:** Mammographic findings in 164 patients with 170 pathologically proven lesions were evaluated by using first DM alone and thereafter with addition of DBT to DM. The perceived utility of adjunct DBT was scored using a rating of 0–2. A score of 0 indicating that DM plus DBT was comparable to DM alone, 1 indicating that DM plus DBT was slightly better, and 2 indicating that DM plus DBT was definitely better. **Statistical Analysis:** McNemar Chi-squares test, Fisher's exact test. **Results:** On DM, 149 lesions were characterized mass with or without calcifications, 18 asymmetries with or without calcifications, 2 as architectural distortion, and 1 as microcalcification alone. Adjunct DBT helped in better morphological characterization of 17 lesions, with revelation of underlying masses in 16 asymmetries and one architectural distortion. Adjunct DBT was perceived to be slightly better than DM alone in 44.7% lesions, and definitely better in 22.9% lesions. Lesions showing score 1 or 2 improvement were significantly higher in heterogeneously and extremely dense breasts ($P < 0.001$). **Conclusions:** Adjunct DBT improves morphological characterization of lesions in patients with breast cancer. It highlights more suspicious features of lesions that indicate the presence of cancer, particularly in dense breasts.

Keywords: *Breast cancer, digital breast tomosynthesis, digital mammography, mammography*

Introduction

Mammography is the most widely used imaging modality for detection and characterization of breast lesions. Breast cancer may present as mass, calcifications, architectural distortion, or asymmetry on mammography. However, the risk of cancer (positive predictive value) associated with different morphological types varies. Asymmetry is associated with lower likelihood of cancer in screening examinations than are masses, calcifications, and architectural distortion.[1] Similarly, characterization of lesion margin is also very important as spiculated margins are highly suggestive of malignancy.[2] Identifying findings with very high- or low-positive predictive values may lead to improved mammographic accuracy and better assignment of Breast Imaging Reporting and Data System (BI-RADS) category. However, an important limitation of mammography is the masking of cancers in the dense parenchyma.[3]

Digital breast tomosynthesis (DBT) is a recent addition to the equipment used for digital mammography (DM) in which the X-ray tube moves in an arc during the examination and acquires a series of low-dose two-dimensional projections.[4] The projection images obtained are reconstructed into thin slices of 1 mm thickness each, which minimizes the effect of overlapping tissue and helps in detection of subtle abnormalities. Previous studies in the diagnostic environment have concluded that adjunct DBT is particularly useful for noncalcified lesions, including asymmetries and better delineates lesion margins as compared to DM alone.[5] Roth *et al*. also made similar observations and found adjunct DBT useful as a problem-solving tool.[6] They suggest that DBT could reduce the need for additional views due to its improved capability of

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analyzing lesion margins, as well as better triangulation of lesions seen on one view only.

In India, screening for breast cancer is not common place. Indian patients with breast cancer tend to be young and often present with large tumors.[7] Due to the delayed presentation, most breast cancer patients have abnormalities evident on DM images itself. Whether the addition of DBT, a technique developed for detection of early breast lesions, has any role in patients with symptomatic breast disease remains unclear. Asian women tend to have denser breasts, DBT is a promising tool as it improves characterization of lesions in nonfatty breasts.[3,8] We, therefore, decided to interrogate whether the addition of DBT improves the characterization of lesions in breast cancer patients.

Subjects and Methods

We conducted a retrospective study on women who had been diagnosed with invasive breast carcinoma, to assess the mammographic characteristics of lesions on DM, and the impact of the addition of DBT to DM on the characterization of breast lesions. This study was reviewed by the institutional ethics committee, which waived the requirement of informed consent.

Study subjects

Review of records from the Department of Pathology at our institution during the period from October 2013 to September 2014 identified 289 women with breast cancer. Pre-treatment mammograms were available for review in 164 breast cancer patients, among whom 128 had histological, and 36 had a cytological diagnosis.

Mammography - image acquisition protocol

Bilateral mammograms had been performed on Selenia dimensions mammographic system (Hologic, USA) using "combo-mode" in cranio-caudal and mediolateral oblique projections, acquiring a traditional DM and a DBT scan during the same breast compression. The total time taken for acquisition of DBT view on each side was approximately 3 s and mean radiation dose for single breast view in combo-mode was about 1.45 mGy. The images were reviewed using a mammographic workstation (Hologic Inc., Securview) that included two Barco 5.0-megapixel monitors.

Mammogram analysis

Mammograms were evaluated according to the American College of Radiology Breast Imaging Reporting and Data System lexicon.[9] In each case, bilateral scans were jointly reviewed by two radiologists with 7 and 10 years' experience in breast imaging. Obviously benign looking lesions such as small intra-mammary nodes and benign calcifications were not recorded.

In the first session, lesion number, location, morphological type, and margins were recorded along with breast composition on DM alone. In cases with multiple lesions or bilateral disease, each lesion was assessed separately. The overall breast composition was categorized as predominantly fatty, scattered fibro-glandular, heterogeneously dense and extremely dense, respectively. In the second session lesion number, location, morphological type, and margins were recorded after addition of DBT to DM. In addition to the above assessment, the observers also scored the perceived utility of addition of DBT to DM using a subjective DBT rating. Impact of adjunct DBT was scored as 0, if DM plus DBT was comparable to DM alone. Score 1 indicated that DM plus DBT was slightly better than DM alone. Score 2 indicated that DM plus DBT was definitely better than DM alone, perceived as significant improvement in lesion visibility, or change in morphological type or margins,

Statistical analysis

Lesions without pathological confirmation were excluded from statistical analysis**.** Comparisons in proportions of the lesions among the groups (no change, slightly better, and definitely better) have been performed using Chi-square test. To test the improvement in morphological/margin characterization of lesions by DM plus DBT method over DM alone, McNemar Chi-squares test have been used. A two-sided or one-sided $P < 0.05$ has been considered to be statistically significant. Fisher's exact test was used to assess association between DBT rating groups and different breast compositions. Statistical package for social sciences version 22 (SPSS-22, IBM, Chicago, USA) have been used to analyze the data.

Results

Mean age of study subjects was 49.0 ± 11.6 years, ranging from 25 to 82 years. Largest age-group in our patient population was 41–60 years (59.4%). Of the 164 women, predominantly fatty, scattered fibro-glandular, heterogeneously dense, and extremely dense breasts were found in 38, 51, 63, and 12 women, respectively.

In 164 patients, DM identified 181 lesions, whereas DM plus DBT identified 185 lesions. A total of 162 patients had single breast involvement, whereas 2 had bilateral disease. Pathological diagnosis of all lesions was not available in many cases of multi-focal/multi-centric involvement, as treatment was initiated on the basis of histopathology/cytological proof from the index lesion only. The 4 additional lesions which were only detected after addition of DBT to DM were not pathologically proven. Thus, 170 lesions had proven diagnosis.

The largest dimension of the lesion was ≤20 mm in 20 (11.8%), 21–50 mm in 91 (53.5%) and more than 50 mm in 59 (34.7%) lesions. In this study, out of 170 lesions, 32.4% had no change observed, 44.7% some change and 22.9% were perceived definitely better after addition of DBT as compared to r DM alone. Chi-square test revealed that there was a significant difference in proportions of the

lesions among three DBT groups (P = 0.002, two-sided). Based on mammographic features on DM alone, 87 of 170 lesions were characterized as masses, 62 as masses with calcifications, 5 as asymmetry, 13 as asymmetry with calcification, 2 as architectural distortion, and 1 as microcalcification alone. After addition of DBT to DM, these lesions were categorized as masses in 92, masses with calcifications in 74, asymmetry in 1, asymmetry with calcification in 1, architectural distortion in 1, and microcalcification alone in 1 patient. McNemar's Chi-square test revealed that difference in proportions in masses (with and without calcification) detected by DM alone and DM plus DBT was statistically significant (87.6% vs. 97.6%, $P < 0.001$, one-sided). Impact of adjunct DBT on the morphological characterization of lesions is shown in Figure 1.

Asymmetries formed the second largest group of abnormalities (18/170, 10.6%) if only DM findings are considered; on the addition of DBT, underlying masses were revealed in 16 (88.9%) of 18 such lesions [Figure 2].

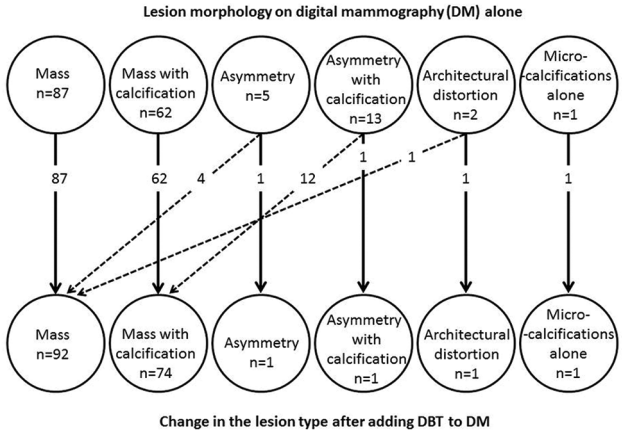

Figure 1: Impact of digital breast tomosynthesis on morphological characterization of 170 pathologically proven lesions in 164 breast carcinoma patients

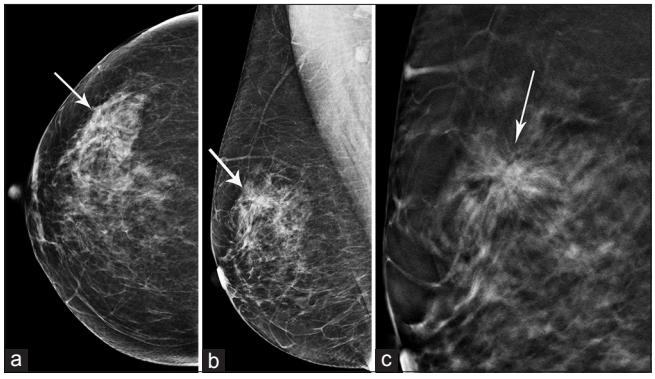

Figure 3: (a-c) A 48-year-old woman presenting with a vague right breast lump. Right cranio-caudal (a) and medio-lateral oblique (b) views showing architectural distortion (arrow) in upper outer quadrant.(c) Digital breast tomosynthes image (Magnified) of right medio-lateral oblique view of corresponding region revealing an underlying mass (arrow)

In one case seen as architectural distortion on DM, the addition of DBT revealed a spiculated mass [Figure 3]. Hence, adjunct DBT changed the characterization of lesions (morphological type) in 17 of the 170 lesions.

Adjunct DBT was able to demonstrate mass margins more clearly as compared to DM alone [Figure 4]. Of the 48 mass lesions with indistinct margins on DM, 10 were found to be micro-lobulated and 18 as having spiculated margins on the addition of DBT. Of the 8 circumscribed masses on DM, 2 showed indistinct margins on DBT. Among 21 non-mass lesions (asymmetry, architectural distortion, and microcalcifications) described on DM alone, 17 revealed mass on the addition of DBT; 5 with indistinct, 1 with micro-lobulated and 11 with spiculated

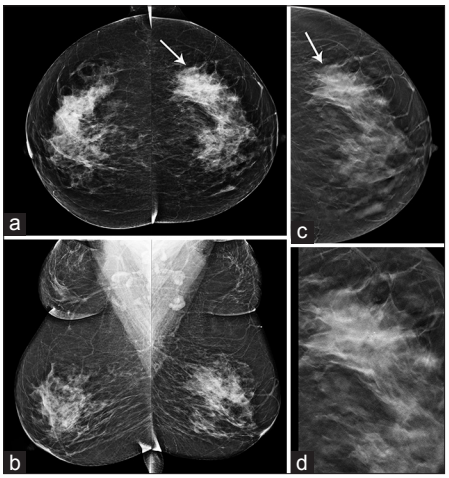

Figure 2: (a-d) A 50-year-old woman presented with left breast lump. Bilateral cranio-caudal (a) and medio-lateral oblique (b) digital mammography views showing heterogeneously-dense parenchyma with focal asymmetry with calcifications in left upper-outer quadrant (arrow). In cranio-caudal digital breast tomosynthesis view (c), left breast reveals a dense, irregular mass with fine pleomorphic calcifications (arrow). Magnified image of digital breast tomosynthesis view (d)

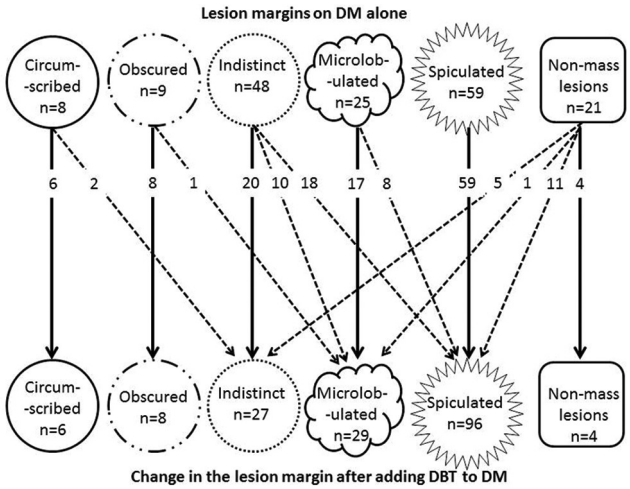

Figure 4: Impact of adjunct digital breast tomosynthesis on margin characterization of 170 pathologically proven lesions in 164 breast carcinoma patients. Nonmass lesions include asymmetry, asymmetry with calcification, architectural distortion and microcalcifications alone

margins. McNemar's Chi-square test revealed that difference in proportions in spiculated margins detected on DM alone and DM plus DBT was statistically significant (34.7% vs. 56.5%, $P < 0.001$, one-sided).

Fisher's exact test indicated that there was a significant difference in proportions of DBT rating among different breast compositions ($P < 0.001$) [Table 1]. A high proportion of lesions showed DBT rating score of 1 or 2 in heterogeneously dense (54/66; 81.8%) and extremely dense breasts (9/12; 75%) as compared to predominantly fatty (16/39; 41.0%) and scattered fibroglandular parenchyma (36/53; 67.9%).

Discussion

Mammography is the only screening tool which has been shown in randomized controlled trials to confer a survival benefit.[3,10,11] Whereas it is 80% sensitive in fatty breasts, its sensitivity falls as low as 30% in dense breasts.[12] The inherent limitation of DM is tissue superimposition which may obscure a lesion or mimic a lesion, a phenomenon that is more likely in denser breasts. Several studies have shown that adjunct DBT, through a reduction in tissue superimposition, is useful in both screening and diagnostic practice.[6,13]

Nearly half of our patients had heterogeneously or extremely dense breasts. This would be expected since 60.3% of our patients were below 50 years of age. This is comparable to data from Breast Cancer Surveillance Consortium in which approximately 55%–60% of patients had dense breasts.[14] More than half of the lesions (53.5%) were 2–5 cm in size and a significant proportion (34.7%) of lesions were larger than 5 cm. This is due to late presentation and lack of routine screening in our population. Based on combined DM and DBT findings, most of our patients (97.6%) had mass-related lesions, whereas only1.2% had asymmetries, 0.6% had architectural distortion, and 0.6% micro-calcifications alone. This is different from other studies where the proportion of masses, asymmetries and calcifications are more uniformly distributed.[5]

Malignancies can be found in 0%–14% of asymmetries on breast tissue biopsies; hence, these groups of mammographic findings pose an imaging challenge.[5] Asymmetries formed the second largest group 18/170 (10.6%) of abnormalities in our study if only DM findings are considered. Underlying masses were revealed in a significant number (16/18, 88.9%) of asymmetries on adding DBT, thus increasing lesion conspicuity and confidence of reporting. The TOMMY trial in the UK has demonstrated higher sensitivity of DM plus DBT over DM (92% vs. 89%) where the dominant radiological feature is mass.[15] Poplack *et al*. suggested that DBT is superior to diagnostic mammography, especially in case of masses.[16]

In our study, DBT was able to reveal more suspicious features in mass lesions, due to better characterization of lesion margins. Among 21 nonmass lesions described on DM, 11/21 (52.4%) revealed masses with spiculated margins on DBT. Of the 48 mass lesions with indistinct margins on DM, 10/48 (20.8%) revealed micro-lobulated margins, and 18/48 (37.5%) revealed spiculated margins on DBT. Andersson *et al*. showed that cancer visibility was superior on DBT compared to DM, and significant number of lesions were upgraded as per BI-RADS classification when DBT was compared with one view or two view diagnostic mammography.[17]

Adjunct DBT found superior rating (score 1, 2) in 67.6% lesions in our study. Comparable results were obtained by Hakim *et al*., who found DBT to be superior to diagnostic mammography in 50% of cases.[18] In the study by Yang *et al*., 58.8% of mass lesions had a superior rating on DBT versus DM alone.[5] In our study, 45.7% of patients had heterogeneously or extremely dense breasts, and in these patients adjunct, DBT showed higher rating (score 1 or 2) in 81.8% and 75% lesions, respectively. A direct relationship was demonstrated between higher DBT score and breast density. This finding is corroborative to study by Mun *et al*.[19]

The major limitation of our study is that sensitivity or specificity of adjunct DBT could not be evaluated since only pathologically proven malignancies were included. We evaluated the role of adjunct DBT in the diagnostic environment; however, our "diagnostic environment" is not comparable to developed countries where most diagnostic mammograms are performed as recalls from abnormal screening. In our study, almost all patients had palpable lesions or other symptoms, whereas in the study by Yang *et al*., 29/59 (52%) patients were asymptomatic.[5]

The controversy raised by this study are, that if lesions are at least partially visible on DM, what is the utility of adjunct DBT. However, it is a known fact that some palpable breast lesions have inflammatory etiology, especially in developing countries; and revelation of underlying microlobulated or spiculated mass in such cases is an important clue for making the correct decision. In a review article on breast tuberculosis by Tewari and Shukla, the authors stated that "mammogram in breast

Table 1: Subjective digital breast tomosynthesis rating of 170 lesions in different breast compositions

Association between DBT rating and breast composition				
Breast composition	**No change (0)**	**Slightly better (1)**	**Definitely better (2)**	**Total**
Predominantly fatty	23	13	3	39
Scattered fibro-glandular	17	28	8	53
Heterogeneously dense	12	29	25	66
Extremely dense	3	6	3	12
Total	55	76	39	170

Fisher's exact test: $P<0.001$. DBT: Digital breast tomosynthesis

tuberculosis is of limited value as the findings are often indistinguishable from carcinoma breast."[20] Although this is an old review (2004) based on findings on conventional mammograms, the application of DBT to evaluate such cases could be a direction for future research.

Conclusion

Adjunct DBT is useful for improving characterization of malignant breast lesions. It highlights more suspicious characters of the lesion thus increasing the confidence of reporting. It is more useful in patients with dense breasts compared to fatty breasts.

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Conflicts of interest

There are no conflicts of interest.

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