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RESEARCH ARTICLE

Digital breast tomosynthesis for early detection of malignant breast microcalcification: A hospital-based cross-sectional study

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ABSTRACT

Background: Breast cancer is the leading cause of cancer-related deaths in women. Early detection by screening is crucial for improved survival. Digital breast tomosynthesis (DBT) may offer better visibility than conventional screening. This study aims to assess the diagnostic accuracy of DBT in detecting malignant breast microcalcifications compared to histopathological findings.

Methods: This cross-sectional study was done at the Department of Radiology and Imaging, Bangabandhu Sheikh Mujib Medical University, Dhaka, from July 2022 to June 2023 and enrolled 35 women suspected of having breast cancer. Each patient underwent DBT and histopathology tests. The diagnostic accuracy of DBT in detecting malignant breast microcalcifications was assessed compared to the gold standard of histopathology.

Results: The average age of the participants was 48.6 years. Palpable breast lumps (91.4%) were the most common clinical presentation. Among them, 80% had malignant microcalcifications diagnosed by DBT, primarily with linear (40.0%) and segmental (28.6%) distribution. Histopathology identified 80% of cases as malignant, with ductal carcinoma in situ (34.3%) being the most prevalent type. DBT demonstrated high sensitivity (100%) and specificity (85.7%) in detecting malignant microcalcifications, resulting in an overall accuracy of 97.1%.

Conclusions: DBT has high diagnostic accuracy for detecting malignant breast microcalcifications and can be considered a valid tool for the early detection of breast microcalcifications, particularly in the context of diagnosing breast cancer.

Keywords: *breast cancer, digital breast tomosynthesis, microcalcification, accuracy*

INTRODUCTION

Worldwide, breast cancer is the fourth leading cause of cancer mortality in women, with an estimated 2.3 million new cases and 666,000 deaths in 2022.[1] In Bangladesh, 12,989 new cases of breast cancer were diagnosed, and 6,162 deaths were reported in 2022. The 5-year prevalence rate of breast cancer is estimated at 42.4 per 100,000.[2] However, women of reproductive age (15-49) are particularly vulnerable, with an incidence rate of 19.3 per 100,000.[3] Furthermore, nearly 90% of breast cancer cases in Bangladesh are diagnosed at advanced stages (III-IV), which is concerning and increasingly common.[4]

Early detection of breast cancer is crucial, as it can increase the potential survival rate by up to 100% for stage I diagnoses, compared to 24% for stage IV cases after 8 years.[5] For this reason, effective screening methods are of paramount importance. Digital breast tomosynthesis (DBT) is an innovative imaging technology that utilises varied projection angles to reconstruct three-dimensional (3D) images. This technology improves detection in dense glandular tissue, offering detailed lesion visualisation and increasing the accuracy of breast cancer diagnosis.[6] DBT may reveal more cancers that would otherwise go undetected during traditional screenings.[7] Despite

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HIGHLIGHTS

1. Digital breast tomosynthesis can be a valuable screening tool for breast cancer detection due to its ability to differentiate between benign and malignant microcalcifications.
2. Given the uncertainty of certain breast lesions, it is essential to examine whether it (digital breast tomosynthesis) can improve the diagnosis of breast cancer.
3. Digital breast tomosynthesis demonstrated high diagnostic accuracy in detecting malignant breast microcalcifications in this hospital-based study.

limitations, such as challenges in visualising lesions dominated by calcifications,[8] recent advancements in DBT have improved the visualisation of calcifications, reducing the likelihood of missing malignant calcifications during screening.[9]

DBT uses a quasi-three-dimensional (3D) technique, reducing blur for structures in the focal plane,[7] and producing a series of images that helps radiologists navigate through the breast parenchyma and make lesions more noticeable.[10] DBT's radiation hazard is nearly half that of the DBT plus full-field digital mammography (FFDM) screening protocol.[11] Moreover, examination time is diminished as FFDM acquisition time is no longer necessary.[9] Several studies have demonstrated the superior image quality of DBT in characterising masses and asymmetry, reducing recall rates, and enhancing efficiency in cancer detection.[12, 13, 14] Its superiority in detecting microcalcifications related to malignancy has been claimed. However, a consensus has yet to be reached.[15, 16]

Given the lack of consensus regarding the characterisation and detection of microcalcifications using DBT, this study aimed to examine the accuracy of DBT in detecting breast microcalcifications compared to the current gold standard of histopathology.

METHODS

Study design and population

This cross-sectional study was conducted from July 2022 to June 2023. During this period, 45 eligible female patients with breast lesions visited the Department of Radiology and Imaging of Bangabandhu Sheikh Mujib Medical University (BSMMU) for the DBT procedure. Patients were selected through convenience sampling based on predefined criteria: females aged 18 or older, presenting with breast lumps or signs of malignancy, willing to undergo DBT and biopsy, and providing consent. Out of 45 eligible patients, six did not give consent, three were excluded because the clinician did not recommend a histopathology test, and one was excluded due to pregnancy. After these exclusions, the final sample consisted of 35 patients.

This study aimed to detect all malignant microcalcifications without missing any, thus the sample size calculation was based on sensitivity using Buderer's formula. Based on expected sensitivity of 92%, an expected specificity of 71%, and a 50% assumed prevalence with 10% precision, the estimated sample size was 57. However, we could recruit only 35 patients for this study.

Informed written consent was obtained from each participant after explaining the study's aims, procedures, risks, and benefits, while assuring strict confidentiality and anonymity. Participants had the right to withdraw at any stage of the study. Proper confidentiality was maintained by coding the research data, storing it securely, and restricting access to authorized personnel, with each patient assigned a unique ID number for anonymity.

Demographic, clinical, and previous laboratory and imaging data were collected from the participants. DBT and biopsy procedures were conducted in the Radiology and Imaging, and Pathology departments at BSMMU. After assessing microcalcifications through DBT, patients underwent biopsy either with DBT or ultrasound guidance, depending on visibility.

DBT Scanning technique

Image acquisition: DBT examinations were performed using a FUJIFILM Digital Mammography System (FDR MS-3500) with 3D-DBT technology. All patients underwent DBT in Craniocaudal (CC) and Mediolateral oblique (MLO) projections, carried out by registered radiologic technologists experienced in mammography to ensure accuracy and consistency. Each breast was carefully compressed and positioned for the procedure.

The 3D-DBT technique involved capturing 15 low-dose projection images, with a 0° scan angle for CC and 45° for MLO. These 2D projections were then reconstructed into 1 mm slices, forming a 3D image of the breast. The images were displayed on liquid-crystal display (LCD) screens for interpretation. Additional views were unnecessary, as digital image processing allowed for zooming, contrast adjustment, brightness control, inversion, and other techniques to enhance lesion detection. Standardization of image acquisition across various patients and technologists was achieved through the DBT machine's built-in settings, which automatically regulated imaging variables like exposure, positioning, and compression, thus reducing operator variability. Patient variability, primarily due to differences in breast composition, was minimised by applying the appropriate compression tailored to each patient's breast type.

Image analysis: The DBT images were transferred to the workstation for evaluation. Two radiologists (SS, RP) with 3-5 years of breast imaging experience independently reviewed them. A third radiologist (MSS), with over 10 years of experience, further examined the images to minimize bias. All radiologists were blinded to clinical data and pathology results. Various DBT features were individually assessed, including breast density, lesion size, type (mass or focal asymmetry), characteristics (shape, margin, and density), calcifications (morphology and distribution), and any other suspicious abnormalities.

The probability of malignancy for DBT findings was classified using the American College of Radiology Breast Imaging Reporting and Data System (BI-RADS) score,[17] which includes the following categories: a) BI-RADS 1, indicating a negative result; b) BI-RADS 2, denoting a benign finding; c) BI-RADS 3, suggesting a probably benign condition; d) BI-RADS 4, indicating a suspicious abnormality; and e) BI-RADS 5, highly suggestive of malignancy.

Breast density was assessed by the American College of Radiology (ACR) BI-RADS scale,[18] with four categories: Type A: The breasts are almost entirely fatty; Type B: There are scattered areas of fibroglandular density; Type C: The breasts are heterogeneously dense, which may obscure small masses; and Type D: The breasts are extremely dense, which lowers the sensitivity of mammography. The results of DBT for each patient were compared in terms of main radiological features, BI-RADS classification, and diagnostic performance.

Histopathology as the reference standard

The definitive diagnosis was established through histopathologic findings after examination of ultrasonography-guided biopsy (n=20) and DBT-guided biopsy (n=15). Two experienced pathologists reviewed all specimens and reached a consensus. In case of disagreement, they re-examined the slides together, considering clinical history, imaging, and laboratory results to ensure accurate diagnoses.

Statistical Analysis

Frequencies and percentages were presented for all categorical variables. The diagnostic performance of DBT for detecting malignant microcalcifications in the breast was assessed using a 2x2 contingency table analysis for sensitivity, specificity, and accuracy of DBT in detecting malignant microcalcification. Accuracy was calculated as the sum of true positives and true negatives divided by all subjects. Corresponding 95% confidence intervals were calculated for the sensitivity, specificity, and accuracy of the DBT test. The data were analysed using SPSS software version 23.0.

RESULTS

A total of 35 female patients were included in the study, ranging from 37 years to 72 years (mean age 48.6 ± 7.2). Among the patients, 20 (57.1%) were from urban areas, and 15 (42.9%) came from rural areas. The most common marital status was married, reported by 27 patients (77.1%). In terms of education, 19 patients (54.3%) had a primary level or lower, while 11 (31.4%) had completed secondary or higher secondary education. The most common occupation among the patients was housewife, reported by 26 patients (74.3%) **(TABLE 1)**.

Common clinical presentations included palpable lumps (91.4%) and breast pain (37.1%). Hypertension and diabetes mellitus were present in 51.4% and 37.1% of patients, respectively **(TABLE 2)**.

TABLE 1 Socio-demographic characteristics of the study participants (n=35)

Variables	Frequency	Percentages
Location		
Urban	20	57.1
Rural	15	42.9
Marital status		
Currently married	27	77.1
Widowed	6	17.1
Divorced	2	5.7
Level of education		
Up to primary	19	54.3
Secondary and higher secondary	11	31.4
Graduate	5	14.3
Occupational status		
Home maker	26	74.3
Manual labourer	6	17.1
Others	3	8.6

DBT findings revealed that type B was the most common breast composition type, present in 30 (85.7%) patients. Microcalcification was found in 80% of the cases. The distribution mostly showed a linear pattern in 14 (40%) patients, followed by a segmental pattern in 10 (28.6%) patients. Among the calcification, DBT detected 29 (82.9%) cases of a malignant nature and 6 (17.1%) cases of a benign nature **(TABLE 3)**.

TABLE 2 Clinical findings of the study participants (n=35)

Variables	Frequency	Percentages
Involving breast		
Right breast	18	51.4
Left breast	17	48.6
Clinical presentation		
Palpable lump	32	91.4
Pain in the breast	13	37.1
Nipple discharge	7	20.0
Overlying skin thickening	5	14.3
Retracted nipple(s)	5	14.3
Comorbid conditions		
Hypertension	18	51.4
Diabetes mellitus	13	37.1
Ischemic heart diseases	3	8.6
Menstrual status		
Premenopausal	19	54.3
Post-menopausal	16	45.7
H/O previous breast cancer	2	5.7
H/O breast cancer in the family	9	25.7
H/O other malignancy in the family	2	5.7

H/O indicates history of

Histopathology findings revealed that 28 (80%) patients had malignant and 7 (20%) had benign calcification. The most frequent malignant lesion was ductal carcinoma in situ presented in 12 (34.3%) patients, followed by infiltrating ductal carcinoma in 8 (22.9%) patients. The most common benign lesion was fibroadenoma in 3 (8.6%) patients **(TABLE 4)**. The breast calcification was characterised based on the BI-RADS category. BI-RADS 3 or below were considered benign, while BI-RADS 4 and above denoted malignant calcification.

DBT successfully diagnosed all cases of BI-RADS 3 as benign and BI-RADS 5 as malignant calcification. However, it falsely diagnosed one case as BI-RADS 4 of a malignant nature, which in reality was of a benign nature. Overall, DBT had 100% sensitivity and 85.7% specificity for diagnosing malignant microcalcification of the breast, considering BI-RADS 4 and 5 as suggestive of malignancy, with an overall accuracy of 97.1% **(TABLE 5)**.

DISCUSSION

The DBT represents an advancing technology that can potentially enhance the detection and characterisation of breast lesions. While DBT is anticipated to address certain limitations inherent in mammography, the available data on its efficacy in a diagnostic context remains limited.[6, 7, 15, 16] This study demonstrated that DBT has a high accuracy in detecting malignant breast microcalcifications, highlighting its effectiveness as a critical tool in breast cancer detection.

The study participants exhibited a broad age range consistent with findings from several earlier studies, by Teertstra *et al.*, Byun *et al.* Roganovic *et al.* and Chowdhury *et al.*, which indicated that breast cancer can manifest in women of various ages, with a higher likelihood in later stages.[12, 15, 19, 20] Most participants in our study had primary or below level education, aligning with findings from Begum *et al.* Limited educational attainment is often associated with a lack of awareness regarding breast cancer and preventive measures, which may contribute to delayed diagnosis.[21] Additionally, most patients were housewives, a trend similar to those reported by Chowdhury *et al.* and Begum *et al.* Being a homemaker may be linked to reduced access to healthcare services and delayed disease detection, leading to poorer health outcomes.[20, 21]

TABLE 3 DBT features of the breast lesions present in the study participants (n=35)

Features	Frequency	Percentages
Composition of breast		
Scattered areas of fibroglandular density (B)	30	85.7
Heterogeneously dense, which may obscure small masses (C)	5	14.3
Site of lesion		
Upper and outer quadrant	13	37.1
Upper and inner quadrant	9	25.7
Lower and outer quadrant	5	14.3
Lower and inner quadrant	3	8.6
Retro-areolar	5	14.3
Type of calcification		
Micro	28	80
Both (micro and macro)	7	20
Distribution of calcification		
Linear	14	40.0
Segmental	10	28.6
Grouped	7	20
Regional	3	8.6
Diffuse	1	2.9
Overlying skin condition		
Normal	23	65.7
Mild thickening	12	34.3
Nature of calcification		
Benign	6	17.1
Malignant	29	82.9

The key clinical presentations were palpable breast lumps and pain. Koo *et al*. found that palpable lumps were the most common presenting symptom in breast cancer, while breast pain and nipple abnormalities were notable among non-lump symptoms. Since non-lump symptoms often lead to delayed treatment, raising awareness about them is crucial for earlier breast cancer detection.[22]

This study identified microcalcifications in 80% of cases, with mostly linear and segmental distribution. Kuwabara *et al*. had highlighted the importance of calcification patterns in lesion characterization, noting a significant association between continuous segmental distribution and malignancy.[23] Breast calcifications can vary in appearance, with distinct morphological features often indicating their underlying causes.[24] Linear or segmental calcifications are considered high-risk and more likely malignant compared to clustered, moderately suspicious calcifications. However, benign types like vascular or thick linear calcifications can also exhibit linear patterns, highlighting the need to evaluate both morphology and distribution for accurate assessment.[25]

TABLE 4 Histopathological findings of the breast lesions present in the study participants (n=35)

Histopathology findings	Frequency	Percentages
Benign	7	20.0
Fibroadenoma	3	8.6
Benign phyllodes tumour	2	5.7
Granulomatous mastitis	1	2.9
Fibrocystic change	1	2.9
Malignant	28	80.0
Ductal carcinoma in situ	12	34.3
Infiltrating ductal carcinoma	8	22.9
Invasive ductal carcinoma	7	20.0
Invasive lobular carcinoma	1	2.9

In numerous cases, 2D mammography images can cause confusion regarding lesion distribution and the source of increased density, whether from breast tissue or calcifications.[23] DBT can clarify this by verifying the continuity of calcifications in depth and identifying the sources of density, thereby improving malignancy prediction, particularly for lesions with complex distribution.[7] **FIGURE 1** illustrates the DBT results for a female patient with type-c breast density and a palpable lump. Notable findings included soft tissue opacity with spiculated margins, segmental clustered microcalcifications, parenchymal distortion, and an enlarged axillary lymph node.

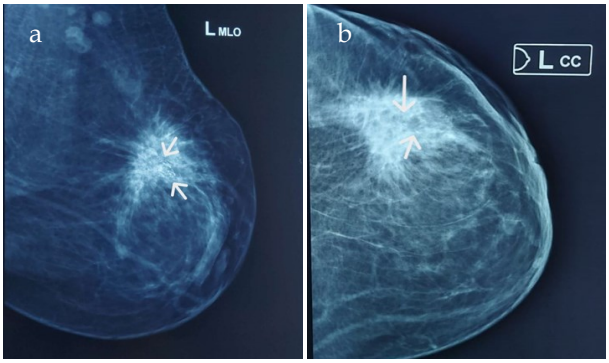

FIGURE 1 A 45-year-old woman presenting with a palpable lump in the left breast. (a) Mediolateral oblique and (b) craniocaudal DBT images reveal a type-c breast showing a soft tissue opacity with a spiculated margin in the upper and outer quadrant of the left breast. Multiple internal microcalcifications (arrow marks) are seen (Segmental, clustered) and distortion is present in the surrounding parenchyma.

The histopathological analysis revealed a predominance of malignant tumours, with ductal carcinoma in situ being the most common type. Salvatorelli *et al*. stated that ductal carcinoma in situ is frequently linked to microcalcifications and is thought to be a precursor to

TABLE 5 **Diagnostic accuracy of digital breast tomosynthesis (DBT) for detecting malignant breast microcalcifications compared to histopathological findings**

DBT	Histopathology		Total	Validity indices
	Malignant	Benign		(95% confidence interval)
Malignant	28 (a)	1 (b)	29	Sensitivity 1.0 (0.87 – 1.0)
Benign	0 (c)	6 (d)	6	Specificity 0.86 (0.49 – 0.97)
Total	28	7	35	Accuracy 0.97 (0.85 – 0.99)

*Sensitivity = a / (a + c), specificity = b / (b + d), accuracy = (a + d) / (a + d + b + c)

invasive breast cancer types.[26] Tumour cell invasion in ductal carcinoma in situ occurs during tumour growth and significantly affects patient prognosis. While conventional mammography struggles to evaluate this process solely through calcifications, DBT can identify increased density associated with overlapping clusters of calcifications.[23]

In our study, both USG-guided and DBT-guided techniques were used for biopsies, which could raise concerns about potential bias. Though USG is effective for palpable lesions, it struggles with non-palpable lesions or occult microcalcifications making representative tissue sampling difficult. In contrast, DBT-guided biopsy allows for precise visualization of these challenging lesions, leading to more accurate sampling. Combining both methods reduced bias and ensured optimal tissue collection, as relying solely on USG risks incomplete sampling. [27, 28]

In this study, DBT demonstrated a high accuracy of 97.1% in detecting malignant breast microcalcifications, with a sensitivity of 100% and a specificity of 85.7%, using BI-RADS 4 as the cut-off point. As the only premier postgraduate university hospital and cancer referral center in Bangladesh, Bangabandhu Sheikh Mujib Medical University attracts cancer patients from across the country.[29] Its exclusive use as the study's sample and a smaller sample size may have increased the proportion of malignant cases, contributing to the observed 100% sensitivity. Liu *et al.* reported a high sensitivity but moderate specificity of DBT for detecting malignant breast lesions.[30] Similarly, Seo *et al.* and Li *et al.* found DBT to exhibit high accuracy in characterising malignant calcifications. [31, 32]

In this study, one case initially classified as BI-RADS 4, suggesting malignancy, was later identified as a fibro cyst. This discrepancy may arise because fibro cysts can appear opaque on DBT imaging if they contain significant fibrous tissue, potentially confusing them with calcifications. Therefore, a critical analysis of influencing variables and a multidisciplinary approach are essential for improving diagnostic accuracy.

This study, conducted in a tertiary care hospital with a limited sample selection, may restrict the generalizability of our results. However, multiple studies and meta-analyses with broader demographics and population-level settings have consistently shown DBT's superior diagnostic performance in detecting early breast cancer.[33, 34]

This study has several limitations. Firstly, it did not address DBT's performance across different breast density categories due to the limited patient availability and imbalanced sample sizes. Additionally, the use of a convenience sampling method may introduce non-representative bias, and the small sample size limits the statistical power, affecting the generalizability of the results.

Conclusion

DBT plays a crucial role in accurately identifying microcalcifications in the breast. Its remarkable diagnostic accuracy and capability to differentiate between benign and malignant microcalcifications make DBT an important tool for early breast cancer detection. However, it is not recommended for population-level screening due to higher radiation exposure, longer procedural times, reduced patient comfort, and lack of availability at local levels. The results of this study are particularly relevant to tertiary hospital settings like BSMMU, where advanced diagnostic tools are accessible. Further research with a larger, more diverse sample size is needed to validate these findings.

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Author contributions

Conception and design: MSS, BB, SNS. *Acquisition, analysis, and interpretation of data:* MSS, PC. *Manuscript drafting and revising it critically:* MSS, BB, SNS, PC, SS, MS, AKS. *Approval of the final version of the manuscript:* MSS, BB, SNS, PC, SS, MS, AKS. *Guarantor of accuracy and integrity of the work:* MSS.

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Conflict of interest

We do not have any conflict of interest.

Ethical approval

Ethical clearance was obtained from the Institutional Review Board of BSMMU (Memo No.: BSMMU/2022/8946, dated 4 Sep 2022.

Data availability statement

We confirm that the data supporting the findings of the study will be shared upon reasonable request.

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