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A comparison of full-field digital mammography (FFDM) with digital breast tomosynthesis (DBT) in the detection of microcalcifications by correlating mammographic and pathologic findings

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Abstract

Introduction: Breast micro-calcifications primarily represent benign conditions; they might be regarded as the earliest presentations of malignancies. As a well-known procedure, full-field digital mammography (FFDM) is a 2-dimensional (2-D) imaging modality most frequently used in breast cancer screening. DBT, i.e., digital breast tomosynthesis, on the other hand, is a 3- 3-dimensional (3-D) modality increasingly attracting the attention of researchers in the field for clinical applications.

Objectives: The present study compares FFDM values against DBT technique data- considered a valuable means of screening breast cancers.

Patients and Methods: This is a cross-sectional study conducted on 92 suspected breast cancer patients who underwent screening assessments using both FFDM and DBT. The breast calcification and density categories were identified according to ACR BI-RADS (American College of Radiology Breast Imaging- Reporting and Data System). The calcifications were categorized as benign (BIRADS 2 and 3) or malignant (BIRADS 4 and 5). The histopathological findings from the biopsied lesions were considered the gold standard for breast cancer diagnosis. The outcomes of FFDM and DBT were compared.

Results: The total sensitivity of DBT in identifying benign versus malignant lesions was 96.7%. In the case of FFMD, the sensitivity value was 90.2%. On the other hand, both modalities revealed similar specificity, accounting for 8.7%. The area under the curve (AUC) accounted for 0.527 for DBT and 0.505 for FFDM. The overall agreement coefficient for the two radiologists in the identification of micro-calcifications accounted for 0.613 (95% CI: 0.394-0.823). This agreement coefficient for FFDM was 0.676 (95% CI: 0.412, 0.940), and the value for the DBT procedure was 0.517 (95% CI: 0.147, 0.887).

Conclusion: According to the current study, DBT can be considered a powerful tool in screening and diagnosing microcalcifications such as FFDM in breast tissue. Although the sensitivity of DBT is remarkably high, its specificity is not justifiable.

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Introduction

Breast calcification is a common manifestation in breast cancer screenings. Micro-calcifications mostly represent benign conditions. However, they might indicate an early sign of malignant disease (1). Therefore, precise characterizations should be applied considering the morphology and distribution of the micro-calcified tissues to stratify the lesions and facilitate decision-making for further follow-up (2). In this connection, the Breast Imaging-Reporting and Data System (BI-RADS) of the American College of Radiology (ACR) is widely applied to explain the morphology, distribution as well as breast calcifications categories e.g., commonly observed calcifications and types of calcifications having suspicious morphology (3,4). Nevertheless, certain micro-calcifications remain suspicious, particularly those sand-like micro-calcifications usually indicating malignant lesions (5). Hence, identifying suspicious lesions is critical and still a matter of debate.

Full-field digital mammography (FFDM)—as conventionally applied—is one of the most popular and widely employed procedures for screening and early diagnosis of breast cancer. The technique is a 2-dimensional (2-D) imaging modality (6). The FFDM procedure displays certain inevitably inexplicable constraints arising from its inability to precisely make a distinction between lesions being suspicious from those of contiguous

Key point

In this cross-sectional study involving 92 suspected breast cancer patients, the efficacy of FFDM and DBT in screening microcalcifications was evaluated. Microcalcifications are often benign but can signal early malignancies. DBT, a 3-dimensional imaging modality, gained attention for breast cancer screening. The study assessed calcification and density categories based on ACR BI-RADS, using histopathological findings as the gold standard. DBT demonstrated higher sensitivity (96.7%) in distinguishing benign and malignant lesions compared to FFDM (90.2%). Specificity was comparable (8.7%) between modalities, however, DBT showed lower overall agreement (0.517) than FFDM (0.676). The study concludes that while DBT is a potent tool for microcalcification screening, its specificity may raise concerns.

overlapping tissues (7). The inadequate sensitivity and high rates of false-positive cases in dense breast tissue are one of the critical shortcomings when FFDM is administered (2). As a modality, DBT or digital breast tomosynthesis is a 3-D imaging modality widely attracting the attention of researches for application in breast cancers screenings and assessments. The tendency to use DBT is attributed to its ability to surmount the limitations inherent in mammography, particularly superimposition of tissues resulting from multiple x-ray projection acquisitions as well as reconstruction of images having pseudo-tomographic natures (8,9). Regardless of optional technical parameters attached to each modality, the values of applying DBT in assessing masses, asymmetries and architectural distortions are adequately discussed and verified (10). Nevertheless, the evaluation of micro-calcifications by DBT has not been well-documented and elucidated (11). Numerous efforts have been made to compare the efficacy of DBT vis-à-vis FFDM in differentiating benign and malignant micro-calcifications. Indeed, the data in this regard is controversial. Some studies claim that DBT sensitivity in characterization of micro-calcified lesions is similar to that of FFDM (5,12). While others oppose this view and present arguments as to the superiority of either DBT or FFDM (13-15). Given this situation, the current study aims to compare these modalities in terms of detecting and characterizing micro-calcifications.

Objectives

Our study aims to compare the sensitivity and accuracy of FFDM with DBT in detecting suspicious microcalcifications by correlating mammographic and pathologic findings.

Patients and Methods

Participants of the study

The present study was conducted as a retrospective cross-sectional one on 92 patients—receiving breast examinations because of unnaturally suspicious masses. They required imaging for probable malignancy. These patients were referred to Ghasr-e-Nour imaging and radiology center as a private clinic offering DBT and FFDM imaging from March 2020 to May 2021.

The study included patients who both underwent DBT and FFDM examinations. Further, the pathological study of their biopsied tissues was available. Exclusion criteria were defined as those with typical manifestations of benign lesions in mammography, pregnancy, or lactating and having a history of breast surgery or breast treatment.

Imaging acquisition

The patients under study underwent DBT and FFMD imaging for both breasts in the craniocaudal and mediolateral oblique positions using a standard DBT system(Hologic Selenia Dimensions Mammography system manufactured in the USA). The following are the specifications of the imaging machines: Digital detector in size of 240 × 290 mm and pixel size of 70 mµ. With the help of standard imaging phantom in combo mode, i.e., DBT and FFDM, the mean doses for glandular radiation doses for FFDM, DBT, and combo mode in a single view- in the mentioned order-were approximately determined at 1.25, 1.65, and 2.90 mGy. DBT examinations were conducted right after the FFDM procedure in the same compression mode, i.e., combo mode applying AEC (automatic exposure control) performed by the same technician. Regarding the DBT procedure, simultaneous with the x-ray tube rotation through an arc of −7.5 to +7.5°, a sequence of low-dose 2-D images of 1 mm-thickness were acquired. This was carried out while the breast stayed in a fixed position compressed. Using an automatic technique of filtered back projections, the latter images were reconstructed in the form of a series of slices of one-millimeter thickness.

Analyzing images

Two radiologists who were experts at assessing breast imaging interpreted the images. These radiology specialists participated through the entire course of FFDM and DBT interpretations. The images were displayed in standard hanging protocols.

The images were assessed per breast and not per patient. The study was conducted double-blindly. Primarily, each radiologist interpreted FFDM images randomly while he/she was unaware of the patient's clinical information or the DBT images. The findings were assigned a BI-RADS category. Similarly, they interpreted DBTs randomly. To minimize the potential biases, the assessments of DBTs and FFDMs were executed at an interval of one month (16). Whenever the BI-RADS categories—occurring within an identical image modality—were a source of difference among the radiologists, a consensus was reached through holding a discussion session (17).

Besides, as per ACR BI-RADS categories guidelines, breast densities were differentiated as follows: Almost wholly fatty (F), Randomly distributed fibro glandular (S), Heterogeneously dense (HD), and extremely dense (ED) (3).

Breast suspicious calcifications were categorized according to BI-RADS classification (3), according to which the lesions were defined as positive or negative. Those classified as BI-RADS 2 and 3 were considered negative, while those categorized as BIRADS 4 and 5 were defined as positive. As the study was conducted as a retrospective one, the following categories were not applicable: Categories 0 (i.e., those cases requiring extra imaging evaluation or those cases with prior mammograms for the sake of comparison); category1 (considered negative): and category 6 (cases with malignancy proven through biopsy). The histopathological findings were considered the gold standard for diagnosing breast cancer (2).

Statistical analysis

To feed the data for statistical analysis, SPSS software version 23 (SPSS Inc., Chicago, IL, USA) was employed. To present the nominal data, absolute frequencies and percentages were utilized. We also exploited general estimation equations (GEE) to compare the two methods and the two interpreters regarding measuring accuracy, sensitivity, and the parameter of specificity. In this way, we could consider several measures for each case. Two distinct models were employed. (a) A bipartite model of repeated measures considering inter-subject parameters 'method', and 'rater' alongside the interaction. (b) A tripartite mixed model incorporating the between-subject parameter-'lesion type' (benign vis-à-vis malignant) also including all resulting bipartite and tripartite three interactions. Also presented is a model-based 95% confidence interval (CI) as developed by Wald. Furthermore, the receiving operating characteristics (ROC) calculations were provided separately for each reader and method based on the BI-RADS ratings. The ROCs were compared using the DeLong method, and a significance level of less than 0.05 was significant for the *P* value.

Results

In the current study, 92 imaging and biopsied tissues were evaluated. The average age of the patients studied was 49.09 ± 7.65 years old (range: 33-70 years of age). Table 1 demonstrates the distribution of breast tissue density according to ACR, where most tissues studied were classified as highly heterogeneously dense instances (46.7%) followed by scattered fibroglandular (40.2%). The pathological study of the lesions revealed that half of the biopsies were malignant (Table 2).

The sensitivity and specificity of FFDM and DBT in the identification of micro-calcifications in benign (BIRAD 2-3) and malignant (BIRAD 4-5) categories are shown in Table 3. The total sensitivity of DBT was 96.7% and that of FFMD was 90.2%, while both modalities revealed similar specificity accounting for 8.7%. The area under the curve (AUC) accounted for 0.527 for DBT, a value more than 0.505 measured for FFDM. The measured sensitivity, specificity and AUC by radiologist #1 for DBT were 97.8%, 10.9% and 0.511, respectively. The obtained values were higher in DBT compared to FFDM. Radiologist # 2 presented higher specificity for FFDM (10.9%) compared with DBT (6.5%); whereas other entities were superior in DBT. Detailed information is provided in Table 3.

The overall agreement coefficient for the two radiologists in the identification of micro-calcifications accounted for 0.613 (95% CI: 0.394-0.823). This agreement coefficient for FFDM was 0.676 (95% CI: 0.412, 0.940) for FFDM and 0.517 (0.147, 0.887) for DBT.

Table 1. Clinical characteristics of lesions

Variable	No. (%)
Breast tissue density	
Heterogeneously dense	43 (46.7)
Scattered fibroglandular	37 (40.2)
Extremely dense	7 (7.6)
Fatty	5 (5.4)
Pathological outcomes	
Malignant	46 (50)
Benign	46 (50)
Benign lesions	
Atypical ductal hyperplasia	14 (30.4)
Hyperplasia with calcification	15 (32.6)
Fat necrosis	2 (4.3)
Fibrocystic changes	1 (2.2)
Flat epithelial atypia	7 (15.2)
Papillomatosis	1 (2.2)
Sclerosing adenosis	6 (13)
Malignant lesions	
Ductal carcinoma in situ	34 (73.9)
Invasive ductal carcinoma	12 (26.1)

Table 2. Consistency between pathological and imaging investigations

Pathology		Imaging	
		Benign	Malignant
FFDM	Benign	8 (8/69)	9 (9.78)
	Malignant	84 (91.30)	83 (90.21)
DBT	Benign	8 (8.69)	3 (3.26)
	Malignant	84 (91.30)	89 (96.73)
Total		92 (100)	92 (100)

Discussion

According to our study and experience, DBT with a narrow scan-angle shows superior performance over FFDM procedure in detecting and characterizing microcalcified breast tissues in the clinical settings. Although the evaluations of microcalcifications were variably influenced by the readers, this was not the case with the modality by which the tissues were assessed. We achieved significant sensitivity of over 95% for DBT in the assessment of microcalcifications across the board and by each reader separately showing overall superiority of DBT

Table 3. Sensitivity and specificity of FFDM and DBT modalities in identification of breast micro-calcifications

	Overall			Radiologist 1			Radiologist 2		
	AUC	Sensitivity	Specificity	AUC	Sensitivity	Specificity	AUC	Sensitivity	Specificity
FFDM	0.505 (0.431, 0.580)	90.2 (83.6, 96.2)	8.7 (3.8, 16.4)	0.500 (0.394, 0.606)	91.3 (79.2, 97.6)	8.7 (2.4, 20.8)	0.543 (0.436, 0.648)	91.3 (79.2, 97.6)	10.9 (3.6, 23.6)
DBT	0.527 (0.452, 0.601)	96.7 (90.8, 99.3)	8.7 (3.8, 16.4)	0.511 (0.404, 0.617)	97.8 (88.5, 99.9)	10.9 (3.6, 23.6)	0.511 (0.404, 0.617)	95.7 (85.2, 99.5)	6.5 (1.4, 17.9)

Abbreviations: FFDM; Full field digital mammography, DBT; Digital breast tomosynthesis, AUC; Area under curve.

over FFDM. The significant point in our study is the low specificity found for both modalities accounting for at mot 10%. Although it was found that DBT is relatively superior to FFDM, the assessed inter-reader agreement of our study was not remarkably high, albeit acceptable.

Despite the typical breast lesions having critical features and which can be diagnosed easily using diverse modalities, the precise identification and microcalcification characterization plays a pivotal role in the adopted approach toward managing lesions in breast tissues. Since ten years ago, initial investigations have shown inclination toward DBT administration for evaluating microcalcifications (1,11,18). The preliminary studies have revealed that the capability of DBT to appropriately visualize microcalcifications is widely dependent on such diverse factors as DBT system, range of angular scanning, the number of projections, both characteristics and reconstruction algorithms specific to the detector. In continuation they found out that not only the performance of DBT is not inferior to the routine FFDM for the detection of microcalcified breast tissues, but also it can act as powerfully in case of appropriate image acquisition and reconstruction protocols (19, 20).

Li et al performed a research study on 312 breast tissues to compare the capability of FFDM in differentiating benign and malignant breast cancers. They determined that DBT exhibited significantly higher ability in distinguishing malignant microcalcifications as compared with FFDM (87.9% versus 75.2%); but not benign ones in premenopausal (88.4% versus 78.8%), postmenopausal (90.2% versus 77.2%) and dense breast cases (89.4% versus 81.9%) (2). Another large screening study conducted retrospectively by Giess et al had an assessment of FFDM and DBT of 68794 patients. They noticed similar outcomes for each modality to correctly diagnose breast cancer in microcalcified specimens. However, assessing those cases who had performed both modalities, DBT performance exhibited better results (21). Additionally, Clauser and colleagues performed a similar study where they showed that DBT functioned as well as FFDM. However, in their study they noticed a remarkable difference in inter-reader interpretations of images (12). Despite the fact most studies given in the relevant literature claim DBT exhibits higher and better accuracy than FFDM – in characterizing benign versus malignant microcalcification lesions – few studies have presented contrary outcomes (14).

The inconsistency observed in their findings may partially be attributed to the size of the study population as the study of fewer cases might lead to the possible inaccuracies. Viewed from another perspective, readers' experience and inter-reader agreement can deeply affect the outcome. High inter-reader diversity might potentially lead to wide variation in diagnoses. Limited number of studies have presented negligible effects of inter-reader differences on the accuracy, sensitivity and specificity of different methods in predicting the probability of malignancies (16,22). Dibble and colleagues found that using DBT technique brings about a reduction in inter-reader variability, an increase in readers' confidence, and an enhanced sensitivity in detecting distortions in breast architecture (16). It is to be noted that the experience, expertise and accuracy of the radiologist responsible for reading the mammography images plays a crucial role in forming a correct diagnoses with FFDM or DBT modalities. However, an acceptable level of agreement was observed in the readers of our study. Other studies, which have not assessed this issue, have insisted on the significance of readers' expertise to accurately assess variable breast architectural tissues and employed experienced radiologists to minimize the probable inter-reader biases (2,17).

The current study has been performed in narrow angle projections, similar to that of Li et al (2). Since the detectability of the DBT procedure highly dependent upon the angle of scan, our results might exhibit differences with other research studies (12,15). In wide-angle scans, owing to the fact that higher ranges of tissues are scanned by x-ray and as the dose for each projection is reduced, the signal received by the detector might come lower. While at this time, there might be an increase in the relative noise produced. This conditions might potentially give rise to a decrease in small structures visibility – microcalcifications being in the top list (15). FFDM images are sharper than those obtained through DBT technique. For in DBT, pixel pitches are of higher dimensions than that of 2-D mammography. Besides, geometric blurring, particularly in wide-angle DBT, is another disfavored characteristic of DBT. This incident comes about due to the movement of the tube and comparative increase occurring in each projection (15). Nevertheless, DBT superiorities outweigh the mild blurring of the images when applied in breast cancer screening and diagnosis (23-25).

This study showed that DBT functions more efficiently in diagnosing malignant lesions based on pathological studies when compared with benign lesions. Consistent outcomes were achieved for FFDM as well. Another study by Li et al, however, opposes this finding. It is to be reminded that they did not equalize the number of malignant and benign lesion cases in their study(2). It is worthy of note that previous studies have ranged malignant microcalcified lesions in 10 to 39% of their subjects studied, which statistics accounts for half of the samples given in this report (26,27).

Conclusion

As per findings of the present study, DBT was relatively superior to FFDM in screening and diagnosing microcalcifications in breast tissues. And although the sensitivity of DBT is notably high, its specificity is not justifiable. The inter-reader agreement of this study was satisfactorily acceptable for both FFDM and DBT assessments.

Limitations of the study

Small sample population and lack of further demographic information of the patients were the most significant limitations of the present research study.

Authors' contribution

Conceptualization: Maryam Farghadani, Bahar Ghadiri-faraz, Maryam Riahinezhad, Sahar Sarami
Data curation: Maryam Farghadani, Sahar Sarami
Formal analysis: Sahar Sarami
Funding acquisition: Maryam Farghadani, Bahar Ghadiri-faraz, Maryam Riahinezhad, Sahar Sarami
Investigation: Sahar Sarami
Methodology: Maryam Farghadani, Sahar Sarami
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Visualization: Maryam Farghadani, Bahar Ghadiri-faraz, Maryam Riahinezhad, Sahar Sarami
Writing–original draft: Sahar Sarami
Writing–review and editing: Sahar Sarami

Conflicts of interest

The authors declare that they have no competing interests with any institution and organization.

Ethical issues

The research conducted in this study adhered to the principles outlined in the Declaration of Helsinki, which has been approved by the Ethics Committee of Isfahan University of Medical Sciences (Ethical code#IR.MUI.MED.REC.1399.767). Due to the retrospective design of the study, no consent was obtained. However, at the time of performing imaging procedure, the patients were informed of the potential use of the data for clinical investigations and reassured as to the confidentiality of their personal information. This study was extracted from Sahar Sarami's specialty dissertation on imaging and radiology, department of imaging and radiology of this university (Thesis #399686). The authors have fully complied with such ethical issues as avoidance of plagiarism, data fabrication or double publication.

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