Exp Oncol 2020
42, 3, 1–5

Experimental ONCOLOGY

DETECTION OF BREAST CANCER PRESENTING AS A MASS IN WOMEN WITH DENSE BREASTS — DIGITAL BREAST TOMOSYNTHESIS VERSUS FULL-FIELD DIGITAL MAMMOGRAPHY

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Aim: **To evaluate the sensitivity and specificity of digital breast tomosynthesis compared with full-field digital mammography in detection of breast cancer presenting as a mass in women with dense breasts.** ***Materials and Methods:*** **This study included 347 asymptomatic and symptomatic patients with dense breasts who underwent full-field digital mammography, digital breast tomosynthesis and hand-held full breast ultrasound. 57 core-needle biopsies were performed. Pathology included 31 invasive cancers and 26 non-cancerous lesions.** ***Results:*** **Sensitivity of full-field digital mammography was 61.3% [0.422–0.789] and sensitivity of digital breast tomosynthesis was 77.4% [0.589–0.904]. Specificity of full-field digital mammography was 92.7% [0.893–0.953] that was 2.2% lower than the specificity of digital breast tomosynthesis — 94.9% [0.919–0.971].** ***Conclusion:*** **Results of our study showed superior sensitivity and specificity of digital breast tomosynthesis compared to full-field digital mammography for detection of malignant masses in women with dense breasts.**

Key Words: **digital breast tomosynthesis, full-field digital mammography, breast cancer, dense breast.**

DOI:

The role of digital breast tomosynthesis (DBT) in medical practice has been increasing continuously over the last decade. A number of early clinical studies has showed a higher accuracy of DBT compared to standard full-field digital mammography (FFDM) [1].

DBT is a form of limited-angle tomography [2]. During acquisition of tomosynthesis images, an X-ray source takes a series of low-dose exposures, providing multiple images of the breast in different planes that are 3D reconstructed, while moving in a limited arc above the compressed breast [2].

Large multicenter studies have identified major advantages of DBT as compared to FFDM, but the role of tomosynthesis for women with dense breasts has not been fully established yet [3].

Breast density is relative amount of radiopaque epithelial and stromal tissue elements compared with the amount of radiolucent fatty tissue seen in mammography [4]. Usually palpable breast firmness during physical examination does not correlate with mammographic density [4].

Younger, pre- or perimenopausal women are known to have a higher proportion of dense breast tissue, as breast density decreases with age [5]. Breast tissue is subject to physiologic involution changes when glandular tissue is being replaced by fat, thus breasts become less dense and more mammographically transparent with age [5].

Higher breast density is reported to be one of the main risk factors for breast cancer (BC) [4]. Different parenchymal densities were first described by Leborgne and were later described as one of possible BC risk factors by Wolfe [6]. The fourth edition of Breast Imaging-Reporting and Data System (BI-RADS) Atlas introduced density distribution by percentage ratio of fat and fibroglandular tissue (< 25% of glandular tissue — 1 category, 25–50% of glandular tissue — 2 category, 51–75% of glandular tissue — 3 categories and > 75% — glandular tissue 4 category) [7].

However, in the newest 5th edition American College Radiology returned to original description of breast density, which was used in the first editions, and removed the numeric values to avoid confusion with BI-RADS diagnostic categories and replaced the numbers with the letters 1-A, 2-B, 3-C, 4-D [8]. Now breast density is based on the visual assessment of the breast parenchyma by interpreting radiologist and does not correspond to the percentage of fat and fibroglandular tissue [8].

The aim of the study was to compare sensitivity and specificity of DBT and FFDM in detection of BC represented as a mass in women with dense breasts (categories C and D according BI-RADS Atlas).

MATERIALS AND METHODS

The institutional review board approved this study and waived the need for informed consent due to its retrospective character.

Submitted: January 27, 2020.
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Abbreviations used: AUC – area under the curve; BC – breast cancer; BI-RADS – breast imaging-reporting and data system; DBT – digital breast tomosynthesis; FFDM – full-field digital mammography; HHUS – hand-held full breast ultrasound; MCs – microcalcifications.

1383 patients underwent FFDM, DBT and handheld full breast ultrasound (HHUS) from January 2015 to December 2017 at the State Institution "Institute of Nuclear Medicine and Diagnostic Radiology of the National Academy of Medical Science of Ukraine". BI-RADS categories were utilized for interpretation of all studies. Mammographic breast density was categorized according BI-RADS 5th Edition.

1036 patients were excluded from this analysis. Exclusion criteria were: BI-RADS-1 category; low breast density, microcalcifications (MCs) or architectural distortion as a main finding, lack of pathology diagnosis or imaging follows up.

Only patients with dense breasts (categories C and D) with mass on any imaging modality were included. First imaging modality was FFDM followed by DBT and HHUS in order to establish correlation with mammographic findings. Biopsy was conducted under imaging modality where lesion was seen the best. All BI-RADS 4 and 5 lesions underwent biopsy with pathology. Benign nature was determined by imaging follow up for 2 years.

This study included 347 patients with dense breasts (C and D). Age of the patients ranged from 32 years to 83 years with mean age of 52 years. A total of 57 breast lesions were examined by pathology, revealing 31 invasive cancers, and 26 non-cancers findings.

All patients underwent bilateral mammography in "COMBO" mode in two standard projections (CC and MLO) as a first step of imaging examination on Selenia Dimensions Mammography unit (Hologic, USA). This step incorporated digital mammography and tomosynthesis, including synthesized images.

In "TOMO" mode, X-ray tube moves in an arc over the compressed breast capturing multiple images of each breast from angles –7.50° to +7.50°. The obtained images are then reconstructed into 1 mm thick slices.

The interpretation of the images was performed on 2 monitors with a matrix resolution of 5 Mpc by dedicated breast radiologist. Interpretation of mammograms was performed using special algorithm: in its original size; enlarged images by quadrants (upper lateral, upper medial, lower medial, lower lateral); in inverse mode.

HHUS was performed on a Toshiba Viamo US system with a linear probe centered at 9.0 MHz by experienced breast radiologist.

The specificity and sensitivity for DBT and FFDM was determined using ROC analysis. EasyROC server was used as a computing R-tool for this statistical analysis [9]. The differences were considered significant at *p*-value < 0.05.

RESULTS

Analysis of the results showed that sensitivity of FFDM was 61.3% [0.422; 0.789]; sensitivity of DBT was 77.4% [0.589; 0.904] (Table), what was considered statistically significant ($p < 0.05$).

Specificity of FFDM was 92.7% [0.893; 0.953], specificity of DBT was 94.9% [0.919; 0.971] (see Table) what was not statistically significant.

The specificity and sensitivity for DBT and FFDM are shown in Table, with the corresponding graphical interpretation of the ROC-dependence (Fig. 1).

There was statistically significant difference between DBT area under the curve (AUC) and FFDM AUC. Difference = 0.0917 [0.025; 0.158], $p = 0.0017$.

As we see in Example 1 (Fig. 2), dense fibroglandular breast tissue obscured suspicious mass in lower inner quadrant of the right breast on FFDM. But DBT showed an irregular mass with spiculated margin that was also visible during HHUS examination. Core-needle biopsy showed invasive ductal carcinoma.

Example 2 (Fig. 3) shows the similar situation, when dense fibroglandular breast tissue partially obscured suspicious mass in upper outer quadrant of the left breast on FFDM but DBT scans showed an irregular mass with spiculated margin that was also visible on ultrasound. Core-needle biopsy confirmed invasive breast cancer.

DISCUSSION

DBT is a new modality for Ukrainian breast imaging. It first appeared in State Institution "Institute of Nuclear Medicine and Diagnostic Radiology of the National Academy of Medical Science of Ukraine" in 2014 [10]. Although there is a growing number of publications on this imaging modality, DBT was never validated on Ukrainian population and thus it was very important to compare DBT with FFDM for breast cancer detection in our setting.

Dense fibroglandular tissue is the most important inherent limitation of mammography [11].

Because breast density adversely affects sensitivity and specificity of FFDM due to its masking effect and also serves as an independent risk factor of BC, we decided to select women with dense breasts for our study [12].

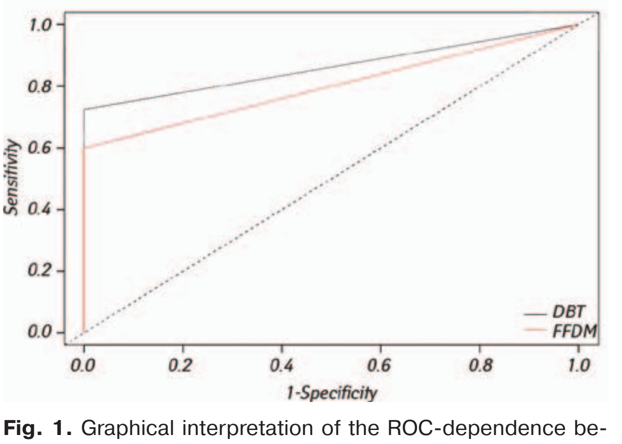

Fig. 1. Graphical interpretation of the ROC-dependence between DBT and FFDM

Table. Sensitivity and Specificity for DBT и FFDM

	DBT			FFDM		
	Point Estimate	Lower 95% CL	Upper 95% CL	Point Estimate	Lower 95% CL	Upper 95% CL
Sensitivity	0.774	0.589	0.904	0.613	0.422	0.782
Specificity	0.949	0.919	0.971	0.927	0.893	0.953

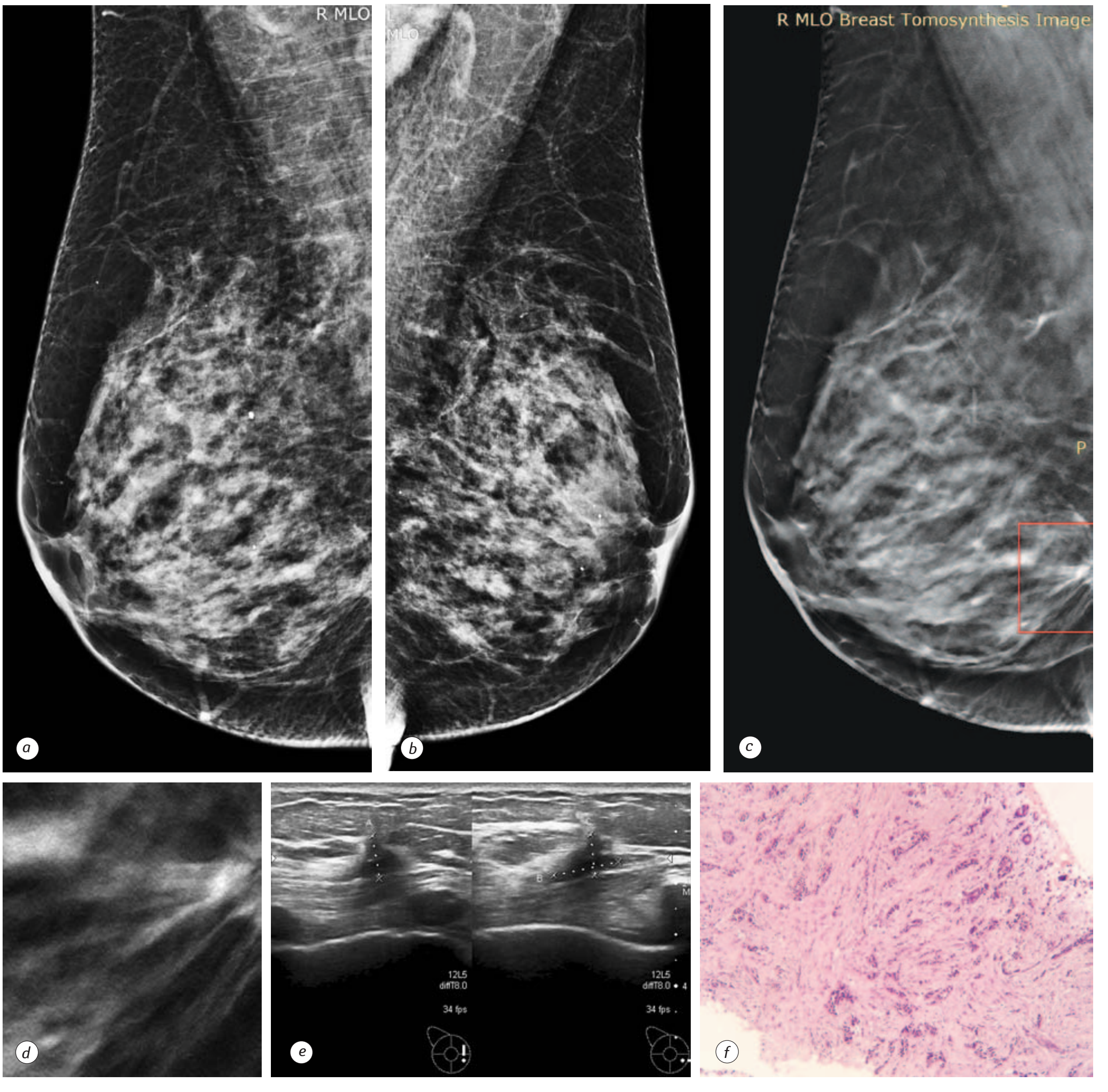

Fig. 2. A 51-year old asymptomatic female with no personal or family breast cancer history attended her first screening mammography. Dense fibroglandular breast tissue obscured suspicious mass in lower inner quadrant of the right breast on mammography. DBT showed an irregular mass with spiculated margin that was also visible on ultrasound. Core-needle biopsy showed invasive ductal carcinoma. *a, b* — mammography RMLO and LMLO views; *a, c, d* — Rmlo — view, Rmlo Breast Tomosynthesis Image, magnification of ill-defined spiculated mass on Tomo scans; *e* — ultrasound image of suspicious mass; *f* — breast invasive carcinoma G2 of no special type. Stained with hematoxylin-eosin, magnification × 100

The sensitivity of 2D mammography is dramatically reduced (25–60%) in women with dense breasts (BI-RADS C and D) [11]. Adding ultrasound screening can increase breast cancer detection rates by 1.9–4.2%, depending on the population [13].

Considering all above, HHUS with ultrasound-guided 14-gauge core needle biopsy were methods of control for lesions in dense breasts. Sonographically guided 14-gauge core needle biopsy is an accurate method for evaluating breast masses [14].

One of the main advantages of DBT is better characterization of mass margin [15]. Andersson *et al.* [16], compared BC visibility in one-view DBT with BC visibility in one- or two-view FFDM. Authors demonstrated that the BC visibility on DBT is better to FFDM and suggested that DBT may have a greater sensitivity for BC detection [16].

Rafferty *et al.* [17] demonstrated a persistent and statistically significant increase of up to 7.2% in diagnostic accuracy and significant reduction in callback rate of up to 38.6% when DBT was added to FFDM [17]. The addition of DBT led to a significant improvement in tumor characterization for non-calcified tumors (group 1 — 8.8%, group 2 — 10.4%), whereas for tumors with MCs the difference was not significant [17].

Aim of another study was to determine the difference in diagnostic accuracy of film-screen mammography and FFDM with adding of DBT in patients recalled for assessment after screening examination [18]. The scientists emphasized that impact for soft-tissue

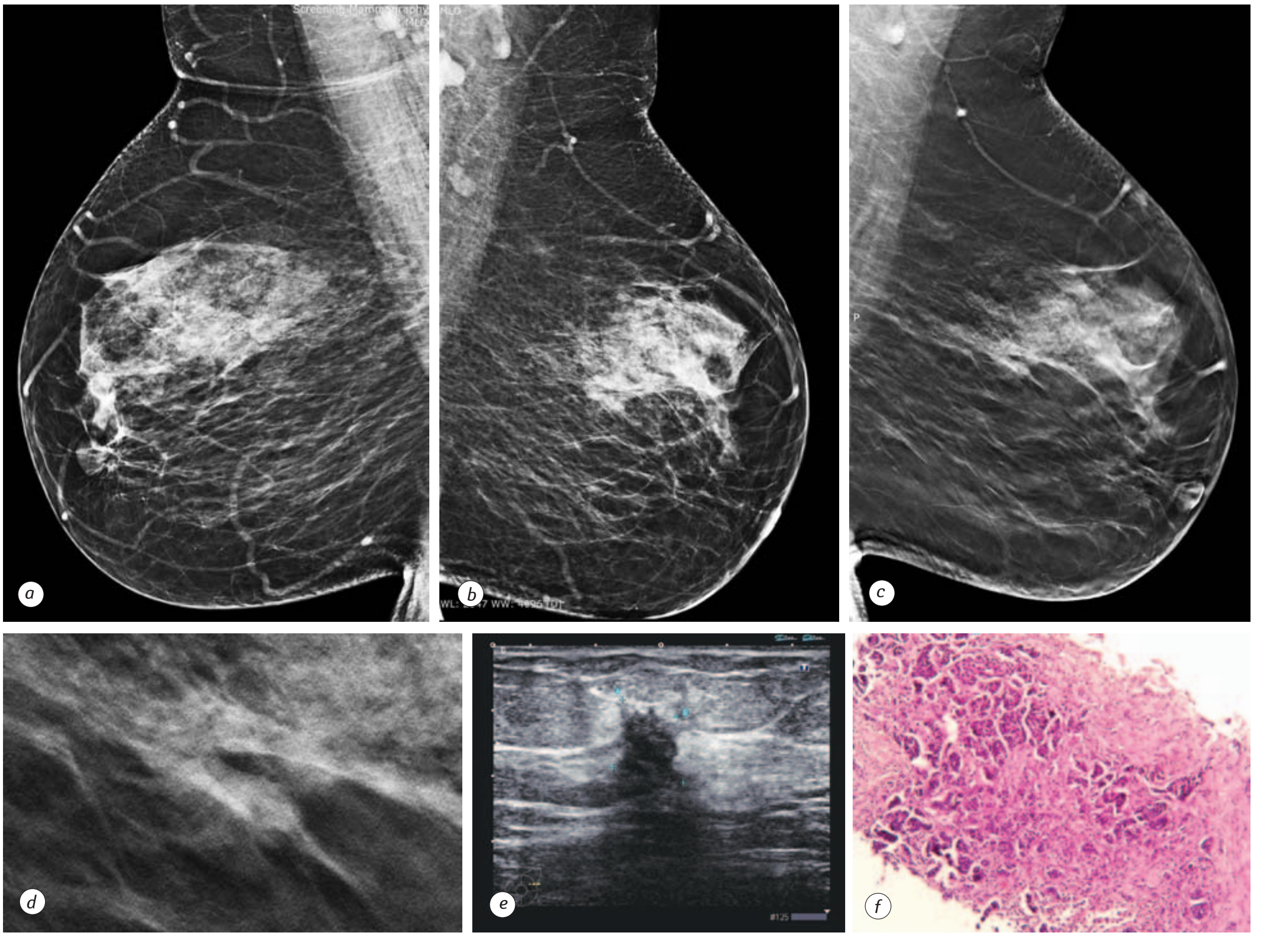

Fig. 3. A 56 years old female with focal pain in the left breast with no personal or family history of breast cancer attended diagnostic mammography. Dense fibroglandular breast tissue partially obscured suspicious mass in upper outer quadrant of the left breast on mammography. DBT showed an irregular mass with spiculated margin that was also visible on ultrasound. Core-needle biopsy confirmed invasive breast cancer. *a, b* — mammography RMLO and LMLO views; *b, c, d* — Lmlo — view; Lmlo Breast Tomosynthesis Image; magnification of ill-defined spiculated mass on Tomo scans; *e* — Ultrasound image of suspicious mass; *f* — breast invasive carcinoma G2 of no special type. Stained with hematoxylin-eosin, magnification × 100

lesions was much greater (AUC was 0.9905 with the addition of DBT and AUC was 0.9201 for FFDM combined with film-screen mammography ($p = 0.0001$)) than for MCs (AUC was 0.7920 with the addition of DBT and AUC was 0.7843 for FFDM combined with film-screen mammography combined ($p = 0.3182$)) what correlates with our study where we also noted better accuracy of DBT in comparison with FFDM for soft-tissue lesions [18].

Another study compared diagnostic performance of DBT and mammographic spot views in 67 women with masses [19]. DBT and mammographic spot views showed similar breast masses characterization in terms of visibility, reader performance, and BI-RADS assessment [19]. These results proposed that mammographic spot views might not be mandatory for mass assessment when DBT was made [19].

Our study also showed superior sensitivity and specificity of DBT compared to FFDM for masses in women with dense breasts. The results of our study are in line with the results of other published studies [15–19].

Our study has some major limitations. There was only one breast radiologist performing the imaging and biopsies. Due to its retrospective nature interpreting radiologist knew the biopsy results beforehand and this could potentially introduce a bias in BI-RADS assessment. The number of cancer cases in our sample was limited and we did not include other findings such as microcalcification, architectural distortion and asymmetries in this analysis.

CONCLUSIONS

In this study, two-view DBT was compared with two-view FFDM for the detection of BC represented by mass in women with dense breasts. Results of our study showed superior sensitivity and specificity of DBT compared to FFDM. BC detection in women with dense breasts can be improved by routine use of DBT.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest, no relationships with any companies, whose products or services may be related to the subject matter of the article.

AUTHOR’S CONTRIBUTION

T.M. Babkina — idea and concept of research, I.M. Dykan — data collection and processing, A.V. Gurando — wrote the paper, D.M. Suleimenova — editing, data analysis, T.M. Kozarenko, Ye.M. Bozhok — literature analysis, V.A. Stuley — statistical analysis.

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