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Original Article

Digital breast tomosynthesis and ultrasonography: diagnostic performance and effect on recall rates versus digital mammography in category 0

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Abstract: The purpose of this study was to compare diagnostic performance and screening recall rates of digital breast tomosynthesis (DBT) and ultrasound (US) added to digital mammography (DM) in the category 0. This study was approved by the local ethics committee and informed consent was obtained. The additional breast US and DBT performed 216 women categorized as BI-RADS category 0 according to screening DM between January 2014 and February 2015. A total of 22 women that previously underwent breast surgery, radiotherapy, chemotherapy were excluded. Finally 194 patients were enrolled in this study. The DM+DBT images and DM+DBT images with US images of patients were independently reviewed by three breast radiologists and than recategorized according to BI-RADS category. Among 194 lesions, 165 (85%) were benign and 29 (14.9%) were malign. DBT reduced recall rate by 70%. For DBT, sensitivity, specificity, PPV, NPV and diagnostic accuracy were 97%, 82%, 48%, 99%, and 84%, whereas for US sensitivity, specificity, PPV, NPV and diagnostic accuracy were 93%, 79%, 47%, 98%, and 81%, respectively. AUC value was 0.89 and 0.86 for DBT and US. In conclusion, DBT reduced recall rates. DBT showed better diagnostic performance than breast US for category 0. Reduction in RR was independent from breast parenchymal patterns.

Keywords: Screening mammography, digital breast tomosynthesis, ultrasonography, diagnostic performance, recall rates

Introduction

Conventional mammography is the most effective method of breast cancer screening [1]. It's sensitivity is high as 80-98% in the fatty breasts, but it decreases down to 30-48% in dense breasts [2]. Nevertheless, the risk of developing breast cancer is 2-6-fold higher for women having dense breast [3]. The diagnostic performance of full-field digital mammography (DM) is superior to conventional mammography in especially women with dense breast tissue. However, DM as well has limitations. Small lesions in particular may be hidden in dense breast parenchyma and may be overlooked [4]. For this reason, ultrasonography (US) is widely used for complementary purpose in dense breasts and increases the rate of detecting cancer. Earlier studies determined that mammography together with US 4.2-fold enhances the rate of detecting cancer in 1000 women screened. However, leading to unnecessary biopsy and additional methods due to negative biopsy results and high false-positivity rates are among the disadvantages [5].

The rate of diagnosing unknown or clinically insignificant lesions has increased along with the use of screening mammography, which leads to over treatment [6]. Moreover, false images appear due to superposition of breast parenchyma. Thus the patient is unnecessarily recalled, which causes anxiety, and the increasing cost [7]. Digital breast tomosynthesis (DBT) provides three-dimension sectional imaging [8]. This method allows elimination of glandular tissue superposition, which is a problem particularly in the dense breasts, and makes the detection and characterization of lesion easier [9]. And also, it is reported that DBT is superior to film mammography in assessing the masses, parenchymal distortions and asymmetric densi-

Table 1. Histopathological verification

Histology	Lesions	*%*
Malignant[c]	29	*72.5*
Invasive Ductal Carcinoma[a]	25	*86.20*
DCIS[a]	2	*6.89*
Medullary Carcinoma[a]	1	*3.44*
Invasive Lobular Carcinoma[a]	1	*3.44*
Benign[c]	11	*27.5*
Fibroadenoma[b]	2	*18.18*
Benign Cytologyi[b]	2	*18.18*
Mastitis[b]	2	*18.18*
Adenosis[b]	1	*9.09*
Granulomatous mastitis[b]	1	*9.09*
Fat Necrosis[b]	1	*9.09*
Breast Tissue[b]	1	*9.09*
Cyst[b]	1	*9.09*

[a]Percentages are calculated on 29 malignant lesions. [b]Percentages are calculated on 11 benign lesions. [c]Percentages are calculated on 40 malignant and benign lesions. DCIS: Ductal carsinoma insitu.

Table 2. Summary of malignant cases

Case No	Age	DM Finding	BI-RADS (US)	BI-RADS (DBT)	Breast Pattern
1	63	SM	5	5	A
2	52	PD	5	4c	B
3	52	AD	5	5	B
4	64	SM	4C	5	B
5	41	SM	4A	5	C
6	50	PD	4A	3	D
7	62	SM	2	5	B
8	54	AD	4C	5	B
9	69	SM	5	5	B
10	66	PD	3	5	B
11	47	AD	4A	1	C
12	87	SM	5	5	B
13	57	SM	0	5	C
14	41	SM	5	5	C
15	55	SM	5	5	B
16	69	SM	5	5	A
17	86	SM	5	5	A
18	45	PD	4A	4c	B
19	52	SM	4A	4c	C
20	47	SM	5	5	C
21	45	PD	5	3	D
22	76	SM	4B	4c	A
23	51	PD	4C	5	C
24	51	PD	4C	4c	C
25	64	AD	4C	5	B
26	51	AD	5	5	B
27	40	SM	5	5	D
28	63	SM	4C	5	B
29	50	SM	5	5	B

PD: Parenchymal Distortion, AD: Asymmetric Density, SM: Superposed Mass.

ties [10]. The first studies conducted in the Unites States of America and Europe demonstrated that DBT used in screening programs increases the diagnosis of invasive malignant lesion and decreases the number of patients recalled because of false-negative mammography and nonspecific images [11].

The purpose of this study was to compare diagnostic performance with DBT and US and to identify their effects on the recall rates for breasts with category 0 at digital mammography.

Materials and methods

This study was approved by the local ethics committee and informed consent was obtained. We reviewed retrospectively the electronic medical records of 3508 women who underwent screening DM in our Breast Unit between January 2014 and February 2015. Of these patients, 216 women categorized as BI-RADS category 0 (incomplete, need additional imaging evaluation) according to DM were performed additional breast ultrasound and DBT. A total of 22 women that previously underwent breast surgery, radiotherapy, chemotherapy were excluded. Thus, the remaining 194 patients were finally enrolled in this study.

Image acquisition

All patients were underwent DM in standart positions and DBT in a one position mediolateral oblique (MLO) using a commecially avaliable device (Mammomat Inspiration, Siemens, Erlangen, Germany) used by two experienced technician. The device had high milliamp, an X-ray tube containing tungsten anode material and aluminum, silver and rhodium filters and extending up to 15 degrees, and automatic exposure system that takes the component and thickness of the breast as the basis. After acquisition, data from the projection images were combined to create a full 3D-image set of 1 mm slices of the breast. The images obtained by DM and DBT were stored at the workstation.

US (Aplio XG; Toshiba, Tokyo, Japan) was performed with 12 MHz linear probe on radial/antiradial plane while the patient was in supine position. US examination

Table 3. Recall rates of patients when DBT and US were added

Recall		Number of Patients	Percentage of Patients (%)
Recall DBT	No	136	70.1
	Yes	58	29.9
	Total	194	100.0
Recall US	No	116	66.7
	Yes	58	33.3
	Total	174	100.0

was performed by two radiologists specialized in breast imaging who have studied in same unit for 5 and 15 years. Their DICOM images of US were stored in our medical data system.

Image analysis

The images were evaluated by three radiologists specialized in breast imaging and with experience ranging from 5 to 15 years in reading mammograms. The readers were blinded to the histopathologic information independently. The DM+DBT images and DM+DBT images with US images of patients were independently reviewed by three breast radiologists and than recategorized according to BI-RADS category. Parenchymal patterns on mammograms were classified according to The American College of Radiology (ACR); type A: fat tissue is dominant in the entire breast tissue, type B: scattered fibroglandular densities in addition to the dominant fat tissue, type C: breast parenchyma has heterogeneous density, type D: breast parenchyma is extremely dense [12].

Pathology results of US-guided needle biopsy or surgical excision biopsy material were considered as reference standard. In the cases in which biopsy was not performed, reference standard was follow up of at least two years. Final BI-RADS category of each patient was determined according to these references.

Statistical analysis

Mammographically, all patients in the study were considered BIRADS category 0 and were hold that they will be recalled. In the present study, when DBT and US were added to DM, we used the statement *"Yes"* when recall was necessary and *"No"* when recall was not necessary.

Patients who were stable during follow-up and the patients with benign biopsy results were considered true negative (TN) unless they were recalled by the reader, otherwise they were considered false positive (FP). Patients with malignancy on histopathological examination were considered true positive (TP) unless they were recalled by the reader, otherwise they were considered false negative (FN). Comparison was made in terms of final results obtained from the evaluation of DM+DBT, DM+US and standard references, diagnostic performance, TP, TN, FP and FN rates, and AUC (area under the ROC curve) values. Based on these rates, diagnostic performance, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic accuracy of DBT and US, which were performed after DM, were obtained. Sensitivity (TP/(TP+FN)), specificity (TN/(TN+FP)), positive predictive value (TP/(TP+FP)), negative predictive value (TN/(TN+FN)) and diagnostic accuracy ((TP+TN)/(TP+FP+TN+FN)) rates were calculated. In addition, AUC value was calculated to decide whether DBT and US results is better in terms of diagnostic accuracy. Diagnostic performance was presented as ratio (percentages) and 95% confidence interval.

The relation between recall rates with DBT and US and the breast parenchymal pattern was investigated by chi-square test. The level of statistical significance was predetermined to be $P<0.05$. R Studio Version 3.2.1 program was used for the statistical analyses.

Results

Patients

The mean age of 194 patients enrolled in the study was 52 years (range 39-87 years). Digital mammography showed focal asymmetric density in 35%, suspicious parenchymal distortion in 19%, and a mass with contour superposed by the parenchyma in 46% of the patients. With regard to the distribution of parenchymal pattern, 7%, 31%, 43%, and 19% had type A, B, C and D parenchymal pattern, respectively.

Of the patients, 73 patients (38%) were stable during follow-up two years, and 81 patients (42%) were considered negative for pathology based on the DBT and US.

Table 4. Diagnostic Performance of Digital Breast Tomosynthesis and Ultrasonography

	DBT (n = 194)		*US (n = 174)*	
	Ratio	*95% CI (%)*	*Ratio*	*95% CI (%)*
Sensitivity	28/29 (%96.55)	82.24-99.91	27/29 (%93.10)	77.23-99.15
Specificity	135/165 (%81.82)	75.07-87.38	114/145 (%78.62)	71.05-84.99
Accuracy	163/194 (%84.02)	78.86-89.19	141/174 (%81.03)	75.21-86.86
Negative Predictive Value	135/136 (%99.26)	95.97-99.98	114/116 (%98.28)	93.91-99.79
Positive Predictive Value	28/58 (%48.28)	34.95-61.78	27/58 (%46.55)	33.34-60.13
AUC	0.89	0.84-0.93	0.86	0.80-0.91

AUC: Area under the ROC curve. DBT: Digital Breast Tomosynthesis. US: Ultrasonography. CI: Confidence Interval.

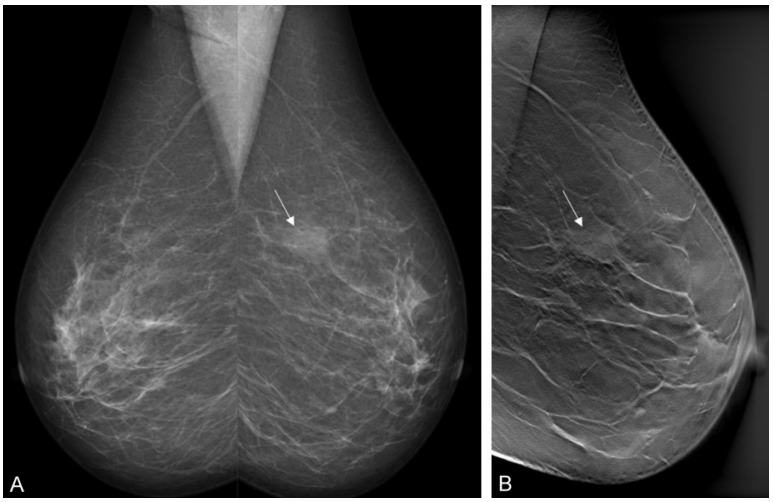

Figure 1. Mediolateral oblique digital mammography view (A) shows asymmetry (arrow) of the left upper breast. However, the lesion is not depicted on the craniocaudal view. The final assessment was BI-RADS category 0, needs further evaluation. On digital breast tomosynthesis (B), suspicious lesion was not detected in the area. The finding was interpreted as tissue superimposition.

Lesion-based distribution of the final pathological findings is reported in **Table 1**. Histopathological samples were collected from 40 patients (20%) of the patients. Histopathological examination revealed malignancy in 29 and benign pathology in 11 patients. On final assessment, malignant and benign lesion (added negative findings) were detected in 29 (15%), 165 (85%) of 194 patients, respectively.

Analysis of the patients with malignant mass in terms of parenchymal pattern is reported in **Table 2**. It was classified as non-dense in 18/29 (62%) patients, whereas 11/29 (38%) patients had dense breasts. In non-dense breasts (type A, B), DBT suggested biopsy in all of 18 cases whereas US suggested biopsy in 16 cases. However, in heterogeneous breasts (type C), DBT suggested biopsy in all but US suggested biopsy in 7 of these patients and suggested additional imaging in one case. Histopathological examination revealed invasive lobular carcinoma in the case in whom biopsy was not recommended with US. For the pattern D, addition of DBT recommended biopsy in one of three cases with malignancy, while the addition of US recommended biopsy for all. Biopsy results revealed invasive ductal carcinoma in two cases, of whom DBT did not recommend biopsy.

Recall and diagnostic performance

In **Table 3**, we report the recall rate of DBT and US. Recall was not required in 70% of the patients with addition of DBT to DM. Evaluating US findings together with DM, recall was not considered in 67% of the patients.

With regard to the diagnostic performance of additional DBT and US procedures, the sensitivity was 96% and 93%; specificity was 82% and 79%; diagnostic accuracy was 84% and 81%; NPV was 99% and 98%; and PPV was 48% and 47%, respectively. The results are shown in **Table 4**. Moreover, AUC value was 0.89 for DBT and 0.86 for US. Based on these outcomes, we can say that diagnostic performance is superior for DBT according to US.

BI-RADS categorization of the patients with malignancy based on DBT and US findings are summarized in **Table 2**.

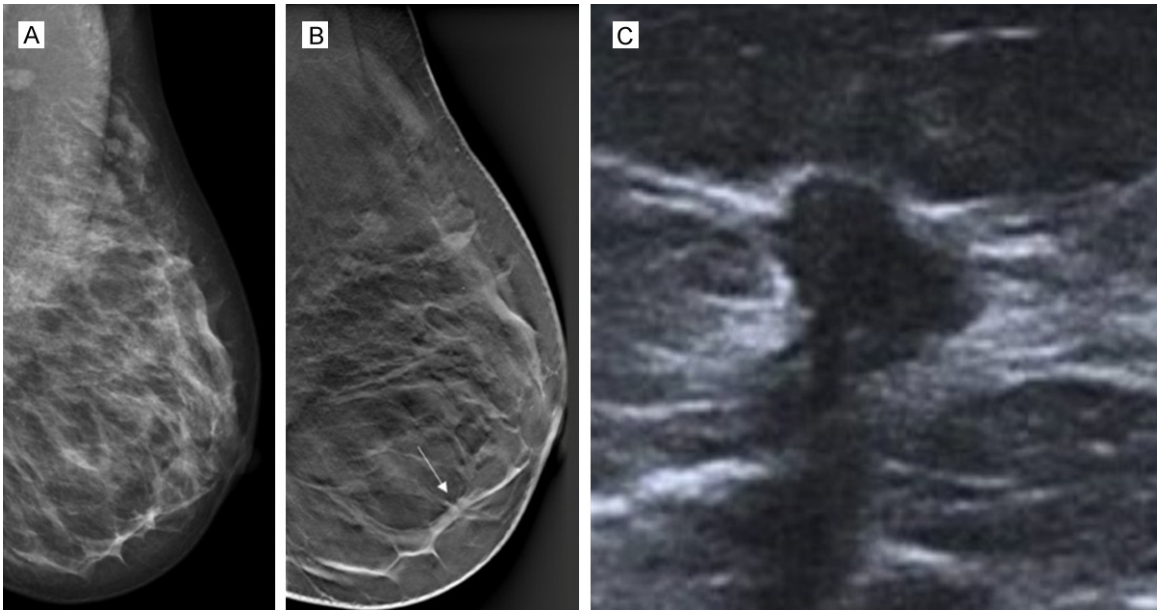

Figure 2. Craniocaudal digital mammography view (A) shows heterogeneously dense breast. On craniocaudal digital breast tomosynthesis (B), a spiculated mass (arrow) was detected on left breast. On ultrasound (C), a hypoechoic mass with irregular shape was observed and assessed as category 4C. The mass was confirmed as invasive ductal carcinoma.

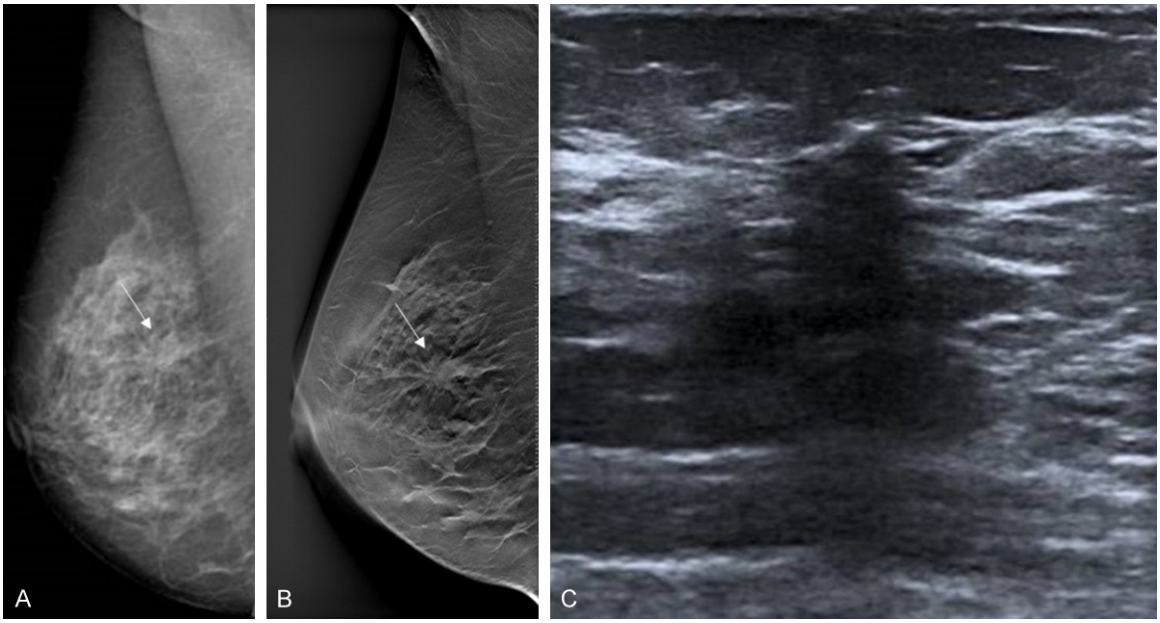

Figure 3. Mediolateral oblique digital mammography view (A) shows structural distortion (arrow) on the heterogeneously dense breast. On digital breast tomosynthesis (B), a spiculated mass (arrow) was detected at the center of right breast and assessed as category 5. On ultrasound (C), a hypoechoic area with blurred contours was observed and assessed as category 4B. The mass was confirmed as sclerotic tissue.

Patients with suspicious findings on digital mammography and have been estimated true or false for malignancy with the addition of DBT and US, are demonstrated on **Figures 1**-**3**.

No statistically significant relation was determined between recall rates of DBT and US and breast parenchymal pattern. The results were as following and summarized in **Table 5**: *Chi-*

Table 5. Comparison of DBT and US recall findings according to the pattern

		Pattern (%)						
		A	B	C	D	Total	*Test (CC)*	*p*
DBT	Yes	5 (2.6)	18 (9.3)	20 (10.3)	15 (7.7)	58	4.091 (0.144)	0.251
	No	9 (4.6)	42 (21.6)	64 (33)	21 (10.8)	136		
	Total	14	60	84	36	194		
US	Yes	4 (2.3)	18 (10.3)	24 (13.8)	12 (6.9)	58	0.759 (0.066)	0.859
	No	7 (4)	31 (17.8)	56 (32.2)	22 (12.6)	116		
	Total	11	49	80	34	174		

Test (CC): Chi-square (Contingency Coefficient).

square = 4.091, P = 0.251 and Chi-square = 0.759, P = 0.859, respectively.

Discussion

Many studies have been conducted on the recall rate of DBT in the literature. It has been reported that DBT reduced recall rate by 40%, 43-58% and 32%, respectively, in the retrospective studies conducted in screening or selected cases [13-15]. In two different studies comparing two groups that underwent DBT at the same and different times, it was emphasized that DBT reduces the recall rate by 15% and 25-82%, respectively [16, 17] Another comparative prospective study showed that DBT dropped to less than 15% in recall rate [11]. However, some researchers have reported that the recall rate increases with the addition of DBT [18, 19]. This may be due to insufficient DBT experience of centers or a low recall rate with DM.

Takamotom et al [20], who investigated the role of DBT in the diagnosis of breast cancer, reported the superiority of DBT in diagnosing mass, focal asymmetric density and parenchymal distortion. In a similar study, Lee et al [21], demonstrated that diagnostic performance of DBT is superior to US in category-0 dense breasts and emphasized that DBT reduces the false positive rates and short-interval follow-up. In a similar study, in which the majority of cases had dense breasts, diagnostic performances of DBT and US for breast mass characterization were found comparable [22]. Elizalde et al [23] investigated fatty and dense breasts together and found no significant difference between DM+DBT and DM+US in terms of diagnostic performance.

Our study showed that DBT was more accurate than DM and US for recall in screening patients and DBT decreased the recall rate by 70%. This significantly high reduced recall rate of DBT may be related that it was including only selected cases of BI-RADS category 0. Moreover, we determined that DBT not only decreased the recall rate but also displayed a diagnostic performance superior to US. In particular, based on the analysis of malignancy cases, the accurate estimation performance of DBT compared to US was superior to A-B patterns breasts, comparable to C pattern breasts. But, we found that it is lower for D pattern breasts. This may be due to the fact that DBT can not sufficiently clarify the characteristics of mass in D pattern breasts. In fact, in a similar study, Kim et al [22] compared DBT and US for mass characterization and found the diagnostic performance comparable between two methods.

We think the role of DBT on recall rate is comparable with US even better in the B-C pattern breasts, but DBT has no the effect in dense breasts. Moreover, we showed that US has additional role on recall rate in this group. But, the number of women with dense breast tissue is very small in our study group. For this reason, we believe that it is necessary to undertake new research studies for the role of DBT on recall rate in especially dense breasts to guide future screening programmes.

The present study has some limitations. First, we used DBT for diagnostic purpose because all of our patients were BIRADS-0. So, we were unable to evaluate the use of DBT for screening purpose and its role in detecting early-stage breast cancer. Second, the number of cases with dense breast is too small.

Conclusion

Addition of DBT reduces the recall rate by 70% in BI-RADS-0 breasts independent from the

parenchymal pattern. DBT could be added to DM with one position in screening programmes, US must be added as complemantary to DM/DBT especially in dense breasts.

Disclosure of conflict of interest

None.

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