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Original Article

Comparative study on diagnosis efficacy of digital breast tomosynthesis and color Doppler ultrasound for breast lesions

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Abstract: Early detection and screening of breast cancer has important clinical significance. This study aimed to compare the diagnosis efficacy of digital breast tomosynthesis (DBT) and color Doppler ultrasound for breast lesions. Patients with breast lesions were enrolled (1065 patients), among which 194 cases had complete pathological examination data. Using breast imaging reporting and data system (BI-RADS) classification as the criteria, the distribution differences among DBT, ultrasound, and DBT + ultrasound in diagnosis of breast lesions were analyzed. Based on the pathological results of 194 cases, the diagnostic efficacies of three diagnostic models were compared. Results showed that, there was significant difference in BI-RADS distribution between DBT and ultrasound (P=0.001), no significant difference between DBT and DBT + ultrasound (P=0.258), or between ultrasound and DBT + ultrasound (P=0.394). All three diagnostic models could distinctly discriminate the malignant and benign breast lesions (all P<0.001). The analysis with multi-group independent-sample Kruskal-Wallis rank sum test showed χ^2=14.982 and P=0.001, indicating there was difference among three diagnostic models. DBT obviously preceded ultrasound in the sensitivity, missed diagnosis rate, accuracy, and negative predictive value. Ultrasound was superior to DBT in displaying cystic lesions. The specificity of ultrasound in determining benign masses was better than DBT. The sensitivity of DBT + ultrasound was 100%, with a missed diagnosis rate of 0.000, and the negative predictive value also reached 100%. The combination of DBT and ultrasound can improve the diagnostic efficacy of breast lesions, compared with single DBT or ultrasound.

Keywords: Digital breast tomosynthesis, ultrasound, BI-RADS, breast lesions, diagnostic efficacy

Introduction

Breast cancer is a common malignant tumor in women. The incidence of breast cancer has ranked first place among female cancers. The incidence of breast cancer accounts for 85% of the total number of women patients aged 35-70 years [1]. Clinical practice proves that the early cure rate of breast cancer can reach as high as 97% [2]. Therefore, the early detection and screening of breast cancer has important clinical significance. Digital breast tomosynthesis (DBT) is a new imaging technology which uses different projection angles to reconstruct the 3D images. It can improve the detection ability of fiber dense glandular tissue and displaying ability of lesion morphology, thus increase the sensitivity and specificity of breast cancer diagnosis [3]. This technique can display the foci which are concealed by normal tissue in traditional X-ray photography, and improve the diagnosis accuracy [4, 5]. This study compared the distribution of breast imaging reporting and data system (BI-RADS) classification and diagnostic efficacy among three diagnostic models including DBT, ultrasound, and DBT + ultrasound for breast lesions, and analyzed their advantages. The objective was to provide a reference for further application of DBT and ultrasound to diagnosing breast lesions.

Subjects and methods

Subjects

One thousand and sixty-five patients with breast lesions treated in XXX hospital from May 2013 to July 2015 were enrolled in this study. Their ages were 25-85 years old, with average

Table 1. Distribution of BI-RADS classification in three diagnostic models

BI-RADS grade	DBT	Ultrasound	DBT + ultrasound
0	28 (2.63%)	2 (0.19%)	1 (0.09%)
1	4 (0.38%)	21 (1.97%)	4 (0.38%)
2	481 (45.16%)	310 (29.11%)	443 (41.79%)
3	213 (20.00%)	388 (36.43%)	268 (25.28%)
4A	97 (9.11%)	178 (16.71%)	117 (11.04%)
4B	134 (12.58%)	93 (8.73%)	123 (11.60%)
4C	54 (5.07%)	38 (3.57%)	50 (4.69%)
5	54 (5.07%)	35 (3.29%)	59 (5.53%)
Total	1065 (100%)	1065 (100%)	1065 (100%)

BI-RADS, breast imaging reporting and data system; DBT, digital breast tomosynthesis.

Table 2. Pairwise comparison of BI-RADS distribution in three diagnostic models

Model	χ^2	P
DBT *vs.* DBT + ultrasound	-77.526	0.258
DBT *vs.* ultrasound	-148.012	0.001
Ultrasound *vs.* DBT + ultrasound	70.486	0.394

BI-RADS, breast imaging reporting and data system; DBT, digital breast tomosynthesis.

age of 42.01±8.8 years. The patients had complete breast color Doppler ultrasound and DBT data collected. Among the 1065 patients, 194 cases had complete pathological examination data. This study was approved by the ethics committee of Fujian Medical University. Written informed consent was obtained from all participants.

Inspection methods

DBT inspection was performed at the craniocaudol and mediolateral oblique in all patients, using the Selenia® Dimensions® Digital breast 3D tomography system (Hologic Inc., MA, USA). In each inspection, the X-ray tube was rotated within 15°, with one time of low-dose exposure at for every 1° rotation. The 15-frame images were obtained, for reconstructing a series of high-resolution tomographic images. Finally the DBT images were obtained at the same body position (COMBO mode). The color Doppler ultrasound examination (EUB-6500, Hitachi Medical Corp., Tokyo Japan) was also performed to all patients and was operated by a physician specializing in ultrasound for more than 4 years.

Evaluation of examination outcome

DBT and color Doppler data in all patients were recorded. Using BI-RADS classification as the criteria, the distribution differences among DBT, ultrasound, and DBT + ultrasound in diagnosis of breast lesions were analyzed. Based on the pathological results of 194 cases, the diagnostic efficacies of three diagnostic models were compared. The images of each patient were read by four doctors, and a consistent consultation was obtained.

Statistical analysis

All statistical analysis was carried out using SPSS 17.0 software (SPSS Inc., Chicago, IL, USA). The enumeration data are presented as the number and rate. The comparison between two groups was performed using χ^2 test, and that among multiple groups performed using multi-group independent-sample Kruskal-Wallis rank sum test. $P<0.05$ was considered as statistically significant.

Results

Distribution of BI-RADS classification in three diagnostic models

The distribution of BI-RADS classification in DBT, ultrasound, and DBT + ultrasound models are shown in **Table 1**. DBT and ultrasound models were performed in 1065 patients, respectively, and the DBT + ultrasound model was performed in 1065 patients. The pairwise comparison results of three diagnostic models are shown in **Table 2**. There was a significant difference of BI-RADS distribution between DBT and ultrasound (P=0.001), with no significant difference between DBT and DBT + ultrasound (P=0.258) or between ultrasound and DBT + ultrasound (P=0.394). The analysis with multi-group independent-sample Kruskal-Wallis rank sum test showed $\chi^2=14.982$ and P=0.001, indicating there was a difference among the three diagnostic models.

Diagnostic efficacy of three diagnostic models

The diagnostic efficacies of three models were compared using pathological results as the criteria. Results are shown in **Table 3**. All three diagnostic models could distinctly discriminate

Table 3. Diagnostic results of the three diagnostic models

		Pathological results		Total	χ^2	P
		Malignant	Benign			
DBT	Malignant	71 (98.61%)	71 (58.20%)	142 (73.20%)	37.694	<0.001
	Benign	1 (1.39%)	51 (41.80%)	52 (26.80%)		
	Total	72 (100%)	122 (100%)	194		
Ultrasound	Malignant	62 (86.11%)	30 (24.59%)	92 (47.42%)	68.731	<0.001
	Benign	10 (13.89%)	92 (75.41%)	102 (52.58%)		
	Total	72 (100%)	122 (100%)	194 (100%)		
DBT + ultrasound	Malignant	72 (100%)	32 (26.23)	104 (53.61%)	99.079	<0.001
	Benign	0	90 (73.77%)	90 (46.39%)		
	Total	72 (100%)	122 (100%)	194		

DBT, digital breast tomosynthesis.

Table 4. Indexes related to three diagnostic models

Index	DBT	Ultrasound	DBT + ultrasound
Sensitivity	0.986	0.861	1.000
Missed diagnosis rate	0.014	0.139	0.000
Specificity	0.418	0.754	0.738
Misdiagnosis rate	0.582	0.246	0.262
Prevalence rate	0.371	0.371	0.371
Accuracy	0.732	0.474	0.536
Positive predictive value	0.500	0.674	0.692
Negative predictive value	0.981	0.902	1.000
Positive likelihood ratio	1.694	3.502	3.813
Negative likelihood ratio	0.033	0.184	0.000
Youdens index	0.404	0.615	0.738

DBT, digital breast tomosynthesis.

the malignant and benign breast lesions (all P<0.001). The related indexes are shown in **Table 4**, and the receiver operating characteristic (ROC) curve are shown in **Figure 1**. DBT obviously preceded ultrasound in the sensitivity, missed diagnosis rate, accuracy, and negative predictive value. Ultrasound was superior to DBT in displaying the cystic lesions. The specificity of ultrasound in determining benign masses was better than DBT. The area under ROC curve (AUC) of ultrasound was 0.808, which was greater than that of 0.702 of DBT. The sensitivity of DBT + ultrasound was 100% with missed diagnosis rate of 0.000, and the negative predictive value also reached 100%. This indicates that DBT + ultrasound has superior diagnostic performance, compared with single DBT or ultrasound.

Advantages of DBT and ultrasound with BI-RADS classification

DBT could more accurately determine the morphology, size, and distribution of malignant calcification foci. The typical malignant calcification foci could be determined as BI-RADS. The color Doppler ultrasound was not ideal for the diagnosis of calcification. Most of pathologically confirmed invasive ductal carcinomas were diagnosed as ductal carcinoma *in situ* by ultrasound (**Figure 2**). DBT was superior to ultrasound in determining the structure distortion (**Figure 3**). Ultrasound had great superiority in determining the cystic lesions which sometimes could not be displayed by X-ray (**Figure 4**). For cases with infiltrating ductal carcinoma after breast augmentation by injection with hydrogel, due to unclear boundary of hydrogel and gland tissue, the lesion was difficult to be displayed. However, this could be clearly revealed by ultrasound (**Figure 5**).

Discussion

DBT imaging is a high-level technology based on flat panel detection. This method is carried out through a series of different angles to carry on the fast collection to the mammary gland, and then obtain the small-dose projection data from different projection angles. In this method, the images can be reconstructed at any level parallel to the detector plane [6]. DBT is different from full-field digital mammography (FFDM) in scanning mode, imaging angle and parameters. DBT method can solve the overlapping problems of traditional 2D FFDM imaging, and improve the image quality. Although the radiation dose is also increased compared to conventional FFDM, but it is still lower than the maximum limit (3mGy) which is prescribed by FDA. Some scholars [7] believe that, if the

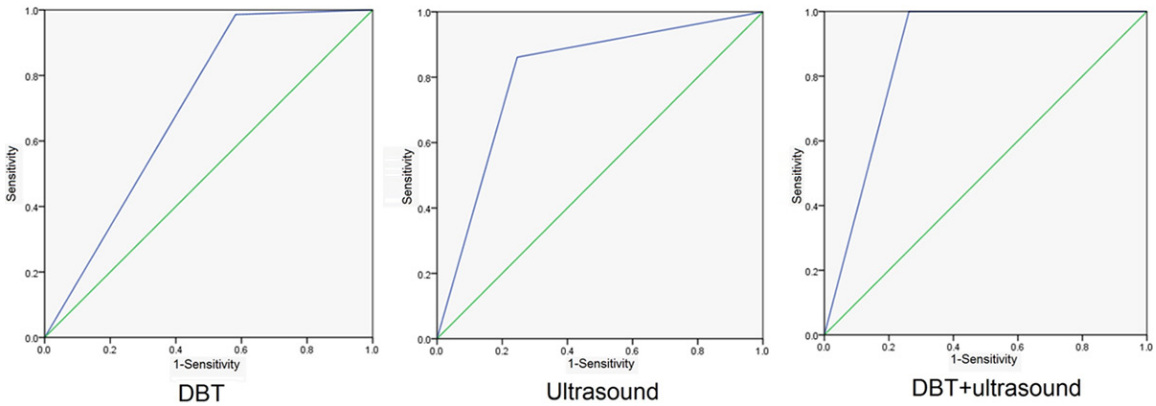

Figure 1. ROC curves of three diagnostic models. DBT: AUC, standard error, *P* value and 95% CI were 0.702, 0.036, 0, and 0.631-0.774, respectively; Ultrasound: AUC, standard error, *P* value and 95% CI were 0.808, 0.033, 0, and 0.743-0.872, respectively; DBT + Ultrasound: AUC, standard error, *P* value and 95% CI were 0.869, 0.026, 0, and 0.819-0.919, respectively. ROC, receiver operating characteristic; AUC, area under ROC curve; CI, confidence interval.

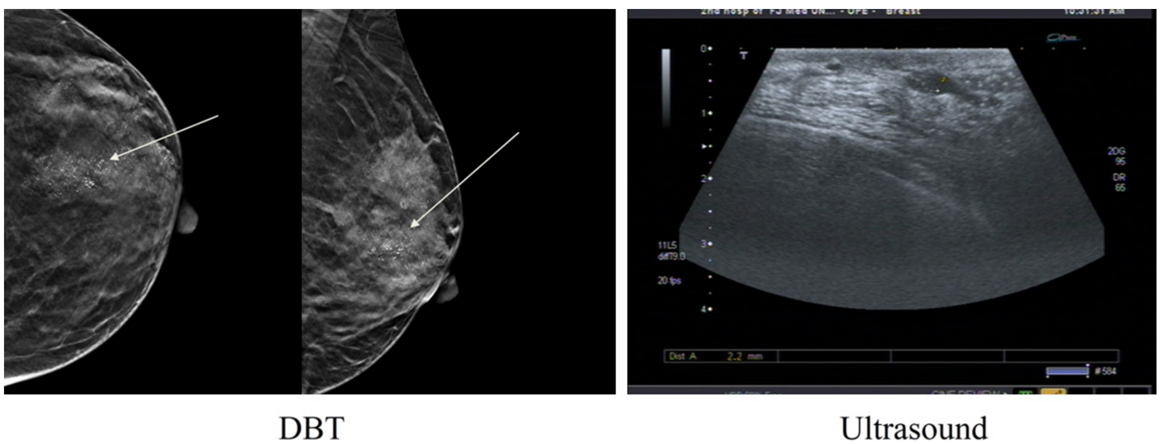

Figure 2. DBT and ultrasound for breast ductal carcinoma in situ. DBT, digital breast tomosynthesis.

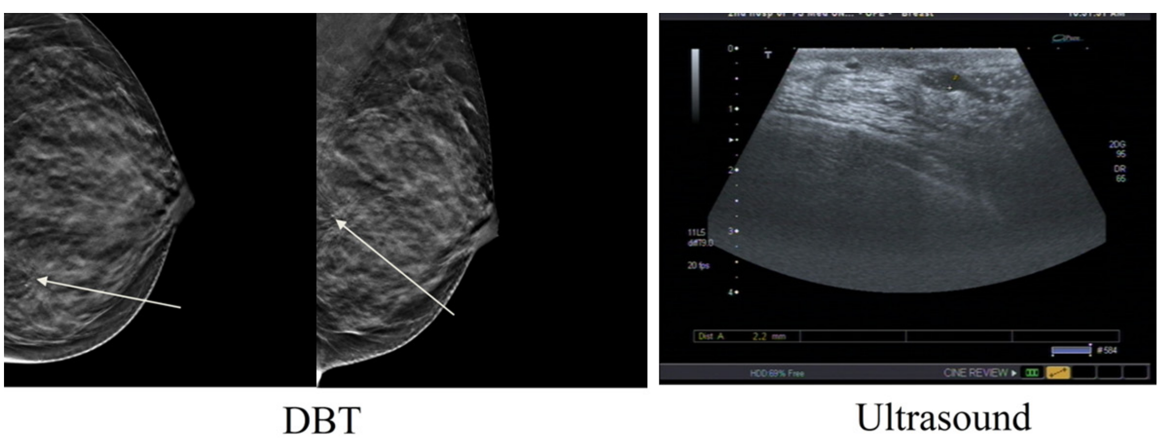

Figure 3. DBT and ultrasound for breast lobular carcinoma. DBT, digital breast tomosynthesis.

DBT can improve diagnostic efficiency, the slightly high radiation dose can be accepted. Because DBT has a high diagnostic rate, the breast reexamination rate is low. To a certain

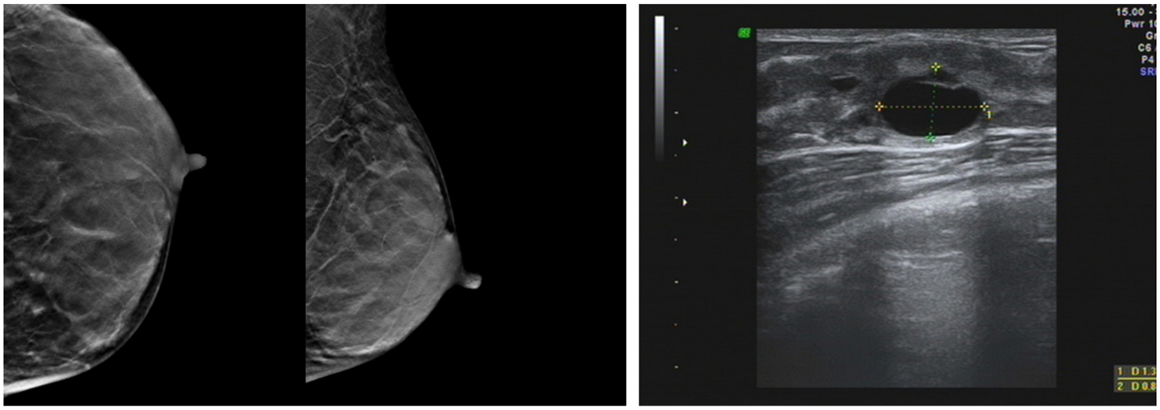

Figure 4. DBT and ultrasound for breast cystic lesions. DBT, digital breast tomosynthesis.

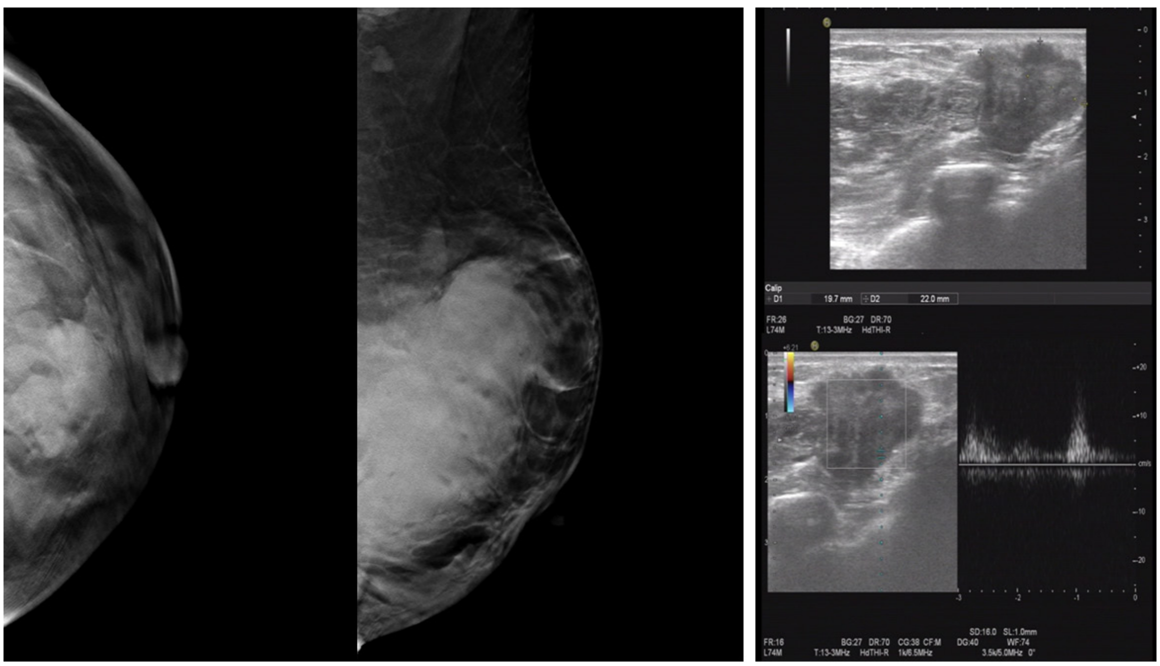

Figure 5. DBT and ultrasound for breast ductal carcinoma after breast augmentation. DBT, digital breast tomosynthesis.

extent, the exposure dose of DBT is much smaller than the radiation dose accumulated in the conventional FFDM examination. Previous literature [8, 9] report that the clinical research of DBT is mainly focused on the comparison with conventional FFDM. At present, most of research results show that the diagnostic value of DBT combined with FFDM is higher than single FFDM [10, 11]. The advantages of DBT are mainly that it can improve the sensitivity of screening diagnosis and accuracy of tumor size assessment and reduce the recall rate. Gennaro et al. [12] found that, DBT can significantly reduce the recall rate of patients. Förnvik et al. [13] report that, DBT has a significant advantage in tumor size assessment compared with FFDM, but there is no significant difference in tumor classification.

Our previous study [14] shows that the AUC of FFDM is 0.805, and it is 0.941 under the COMBO mode. The sensitivity of FFDM under

COMBO mode at the optimal cut-off of is 82.9%, which is higher than 60% of FFDM. The specificities of two methods are the same (93.2%). In this study, the sensitivity of DBT is 98.6%, which is significantly higher than 82.9% in in previous study [14]. This is due to the further understanding of sectioned images and increased determination of malignant signs. However, the specificity decreased from 93.2% to 41.8%. The reason is that, following the BI-RADS classification principle (2013 edition), the 4B-grade lesion is moderately possibly malignant, so it needs to be histologically diagnosed (malignant probability between 10% and 50%). In addition, we feared the missed diagnosis of breast cancer. Therefore, the 4B-grade cases were included with benign lesions. In statistical treatment, 4B grade was classified as malignant lesions. This resulted in the decreased specificity for this group. DBT + ultrasound can thus increase the specificity to 73.8%.

Color Doppler ultrasound not only has the advantages of 2D ultrasound image, but also provides a wealth of information on the hemodynamics [15], so it can significantly increase the diagnosis level of breast disease. However, the breast color Doppler ultrasound also has certain limitation. First, the sensitivity of color Doppler ultrasound to breast cancer-negative cases diagnosed by palpation is low. Micro calcification cannot be found, the mass sentus cannot be displayed, and small lesions or atypical cases are difficult to be detected [16]. Therefore, the accuracy rate of diagnosis is not ideal. In this study, the accuracy of ultrasound was 47.4%, which is lower than 73.2% of DBT. In addition, ultrasound can form the sound shadow behind the nipple, so it is easy to lead to missed diagnosis. Second, the color signal is affected by the instrument performance, instrument regulation, operation technology, histological characteristics of the tumor, and the tumor size [17]. There are overlapping or crossing phenomena in the differentiation of benign and malignant tumors. Third, the technology level of checking and the carefulness of operation can greatly affect the color Doppler ultrasound. The operating time is relatively long, so it is not suitable for large scale census [18]. If the ultrasonic examiner has no patience, it will easily cause missed diagnosis for larger breast or obese patients. The missed diagnosis rate of ultrasound is 13.9%, and that of DBT is only 1.4%. Finally, the subjective influence on color Doppler ultrasound is greater, and the results of different physicians may have different results, so it is difficult to obtain accurate contrast images.

This study finds that DBT is superior to color Doppler ultrasound in sensitivity, missed diagnosis rate, accuracy, and negative predictive value for diagnosis of breast lesions. Therefore, it has a great advantage for breast cancer screening. Ultrasound is superior to DBT in displaying cystic lesions, with better specificity of determining benign tumor than DBT. The sensitivity of DBT + ultrasound is 100% with a missed diagnosis rate of 0.000, and a negative predictive value that reaches 100%. This indicates that DBT + ultrasound can achieve superior diagnostic efficacy and has high clinical promotion value. Nevertheless, this study still has some limitations. The sample size of this study was relatively small. Larger sample sizes will make the results more convincing. In our future studies, the sample size will be further increased for obtaining better results.

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Disclosure of conflict of interest

None.

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