RESEARCH ARTICLE

Role of Breast Tomosynthesis in Diagnosis of Breast Cancer for Japanese Women

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Abstract

Introduction: Mammography is the most basic modality in breast cancer imaging. However, the overlap of breast tissue depicted on conventional two-dimensional mammography (2DMMG) may create significant obstacles to detecting abnormalities, especially in dense or heterogeneously dense breasts. In three-dimensional digital breast tomosynthesis (3DBT), tomographic images of the breast are reconstructed from multiple projections acquired at different angles. It has reported that this technology allows the generation of 3D data, therefore overcoming the limitations of conventional 2DMMG for Western women. We assessed the detectability of lesions by conventional 2DMMG and 3DBT in diagnosis of breast cancer for Japanese women. Methods: The subjects were 195 breasts of 99 patients (median age of 48 years, range 34~82 years) that had been pathologically diagnosed with breast cancer from December 20, 2010 through March 31, 2011. Both conventional 2DMMG and 3DBT imaging were performed for all patients. Detectability of lesions was assessed based on differences in category class. Results: Of the affected breasts, 77 (75.5%) had lesions assigned to the same categories by 2DMMG and 3DBT. For 24 (23.5%) lesions, the category increased in 3DBT indicating improvement in diagnostic performance compared to 2DMMG. 3DBT improved diagnostic sensitivity for patients with mass, focal asymmetric density (FAD), and architectural distortion. However, 3DBT was not statistically superior in diagnosis of the presence or absence of calcification. Conclusions: In this study, 3DBT was superior in diagnosing lesions in form of mass, FAD, and/or architectural distortion. 3DBT is a novel technique that may provide a breakthrough in solving the difficulties of diagnosis caused by parenchyma overlap for Japanese women.

Keywords: Breast tomosynthesis - mammography - breast cancer - Japanese women

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Introduction

Mammography is the most basic technique in diagnostic imaging of the breast, despite the various modalities are now used (Humpherey et al., 2003). Conventional 2D mammography (2DMMG) is a modality that breast tissue is visualized as a two-dimensional image. Parenchymal overlap, which may cause significant obstacles to detect abnormal lesion, is often shown in conventional 2DMMG. In particular, limitations of diagnosis in dense or heterogeneously dense breasts are well known in terms of sensitivity and specificity (Carney et al., 2003; Leconte et al., 2003).

The concept of tomosynthesis had been proposed since 1980s, however, the quality of the detectors and other technical barriers did not reach the level that would permit its utilization. Nowadays, advancements in digital detector technology have enabled its application in clinical practice (Andersson et al., 2008; Hakim et al., 2010; Helvie, 2010; Teertstra et al., 2010; Williams et al., 2010; Vecchio et al., 2011). In 3D digital mammography tomosynthesis (3DBT), tomographic images are reconstructed from multiple projections acquired from different angles. This technique allows the generation of 3D data and resolves the problem of tissue overlap. It was reported that the advantage of this technique is to improve the diagnostic accuracy by better visibility of the low contrast features that are hard to depict in conventional 2DMMG due to breast tissue overlap for Western women (Gur, 2007; Park et al., 2007; Michell et al., 2012; Alakhras et al., 2013; Houssami et al., 2013; Skaane et al., 2013; Zuley et al., 2013).

The aim of our present study was to evaluate the role of breast tomosynthesis in diagnosis of breast cancer for Japanese women. We therefore performed a 3DBT study assessing its diagnostic performance for a series of breast cancer patients, making comparison with conventional 2DMMG.

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Materials and Methods

Patients

With the approval of the institutional review board (IRB), a total of 110 patients (34~82 years of age, median age of 48 years) that had been pathologically diagnosed with breast cancer were imaged by both 2DMMG and 3DBT from December 20, 2010 to March 31, 2011. The analysis was performed with the breasts divided into affected breasts diagnosed pathologically as breast cancer with core needle biopsy (n=102) and unaffected breasts (n=93). All patients gave their informed consent before participating in this study. Patients with lesions completely removed by stereotactic vacuum-assisted breast biopsy, and those with history of open biopsy and/or surgery that affect breast architecture were excluded from the further analysis. Eventually, 99 patients (195 breasts) were included in this study. The detectability of lesions was assessed and compared by 2DMMG and 3DBT, based on category class and morphology of the lesions.

Diagnostic methods

Lesion category was assessed based on the agreement of two breast professional radiologists with grade A certification of the central committee on quality control of mammographic screening in Japan. Assessment of category was performed in accordance with the third edition of the Japan radiological society mammography guidelines. Breast Imaging-Reporting and Data System (BI-RAD) which is published by the American Colleage of Radiology is grobally used.. The system was designed to standardize reporting. The Japan radiological society mammography guidelines share similality with BI-RAD.

The Japan radiological society mammography guidelines Assessment categories are i) Negative. ii) Benign finding(s). iii) Probably benign. iv) Suspicious abnormality. v) Highly suggestive of malignancy.

In the interpretation of the radiograms, the Mediolateral-oblique (MLO) and Cranio-Caudal View (CC) images obtained by 2DMMG were evaluated at first. After assessment by 2DMMG, images obtained by 3DBT. In 2DMMG, as usual, the interpretation of the radiograms was used two screens on one monitor, the left and right sides of the MLO image on a double monitor, and the CC image on 4 screens. Next, the MLO and CC images were displayed on a one-screen monitor, and post processing such as magnification and changes of the window level for the respective images was performed. In 3DBT, basically, images were displayed on a one-screen monitor and observed as a continuously repeated video. If there were any remarks of even the slightest interest, the frame of the original image was assessed repeatedly.

Tomosynthesis system

A digital breast tomosynthesis system (Selenia Dimensions, Hologic, Bedford, MA, USA) was used for patient imaging. The system supported both 2DMMG and 3DBT imaging. In tomosynthesis imaging, 15 projections are acquired over a 15° angular range (-7.5° to +7.5°). These projections were used to reconstruct tomographic images of the breast with 1mm slice thickness.

Statistical analysis

In the statistical analysis, χ^2 test was used to investigate whether category sensitivity was correlated with the presence or absence of mass, FAD, calcifications, and distortion. Multivariate logistic regression analysis was performed based on the results of the χ^2 test to investigate the variables that affect category sensitivity. Statistical analysis was carried out with $p<0.05$ to indicate a significant difference. These statistical analyses were conducted using SPSS version 20.0 (SPSS Inc, Chicago, IL, USA).

Results

A comparison of categories of all 195 breasts is presented in Table 1. Of the affected breasts, 77 (75.5%) had same category in both 2DMMG and 3DBT; for 24 (23.5%) breasts, the category was higher in 3DBT indicating an improvement in diagnostic accuracy compared to 2DMMG. Only in 1 (1%) breast, the category decreased. In 15 (14.7%) breasts, the lesions could not be detected in neither 2DMMG nor 3DBT (Table 2).

The effectiveness of 3DBT was further investigated. The "effectiveness" is defined as an increased in diagnosis category in affected breast, or a decrease in diagnosis category in unaffected breast. Lesions were classified by presence or absence of mass, FAD, calcifications. Some patients had two or more duplicate findings. In our present study, 3DBT was more statistically effective for patients with mass lesion, FAD, or architectural

Table 1. The Comparison of Categories with 2DMMG and 3DBT of All Patients

		2DMMG category					
		1	2	3	4	5	Total
3DBT category	1	83	0	6	0	0	89
	2	0	8	0	0	0	8
	3	7	1	21	0	0	29
	4	0	0	9	19	0	28
	5	0	0	2	10	29	41
	Total	90	9	38	29	29	195

Table 2. The Comparison of Categories with 2DMMG and 3DBT of Affected Breasts

		2DMMG category					
		1	2	3	4	5	Total
3DBT category	1	14	0	1	0	0	15
	2	0	1	0	0	0	1
	3	2	1	14	0	0	17
	4	0	0	9	19	0	28
	5	0	0	2	10	29	41
	Total	16	2	26	29	29	102

Table 3. Category Changes According to Finding Type in Affected Breasts

	No	Category increased cases	OR	OR(95%CI)	p-value
mass	37	13	4.48	1.33~15.13	0.016
FAD	10	5	9.32	1.91~45.36	0.006
calcification	44	7	0.61	0.18~02.02	0.415
distortion	18	8	6.91	1.70~22.57	0.006

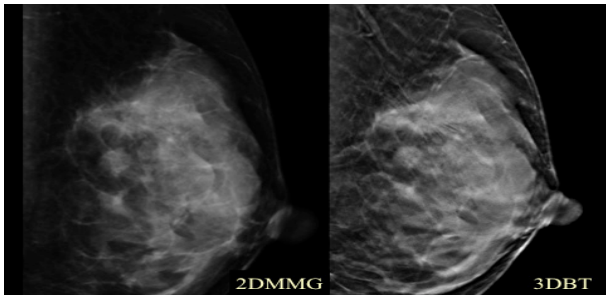

Figure 1. Comparison of 3DBT with 2DMMG in a Patient with a Mass

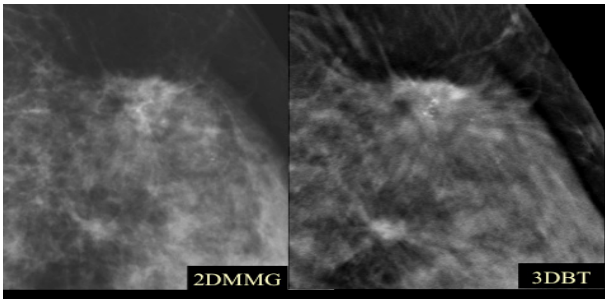

Figure 2. Comparison of 3DBT with 2DMMG in a Patient with Mass and Amorphous Calcifications

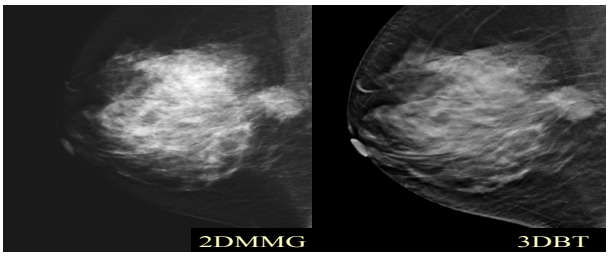

Figure 3. Case in Which 3DBT was not Effective

distortion ($p<0.05$). In addition, 3DBT was not found to be statistically effective in diagnosis of the presence or absence of calcifications ($p=0.415$) (Table 3).

Case1 was a patient with mass-forming invasive breast cancer (Figure 1). The presence of mass in the upper area could be confirmed in the left MLO image even by 2DMMG. Suspicion of malignancy from the margin of a slightly minute serration was judged as category 3. In 3DBT, it was evident that the mass had a clear spiculation strongly pulled into the peripheral breast tissue. It was also understood that part of the mass was denser than normal breast parenchyma, thus, the category was increased to 4. In addition, calcifications could also be easily recognized as an accessory finding.

Case 2 was a patient with invasive breast cancer with mass and grouped amorphous calcifications (Figure 2).This case showed calcifications and distortion that could be detected by 2DMMG. In 2DMMG, it is difficult to detect findings other than calcifications in heterogeneously dense breasts. Therefore, only microcalcifications were detected by 2DMMG. However, in 3DBT, clear and wide-range of distortion in the periphery of the microcalcifications was easily pointed out. The category was judged as 5 based on findings by both 2DMMG and 3DBT.However, in just slice with calcifications, grouped amorphous calcifications could be more clearly identified by 3DBT.

Case 3 was a patient with mass and spiculation-forming invasive breast cancer (Figure 3). When a mass is clearly seen in the dorsal side of normal breast tissue by 2DMMG, most of the periphery mass is surrounded by fat tissue. With 3DBT, clearer visualization is obtained, however, it did not make difference in assessment.

Table 4. The Comparison of Categories with 2DMMG and 3DBT of Unaffected Breast

		2DMMG category					
		1	2	3	4	5	Total
3DBT category	1	69	0	5	0	0	74
	2	0	7	0	0	0	7
	3	5	0	7	0	0	12
	4	0	0	0	0	0	0
	5	0	0	0	0	0	0
	Total	74	7	12	0	0	93

Table 5. Category Changes According to Finding Type of Unaffected Breasts

	No	Category decreased cases	p-value
Mass	7	0	1.000
FAD	5	3	0.001
Calcification	12	0	1.000
Distortion	5	3	0.001

Of the unaffected breasts, the categories of 83 (89.2%) cases given by 3DBT were equivalent to that of 2DMMG; increased in 5 cases (5.4%), and decreased in 5 (5.4%) cases (Table 4). The difference in category judgment between the two modalities was quite few. However, six lesions were diagnosed as FAD and distortion by 2DMMG, which was not detected in 3DBT (Table 5).

Discussion

In general, breasts of Japanese women are relatively small in size, and commonly characterized as dense or heterogeneously dense compared to breasts of Western women. Similar results have been reported in previous studies on Western populations (Andersson et al., 2008; Hakim et al., 2010; Helvie, 2010; Teertstra et al., 2010; Williams et al., 2010; Vecchio et al., 2011; Michell et al., 2012; Alakhras et al., 2013; Houssami et al., 2013; Skaane et al., 2013; Zuley et al., 2013). Our study showed that 3DBT improved the diagnosis accuracy compared to 2DMMG in Japanese female population and 3DBT is a novel technique that may provide a breakthrough in solving the difficulties of diagnosis caused by parenchyma overlap in 2DMMG.

Moreover, quite a few lesions that could not be recognized due to overlapping of the breast parenchyma in 2DMMG could be visualized in 3DBT. There were some lesions that could not be visualized even by 3DBT. Breasts with little fat are as same as those surrounded by breast parenchyma following tomosynthesis similar to the X-ray absorption difference, and are difficult to visualize. 3DBT had been shown to be effective in patients with a mass, FAD, or distortion. It was also shown in this study that 3DBT is not effective for calcifications cases, consistent to results from other studies (Poplack et al., 2007; Spangler et al., 2011).

With regard to masses and FAD, it is difficult to

evaluate margin of the mass or FAD in 2DMMG because the density is almost the same as normal breast tissue.

When 3DBT is used, assessment of mass margins such as the status of spiculation, and visualization of accompanying findings such as the retraction and calcifications of peripheral breast tissue become clear. Therefore, it contributed to the improvement in diagnostic performance. The correlation between lesions with architectural distortions became more evident in 3DBT, contributing to improvement in diagnostic performance.

Calcifications has much higher attenuation compared to normal breast tissue, so it is not difficult to detect even in 2DMMG. Because of that, there was no significant finding in the category difference between 2DMMG and 3DBT. However, compared to calcifications that was detected in overlap in 2DMMG, calcifications at just slice where a lesion was actually present could be detected more clearly in 3DBT. In addition, 3DBT enables stereoscopic recognition of calcification spread. Therefore, it will be a useful modality in the imaging of the extent of resections by surgeons during surgery.

In unaffected breast, the category decrease was observed with 3DBT in cases recognized as FAD or distortion by 2DMMG. Elimination of tissue overlap in the radiogram interpretation using the fault plane was suggested to improve the diagnostic performance. Though the number of patients in this study was small, the results obtained were statistically significant. FAD and distortion are false positives that typically accompany tissue overlap, so the level of contribution by 3DBT to diagnostic performance is high. Therefore, it is expected that 3DBT will be able to decrease recall rate in breast examinations.

When 3DBT was added to 2MMG for 49 breasts (81.3%) with a category of 4 or more, category assessment was not improved. This result indicated that if clear visualization of lesion could be obtained with 2DMMG, the addition of 3DBT had little advantage (Figure 3). When a mass is clearly seen in the dorsal side of normal breast tissue by 2DMMG, most of the periphery mass is surrounded by fat tissue. Therefore, a short spiculation is visualized clarifying presence of an invasive cancer. With 3DBT, clearer visualization is obtained, however, it did not make difference in assessment. Similarly, in fatty breast, there is no effect of overlap of breast parenchyma. However, there is advantage to confirm the presence or absence of accessory lesions.

The limitations of this study are that the number of patients was limited, and that there is the possibility of bias as the radiologists knew that the subjects were breast cancer patients (information on the site of the lesions was not given). However, even in clinical practice, the radiologists read the images with clinical information including pathological results. Therefore, we believe that there was no compromised factors.

In conclusion, we reported here our first clinical study with 3DBT. In lesions with findings of mass, FAD, and distortion, 3DBT is promising to be more effective than 2DMMG, breaking through the limitations of 2DMMG caused by the overlap of breast parenchyma. It is helpful in diagnosis of spread of lesions, and the stereoscopic recognition of calcifications in breast cancer patients. It may reduce recall rate in medical examinations of the breast thereby contributing to the decrease in the economical and psychological stress on patients.

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