Characterization of Breast Lesions: Comparison between Three-dimensional Ultrasound and Automated Volume Breast Ultrasound

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Objective: This study aimed to compare the diagnostic performance of three-dimensional ultrasound (3D-US) and automated breast volume scanner (ABVS) for the characterization of benign and malignant breast lesions.

Methods: Ninety patients who underwent surgery and preoperative conventional ultrasound (US), 3D-US, and ABVS examinations were enrolled in this study. The image quality and adjacent structures of the lesions in the coronal plane were compared. The combination of US, 3D-US, and ABVS for retraction phenomenon of the lesion was compared and the diagnostic performance of each combination was analyzed.

Results: ABVS displayed better image quality and adjacent structures than 3D-US ($P < 0.001$). The area under the curve (AUC) was 0.913, 0.842, and 0.871 for US, 3D-US, and ABVS, respectively. The AUC of the retraction phenomenon of the lesion was 0.732 and 0.810 for 3D-US and ABVS, respectively. When they were combined, US+ABVS showed the highest AUC of 0.924. No significant difference of diagnostic performances was found among conventional US, US+3D-US, and US+ABVS ($P > 0.05$).

Conclusions: Compared with 3D-US, ABVS seems to be superior in showing the retraction phenomenon of breast lesions and in the characterization of breast lesions alone or in combination with conventional US. Although no significant difference was observed between them, both ABVS and 3D-US provided valuable information in the coronal plane and improved our confidence level in breast lesion characterization, especially when combined with the conventional US.

Key words: Breast neoplasms; Ultrasonography; Imaging; Three-dimensional; Automated volume scanner

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Mammography is currently the primary screening and diagnostic tool for the detection of breast cancer. However, the sensitivity of mammography is substantially low for women with high breast density [1, 2]. A study carried out by Mandelson et al. was noted that the mammographic sensitivity was only 30% among women with extremely dense breasts but 80% in women with predominantly fatty breasts [3].

Moreover, women with high density breast have been shown to have an increased risk of developing breast cancer [4]. Therefore, additional imaging techniques, including ultrasound (US) and magnetic resonance imaging (MRI), have been used as a supplement to mammography for the detection of malignancy [5].

For women with dense breast tissue, mammographically occult or subtle cancers can be identified by screening

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with combined US and mammography [1,6,7]. A study with a larger sample size has revealed that the US can detect more breast cancers at a lower stage or with a smaller size compared with physical examination [8]. However, the US is much more operator-dependent than other imaging modalities with a significant learning curve, and the image quality of the US is strongly related to the operator's expertise and skill.

In recent years, three-dimensional US (3D-US) has emerged to provide a new perspective in breast ultrasound [9-11], which could reduce operator dependence for volumetric images of the breast to be acquired in a standardized manner. Additionally, the anatomical planes of interest within the volume can be visualized and reviewed in multiplanar views, including the transverse, sagittal, and coronal planes [12-14]. In the last few years, an automated whole breast ultrasound equipment, i.e., automated breast volume scanner (ABVS), has been increasingly used in breast imaging practice, including detection and characterization [11,15-17], and assessment of treatment response after neoadjuvant chemotherapy [18]. Compared with conventional 3D-US, the advantage of ABVS lies in a large field of view, so that the breast can be fully displayed by only two to four-volume scans [11, 15, 19].

Many studies have compared handheld two-dimensional US and 3D-US for diagnostic performance in the detection and characterization of breast lesions [10,20-22], and several studies have compared handheld two-dimensional US with ABVS from different perspectives [15,23-26]. However, no studies have compared the diagnostic accuracy of ABVS to 3D-US in terms of breast lesion characterization.

Thus, the purpose of our study was to compare the diagnostic performance of ABVS and 3D-US in differentiating benign from malignant breast lesions with histopathologic examination as the reference standard.

Materials and Methods

Patients

This prospective study was approved by our institutional ethics committee, and informed consent was obtained from all patients at the time of examination. From November 2015 to December 2016, 96 consecutive women who underwent preoperative conventional US, 3D-US, and ABVS examinations in our department were enrolled in this study. The indications for the US were abnormal findings on breast imaging, palpable masses, and nipple discharge. Eight women were later excluded from the study for the following reasons: 3 patients without histopathological confirmation, 2 patients with a history of surgical intervention, and 1 patient without

complete US data. Finally, 90 breast lesions in 90 patients were included in the final data analysis.

Conventional US and 3D-US examination

Conventional US and 3D-US examinations were performed by two radiologists (J.Q.Z. and W.W.Z.) with more than 20 years of experience in breast US. Conventional US examinations were performed using a MyLab 90 scanner (Esaote SpA, Genoa, Italy) equipped with a LA523 (4-13 MHz) multiple-frequency linear array transducer while 3D-US images were obtained using same scanner with a BL433 (4-13 MHz) volumetric multiple-frequency linear array transducer. The footprint of the BL433 transducer was 55×28 mm. When acquiring 3D volume data, the field of view was set to 44 mm (maximum), and the scan angle was set to 50° (maximum). The scan plane was mechanically moved by a build-in motor controlled by the scanner system, allowing a uniform volume reconstruction based on the volume acquisition technology developed by Esaote.

During 3D-US scanning, the probe was held still, and the patients were asked to hold their breath for approximately 5 seconds. Subsequently, three perpendicular planes, i.e., sagittal, transverse, and coronal planes, of the target region were displayed simultaneously on the scanner monitor. The acquired 3D volume data and representative sagittal, transverse, and coronal images were then stored on the system hard drive for document and analysis.

ABVS examination

Following the conventional US and 3D-US, ABVS examination was performed using the Acuson S2000 ultrasound unit (Siemens Medical Solutions, Mountain View, CA, USA), combined with 6–14 MHz broadband mechanical transducers. During the examination, the patient was placed in a supine position with both breasts fully exposed. The transducer was covered with a replaceable membrane to allow for adequate contact with the skin. The anterior, posterior, lateral, and medial views were acquired for each breast, and additional views were needed for larger breasts. On average, the total time to complete the examination was 15 min, including patient preparation, probe positioning, and scanning. Once the images were obtained, they were sent to a dedicated workstation for the multiplanar reconstruction of the images, including the transverse, sagittal, and coronal planes.

Image analysis

All images, including conventional US, 3D-US, and ABVS, were reviewed by two radiologists (Y.Z. and Y.J.D.) with more than 10 years of experience in breast US without prior knowledge of the patients' histories, pathological findings, or other imaging results. Based

on the fifth edition of the BI-RADS lexicon for breast ultrasound [27], all characteristics for each technique were reviewed as follows: shape (oval, round, or irregular), orientation (parallel or not parallel), margin (circumscribed, indistinct, micro lobulated, angular, or spiculated), echo pattern (hypoechoic, hyperechoic, isoechoic, anechoic, complex cystic and solid, or heterogeneous), posterior features (no posterior features, enhancement, shadowing, or combined pattern), calcification (presence or absence), and associated features (architectural distortion, ductal changes, skin changes, or edema), and a final BI-RADS category was given for US, 3D-US, and ABVS. A consensus would be obtained if there were any controversies by two readers. The retraction phenomenon reflecting malignant characteristics in the coronal plane was defined as hyperechoic cordlike structures interspersed with hypoechoic interval converging into part or all the lesion periphery [28], which was assessed and interpreted for 3D-US and ABVS images. The retraction phenomenon of 3D-US and ABVS was respectively combined with the conventional US for modified BI-RADS categories. If the retraction existed in conventional US, the BI-RADS categories would upgrade. However, those with BI-RADS 5 could not be upgrade anymore; thus, the receiver operating curve (ROC) of modified BI-RADS categories would obtained and compared.

In addition, the image quality and display of adjacent structures of the lesion in the coronal plane, which can reflect the overall spatial structure of breast lesions, were compared by two radiologists to determine which one was better. The judgment was based on the comprehensive resolution and contrast information of each image. If there was disagreement, a consensus would be reached after discussion.

Pathological analysis

All patients underwent core needle biopsy or surgery within one week after US examination. The final histopathological diagnosis was made by one pathologist with 25 years of experience in breast diseases, and blinded to all imaging results.

Statistical analysis

SPSS (version 21.0; SPSS Inc., Chicago, IL, USA) was used for general statistical analysis and MedCalc 19.05 (MedCalc Software, Mariakerke, Belgium) for ROC analysis using the histological results as the gold standard. The Wilcoxon signed-rank test was used to compare the image quality and display of adjacent structures of the lesion between 3D-US and ABVS. The sensitivity, specificity, area under the curve (AUC), and cut-off value of the BI-RADS category were calculated

and compared among conventional US, 3D-US, and ABVS, respectively. The BI-RADS categories were dichotomized using $> 4A$ as the cutoff value, and the Kappa statistic was calculated for consistency check between any two imaging techniques. $P < 0.05$ was considered statistically significant, and the kappa value was characterized as follows: < 0.4 as slight, $0.4 - 0.75$ as moderate, and ≥ 0.75 as good agreement.

Results

Pathological results

The mean age of all 90 patients was 46.93 ± 13.85 (range 18-78) years old, and the mean diameters of all breast lesions were 20.3 ± 10.2 mm (range, 5.7 - 50.9 mm). Additionally, the pathological results were listed in Table 1. Among the 55 benign breast lesions, 35 cases were fibroadenoma (38.89%), 9 cases were adenosis (10%), and 7 cases were intraductal papilloma (7.78%); while there were 35 malignant lesions, including 27 cases of invasive ductal carcinoma (30%), 4 cases of ductal carcinoma in situ (4.44%), one case of invasive lobular carcinoma (1.11%), one case of mucinous carcinoma (1.11%), one case of metaplastic carcinoma (1.11%), and one case of solid neuroendocrine carcinoma (1.11%).

Table 1 Pathologic results of all patients

Item	Cases
Benign	55
Fibroadenoma	35
Adenosis	9
phyllode tumor	2
Papillary ductal carcinoma	7
Pseudoangiomatous hyperplasia	1
Ductal dilation with cyst	1
Malignant	35
Invasive ductal carcinoma	27
Invasive lobular carcinoma	1
Ductal carcinoma in situ	4
Mucinous carcinoma	1
Metaplastic carcinoma	1
Solid neuroendocrine carcinoma	1
Total	90

Comparison of overall image quality between 3D-US and ABVS

Table 2 illustrated the overall image quality of 3D-US and ABVS. In terms of image quality, there was no significant difference between 3D-US and ABVS ($P = 0.330$). However, for the display of adjacent structures, ABVS was superior to 3D-US with statistical significance ($P < 0.001$). In 51 of the 90 cases, ABVS displayed better image quality of the adjacent structures than 3D-US (Fig. 1-3).

Table 2 Overall image quality of 3D-US and ABVS

Item	Image quality	Display of adjacent structures
3D-US better	16	4
ABVS better	22	51
Similar	52	35

3D-US, three-dimensional ultrasound; ABVS, automated breast volume scanner

Figure 1 A 33-year old woman with invasive ductal carcinoma in the right breast. (A) Conventional ultrasound showed a hypoechoic lesion ($11.2 \times 10.1\text{mm}$) with an oval shape and indistinct margin, and the final category was BI-RADS 4B for US; (B) Based on the findings in 3D-US imaging, the final BI-RADS category was BI-RADS 4B; (C) ABVS images showed the retraction phenomenon in the coronal plane, the final category was increased to BI-RADS 4C. BI-RADS, breast imaging reporting and data system; US, ultrasound; 3D-US, three-dimensional US; ABVS, automated breast volume scanner.

Figure 2 A 62-year old woman with invasive ductal carcinoma in the right breast. (A) Conventional ultrasound showed a hypoechoic lesion ($15.5 \times 10.5\text{mm}$) with an irregular shape, spiculated margin, and posterior shadowing, and the final category was BI-RADS 4C for US. (B) 3D-US images displayed the retraction phenomenon in the coronal plane, the final BI-RADS category remained as BI-RADS 4C; (C) ABVS images showed the retraction phenomenon in the coronal plane, the final category was BI-RADS 4C. BI-RADS, breast imaging reporting and data system; US, ultrasound; 3D-US, three-dimensional US; ABVS, automated breast volume scanner.

Figure 3 A 37-year old woman with intraductal papilloma in the left breast. (A) Conventional ultrasound showed a hypoechoic lesion ($17.5 \times 11.0\text{mm}$) with irregular shape and circumscribed margin and the final category was BI-RADS 4A. (B) Based on the findings in 3D-US imaging, the final BI-RADS category was BI-RADS 4B. (C) ABVS images did not show the retraction phenomenon in the coronal plane, the final category was BI-RADS 4A. BI-RADS, breast imaging reporting and data system; 3D-US, three-dimensional US; US, ultrasound; ABVS, automated breast volume scanner.

Comparison of retraction phenomenon between 3D-US and ABVS

Using 3D-US, 31 breast lesions showed the retraction phenomenon (34.44%), among which 22 lesions were proven to be malignant. Simultaneously, 25 lesions showed this phenomenon by ABVS (27.78%), and 23 cases were confirmed as malignant. For 3D-US, the sensitivity, specificity, and area under the curve (AUC) were 62.86%, 83.64%, and 0.732, respectively, while for ABVS, they were 65.71%, 96.36%, and 0.810, respectively. The AUC of ABVS was higher than that of 3D-US, but no statistical significance was found between them ($P > 0.05$) (Fig. 1 and 2). Specifically, of the 10 lesions that showed the retraction phenomenon in 3D-US but not in ABVS, 7 cases were confirmed to be benign, while 3 cases were malignant. In addition, all 4 lesions showed the phenomenon in ABVS but not in 3D-US were malignant (Table 3).

Diagnostic performances of US, 3D-US, and ABVS individually

The diagnostic performances of the final BI-RADS category by US, 3D-US, and ABVS were individually illustrated in Table 4. For conventional US, the final BI-RADS category was classified as BI-RADS 3 ($n = 18$), BI-RADS 4A ($n = 26$), BI-RADS 4B ($n = 11$), BI-RADS 4C ($n = 15$), and BI-RADS 5 ($n = 20$), with a sensitivity and specificity of 82.86% and 89.09%, respectively. ABVS was classified as BI-RADS 3 ($n = 14$), BI-RADS 4A ($n = 23$), BI-RADS 4B ($n = 15$), BI-RADS 4C ($n = 21$), and BI-RADS 5 ($n = 17$), with a sensitivity and specificity of 80.00% and 81.82%, respectively. For 3D-US, the sensitivity and specificity were 85.71% and 72.73% with BI-RADS 3 ($n = 10$), BI-RADS 4A ($n = 20$), BI-RADS 4B ($n = 15$), BI-RADS 4C ($n = 32$), and BI-RADS 5 ($n = 13$). 3D-US exhibited the best sensitivity, with a value of 85.71%, and conventional US had the highest specificity at 89.09%. In addition, conventional US performed the best with an AUC of 0.913, which was higher than those of 3D-US (0.842) and ABVS (0.871). However, no statistical significance

was found between US and 3D-US ($P = 0.05$) and US vs. ABVS ($P = 0.21$). The kappa value for the BI-RADS category was 0.793 for US and ABVS, 0.644 for US and 3D-US, and 0.663 for 3D-US and ABVS.

Diagnostic performances of US in combination with 3D-US and ABVS

The retraction phenomenon of 3D-US and ABVS was used in the conventional US to modify the BI-RADS category. The modified BI-RADS category was BI-RADS 3 ($n = 17$), BI-RADS 4A ($n = 21$), BI-RADS 4B ($n = 16$), BI-RADS 4C ($n = 9$), and BI-RADS 5 ($n = 27$) when combined with 3D-US. The diagnostic performance showed sensitivity and specificity of up to 85.71% and 89.09%, respectively, in the US+3D-US group. Simultaneously, they were BI-RADS 3 ($n = 17$), BI-RADS 4A ($n = 21$), BI-RADS 4B ($n = 14$), BI-RADS 4C ($n = 8$), and BI-RADS 5 ($n = 30$) when combined with ABVS. The sensitivity and specificity increased to 88.57% and 87.27%, respectively, in the US+ABVS group. The AUC reached up to 0.919 and 0.924 for these two groups. Only the diagnostic performance of 3D-US was significantly improved when combined with US ($P = 0.02$). Although US+ABVS had the best diagnostic performance, no significant difference was found among conventional US, US+3D-US ($P = 0.70$), and US+ABVS ($P = 0.52$) (Table 5, Fig. 4).

Table 3 Retraction phenomenon in 3D-US and ABVS

Item	3D-US	ABVS
Retraction phenomenon		
Presence	31	25
Absence	59	65
Diagnostic performance		
Sensitivity	62.86	65.71
Specificity	83.64	96.36
AUC	0.732	0.810

3D-US, three-dimensional ultrasound; ABVS, automated breast volume scanner; AUC, area under the curve

Table 4 Diagnostic performances of US, 3D-US, and ABVS

Item	BI-RADS category					Diagnostic performances		
	3	4A	4B	4C	5	Sensitivity	Specificity	AUC
US	18	26	11	15	20	82.86	89.09	0.913 (0.835 - 0.962)
3D-US	10	20	15	32	13	85.71	72.73	0.842 (0.749 - 0.910)
ABVS	14	23	15	21	17	80.00	81.82	0.871 (0.784 - 0.933)

US, ultrasound; 3D-US, three-dimensional US; ABVS, automated breast volume scanner; BI-RADS, breast imaging reporting and data system; AUC, area under the curve

Table 5 Diagnostic performances of US in combination with 3D-US and ABVS

Item	Modified BI-RADS category					Diagnostic performances		
	3	4A	4B	4C	5	Sensitivity	Specificity	AUC
US+3D-US	17	21	16	9	27	85.71	89.09	0.919 (0.842 - 0.966)
US+ABVS	17	21	14	8	30	88.57	87.27	0.924 (0.848 - 0.969)

US, ultrasound; 3D-US, three-dimensional US; ABVS, automated breast volume scanner; BI-RADS, breast imaging reporting and data system; AUC, area under the curve

Figure 4 The receiver operating curves (ROC) of conventional US, 3D-US, ABVS individually and 3D-US combined with US, ABVS combined with US. US, ultrasound; 3D-US, three-dimensional US; ABVS, automated breast volume scanner.

Discussion

This study was carried out to compare 3D-US and ABVS in terms of breast lesion characterization, which, to the best of our knowledge, has never been reported previously.

Although the principles and operational systems are different between 3D-US and ABVS, one advantage of these two techniques over the conventional US lies in the multiplanar reconstruction of images, including sagittal, transverse, and coronal planes, which can clearly show the anatomical details and spatial location of the breast lesions, and thus improve the overall diagnostic performance [11].

The image quality of the US should be guaranteed for the characterization of breast lesions. A previous study showed that the image quality of ABVS was identical or superior to that of conventional US in 97.1% of breast cases [29]. Our preliminary results suggested that the overall image quality in the coronal plane was similar for most breast lesions between ABVS and 3D-US, while ABVS was superior to 3D-US in displaying adjacent structures of the lesion. The reason may be the small field of view for 3D-US [14,30], while the ABVS images consisted of a 15.4 cm × 16.8 cm field of view of the breast.

The diagnostic performances of individual US, 3D-US, and ABVS were compared in our study. In a recent meta-analysis of nine studies, the pooled sensitivity, specificity, and AUC were 90.8% (95% confidence interval: 88.3 - 93.0%), 82.2% (80.0 - 84.2%), and 0.93 for ABVS, respectively, and 90.6% (88.1 - 92.8%), 81.0% (78.8 - 83.0%), and 0.94 for conventional US by Wang et al. [15]. In addition, for 3D-US, the pooled sensitivity and specificity were calculated to be 0.923 (95% confidence interval, 0.896 - 0.945) and 0.872 (95% CI, 0.849 - 0.893), which was reported by Lian et al. [22]. The overall diagnostic performance of these three imaging techniques was not as good as described previously, which may be due to the small sample size and selective bias; as for the similar diagnostic capability between 3D imaging and the conventional US, the results conformed to those of previous studies [14,20,31-34]. Compared with 3D-US and ABVS, the BI-RADS category of conventional US performed the best with an AUC value of 0.913, and it was 0.871 for ABVS and 0.842 for 3D-US, and the agreement between US and ABVS was considered as good, in accordance with Girometti et al. [16,24]. At this point, it seemed that a single ABVS could outperform 3D-US; however, no significant difference could be found among them.

The retraction phenomenon in the coronal plane has been reported as a significant and discriminating sign in the differential diagnosis of breast lesions [10,35,36]. Zheng et al. found it to be the best predictor of malignant breast lesions [37]. In our study, the retraction phenomenon differed significantly between benign and malignant breast lesions for both 3D-US and ABVS (Fig. 1 and 2), and the sensitivity and specificity were 65.71% and 96.39% for ABVS, which conformed to the previous literature, with sensitivities ranging from 57.5% to 91.4% and specificity from 92.5% to 100% [35,37-39]. For 3D-US, the sensitivity and specificity were 62.86% and 83.64%, respectively. All four lesions that displayed retraction phenomenon in ABVS but not in 3D-US were confirmed to be malignant (Fig. 1), which indicated that ABVS seemed to be better than 3D-US for this sign, but no statistical significance was found between them. These results indicated that both 3D-US and ABVS

enabled better visualization of the lesion extent and infiltration degree and provided relatively high diagnostic performance.

Besides, the special retraction phenomenon, which was unique to the coronal plane, has been recommended for BI-RADS-US lexicon as an independent descriptor by Zheng et al. [37]. Therefore, the retraction phenomenon in 3D-US and ABVS was further combined to the conventional US for a modified BI-RADS in our study, and the diagnostic efficiency was greatly improved, among which the AUC for 3D-US and ABVS reached up to 0.919 and 0.924 with a significant difference from single 3D-US but not from the conventional US. The results were inspiring because combination could make the best of the advantage of the conventional US and the coronal plane information provided by 3D-US and ABVS. On the other hand, it could avoid the shortcomings of ABVS, which could not provide the vascular and elastic characteristics of breast lesions.

Our study had some limitations. First, there might be a selection bias because the population included women with abnormal findings on imaging, with palpable masses or nipple discharge, but not the screening populations. Second, the analysis based on lesion size, histological types and molecular subtypes were not carried out in our study, which may also affect the results, since ABVS was demonstrated to be better at small or intraductal lesions [24,25]. Third, the sample size was small, and further studies would be needed to confirm this conclusion.

Conclusion

ABVS was superior in displaying the adjacent structure of the breast lesions. Moreover, compared with 3D-US, ABVS seems to be superior in showing the retraction phenomenon and in the characterization of breast lesions by itself or in combination with conventional US. Although no significant difference can be found between them, both ABVS and 3D-US provided valuable information in the coronal plane and improved our confidence in breast lesion characterization, especially when combined with the conventional US.

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Conflict of Interest

The authors have no conflict of interest to declare.

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