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Original Article

Value of ultrasound elastography in diagnosis of BI-RADS 4B breast lesions based on conventional ultrasound

Xia Gong[1], Yi Wang[2], Weihua Wu[1]

[1]*Department of Ultrasound, Shanghai Chest Hospital, Shanghai Jiaotong University, Shanghai 200030, China;* [2]*Department of Ultrasound, Shanghai Huashan Hospital, Fudan University, Shanghai 200031, China*

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Abstract: Background: Breast lesions of Breast Imaging Reporting and Data System (BI-RADS) mean that it is difficult to determine whether they are benign or malignant. By conventional ultrasound, it was hard to make a definite diagnosis for breast lesions of US BI-RADS 4B. The purpose of this study was to explore the value of ultrasound elastography in the diagnosis of breast lesions of US BI-RADS 4B by conventional ultrasound. Material and Methods: Ultrasound elastography was carried out in a total of 151 US BI-RADS 4B patients who were diagnosed via ultrasound and surgically treated. The diagnosis of 188 benign and malignant lesions by ultrasound elastography was analyzed based on postoperative pathological examinations. Results: The sensitivity, specificity and accuracy of elastography in the diagnosis of breast lesion were 91.67% (66 of 72), 88.79% (103 of 116), and 89.89% (169 of 188) respectively. Using a ratio of 1.5 as a criterion to determine whether benign or malignant lesion, it is found that the sensitivity, specificity and accuracy of ultrasound elastography were 90.28% (65 of 72), 87.93% (102 of 116) and 88.83% (167 of 188), respectively. Conclusion: Ultrasound elastography can be used as a useful supplement to conventional ultrasound. The combined application of ultrasound elastography and conventional ultrasound could efficiently improve the diagnosis accuracy of BI-RADS 4B breast lesions.

Keywords: Elastography, breast lesion, BI-RADS 4B, diagnosis, ultrasound

Introduction

Breast cancer is one of the most common diseases in women and has a high mortality [1-3]. In 2008, 23% of the new cancer cases were breast cancer, of which 50% incident cases and 60% death cases were in developing countries [1]. In China, the incidence of breast cancer has been increasing in both urban and suburban regions [4]. Currently, ultrasound is the most common way as a screening method because of its advantages: real-time dynamic imaging, simplicity, and noninvasive procedures. Although ultrasound is much more sensitive in detection of tumors compared with other methods, such as palpation and mammography, the specificity of ultrasound is not satisfactory and this limitation leads to an increase in biopsies with a cancer “detection rate” of only 10% to 30% [5]. In 1992, in order to improve the diagnostic quality, the American Association of Radiology and other academic institutions formulated the Breast Imaging Reporting and Data System (BI-RADS) and unified the terminology. The new version of BI-RADS includes the ultrasound diagnosis (BI-RADS), which is mainly a standard terminology and classification of ultrasonographic signs [6]. BI-RADS includes 7 grades from 0 to 6. Grade BI-RADS 4 was subdivided to 4A, 4B and 4C. The breast lesion of BI-RADS 4B means it is difficult to determine whether it is benign or malignant. This study aimed to evaluate the possibility of increasing the ability of breast ultrasound to differentiate benign from malignant masses of BI-RADS 4B breast lesions by the application of ultrasound elastography, and to determine an optimal cutoff value for the traced area ratio by receiver operating characteristic (ROC) analysis for differential diagnosis in future applications.

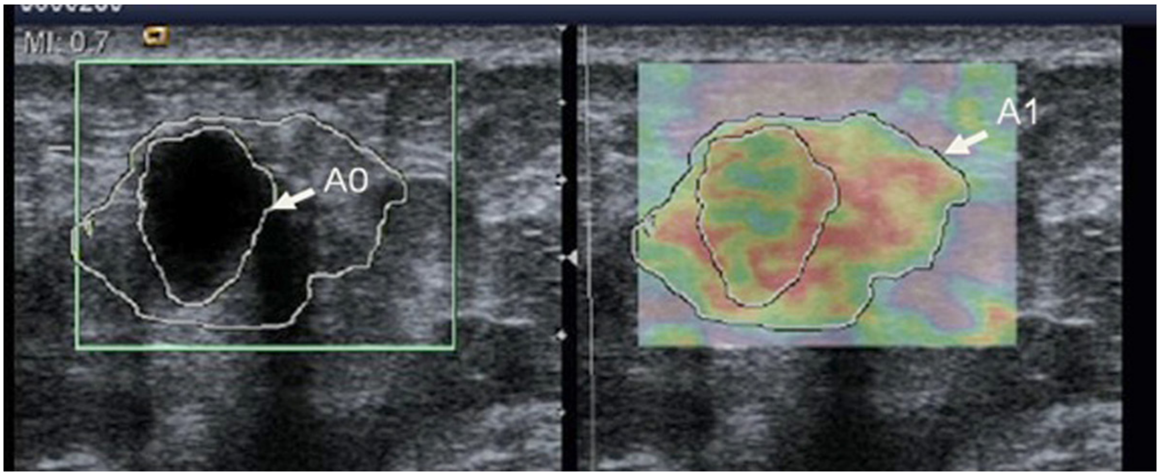

Figure 1. Measurement of the area ratio of elastic images. The area of the mass was detected by conventional ultrasound and defined as A0. The area of the mass was detected again on the elastogram and defined as A1. The ratio of A1 to A0 was considered as the traced area ratio.

Subjects and methods

Patients

This study was approved by the Ethics Committee of Huashan hospital. From July 2013 to January 2014, 151 female patients treated with surgeries in Huashan Hospital were enrolled and reviewed retrospectively in this study. The patients had an average age of 48.92±12.21 years (33-76 years). Informed consent for diagnostic procedures was obtained from each patient. Each patient was examined by conventional ultrasound and ultrasound elastography before surgery. All the patients were exanimated by conventional ultrasound firstly and 188 breast lesions were diagnosed as BI-RADS 4B. These lesions were then examined by ultrasound elastography. After surgeries, breast lesion tissues were acquired and their pathological types were confirmed.

Examination

The ultrasound elastography instrument was the Siemens ACUSON Antares system, of which the probe had a frequency of 5-13 MHz. The images were acquired in a ductal, radial manner, and the elastogram was graded according to the Tsukuba elasticity scores established by Itoh et al. [7].

The patients were examined in a supine position with the arm placed behind the head. For elastography, the same depth, focus position, and gain setting were used as for conventional images. A probe was applied to the breast and focused on the target tumor with and without light pressure. The radiologist who performed real-time imaging was asked to select representative transverse and longitudinal images of solid masses obtained by conventional ultrasound and elastography. Images were saved in a picture archiving and communication system as bitmap files on a hard disk.

Imaging evaluation

In the elastogram, different colors reflected the elastic strain of different tissues: green represented tissues with average hardness of the whole part; red and yellow represented tissue harder than the average hardness; and purple and blue represented tissue softer than the average hardness. When examinations were completed, the elastogram was classified into different grades [8]: 1) if most of the tumor was purple, it was classified as grade 1, indicating that the whole tumor was deformed; 2) if most of the tumor was blue, it was classified as grade 2, indicating that most of the tumor was deformed, but some small parts did not deform; 3) if most of the tumor was green, it was classified as grade 3, indicating deformation of the tumors' boundaries but that the central part of the tumor did not deform; 4) if most of the tumor was yellow, it was classified as grade 4, indicating that the whole tumor did not yield to deformation; and 5) if most of the tumor was red, it was classified as grade 5, indicating that the whole tumor and the peripheral tissues did not deform.

Table 1. Elastographic grading of breast lesions

Pathological examination	Stage 1-3		Stage 4 and above		Total
	Case number	Ratio (%)	Case number	Ratio (%)	
Benign	103	88.79	13	11.21	116
Malignant	6	8.33*	66	91.67*	72
Total	109		79		188

χ^2=118.05, *P<0.001 compared with the Benign group.

Table 2. Elastographic area ratio of breast lesions

Pathological examination	Case number	Area ratio		
		Minimal value	Maximal value	Mean
Benign	116	0.98	1.62	1.20±0.22
Malignant	72	1.04	2.70	1.95±0.61*
Total	188			

Note: t=5.787, *P=0.000<0.001 compared with the Benign group.

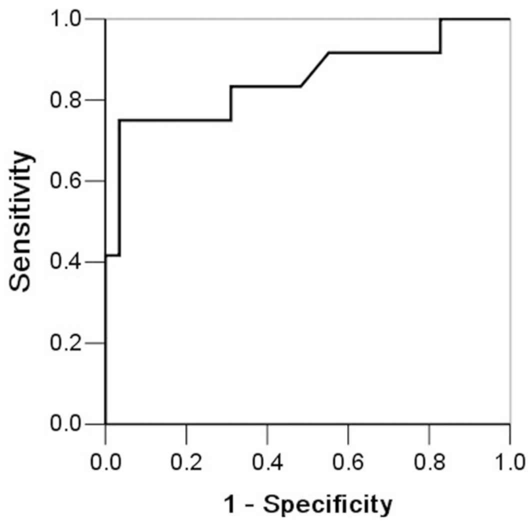

Figure 2. The ROC curve of the elastographic area ratio shows the accuracy of the lesion area ratio diagnosis based on the pathological examinations.

In addition, traced area ratios were calculated. The exact methods for measuring the ratio are described as follows. First, the area of the mass was detected by the conventional ultrasound and defined as A0. Then the area of the mass was detected again by the elastogram and defined as A1. The ratio of A1 to A0 was considered as the traced area ratio (**Figure 1**).

Data analysis

All data was imported into Microsoft Excel 2003 (Microsoft Corporation, Redmond, WA), and all the statistical analyses in this study were conducted with SPSS (SPSS Inc, Chicago, IL). The pathological diagnosis as a gold standard, the elastic hardness grade of the breast lesion was analyzed by using chi-square test, the lesion area ratio was analyzed by using t-test, and the function of area ratio in the diagnosis of the benign/malignant breast lesion was evaluated by using the ROC curve. In the meanwhile, the sensitivity [true positive/(true positive + false negative) × 100%], specificity [true negative/(true negative + false positive) × 100%], and accuracy [(true accurate number/total patient number) × 100%] of the elastographic diagnosis were evaluated.

Results

Diagnosis performance

Based on the elastography grading criteria, the 188 BI-RADS 4B lesions were analyzed by using ultrasound elastography. Usually, lesions of Grade IV and above were malignant [9, 10]. As shown in **Table 1**, of the 116 cases with benign lesions, 103 were Grade III and under (88.79%), and 13 were Grade IV and above (11.21%); of the 72 cases of malignant lesions, 6 were below Grade III (8.33%), and 66 were Grade IV and above (91.67%). The results of the chi-square test revealed that the two groups had a significant difference between them (P<0.001). Hence, the sensitivity, specificity and accuracy of elastography in the diagnosis of breast lesion were 91.67% (66 of 72), 88.79% (103 of 116), and 89.89% (169 of 188) respectively.

Area ratio

The area ratios under different pathological conditions are listed in **Table 2**. The area ratio of the benign and malignant lesions showed a significant difference (P<0.001), and the malignant lesions showed greater changes in the lesion area compared to the benign lesions.

ROC curve of area ratio

The accuracy of the lesion area ratio diagnosis was evaluated by using the ROC curve based on the pathological examinations (**Figure 2**). The area covered by the curve was 0.921, with a 95% confidence interval of 0.878-0.963

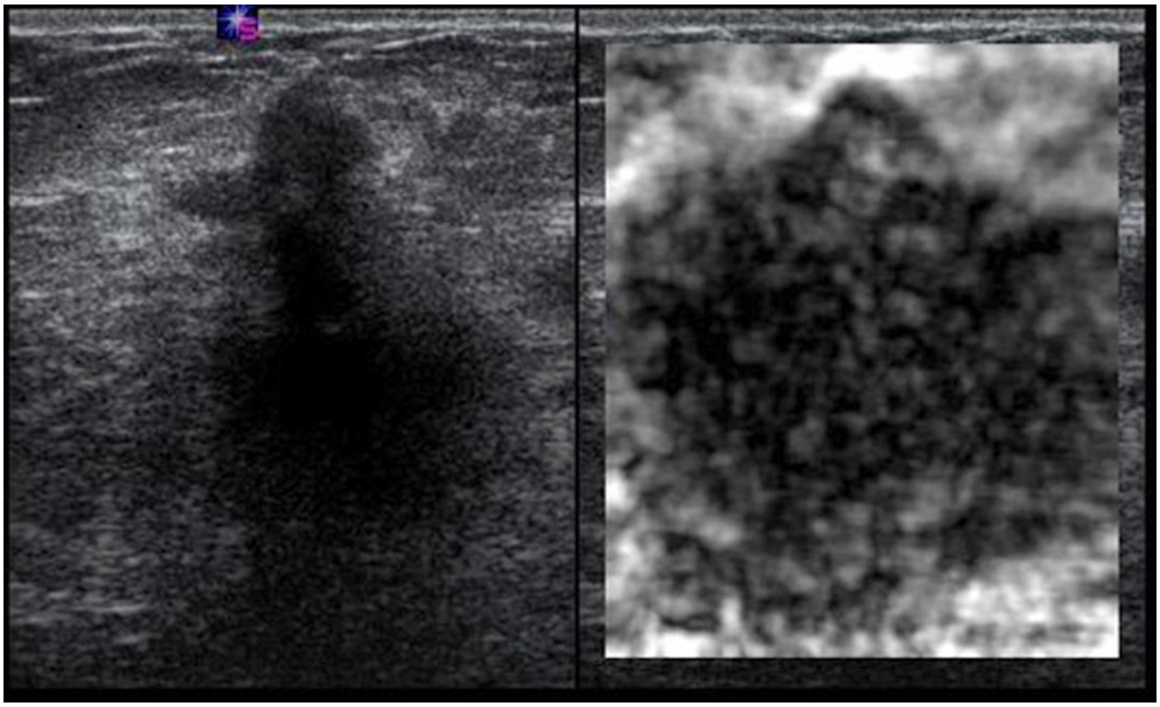

Figure 3. The lesion border is clearly indicated by elastography for fiber hyperplasia lesion. Obvious fiber hyperplasia was observed in the malignant lesions, which appeared as obvious ultrasound attenuation behind the lesion in gray scale sonography. However, due to the increased hardness in the elastic image, the edge of the lesion can be well indicated.

($P<0.001$). At the ratio of 1.5, the Youden index reached the highest peak (Youden index = sensitivity + specificity -1). Hence, the area ratio of 1.5 can be used as the standard to determine whether the lesion is benign or malignant. With this standard, the sensitivity, specificity and accuracy of elastography in the diagnosis of malignant lesions were 90.28% (65 of 72), 87.93% (102 of 116) and 88.83% (167 of 188), respectively.

Discussion

BI-RADS is an international guideline for the diagnosis of breast lesions. The system has 7 different grades, from 0 to 6, of which grade 4 includes all lesions with a 3 to 95% chance of being malignant. The grade 4 cases can be divided into three subgroups, 4A, 4B and 4C, which represent low probability, medium probability and strong probability of malignancy, respectively. As the malignant breast lesions always show obvious overlap in the conventional ultrasound performance, it is critical to develop an accurate diagnosis tool for BI-RADS 4B breast lesions [9]. In the present study, it was found that the newly developed ultrasound elastography technology could be a powerful tool for the diagnosis of breast lesions. Since Ophir et al. raised the concept of ultrasound elastography in 1991 [10], elastography has gained a wide attention from researchers. A lot of evidences have suggested that the combined application of ultrasound elastography, conventional gray scale ultrasound, and Doppler ultrasound not only can significantly improve the accuracy for the diagnosis of benign/malignant breast lesions, but it can also efficiently reduce the false negative cases, and thus has become an important clinical approach [11-13].

In the present study, we found that for the BI-RADS 4B lesions confirmed by conventional ultrasound, the diagnostic sensitivity and specificity of ultrasound elastography reached 91.67% and 88.79%, respectively. As BI-RADS 4B lesions were difficult to be diagnosed by conventional ultrasound, the result showed that ultrasound elastography could be applied to “upgrade” or “downgrade” the ultrasound-detected lesions. Hence, ultrasound elastography can be used as an important supplemental tool of conventional ultrasound, which is consistent with the previous study [14].

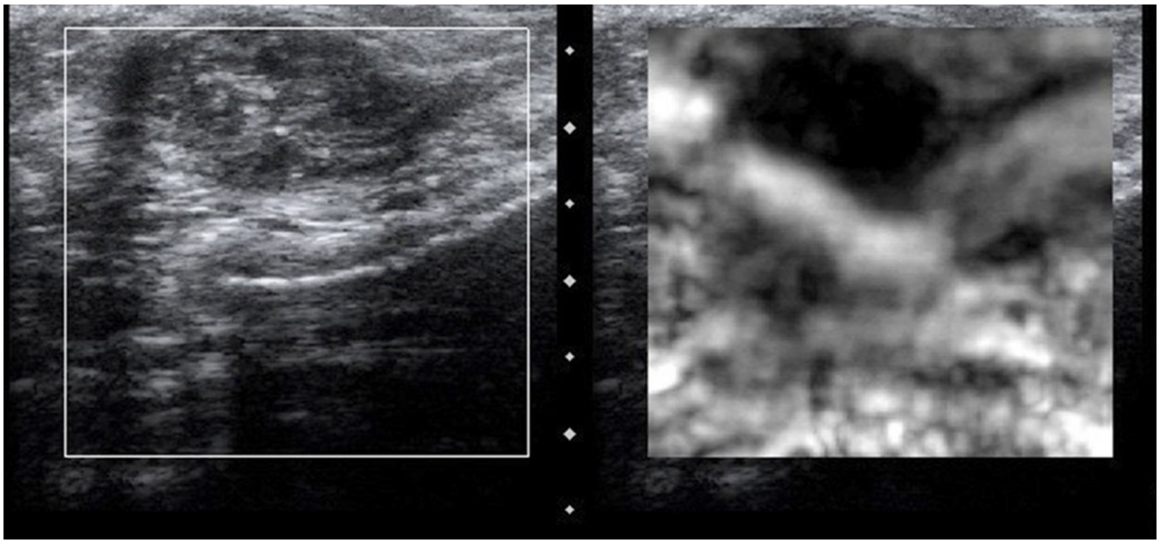

Figure 4. The features of the lesion edge such as spiculation and crab-like infiltration can be clearly indicated in the elastic images.

In recent years, quantitative analysis based on elastography has been used to determine breast malignancy. For instance, the strain ratio has been used to improve the accuracy of the diagnoses [15, 16]. Furthermore, the area ratio can also be used to determine the malignancy. The malignancy is often composed of hard lesions connected to the surrounding tissues, which reduces the activity and elasticity of the lesions [17]. Hence, the elastographic area ratio would be increased. Garra et al. [18] observed obvious fiber hyperplasia in the malignant lesions, which appeared as obvious ultrasound attenuation behind the lesion in gray scale sonography. However, due to the increased hardness in the elastic image, the edge of the lesion can be well indicated (**Figure 3**).

Krouskop et al. [19] reported that the hardness of the breast fibrous tissue was 10-100 times that of the adipose tissue. Due to the infiltration of the malignant lesions into the surrounding tissues, the lesions are compactly associated with these tissues with irregular borders, and thus have poor motility and a correspondently larger elasticity coefficient. As a result, the infiltrating part of the lesion, which has distinct hardness compared to the associated tissues but which cannot be indicated by conventional ultrasound, would clearly appear in the elastic images. Moreover, the features of the lesion edge such as spiculation and crab-like infiltration can be clearly indicated in the elastic images (**Figure 4**).

In the previous study by Hall et al [20], 1.2 was used as the area ratio threshold, and a sensitivity of 100% and a specificity of 75.4% were used to characterize breast tumors in a series of 169 tumors. Sun et al [21] set a criterion of 1.5 as the ratio for differentiating malignant and benign breast tumors. They found that the sensitivity, specificity, and accuracy were 82.8%, 87.8% and 81.1%, respectively. Results of this study indicated that the area changes of the malignant lesions were much larger than the benign lesions. In this study, it was defined that the area ratio of 1.5 was a threshold to determine the malignancy, the sensitivity, specificity and accuracy of the area ratio in the diagnosis of malignancy were 90.28%, 87.93% and 88.83%, respectively, which is consistent with Sun et al. [21] but different from other studies [22]. Although simple usage of the area ratio did not show any significant advantage in sensitivity and accuracy, its specificity demonstrated significant superiority. This result showed that "tuning" a ratio threshold to an individual observer can produce good results, but finding a single generalizable threshold may be difficult [23].

Conclusion

In summary, ultrasound elastography can accurately indicate the relative elastic hardness of breast lesions. The elastic grading, images and area ratio are useful parameters to determine the BI-RADS 4B breast malignancy. Therefore, the combined application of ultrasound elastography and conventional ultrasound could efficiently improve the diagnostic accuracy of BI-RADS 4B breast lesions.

Disclosure of conflict of interest

None.

Address correspondence to: Weihua Wu, Department of Ultrasound, Shanghai Chest Hospital, Shanghai Jiaotong University, 241 West Huaihai Rd, Xuhui Disctrict, Shanghai 200030, China. Tel: 0086-21-22200000; E-mail: wuweihuadoc@sina.com

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