The diagnostic value of strain elastography for BI-RADS category 4 lesions

Meng Dong
Yichang Central People's Hospital, State Administration of Traditional Chinese Medicine, China Three Gorges University

Bingyi Zhang
Yichang Central People's Hospital, State Administration of Traditional Chinese Medicine, China Three Gorges University

Chenghui Fu
Yichang Central People's Hospital, State Administration of Traditional Chinese Medicine, China Three Gorges University

Xingdong Xu
Yichang Central People's Hospital, State Administration of Traditional Chinese Medicine, China Three Gorges University

Boyuan Xing
xingboyuan0306@163.com

Yichang Central People's Hospital, State Administration of Traditional Chinese Medicine, China Three Gorges University

Research Article

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Abstract

Purpose

To investigate the diagnostic value of strain elastography for Breast Imaging Reporting and Data System (BI-RADS) category 4 lesions.

Methods

We recruited a total of 224 patients (259 lesions in all) who were diagnosed with BI-RADS category 4 lesions from July 2021 to December 2022.The sensitivity (SEN), specificity (SPE), positive predictive value (PPV), negative predictive value (NPV) and accuracy (ACC) of conventional ultrasound (US), the elasticity score method, the strain ratio method, a combined group and logistic regression model for the diagnosis of BI-RADS category 4 lesions were calculated. Compare the area under the curve (AUC) values and evaluate the diagnostic value. $P < 0.05$ was considered statistically significant.

Results

Of the 259 BI-RADS category 4 lesions,163 were benign and 96 were malignant. The AUC values of five methods: Logistic regression model > combined group > strain ratio method > conventional US > elasticty score method. The combined group was higher than that for the conventional US and elasticity score method. The AUC of the strain ratio method was higher than that of the elasticity score method, and the AUC of the logistic regression model was higher than the strain ratio method; these differences were all significant ($P < 0.05$).

Conclusion

Strain elastography has high diagnostic value for BI-RADS category 4 lesions, and the strain ratio method was superior to elasticity score method. The efficacy of conventional US when combined with the elasticity score for the diagnosis of BI-RADS category 4 lesions was better than that of either method alone.

Introduction

According to the Statistics of Global Cancer in 2020, breast cancer has surpassed lung cancer as the most prevalent malignant tumor in women [1]. The incidence rate and mortality of breast cancer in China are increasing annually, and are expected to increase by 36.27% and 54.01%, respectively, by 2030 [2]. Breast cancer is associated with a range of somatopsychic disorders and the time of detection is known to be closely related to the selection of treatment methods and the patient prognosis. Generally speaking, the earlier breast cancer is detected, the lower degree of surgical trauma, and the better the prognosis [3].

Current breast examination methods include palpation, X-ray, ultrasound (US), and magnetic resonance imaging (MRI). Of these, breast US is recommended as the main screening method for breast cancer, largely due to its simple operation, economy, non-radioactive method, good repeatability and wide applicability [4]. In order to standardize the terminology of breast imaging reporting and facilitate better communication among radiologists, the American College of Radiology (ACR) has developed the Breast Imaging Reporting and Data System (BI-RADS). The fourth edition of BI-RADS, proposed in 2003, recommended describing breast lesions by shape, orientation, margin, boundary, echo pattern, posterior acoustic features, surrounding tissue, calcifications and vascularity. After 10 years of development, the fifth edition of the BI-RADS, developed in 2013, incorporated elastic imaging assessment. The BI-RADS classification is divided into 0–6 categories; of these, 4 categories relate to suspicious malignant nodules (2% < risk level < 95%). According to the degree of risk, the BI-RADS classification can be divided into three categories: a low suspicion for malignancy (4a, likelihood: > 2% to ≤ 10%), a moderate suspicion for malignancy (4b, likelihood: > 10% to ≤ 50%), and a high suspicion for malignancy (4c, likelihood: > 50% to < 95%) [5].

Ultrasonic elastography (UE) technology can evaluate the hardness of breast cancer on the basis of conventional US to judge benign and malignant lesions, thus improving the diagnostic accuracy of breast cancer. Strain elastography (SE) evaluates the hardness of breast lesions in clinical practice *via* two methods: the elasticity score method and the strain ratio method [6]. The elasticity score method can qualitatively evaluate the hardness of breast lesions *via* elastic imaging, while the strain ratio method can semi-quantitatively judge the hardness of lesions by comparing the hardness of glands or fat around the lesions at the same depth [7–8].

In the clinic, the properties of BI-RADS category 3 and 5 lesions are often relatively certain and less controversial, while BI-RADS category 4 lesions are considered as suspicious malignant lesions. When BI-RADS category 4 lesions are evaluated, histopathological examination is recommended. However, the large range of malignant risk (2%-95%) results in significant uncertainty with regards to diagnosis and treatment. Therefore, over the last five years, many researchers have begun to use various new technologies such as radiomics, deep learning, contrast-enhanced ultrasound (CEUS), automated breast volume scanners, and UE, to study BI-RADS category 4 lesions, in order to predict the benign and malignant nature of these lesions, and thus provide certain guidance for diagnosis and treatment [9–12]. Compared to other new technologies, UE is easy to operate and represents a non-invasive form of examination. In most previous studies, UE technology was applied for all breast lesions or non-palpable forms of breast cancer, and confirmed that the combination of elastic imaging technology and conventional US could improve the diagnostic accuracy for benign and malignant breast lesions [13–19].

The purpose of the present study was to evaluate the diagnostic efficacy of BI-RADS category 4 lesions using SE techniques (including the elasticity score method and the strain ratio method), compare these methods with conventional US, and construct a logistic regression model to identify an optimal diagnostic method to improve the accuracy of diagnosing such lesions.

Methods

This study was approved by the Ethics Committee of our hospital and all patients provided signed and informed consent forms prior to examination. The dates of data for research purposes began on 1/July/2021. PJ-KY2020-13 (YJ-KY2020-0017-03)

Patients

This retrospective study analyzed 224 consecutive patients (259 breast lesions in all; mean age, 47.17±12.51 years; range, 22-90 years) who were diagnosed with BI-RADS category 4 lesions in Yichang Central People's Hospital, The First College of Clinical Medical Science, China Three Gorges University between July 2021 and December 2022. All patients with BI-RADS category 4 lesions were examined by the elasticity score method and strain ratio method. The inclusion criteria were as follows: (1) age ≥ 18 years; (2) BI-RADS category 4 lesions, and (3) accurate pathological results were available. The exclusion criteria were as follows: (1) pregnant or lactating; (2) a history of breast biopsy or surgery, and (3) the size of the lesion was > 5cm.

Conventional US and SE examinations

All examinations were performed by two physicians with five years or more of experience in conventional US and elastography; our analyses were performed with Samsung RS80A ultrasound diagnostic equipment operating at 5-12MHz. Each patient was instructed to lie on their back or, if necessary, on their side, to hold their head with both hands, and fully expose their breast. Then, we enabled grayscale mode, and performed multiple cross-sectional scans of each quadrant of the breast and axillary lymph nodes to obtain the maximum cross-sectional view of the lesion. We recorded the location, size, shape, orientation, edge, internal echo, posterior echo characteristics, calcification characteristics, and surrounding tissue echo information of the lesion in strict accordance with the Fifth Edition of the BI-RADS Classification. When the grayscale US exhibited a clear image of a breast lesion, we switched to elastic imaging mode. The selected area of interest was a rectangular area of breast lesion and surrounding normal tissue. We placed the probe perpendicular to the skin and used the probe to create slight vibrations at the lesion site. When the vertical bar on the right displayed one or more green bars, this indicated that the pressure had reached an ideal state. At this point, we recorded an elastic image and obtained an elasticity score. The diagnostic criteria for the elasticity score method referred to the Tsukuba scoring method proposed by Itoh [7], with a score within the range of 1 to 5. Then, we switched to E-Strain mode and placed the region of interest A in the area where the breast lesion was located; the region of interest B was placed in the glandular area at the same depth. We tried to maintain the range of the two regions of interest consistent. Then, the system would automatically calculate the B/A ratio (known as the strain ratio (SR)) and record the corresponding SR for each lesion.

Image analysis

All images are independently analyzed by two ultrasound physicians. Both physicians had more than five years of experience with conventional US, and the US elastography of SE. All disagreements were solved by consultation with a chief physician. For conventional US images, one of the six major malignant signs (irregular shape, non-circumscribed margin, non-parallel growth, posterior echo attenuation, microcalcification, and surrounding tissue changes) were rated as category 4a, two as category 4b, and three as category 4c. BI-RADS category 4a lesions were regarded as benign, while BI-RADS category 4b and 4c lesions were regarded as malignant. For SE, an elasticity score of 1-3 points was considered as benign, and an elasticity score of 4-5 points was considered malignant. The strain ratio method was used to identify benign and malignant lesions based on the optimal diagnostic threshold corresponding to the maximum Youden index. With the combined conventional US and elasticity score method, when the elasticity score was 1-2 points, the BI-RADS 4a lesions evaluated by conventional US were degraded to category 3, category 4b to category 4a, and category 4c to category 4b. When the elasticity score was 3 points, the original BI-RADS classification remained unchanged; when the elasticity score was 4-5 points, the BI-RADS 4a lesions evaluated by conventional US were upgraded to 4b, 4b to 4c, and 4c to 5 (Table 1). BI-RADS category 3 and 4a lesions were regarded as benign, while BI-RADS categories 4b, 4c, and 5 lesions were regarded as malignant. For the logistic regression model group, we determined the benign and malignant lesions based on data obtained from the predictive model.

Table 1 Revised BI-RADS classification obtained by combining conventional US and elasticity score method

BI-RADS	elasticity score		
	1-2	3	4-5
4a	3	4a	4b
4b	4a	4b	4c
4c	4b	4c	5

Statistics analysis

SPSS software (version 25.0 for Windows; SPSS Inc, Chicago, IL, USA) and MedCalc software (version 20.123, Ostend, Belgium) were used to perform statistical analyses. Quantitative data are expressed as mean ± standard deviation. Comparisons of clinical data (age and the maximum size of lesions) and elastic indicators (elasticity score and strain ratio) between benign and malignant breast lesions was conducted using the two independent sample t-test. The comparison of US features (shape, orientation, margin, internal echo, posterior acoustic features, and microcalcification) between benign and malignant breast lesions was conducted using the $\chi 2$ test. Selected factors showing statistically significant differences in the clinical data and US features were used to construct a binary logistic regression model with elasticity indicators as independent variables and pathological properties as dependent variables. Next, we generated ROC curves and analyzed the predictive value of the logistic regression model. Using pathological results as the gold standard, we then calculated the sensitivity (SEN), specificity (SPE), positive predictive value (PPV), negative predictive value (NPV), and accuracy (ACC) for the diagnosis of BI-RADS category 4 lesions using conventional US, the elasticity score method, and a combination of the two methods. Next, we generated an ROC curve based on the SR values, and identified the optimal SR diagnostic threshold and corresponding SEN, SPE, PPV, NPV, and ACC. The comparison of SEN and SPE between the different diagnostic methods was conducted using McNemar's test, the comparison of ACC between different diagnostic methods was conducted using the $\chi2$ test, and the comparison of area under the curve (AUC) data between different diagnostic methods was conducted using the Z-test. $P<0.05$ indicated a statistically significant difference.

Results

General information

The baseline information relating to the patients with BI-RADS category 4 lesions is described in Table 2. In terms of clinical information, the age and the maximum lesion size in the malignant group were significantly higher than those in the benign group($P<0.001$). Furthermore, the US features, shape, margin and microcalcification characteristics differed significantly when compared between the benign and malignant groups. Malignant lesions usually manifest with an irregular shape, a non-circumscribed margin and microcalcifications. With regards to elastic indicators, the elasticity score and strain ratio in the malignant group were significantly higher than those in the benign group (Fig 1). Fig 2 shows the results of a BI-RADS 4a lesion evaluated by conventional US, the elasticity score and the strain ratio from a 29-year-old patient with a left breast lesion with an elasticity score of 2 and a strain ratio of 1.84. Fig 3 shows the results of a BI-RADS 4b lesion evaluated by conventional US, the elasticity score and the strain ratio from a 53-year-old woman with a right breast lesion with an elasticity score of 5 and a strain ratio of 7.25. Fig 4 shows the results of a BI-RADS 4c lesion evaluated by conventional US, the elasticity score and the strain ratio from a 62-year-old woman with a right breast lesion with an elasticity score of 4 and a strain ratio of 2.89.

Table 2. Information for BI-RADS category 4 lesions

Chracteristics	Benign(163)	Malignant(96)	*P* Value
Patients			
Age(y)	42.77±10.22	54.20±12.07	**<0.001***
Lesions			
Maximum size of lesions	1.34±0.65	1.92±0.78	**<0.001***
Conventional US			
Shape			
regular	61	3	**<0.001***
irregular	102	93	
Orientation			
parallel	144	84	0.840
not parallel	19	12	
Margin			
circumscribed	147	24	**<0.001***
not circumscribed	16	72	
Homogeneous echo			
yes	150	83	0.150
no	13	13	
Posterior acoustic features			
absent	147	91	0.189
present	16	5	
Microcalcifications			
absent	127	62	**0.020***
present	36	34	
Strain Elastography			
elasticity score	1.95±0.71	3.80±0.83	**<0.001***
strain ratio	1.50±0.66	3.88±1.64	**<0.001***

BI-RADS=breast imaging reporting and data system;**US**= ultrasound.

* indicates statistically signifificant difference.

Logistic regression model

Multivariate binary logistic regression analysis was conducted on parameters showing statistical significance between the benign and malignant BI-RADS category 4 lesions. Analysis showed that patient age, the maximum size of lesions, the margin of the lesions, elasticity score, and strain ratio were independent influencing factors for distinguishing benign and malignant BI-RADS category 4 leisons (odds ratio [OR]: 1.091, 2.691, 6.074, 10.101 and 24.811, respectively). A logistic regression equation was established as follows: p= -9.029+0.087 × age (years)+0.990 × maximum size of lesions (cm) + 1.804 × not circumscribed margin of lesions + 2.313 × elasticity score ≥ 4 points + 3.211 × strain ratio ≥ 2.30 (Table 3). The logistic regression model judged BI-RADS category 4 lesions as malignant when $P > 0.50$, and benign when $P < 0.50$. Of the 259 lesions, 91 were diagnosed as malignant with 4 false positive cases; 168 cases were diagnosed as benign including 9 false negative cases. The diagnostic values of SEN, SPE, PPV, NPV, and ACC for BI-RADS category 4 lesions using logistic regression models were 90.63% (87/96), 97.55% (159/163), 94.98% (87/91), 95.60% (159/168), and 94.64% (246/159), respectively.

Table 3. Multivariate Logistic regression analysis for BI-RADS category 4 lesions

Indicators	*β*	SE	*Wald χ2*	*P* Value	OR
Age(y)	0.087	0.027	10.190	0.001*	1.091
Maximum lesion size(cm)	0.990	0.403	6.029	0.014*	2.691
Not circumscribed margin on US	1.804	0.627	8.273	0.004*	6.074
Elasticity score≥4	2.313	0.850	7.410	0.006*	10.101
Strain ratio≥2.30	3.211	0.711	20.393	0.001*	24.811
Constant	9.029	1.750	26.616	0.001	0.000

SE=standard error, OR=odds ratio.

* indicates statistically signifificant difference.

A comparison of the five methods

Next, the diagnostic performances of the five methods (conventional US, elasticity score, strain ratio, combined and elasticity score, and logistic regression model) were analyzed in terms of SEN, SPE, PPV, NPV and ACC (Table 4).

Table 4. Comparison of the diagnostic efficacy of five methods for BI-RADS category 4 lesions

Methods	SEN	SPE	PPV	NPV	ACC
conventional US	87.50%	90.18%	84.00%	92.45%	89.19%
ES	73.96%	98.16%	95.95%	86.49%	89.19%
SR	89.58%	93.25%	88.66%	93.83%	91.89%
US+ES	91.67%	95.71%	92.63%	95.12%	94.21%
Logistic regression model	90.63%	97.55%	95.60%	94.64%	94.98%

US=ultrasound, ES=elasticity score, SR=strain ratio, SEN=sensitivity, SPE=specificity, PPV=positive predictive value, NPV=negative predictive value, ACC=accuracy.

The SEN, SPE, PPV, NPV, ACC and AUC of the BI-RADS category 4 lesions diagnosed by conventional US were 87.50%, 90.18%, 84.00%, 92.45%, 89.19% and 0.888, respectively. For the elasticity score method, of the 96 cases of BI-RADS category 4 lesions diagnosed as malignant by pathology, there were 1, 7, and 17 lesions with elasticity scores of 1, 2, and 3, respectively, and 56 and 15 lesions with elasticity scores of 4 and 5 respectively. Of the 163 cases of benign BI-RADS category 4 lesions diagnosed by pathology, 40, 95, and 25 had elasticity scores of 1, 2, and 3, respectively, while 2 and 1 had elasticity scores of 4 and 5, respectively (Table 5). In addition, the SEN, SPE, PPV, NPV, ACC and AUC of the category 4 lesions diagnosed by the elasticity score method were 73.96%, 98.16%, 95.95%, 86.49%, 89.19% and 0.861, respectively.

Table 5. Comparison of elasticity score between benign and malignant BI-RADS category 4 lesions

Pathological results	Elasticity score					Total
	1 point	2 points	3 points	4 points	5 points	
Malignant	1	7	17	56	15	96
Benign	40	95	25	2	1	163
Total	41	102	42	58	16	259

Next, we set a strain ratio of 2.30 corresponding to the maximum Youden index as the optimal diagnostic threshold; the SEN, SPE, PPV, NPV, ACC and AUC of the category 4 lesions diagnosed by the strain ratio method were 89.58%, 93.25%, 88.66%, 93.83%, 91.89% and 0.914, respectively. The SEN, SPE, PPV, NPV, ACC and AUC of the combined group for the diagnosis of category 4 lesions were 91.67%, 95.71%, 92.63%, 95.12%, 94.21% and 0.937, respectively.

In terms of SEN, the methods were ranked as follows: combined group (US+ES) > logistic regression model > strain ratio > conventional US > elasticity score. Differences between the elasticity score method and the other methods were statistically significant (P<0.05); however, comparisons with other groups were not statistically significant. For the SPE, the methods were ranked as follows: elasticity score >

logistic regression model > the combined group (US+ES) > strain ratio > Conventional US. The comparison between the conventional US and the other methods was statistically significant ($P<0.05$). Furthermore, comparisons between strain ratio, elasticity score, and the logistic regression model were statistically significant ($P<0.05$). For the ACC, the methods were ranked as follows: logistic regression model > the combined group (US+ES) > strain ratio > conventional US = elasticity score. The comparison between the combined group (US+ES), conventional US, and elasticity score was statistically significant ($P<0.05$). Furthermore, comparisons between the logistic regression model, conventional US, and the elasticity score were statistically significant ($P<0.05$). Next, ROC curves were generated to compare the diagnostic efficiency of the five methods (Fig 5). By comparing the AUC, we observed the following rank: logistic regression model > the combined group (US+ES) > strain ratio > Conventional US > elasticity score. Comparisons between the conventional US, the combined group (US+ES), and the logistic regression model were statistically significant ($P<0.05$). In addition, the differences between the elasticity score and other groups (excluding the conventional US) were significant; comparisons between the logistic regression model and the strain ratio method were also statistically significant ($P<0.05$) (Table 6).

Table 6. Comparison of the AUC of five methods for BI-RADS category 4 lesions

Methods	US	ES	SR	US+ES	Logistic regression model
US	/	0.3478	0.2918	0.0186*	0.0144*
ES	0.3478	/	0.0104*	0.0002*	0.0001*
SR	0.2918	0.0104*	/	0.1107	0.0269*
US+ES	0.0186*	0.0002*	0.1107	/	0.5902
Logistic regression model	0.0144*	0.0001*	0.0269*	0.5902	/

**P*-value indicates significant difference. US=ultrasound, ES=elasticity score, SR=strain ratio

Discussion

US examination has been widely used for the diagnosis and differential diagnosis of breast lesions. The Fourth Edition of the BI-RADS, proposed in 2003, describes breast lesions by specific aspects, including shape, orientation, margin, internal echo, posterior acoustic features, and microcalcifications, and then classifies these parameters based on the number of malignant signs. These results can be influenced by the experience of the operating physician and other subjective factors [20–21]. Moreover, there was a certain overlap in the conventional US features of benign and malignant breast nodules, thus posing certain difficulties for accurate diagnosis [22]. The Fifth Edition of the ACR-BI-RADS, published in 2013, incorporated elastic evaluation for the description of breast lesions. US elastic imaging technology, as a non-invasive technique, can objectively evaluate the hardness of breast lesions and determine whether lesions are benign or malignant [23]. The malignant risk for BI-RADS category 4 lesions ranges from 2–95%, thus creating significant uncertainty for clinical diagnosis and treatment plans. In the present study, we used conventional US and elastography techniques to evaluate BI-RADS category 4 lesions, and constructed a logistic regression model using clinical data and US features to compare the diagnostic efficacy of various methods. Our aim was to improve the diagnostic accuracy of BI-RADS category 4 lesions and provide reference guidelines to assist clinical physicians when formulating diagnosis and treatment plans for breast lesions.

In the present study, we first found that the age and maximum diameter of breast lesions in the malignant group were higher than those in the benign group; these results were consistent with previous studies [24–26]. Furthermore, Hsu *et. al* reported that age was one of the clinical risk factors for breast cancer; this is partly due to poorer resistance in older subjects [27]. Secondly, in our research, malignant lesions typically exhibited irregular morphology, an irregular margin, and microcalcifications ($P < 0.05$); these findings also concurred with those of Gu *et. al* [26] and Liu *et. al* [28]. Thirdly, the elasticity score and strain ratio of the malignant breast lesions group were higher than those of the benign group, thus indicating that the hardness of malignant breast lesions was higher than that of the benign group; these findings concurred with those of Ozsoy *et. al* [29] and Zhao *et. al* [30].

Our analysis yielded the following regression equation: p = -9.029 + 0.087 × age (years) + 0.990 × maximum size of lesions (cm) + 1.804 × non-circumscribed margin of lesions + 2.313 × elasticity score ≥ 4 points + 3.211 × strain ratio ≥ 2.30. When the patient's age increased by one year, their risk of malignancy increased by 1.091-fold; however, when the maximum diameter of a lesion increased by 1 cm, the risk of malignancy increased by 2.691-fold. When the margin of the lesion was not circumscribed (microlobulated/angular/spiculated), the elasticity score was 4 or 5 points, and the strain ratio was ≥ 2.30, the risk of a lesion being judged as malignant was 6.074-fold, 10.101-fold, and 24.811-fold higher than that of being judged as benign, respectively. Our model incorporated both the elasticity score and strain ratio into the regression equation, and had a high OR value, thus indicating that SE technology contributed to the construction of the model. The logistic regression model in this study exhibited a higher SEN and SPE for the diagnosis of BI-RADS category 4 leisons, with values of 90.63% and 97.55%, respectively, thus indicating that the model exhibited a high detection rate for both benign and malignant BI-RADS category 4 leisons. The model misdiagnosed 9 cases; all of these were judged as benign by the elasticity score method, 8 cases were diagnosed as benign using the strain ratio method, and 1 case was diagnosed as malignant. The pathological types include 6 cases of invasive ductal carcinoma, 1 case of ductal carcinoma in situ, 1 case of metaplastic carcinoma, and 1 case of encapsulated papillary carcinoma. There were 4 misdiagnosed cases; these all were diagnosed as malignant by the strain ratio method, 2 as benign and 2 as malignant using the elasticity score method. Pathological types included 2 cases of intraductal papilloma, 1 case of granulomatous lobulitis, and 1 case of fibroadenoma with calcification. The ROC curve showed that the AUC of this model was 0.941, thus indicating that the established logistic regression model differentiated well between benign and malignant BI-RADS category 4 leisons. The observed goodness of fit for the Hosmer Lemeshow model was 4.160, thus indicating that the model had a good fit.

Of the 96 cases of malignant breast lesions, a total of 12 cases escaped diagnosis by conventional US, including 6 cases of invasive ductal carcinoma, 1 case of ductal carcinoma in situ, 2 cases of ductal papillary carcinoma, 2 cases of adenoid cystic carcinoma of the breast, and 1 case of invasive lobular carcinoma. It is possible that the malignant signs of some malignant tumors were not obvious; Guldogan *et.al* [31] reported that there were fewer malignant signs of adenoid cystic carcinoma of the breast. Of the 163 cases of benign breast lesions, 16 were misdiagnosed by conventional US, including 9 adenomatous nodules, 5 intraductal papillomas, and 2 cases of granulomatous mastitis. There are several reasons that might underline these observations. First, the pathological basis of some cases of breast fibroadenosis is the proliferation of interlobular fibrous tissue, which causes distortion and deformation of lobular acini, thus resulting in malignant signs, including an irregular shape and an uneven margin under conventional US. Furthermore, Yu *et.al* [32] also pointed out that sclerosing adenopathy can develop into atypical hyperplasia and breast cancer, thus making it easy for this condition to be misdiagnosed in clinical practice. Second, granulomatous lobulitis often presents as irregularly shaped and blurry lesions, which can be easily misdiagnosed by conventional US [33]. Liu *et.al* [34] reported that breast cancer and granulomatous mastitis overlaps with conventional US images, including irregular shape, an uneven margin, some visible microcalcifications and posterior echo attenuation, thus making it difficult to distinguish between these diseases. In total, 25 cases escaped diagnosis by the elasticity score method, including 15 cases of invasive ductal carcinoma, 5 cases of ductal carcinoma in situ, 2 cases of medullary carcinoma, 1 case of mucinous carcinoma, 1 case of spindle cell carcinoma subtype of metaplastic carcinoma, and 1 case of papillary carcinoma. Ten cases escaped diagnosis by the strain ratio method, including 6 cases of invasive ductal carcinoma of the breast, 1 case of ductal carcinoma in situ, 1 case of mucinous carcinoma, 1 case of spindle cell carcinoma subtype of metaplastic carcinoma, and 1 case of papillary carcinoma. Several factors may have been responsible for these results. First, intraductal carcinoma in situ is still in the early stages of cancer progression and the desmoplastic reaction is not obvious, thus resulting in a relatively small hardness, thus resulting in a lower elasticity score and strain ratio [30]. Secondly, myeloid and mucinous cancers have a lower hardness due to a high content of mucin and water [35]. Third, the metaplastic carcinoma spindle cell carcinoma subtype is mainly composed of spindle cells (sarcoma-like components); when there are more vascular components in the sarcoma component, the texture is often softer [36]. Three cases were misdiagnosed by the elasticity score method, including 1 fibroadenoma with calcification, 1 granulomatous lobulitis, and 1 intraductal papilloma. Eleven cases were misdiagnosed by the strain ratio method, including 8 cases of breast fibroadenosis and fibroadenoma, 2 cases of intraductal papilloma, and 1 case of granulomatous lobulitis. There are two potential factors that might be responsible for these findings. First, calcification increases the hardness of the nodules, thus resulting in an increase in their elasticity score. Secondly, intraductal papilloma often manifests as papillary hyperplasia within the duct, as well as secondary changes, including fibrosis, bleeding, and necrosis, thus leading to an increase in hardness [37]. Partial granulomatous lobulitis can increase the hardness of fibrous connective tissue due to inflammatory stimulation [38]. In the combined group, we used the elasticity score method to upgrade and downgrade BI-RADS type 4 nodules, with diagnostic SEN and SPE rates of 91.67% and 95.71%, respectively. After adjusting the BI-RADS classification by elasticity score, there were 8 patients with breast cancer, including

5 cases of invasive ductal carcinoma, 1 case of invasive lobular carcinoma and 2 cases of adenoid cystic carcinoma of the breast. These patients were considered as BI-RADS 4a by conventional US, and adjusted to grade 4b when they had an elasticity score of 4; thus, their diagnosis was correct. In a previous study, Zhang *et.al* [39] reported that a gross specimen of adenoid cystic carcinoma is tough or hard during resection and that this may lead to a higher elasticity score. In addition, 10 patients with benign breast nodules were adjusted from BI-RADS 4b to 4a due to an elasticity score of 1 or 2, thus reducing the rate of misdiagnosis. In total, 126 patients with type 4a nodules were adjusted to type 3 (125 benign and 1 malignant) due to an elasticity score of 1 or 2, thereby reducing the need for unnecessary puncture biopsies. Golatta *et.al* [40] reported that the combination of conventional US and elasticity score could reduce BI-RADS 4a lesions to class 3 and reduce the need for unnecessary biopsy in 35.35% of patients; in addition, the missed diagnosis rate was only 1.96%. These results indicate that when compared to individual diagnosis, the use of UE technology can reasonably downgrade and upgrade BI-RADS category 4 lesions, thereby improving the accuracy of diagnosis.

With regards to SEN, the elasticity score method had the lowest diagnostic efficiency of the five diagnostic methods, with a value of 73.96%. There was a statistically significant difference between the elasticity score method and each group. Yoon *et.al* [41] and Han *et.al* [42] used the elasticity score method to evaluate BI-RADS category 4 lesions and obtained a SEN of 75.00% and 89.76%, respectively. The former result was similar to that arising from our present study, while the latter SEN was relatively higher. This may be due to the fact that the cases of intraductal carcinoma in situ in the present study were still in the early stages of cancer progression, and non-obvious desmoplastic reactions can lead to low levels of hardness, as well as mucinous carcinoma, medullary carcinoma and metaplastic carcinoma. Thus, the elasticity score method is unable to identify these malignant lesions, thus resulting in relatively low sensitivity. With regards to the SPE, the five diagnostic methods exhibited high diagnostic value (all > 90.00%) for BI-RADS category 4 lesions, thus indicating relatively few misdiagnosis cases. In contrast, conventional US exhibited the lowest SPE (90.18%) of the five diagnostic methods, while the elasticity score method had the highest SPE (98.16%), thus indicating that the elasticity score method is better at identifying benign lesions in BI-RADS category 4 lesions and could facilitate conventional US, thereby reducing unnecessary puncture biopsy. According to AUC analysis, the conventional US and elasticity score method had a high diagnostic value for BI-RADS type 4 nodules ($0.8 < AUC \leq 0.9$), while the logistic regression model, combined group, and strain rate ratio method had a higher diagnostic value ($AUC > 0.9$). Of the five methods, the AUC of the elasticity score method was the lowest and was lower than that of the strain ratio method, thus indicating that the strain ratio method had a higher diagnostic efficacy for BI-RADS category 4 lesions than the elasticity score method. The AUC of the combined group was higher than that of the conventional US and elastic scoring method.

There are some limitations to this study that need to be considered. First, only SE was used to evaluate BI-RADS category 4 lesions, without involving shear wave elastography. In addition, multimodal evaluation was not conducted in conjunction with other imaging examinations such as mammography or MRI, thus resulting in a single diagnostic technique. Second, when constructing the logistic regression model, no analysis was conducted on other key indicators, such as the blood supply of lesions, axillary lymph node status, and CEUS results. Third, this study involved a small sample size and was a single center study; furthermore, the constructed logistic regression model has not been trained or validated yet; thus, further research is required for further verification and improvement.

Conclusion

Our analyses found that SE had a high diagnostic value for BI-RADS category 4 lesions, and that the strain ratio method was superior to the elasticity score method. The efficacy of conventional US combined with elasticity score for the diagnosis of BI-RADS category 4 lesions was demonstrated to be better than that of either method alone.

Abbreviations

US, ultrasound; MRI, magnetic resonance imaging; ACR, American College of Radiology; BI-RADS, Breast Imaging Reporting and Data System; UE, Ultrasonic elastography; SE, Strain elastography; CEUS, contrast-enhanced ultrasound; SEN, sensitivity; SPE, specificity; PPV, positive predictive value; NPV, negative predictive value; ACC, accuracy; AUC, Area Under the Curve

Declarations

Data availability statement

The raw data are provided in the article/Supplementary material. Further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving human participants were reviewed and approved by the ethics committee of Yichang Central People's Hospital, The First College of Clinical Medical Science, Third-grade Pharmacological Laboratory on Traditional Chinese Medicine, State Administration of Traditional Chinese Medicine, China Three Gorges University.The patients provided their written informed consent to participate in this study.   PJ-KY2020-13 (YJ-KY2020-0017-03)

Author contributions

BX conceptualized and designed the study. MD, BX and CF collected and analyzed the data. MD and BX dafted the manuscript. BX, BZ and XD revised the manuscript. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declared no competing interest.

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Figures

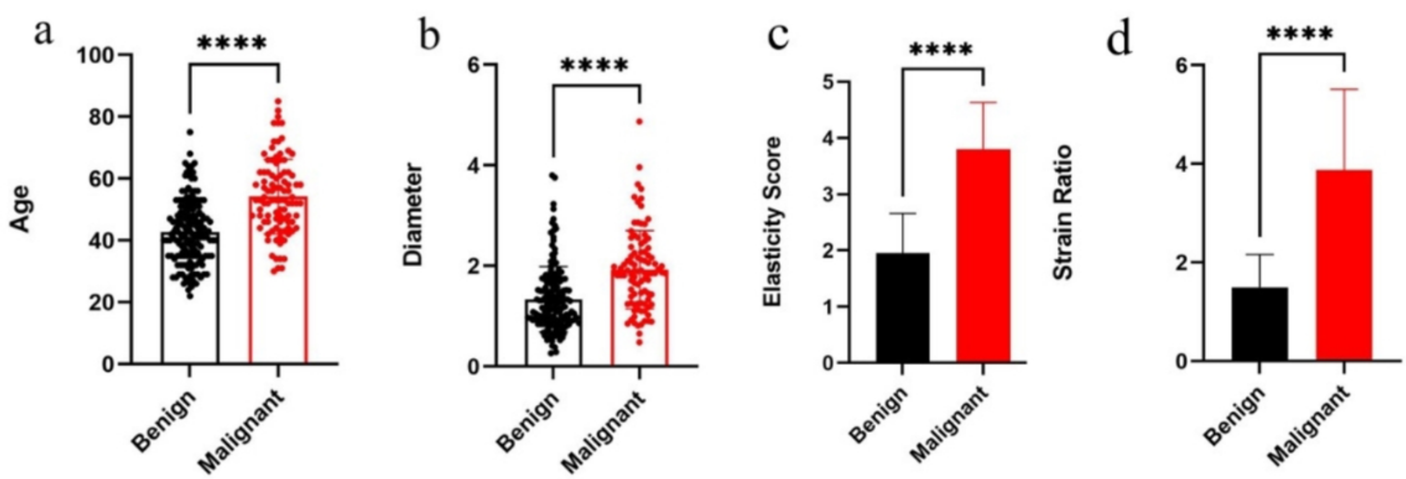

Figure 1

Comparison of clinical characteristics and elastic index between benign and malignant BI-RADS category 4 lesions.

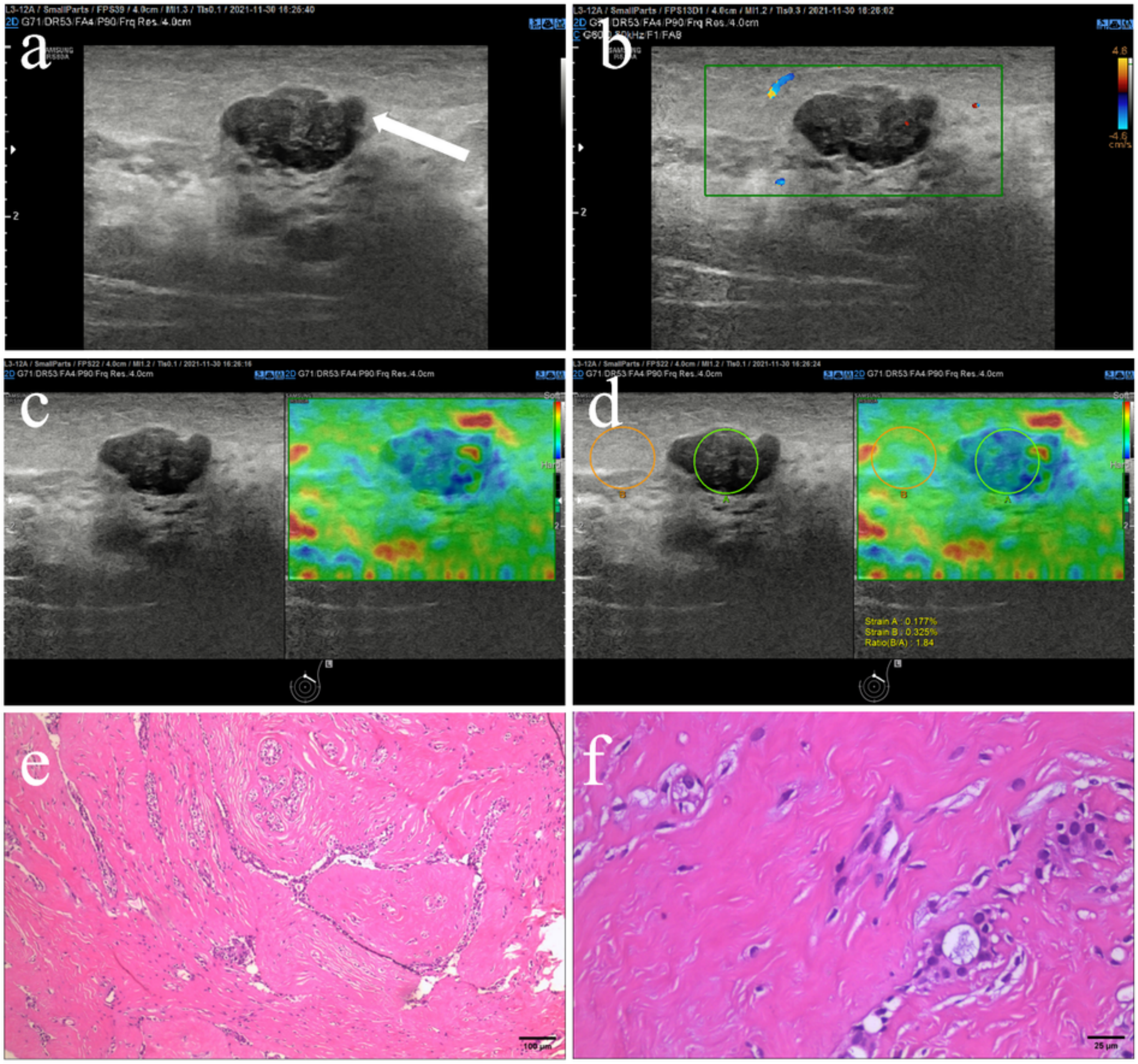

Figure 2

A 29-year-old woman had a lesion on the left breast. The lesion was evaluated BI-RADS 4a by Conventional US for irregular shape (as is shown by the white arrow （**a**） CDFI showed punctate blood flow signals inside the lesion（**b**） with an elasticity score of 2（**c**） with a strain ratio of 1.84（**d**） pathologically confirmed fibroadenosis with fibroadenoma （**e,**HE staining x100）and（**f,** HE staining x400）.

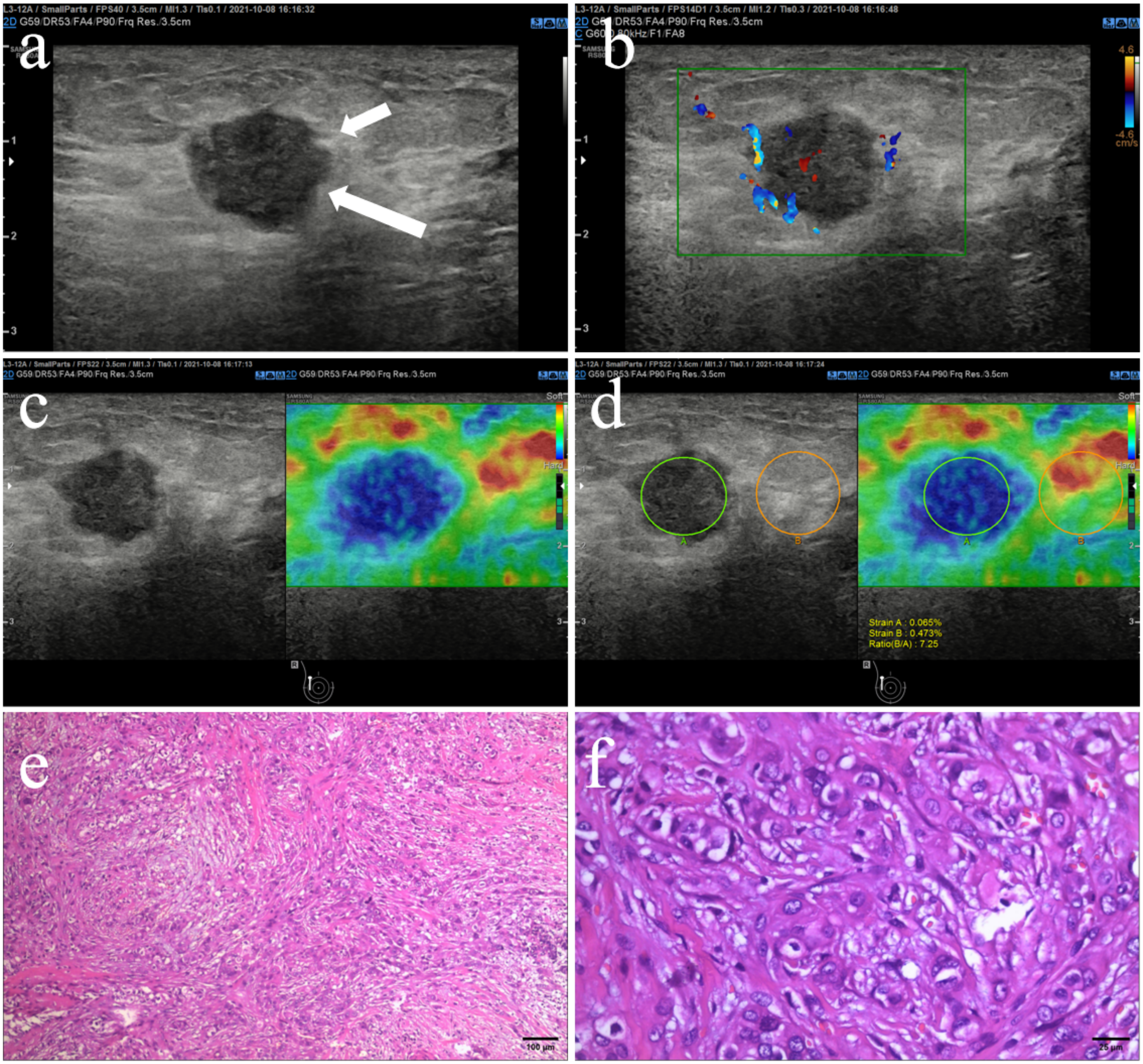

Figure 3

A 53-year-old woman had a lesion on the right breast. The lesion was evaluated BI-RADS 4b by Conventional US for irregular shape (the long white arrow and non-circumscribed margin (the short white arrow)（**a**） CDFI showed blood flow signals both inside and around the lesion（**b**） with an elasticity score of 5（**c**） with a strain ratio of 7.25（**d**） pathologically confirmed invasive ductal carcinoma（**e,** HE staining x100）and（**f,** HE staining x400）.

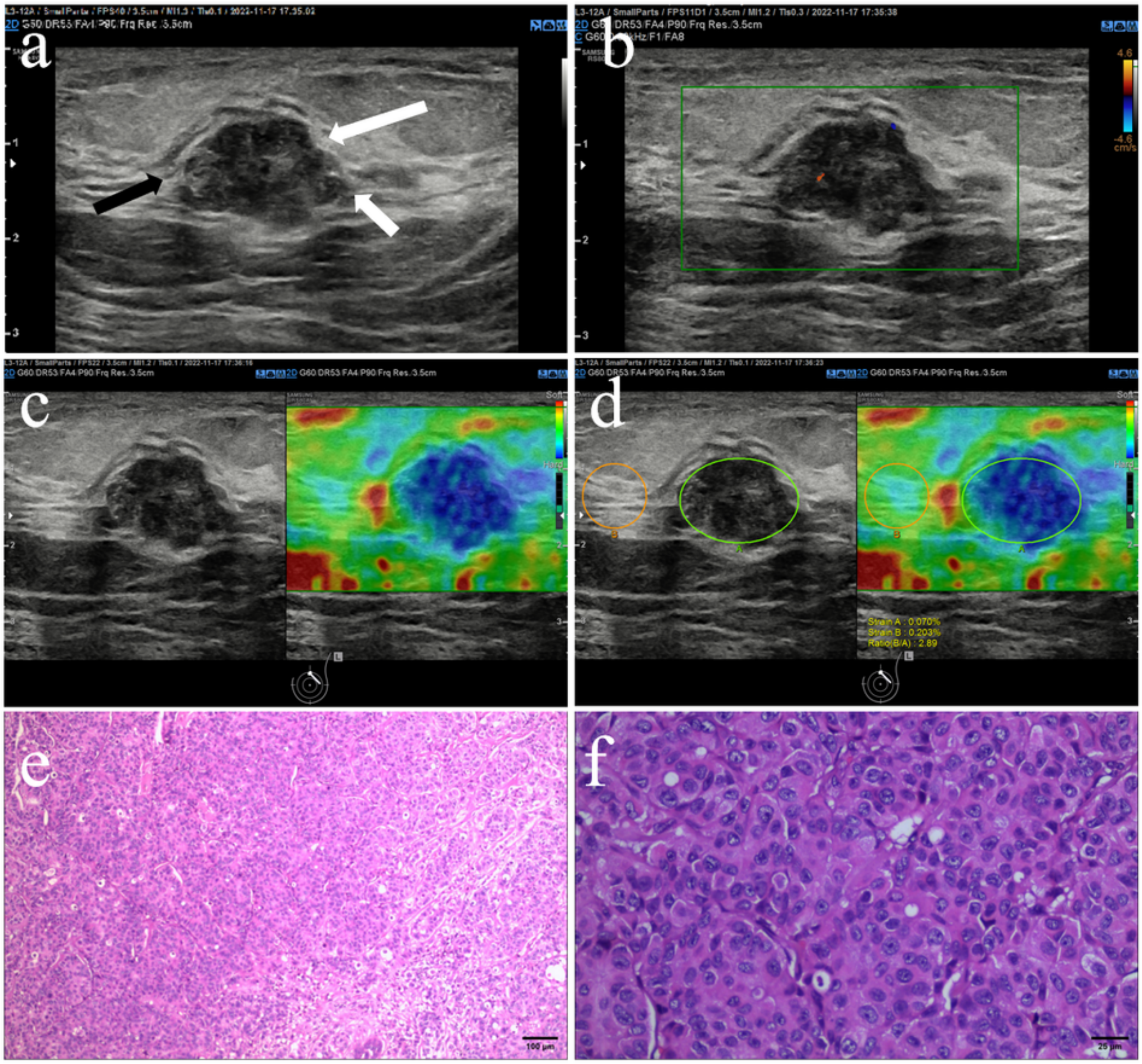

Figure 4

A 62-year-old woman had a lesion on the left breast. The lesion was evaluated BI-RADS 4c by Conventional US for irregular shape (long white arrow), non-circumscribed margin (short white arrow) and microcalcifications (the black arrow)（**a**） CDFI showed punctate blood flow signals both inside and around the lesion（**b**） with an elasticity score of 4（**c**） with a strain ratio of 2.89（**d**）, pathologically confirmed invasive ductal carcinoma （**e,** HE staining x100）and （**f,** HE staining x400）.

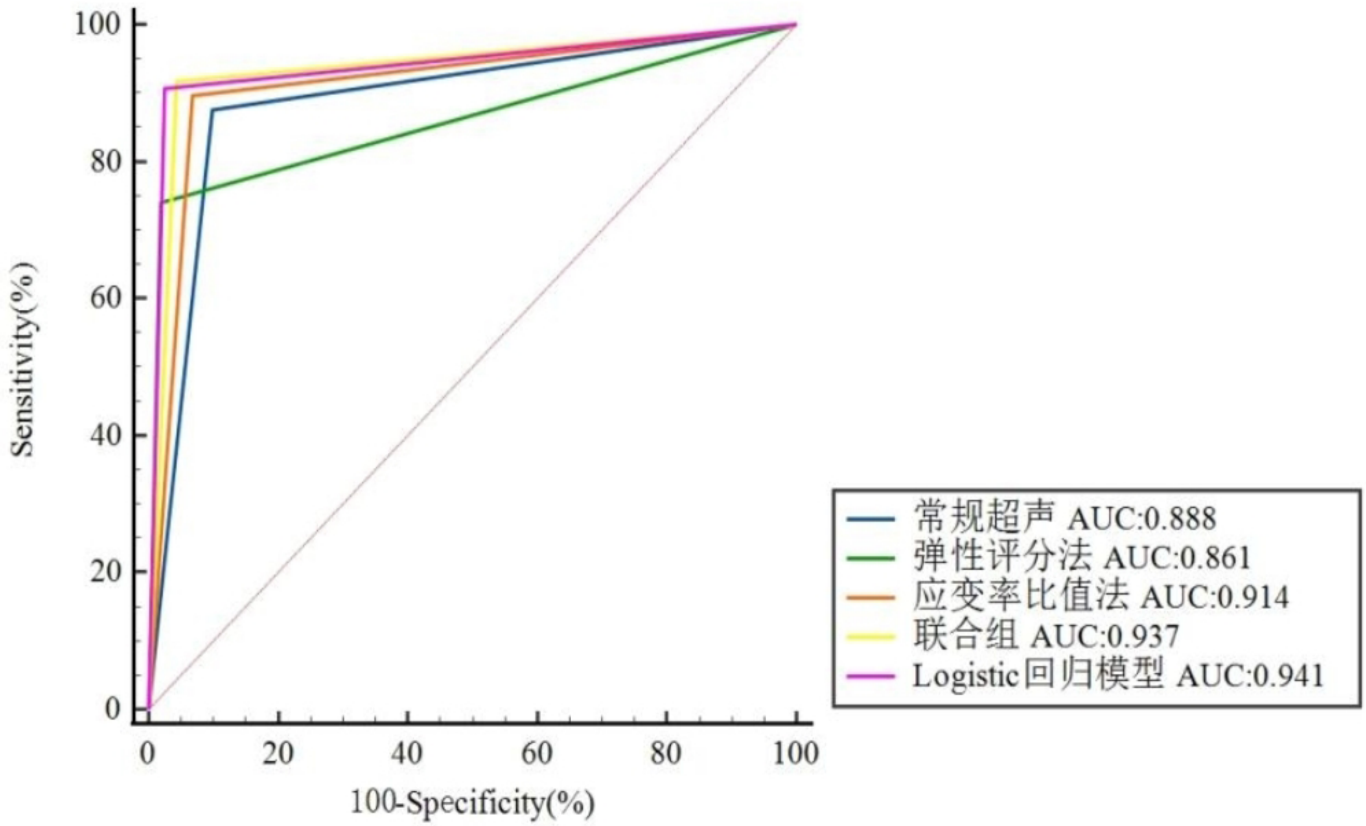

Figure 5

ROC curves for diagnosing BI-RADS category 4 lesions by five methods