RESEARCH

Value of S-Detect combined with multimodal ultrasound in differentiating malignant from benign breast masses

Na Li[1†], Wanling Liu[1†], Yunyun Zhan[1], Yu Bi[1], Xiabi Wu[1] and Mei Peng[1*]

Abstract

Background Ultrasonography (US) still has some limitations in the differentiation of benign and malignant breast masses. Therefore, we introduced new technologies such as S-Detect, microvascular flow imaging (MVFI), and strain elastography (SE) into the examination and compared the multimodal method with Breast Imaging Reporting and Data System (BI-RADS).

Objectives This prospective study aimed to evaluate the value of multimodal diagnostic methods that add S-Detect, MFI, and SR to US in differentiating benign from malignant breast masses.

Methods We recruited 186 patients with 189 masses between July 2021 and March 2022. The masses were examined using US, S-Detect, SR, and MFI before biopsy, and the benign and malignant differentiation value of each and their combination were assessed compared with surgical pathology results using the area under the receiver operating characteristic curve (AUC), accuracy, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). Subgroup analysis by lesion size was also performed.

Results The respective optimal cutoff values of SR and MFI for differentiating benign from malignant masses were 3.15 and 2.45, respectively, and the sensitivity and specificity were 79.3% and 85.6% and 94.6% and 69.1%, respectively. The multimodal AUC (0.907), sensitivity (97.8%), accuracy (90.5%), PPV (84.9%), and NPV (97.6%) were larger than those of each modality ($p < 0.05$), regardless of the mass size.

Conclusions The diagnostic method of S-Detect combined with multimodal ultrasound can effectively improve the diagnostic efficiency of breast masses and is expected to become a routine examination for breast in future for better evaluation the benign and malignancy of breast masses.

Keywords S-Detect, Microvascular flow imaging, Elastography, Multimodal ultrasound, Breast mass

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Background

Breast cancer has recently become the most prevalent malignancy in female individuals [1, 2]. Breast disease has been attracting increasing attention, and it progressively affects younger patients [3, 4]. A study reported that 5-year breast cancer in situ survival rate was 99%, while the 5-year advanced breast cancer survival rate was only 26% [5]. Therefore, early diagnosis and treatment are key for improving patients' survival rate and quality of life [6].

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Ultrasonography (US) is routinely used to examine breast diseases, as it is safe and noninvasive [7]. However, its main limitation is its operator dependency, with low inter-observer consistency and, for some challenging cases, the signs of benign and malignant may be contradictory, which may lead to misdiagnosis [8, 9]. To overcome this problem, researchers have introduced S-Detect, microvascular flow imaging (MVFI), and strain elastography (SE) into the examination to improve the diagnostic efficiency of ultrasound in differentiating benign and malignant breast masses.

S-Detect can effectively improve inter-reader consistency and has good accuracy [9–15]. Microvascular flow imaging is a new microvascular ultrasound imaging technique, and microvascular flow index (MFI) can automatically be determined by delineating the lesion edges on images from MVFI to quantitatively evaluate the abundance of blood flow [16–25]. Elastography evaluates tissue deformation by comparing the stiffness between the tumor and nearby healthy tissue with a high spatial resolution [26–33].

Although the potential benefits of each technique have been reported [9–33], few studies have investigated the effect of combining them when evaluating breast masses. If the three technologies are added to breast ultrasound examination, it may have a positive impact on the diagnostic efficiency of breast masses.

This prospective study aimed to evaluate the value of multimodal diagnostic methods that add S-Detect, MFI, and SR to US in differentiating benign from malignant breast masses.

Methods

The ethics committee of our hospital approved this prospective study, and informed consent was obtained from all patients.

This study was performed between July 2021 and March 2022. We enrolled patients scheduled to undergo diagnostic US at our institution.

Inclusion criteria were as follows: (a) having a relatively isolated breast mass detect by US (ensuring accurate localization during biopsy); (b) have undergone US, MFI, SR, and S-detect examinations before surgery and have clear images; and (c) patients who was over 18 years old. Exclusion criteria were as follows: (a) having a mass too large to measure the SR and/or MFI in a single section (over 6 cm, the maximum diameter of the probe); (b) not having definite pathological results by biopsy; (c) diagnosed with other malignant tumors previously or with a previous history of cancer/treatment; (d) receiving radiotherapy or chemotherapy in the ipsilateral breast; and (e) being pregnant or lactating.

All ultrasound examinations were conducted using the Samsung RS85A ultrasonographic system (Samsung Madison Co. Ltd., Seoul, the Republic of Korea), with 3–12-MHz linear array probes and included grayscale US, SR, MFI, and analysis with S-Detect software. All data in this study were evaluated by two radiologists with over ten years of experience in breast ultrasound and their results were compared with each other. If there was a disagreement between the two, consulted another senior radiologist with over 15 years of experience. This was a prospective study, all patients underwent histopathological evaluation after ultrasound examination, and all biopsies/surgeries are performed under ultrasound guidance.

The patients were maintained in the supine position, fully exposing the breast.

First, a routine ultrasound examination was performed to assess six US features of breast masses according to the BI-RADS classification system. The features included shape, azimuth, edge, internal echo, internal structure, and calcification. Each feature has a corresponding score based on which the mass was assigned a BI-RADS classification (Figs. 1a, 2a, 3a). Masses identified as 4b to 5 were classified as suspected malignancies.

Second, we perform MVFI on breast masses and calculate MFI using images with the most abundant blood flow signal by outlining the lesions' edges on the images (Figs. 1b, 2b, 3b). Each numerical value was averaged after three measurements.

Third, we switched to the SE mode, keeping the probe perpendicular to the target lesion and applying as little pressure as possible. An appropriate sampling box size was selected, image clarity was adjusted, and stability was maintained. Subsequently, the E-Breast was activated to trace the lesion area and normal breast tissue of the same depth (Figs. 1c, 2c, 3c). The stain radio was automatically calculated as the ratio between them by the software. Measurements were made in triplicate, and the average value was used.

Fourth, we scanned the transverse and longitudinal aspects of the breast masses in 2D mode, considered the vertical section maximum diameter as the standard level, and then switched to the S-Detect mode. The software automatically outlined the breast lesion area, and the lesion nature was quickly and automatically evaluated to determine if it was a benign or malignant lesion (Figs. 1d, 2d, 3d).

The respective optimal cutoff values of SR and MFI were determined by receiver operating characteristic (ROC) analysis and the Youden index. When either value was above the cutoff value, the breast mass was determined to be malignant; if not, it was determined to be benign.

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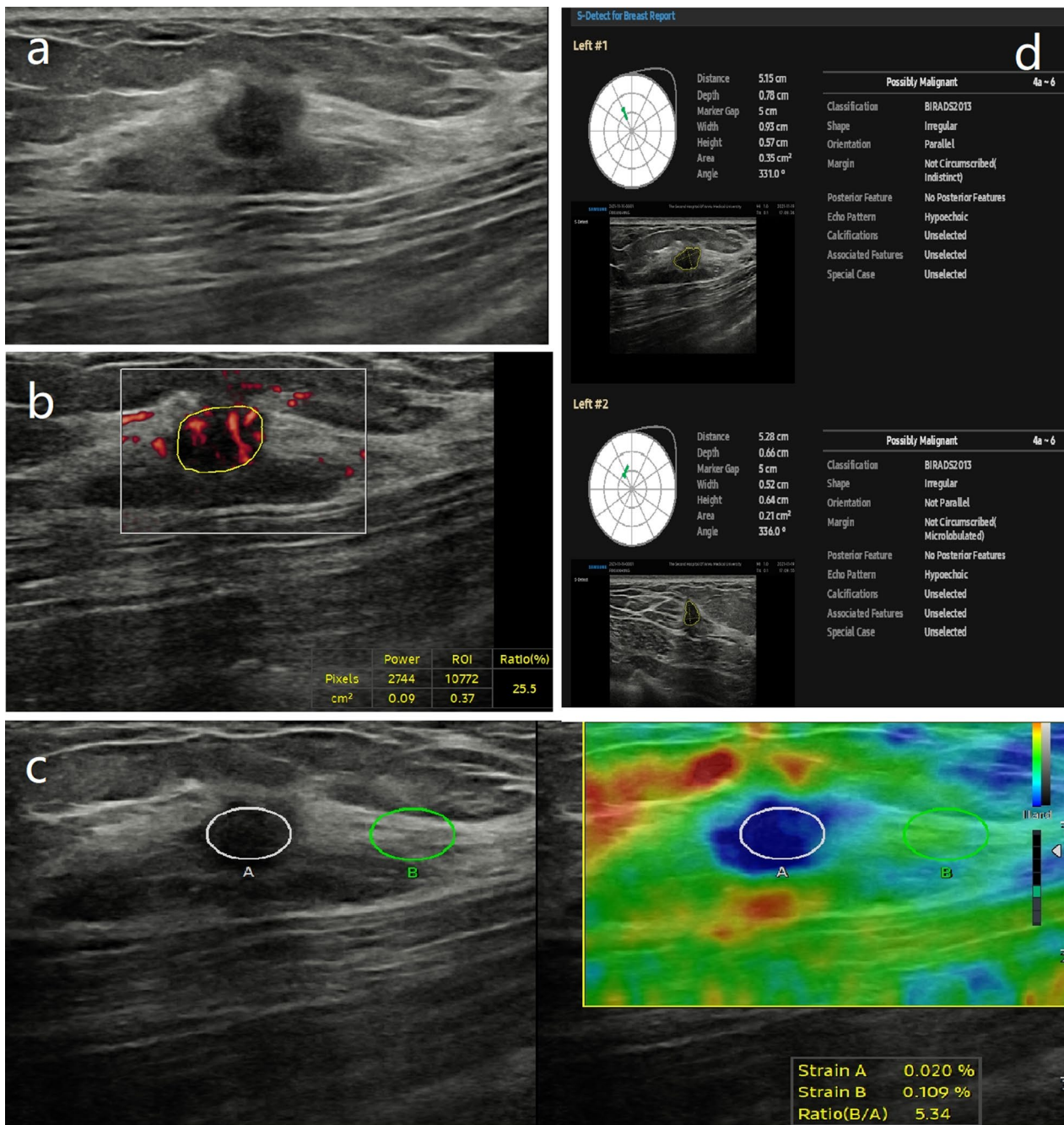
Fig. 1 A 42-year-old female patient with invasive breast ductal carcinoma. The ultrasonographic images of the breast mass long-axis section were assigned a BI-RADS score of 4A (**a**), a vascular index of 25.5 (**b**), and a strain ratio of 5.34 (**c**). The long- and short-axis sections were both judged as malignant by S-Detect (**d**)

We divided the data into eight groups for analysis and comparison: US, US + S-Detect, US + SR, US + MFI, US + S-Detect + SR, US + S-Detect + MFI, US + MFI + SR, US + S-Detect + SR + MFI (the multimodal diagnosis). The combined analysis of US, SR, MFI, and S-Detect was performed according to the long-axis section of the breast mass. The original BI-RADS classification was based on the US; then SR, MFI, and S-Detect examinations were performed. The new BI-RADS combined with various techniques will be upgraded or downgraded based on the results of S-Detect/MFI/SR, and the specific upgrade/downgrade methods was shown in the flowchart

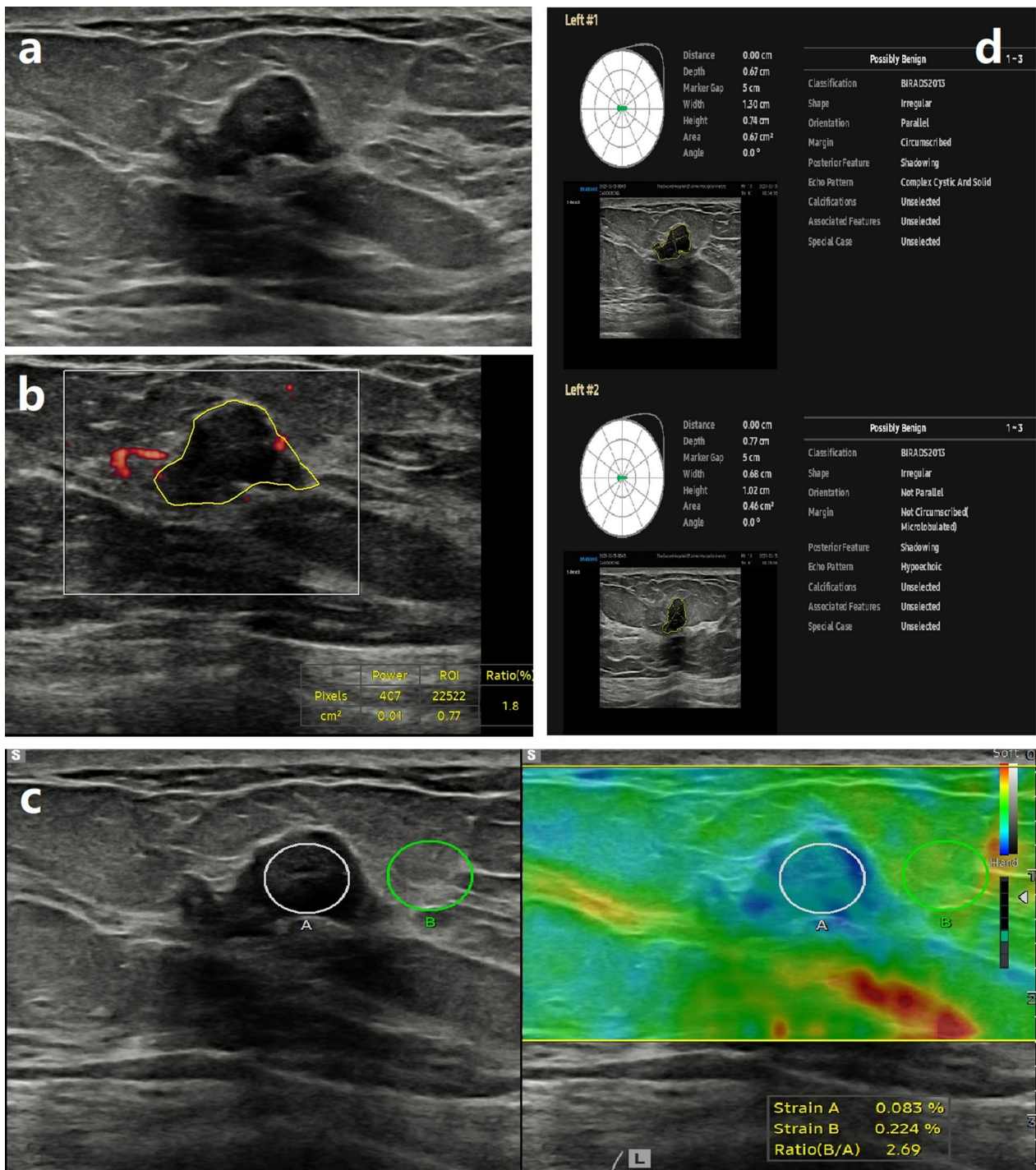Li *et al. Egypt J Radiol Nucl Med*   (2024) 55:22

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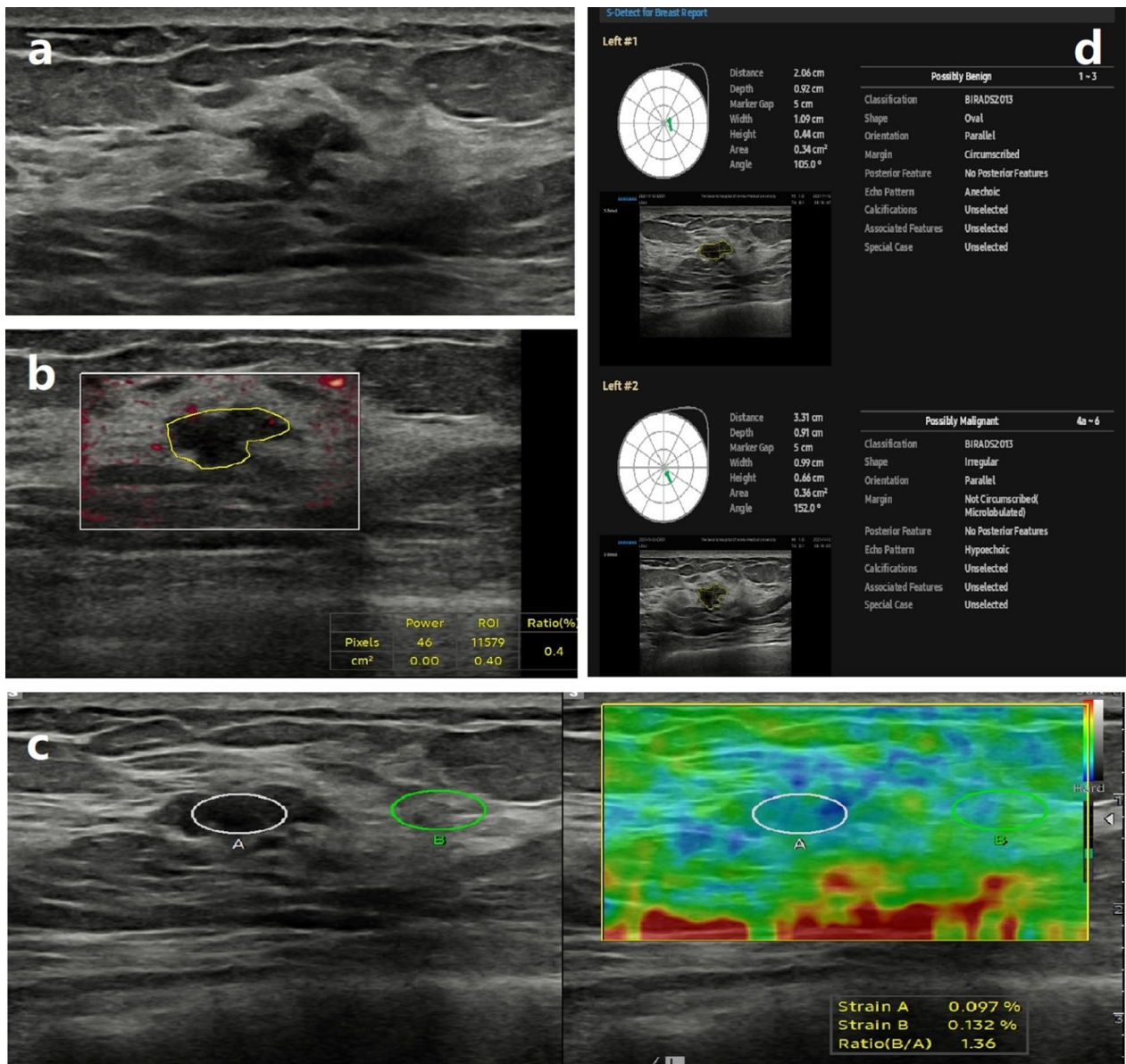
Fig. 2 A 49-year-old female patient with mammary adenosis. The ultrasonographic images of the breast mass long-axis section were assigned a BI-RADS score of 4A (**a**), a vascular index of 0.4 (**b**), and a strain ratio of 1.36 (**c**). The long-axis section was judged as benign by S-Detect (**d**)

(Fig. 4). The masses originally classified as BI-RADS 3 were no longer down-regulated, while the masses of BI-RADS 5 were no longer up-regulated. Masses with a final BI-RADS score between 3 and 4A were judged benign, and those with a BI-RADS score of 4B and above were considered malignant.

We separated the masses by size into masses ≤ 20 mm or > 20 mm. The size of the breast cancer at the time of diagnosis is generally considered as the basic and key factor to determine the clinical outcome [34]. In the tumor–node–metastasis-based staging of breast cancer proposed by the International Union for Cancer Control and the American Joint Commission on Cancer, a tumor with a diameter of less than 20 mm is defined as belonging to stage T1 and a tumor with a diameter of more than 20 mm belongs in stages T2 and above [35, 36]. Therefore, a significant cutoff value of breast mass is 20 mm. The accuracy, sensitivity, specificity, AUC, PPV, and NPV of the US and multimodal diagnostic approaches were analyzed by group. Differences in diagnostic efficiency were compared between the mass size groups and the entire cohort.

Fig. 3 A 50-year-old female patient with intraductal papilloma. The ultrasonographic images of the breast mass long-axis section were assigned a BI-RADS score of 4B (**a**), a vascular index of 1.8 (**b**), and a strain ratio of 2.69 (**c**). The long- and short-axis sections were all judged as benign by S-Detect (**d**)

Quantitative parameters, such as age and size, were represented by mean and standard deviation and compared using the t test. Chi-square test was used to compare the categorical variables (BI-RADS and S-Detect), while the t test was used to compare the continuous variables (SR and MFI) between the

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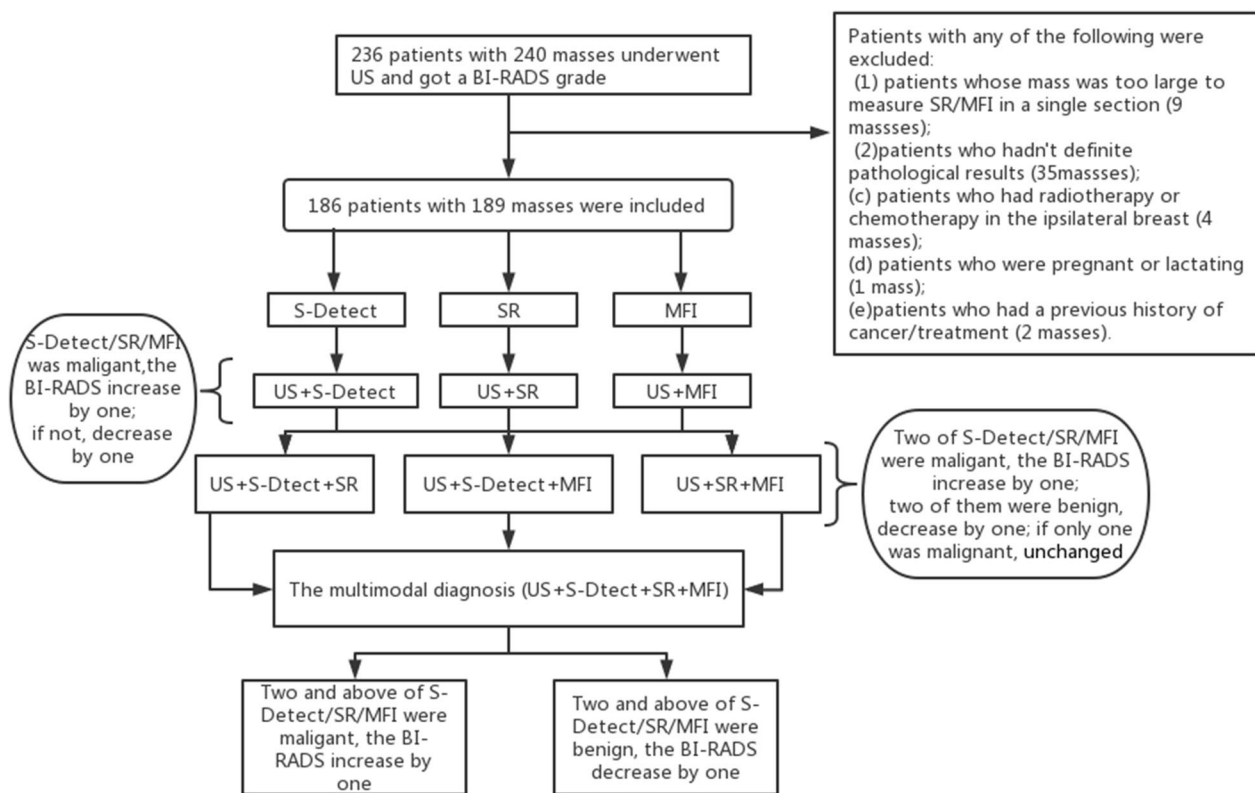
Fig. 4 A study flowchart. BI-RADS: Breast Imaging Reporting and Data System; US: ultrasonography; MFI: microvascular flow index; SR: strain ratio

groups. The *Z* test compared the AUC values. Two-sided statistical significance was set at $P < 0.05$. A Chi-square test was used to compare the size of benign and malignant masses against the mean values of SR and MFI in each group, and the diagnostic efficacy of each group and the US group. Statistical analysis was performed using IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp., Armonk, NY, USA).

Results

Based on the inclusion and exclusion criteria, this study recruited 186 patients (mean age, 47.2 ± 12.7 years) with 189 breast masses (Fig. 4), including 92 malignant (48.7%) and 97 benign (51.3%) masses; the diameters were ≤ 20 and > 20 mm in 98 and 91 masses, respectively. Invasive ductal carcinoma was the most common malignant breast tumor accounting for 79.3% of the malignancies (73/92). Fibroadenoma was the most prevalent benign lesion (49.5%, 48/97; Table 1). The patients with

Table 1 Histopathological diagnosis of the masses and respective MFI and SR values

Malignant				Benign			
Histologic features	N (%)	MFI	SR	Histologic features	N (%)	MFI	SR
Invasive ductal carcinoma	73 (79.3)	12.9 ± 12.2	4.1 ± 3.6	Fibroadenoma	48 (49.5)	5.9 ± 9.0	2.5 ± 1.6
Ductal carcinoma in situ	13 (14.1)	12.2 ± 8.5	3.8 ± 1.5	Mammary adenosis	36 (37.1)	4.8 ± 8.0	2.3 ± 1.2
Mucous carcinoma	4 (4.3)	6.7 ± 6.5	4.4 ± 3.1	Benign phyllodes tumor	4 (4.1)	8.8 ± 8.5	3.3 ± 2.4
Solid papillary carcinoma	1 (1.1)	18.5	3.2	Intraductal papilloma	3 (3.1)	15.8 ± 12.2	2.5 ± 1.1
Neuroendocrine carcinoma	1 (1.1)	8.2	5.9	Usual ductal hyperplasia	3 (3.1)	1.5 ± 1.7	2.1 ± 0.8
				Mastitis	2 (2.1)	10.6 ± 6.6	3.0 ± 1.7
				Mammary cyst	1 (1.0)	1.4	2.8

N: number; MFI: microvascular flow index; SR: strain ratio

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malignant tumors were older than those with benign masses (53.3 ± 11.9 and 41.5 ± 10.6 years; *P* < 0.01) and had larger lesions (28.0 ± 13.8 and 17.8 ± 8.9 mm; *P* < 0.01).

The mean values of the quantitative parameters were all significantly higher in malignant lesions than in benign lesions: MFI (mean, 12.6 ± 11.4 and 5.8 ± 8.6; *P* < 0.01); SR (mean, 4.1 ± 2.2 and 2.4 ± 1.5; *P* < 0.01). The optimal MFI and SR cutoff values for differentiating malignant from benign breast masses were 2.45 and 3.15, respectively, and their AUCs were 0.818 and 0.825, respectively (Fig. 5). The diagnostic sensitivity, specificity, accuracy, PPV, and NPV of US + MFI were 94.6%, 69.1%, 81.5%, 74.4%, and 93.1%, respectively, and those of US + SR were 79.3%, 85.6%, 82.5%, 83.9%, and 81.4%, respectively (Table 2). Most MFI and SR values increased with the lesion's BI-RADS score. The benign/malignant lesion ratio and mean values of MFI and SR for each category are shown in Table 3. Using the pathology examination results as the standard, the combined US and S-Detect assessment had higher sensitivity, accuracy, and NPV (93.5%, 85.2%, and 92.6%, respectively) and a larger AUC (0.911 and 0.862) for differentiating benign from malignant breast masses than US alone (Fig. 5). However, the specificity and PPV of the combined US and S-Detect approach were lower than that of US alone (77.3% and 83.5%; 79.6% and 82.0%, respectively).

The accuracy, specificity, AUC, PPV, and NPV of the US + S-Detect + MFI group increased compared with those of the US group (0.922, 88.4%, 96.7%, 82.4%, 96.3%, respectively); however, the sensitivity decreased (80.4% and 83.5%). The accuracy, sensitivity, PPV, and NPV of the US + S-Detect + SR group compared with the US group increased (86.8%, 90.2%, 83.8%, 90.0%, respectively), and the specificity did not change

significantly (both were 83.5%), while the AUC also increased from 0.862 to 0.914. For the US + MFI + SR group, the accuracy, sensitivity, and NPV increased compared with those of the US group (85.2%, 91.3%, and 90.6%, respectively), while the specificity and PPV decreased (79.4% and 80.8%, respectively), and the AUC increased to 0.923.

The sensitivity, accuracy, PPV, and NPV of the multimodal diagnostic approach (97.8%, 90.5%, 84.9%, and 97.6%, respectively) were significantly higher and the AUC significantly larger (0.939, *P* < 0.001) than those of the other seven groups. The specificity of the multimodal diagnostic was second only to that of the US + SR group; but this finding was not significant (85.6% and 83.5%; *P* = 0.69; Table 2). Using the multimodal diagnostic approach, the score of 61 lesions was downgraded from the original BI-RADS grade, including two incorrectly downgraded malignant lesions; biopsy was correctly avoided for 55 masses; and 106 lesions were upgraded, including 16 incorrectly upgraded benign masses (Table 4).

The AUC between various diagnostic methods showed significant statistical significance (*P* < 0.05). The mean was statistically significant only between the US + MFI and US + SR groups (*P* = 0.025), while there was no significant difference between the other groups (*P* > 0.05).

The multimodal diagnostic AUC, accuracy, sensitivity, and NPV were greater than the corresponding values of the US group in both tumor-size subgroups, particularly in the small mass group that had an AUC of 0.955. The multimodal diagnostic specificity and PPV were slightly lower than in US group (Table 2).
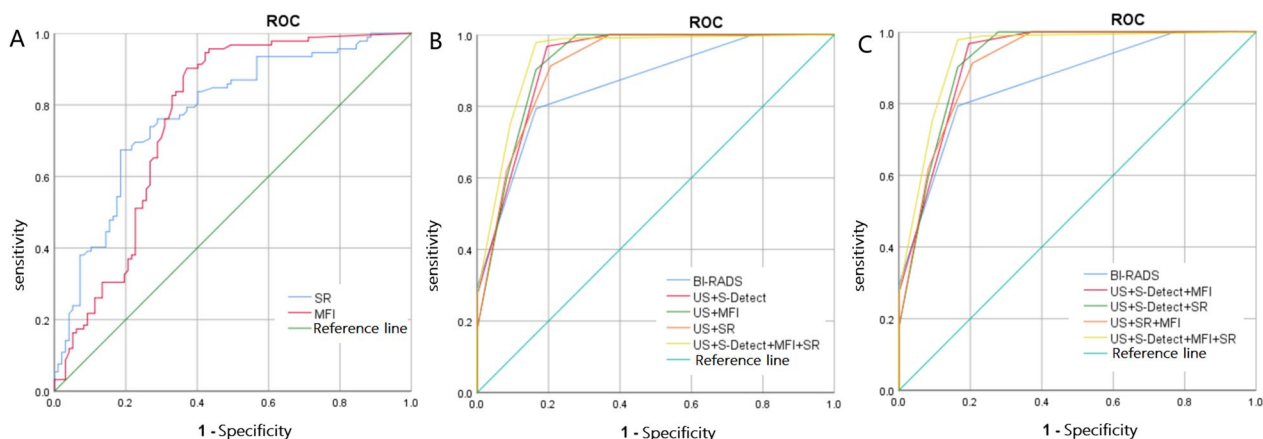
Fig. 5 The receiver operating characteristic curve. ROC of MFI and SR in distinguish between benign and malignant masses (**A**), ROC of US, US + S-Detect, US + MFI, US + SR, and the multimodal diagnostic approach (**B**), and ROC of US, US + S-Detect + MFI, US + S-Detect + SR, US + MFI + SR, and the multimodal diagnostic approach (**C**). US: ultrasonography; MFI: microvascular flow index; SR: strain ratio

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Table 2 Comparison of the diagnostic methods' efficacies of the mass size groups and the entire cohort

Diagnostic method	Size	AUC	Accuracy, %	Sensitivity, %	Specificity, %	PPV, %	NPV, %
US	≤ 20 mm	0.856 (0.772–0.941)	85.7 (78.8–92.6)	75.0 (66.5–83.5)	90.1 (84.2–96.0)	80.0 (72.2–87.2)	88.2 (81.7–94.7)
	> 20 mm	0.841 (0.760–0.923)	76.9 (68.2–85.6)	81.7 (73.9–89.5)	67.7 (58.1–77.3)	83.1 (69.3–90.7)	65.6 (55.8–75.4)
	All masses	0.862 (0.810–0.914)	81.5 (76.0–87.0)	79.3 (73.5,85.1)	83.5 (78.2–88.8)	82.0 (76.5–87.5)	81.0 (75.4–86.6)
US + S-Detect	All masses	0.911 (0.859–0.952)	85.2 (80.1–90.3)	93.5 (90.0–97.0)	77.3 (71.3–83.3)	79.6 (73.9–85.3)	92.6 (88.9–96.3)
	*P**	< 0.001	0.290	< 0.001	0.280	0.670	0.030
US + MFI	All masses	0.896 (0.852–0.939)	81.5 (76.0–87.0)	94.6 (91.4,97.8)	69.1 (62.6–75.6)	74.4 (68.2–80.6)	93.1 (89.5–97.2)
	*P**	< 0.001	> 0.999	< 0.001	0.020	0.190	0.020
US + SR	All masses	0.886 (0.937–0.935)	82.5 (77.1–87.9)	79.3 (73.5,85.1)	85.6 (80.6–90.6)	83.9 (78.7–89.1)	81.4 (75.9–86.9)
	*P**	< 0.001	0.915	> 0.999	0.690	0.740	0.950
US + S-Detect + MFI	All masses	0.922 (0.884–0.960)	88.4 (83.8–93.0)	96.7 (94.1–99.3)	80.4 (74.8–84.0)	82.4 (77.0–87.8)	96.3 (93.6–99.0)
	*P**	< 0.001	0.292	< 0.001	0.575	0.944	0.002
US + S-Detect + SR	All masses	0.914 (0.874–0.954)	86.8 (82.0–91.6)	90.2 (86.0–94.4)	83.5 (78.2–88.8)	83.8 (78.5–89.1)	90.0 (85.7–94.3)
	*P**	< 0.001	0.567	0.040	> 0.999	0.741	0.081
US + MFI + SR	All masses	0.923 (0.884–0.962)	85.2 (80.1–90.3)	91.3 (87.3–95.3)	79.4 (73.6–85.2)	80.8 (75.2–86.4)	90.6 (86.4–94.8)
	*p**	< 0.001	0.397	0.022	0.460	0.824	0.066
US + S-Detect + MFI + SR	≤ 20 mm	0.955 (0.917–0.994)	90.8 (85.1–96.5)	96.9 (93.4–100.4)	87.9 (81.4–94.4)	79.5 (71.5–87.5)	98.3 (95.7–100.9)
	> 20 mm	0.909 (0.843–0.975)	90.1 (84.0–96.2)	98.3 (95.7–100.9)	74.2 (65.2–83.2)	88.1 (81.3–94.9)	95.9 (92.0–99.8)
	All masses	0.939 (0.905–0.974)	90.5 (86.3–94.7)	97.8 (95.7–99.9)	83.5 (78.2–88.8)	84.9 (79.8–90.0)	97.6 (95.5–99.7)
	*P**	< 0.001	0.350	< 0.001	> 0.999	0.590	< 0.001

US: ultrasonography; MFI: microvascular flow index; SR: strain ratio; AUC: area under the receiver operating characteristic curve; PPV: positive predictive value; NPV: negative predictive value

*Comparison with BI-RADS in entire cohort

Table 3 Breast mass distribution and comparison between MFI and SR assessments

Diagnostic method	Malignant	Benign	All masses	MFI	SR	*P**
Mean ages, years	53.3 ± 11.9	41.5 ± 10.6	47.2 ± 12.7			< 0.01
Mean sizes, mm	28.0 ± 13.8	17.8 ± 8.9	22.7 ± 12.6			< 0.01
≤ 20 mm	32	66	98	7.9 ± 10.6	2.9 ± 1.8	< 0.01
> 20 mm	60	31	91	10.5 ± 10.5	3.6 ± 2.2	< 0.01
US	92	97	189	9.1 ± 10.6	3.3 ± 2.0	< 0.01
3	0	22	22	5.3 ± 6.6	2.4 ± 1.1	< 0.01
4A	19	59	78	6.8 ± 11.5	2.6 ± 1.8	< 0.01
4B	46	16	62	12.9 ± 10.9	4.0 ± 2.0	< 0.01
4C	25	0	25	9.8 ± 6.5	3.6 ± 2.1	< 0.01
5	2	0	2	14 ± 11.9	8.8 ± 4.2	< 0.01
MFI	5.8 ± 8.6	12.6 ± 11.4	9.1 ± 10.6			< 0.01
SR	2.4 ± 1.5	4.1 ± 2.2	3.3 ± 2.0			< 0.01
US + S-Detect	108	81	189			< 0.01
US + MFI	117	72	189			< 0.01
US + SR	87	102	189			< 0.01
US + S-Detect + MFI	108	81	189			< 0.01
US + S-Detect + SR	99	90	189			< 0.01
US + SR + MFI	104	85	189			< 0.01
US + S-Detect + MFI + SR	105	83	189			< 0.01

*Comparison between benign and malignant

US: ultrasonography; MFI: microvascular flow index; SR: strain ratio

Table 4 The specific upgraded and downgraded situation of various diagnostic methods

Diagnostic method	Upgrade					Downgrade				
	3 → 4A	4A → 4B	4B → 4C	4C → 5	Total	4A → 3	4B → 4A	4C → 4B	5 → 4C	Total
US + S-Detect	2 (0) *	27 (17)	54 (42)	23 (23)	106 (82)	51 (49)	8 (4)	2 (0)	0 (0)	61 (53)
US + SR	5 (0)	19 (13)	43 (35)	14 (14)	81 (62)	59 (53)	19 (7)	11 (0)	0 (0)	89 (60)
US + MFI	9 (0)	33 (18)	57 (42)	25 (25)	124 (85)	45 (44)	5 (1)	0 (0)	0 (0)	50 (45)
US + S-Detect + SR	0 (0)	15 (11)	39 (31)	14 (14)	68 (56)	48 (48)	4 (3)	2 (0)	0 (0)	54 (51)
US + S-Detect + MFI	0 (0)	20 (16)	50 (38)	23 (23)	93 (77)	40 (40)	1 (1)	0 (0)	0 (0)	41 (41)
US + SR + MFI	2 (0)	17 (12)	39 (30)	14 (14)	72 (56)	42 (42)	1 (1)	0 (0)	0 (0)	43 (43)
US + S-Detect + SR + MFI	2 (0)	23 (19)	58 (48)	23 (23)	106 (90)	55 (55)	4 (2)	2 (2)	0 (0)	61 (59)

*The numbers of parentheses represent the number of successful upgrades and downgrades

Discussion

Ultrasonography is an important method for distinguishing between benign and malignant breast masses [7]. Currently, there are some new ultrasound techniques such as S-Detect, MVFI, and SE [9–29]. Would combining them be more helpful for diagnosing breast masses?

This study explored the application of the S-Detect program and the quantitative parameters of MFI and SR on the basis of US and compared their diagnostic value in differentiating benign from malignant breast lesions.

Our study was performed on 189 patients (92 malignant and 97 benign), unlike Seo et al. [28], who performed their study on 45 patients (20 malignant and 25 benign). And our study was a prospective study, similar to Lee et al. [30], unlike Lee et al. [27] and Zhi et al. [37], whose study was retrospective.

In this study, the sensitivity in the US + S-Detect and US + MFI groups increased, but the specificity and PPV decreased. Our analysis found that this may be due to the inconspicuous malignant characteristics of small tumors, which are often misdiagnosed as benign by conventional ultrasound. However, the addition of S-Detect reduced human error in judging small tumors, and after the addition of MFI, further judgment can be made based on the richness of internal blood flow. Both can avoid the omission of some small malignant lesions, thereby improving sensitivity. However, some large tumors with rapid growth, such as phyllodes tumors and larger fibroadenomas [38, 39], may also have rich internal blood flow signals and irregular morphology, leading to misdiagnosis by MFI and S-Detect, ultimately resulting in lower specificity and positive predictive value.

Wang et al. [13] studied that S-Detect can effectively improve inter-reader consistency and has good accuracy.

Cai et al. [20] studied that the vascular index can be used to appropriately downgrade benign lesions classified as BI-RADS 4, which can improve the diagnostic accuracy and PPV and reduce unnecessary biopsies.

At the same time, this study found that the specificity of the US + SR group was the highest, yet the sensitivity was lower, and the NPV was not significantly increased. The reasons may be that when the malignant mass was small in size, the interstitial reaction was not obvious, the fibrous component arrangement was loose, and the cancer tissue did not infiltrate into the surrounding area. Therefore, the hardness was lower, the elasticity score was lower, and false negatives were prone to occur. Therefore, the sensitivity was lower, and the negative predictive value was not high, even though the specificity was high. As shown in the study by Song et al. [40], it is believed that the hardness of large masses is higher than that in small masses.

Lee et al. [27] studied that the addition of SR in ultrasound improved the accuracy and specificity significantly, while increased the sensitivity, this is similar to our research findings.

This study showed that the highest diagnostic efficacy was achieved when the MFI cutoff value was 2.45. This cutoff value was lower than previously reported values of 2.95 [16] and 3.35 [24], possibly due to differences in the included subjects or the instruments. Chae et al. [16] and Lee et al. [24] used instruments from Aplio, Japan, while we used a diagnostic US instrument from Samsung, Korea, with each instrument coming with measurement software produced by a different company (SMI technology in their case, MVFI technology in ours).

Our study showed that the SR value of malignant masses was larger than that of benign masses, which is similar to the study by Suvannareg et al. [41], Seo et al. [28], Lee et al. [27] and Moon, et al., and our cutoff value of SR was 3.15, while the cutoff of SR in Suvannarerg et al. was 2.78, Seo et al. was 2.63, Lee et al. was 3.57 and Moon et al. [42] was 5.16.

To the best of our knowledge, there are currently few studies that combine these four techniques (US, SR, MFI, and S-Detect) for the diagnosis of breast masses.

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Leng et al. [43] combined routine ultrasonography, elastography, contrast-enhanced ultrasonography and color Doppler, and they showed that multimodal ultrasound is more effective in diagnosing breast lesions.

Lee et al. [27] combined all quantitative values of shear wave elastography and superb microvascular imaging with B-mode US, they showed the combination improved the diagnostic performance in differentiating between benign and malignant breast lesions.

Lee et al. [30] showed that addition of elastography and color Doppler US to B-mode US can increase the PPV of screening US in women with dense breasts while reducing the number of false-positive findings without missing cancers.

Our results indicated that the multimodal diagnostic approach that combined all four techniques had higher AUC, sensitivity, accuracy, PPV, and NPV values than the other seven groups without a loss of specificity (only second to the US + SR group).

All lesions with a BI-RADS score of 3 based on the multimodal diagnostic approach were judged benign using S-Detect, and their SR and MFI were below the respective cutoff values. The BI-RADS score for 61 cases was downgraded, including 55 benign masses being correctly downgraded from BI-RADS 4A to 3. These masses were a mixed variety of benign lesions, so their US images were atypical, resulting in misjudging them as BI-RADS 4A. The multimodal diagnosis could assess these lesions more objectively than US alone, resulting in downgrading these masses, avoiding unnecessary biopsies, reducing the patients' pain and stress, and decreasing overtreatment. Two malignant masses were incorrectly downgraded. One was a mucinous carcinoma, possibly misjudged due to its unique pathological type. Many studies have reported that mucinous carcinoma usually has poor blood supply and because there is more internal mucus, its hardness is also lower [44], resulting in a lower MFI and SR. The other case was an invasive ductal carcinoma, possibly misjudged because of its small size, only 4 mm in diameter, leading to large MFI and SR measurement errors.

Among the 106 upgraded cases, there were 90 malignant lesions correctly upgraded. The ultrasound images of most of these upgraded masses showed insignificant malignant characteristics as the lesions were relatively small. The calculated MFI and SR indicated a high blood flow signal and hard texture, leading to an upgrade of their BI-RADS scores. Multimodal diagnosis can reduce the missed diagnosis rate of smaller breast masses. There were 16 benign masses were incorrectly upgraded, four from BI-RADS 4A to 4B and 12 from BI-RADS 4B to 4C. These lesions included 12 adenopathies with fibrous adenomas, two interstitial fibroses, and two inflammatory lesions. Active hyperplasia of the surrounding tissue may have led to their irregular growth and a strong blood flow signal.

During the subgroup study, we found that multimodal diagnosis had a higher diagnostic efficiency in the small tumor group, with an AUC of 0.955. As shown in the above analysis, small tumors with insignificant malignant characteristics are prone to missed diagnosis by conventional ultrasound, and combining multimodal diagnosis can more effectively evaluate their benign and malignant characteristics. However, regardless of whether it is a large mass group or a small mass group, the accuracy, sensitivity, AUC, and NPV of multimodal diagnosis are greater than the corresponding values of the US group. The specificity of the large mass group is low, and the reason is as shown above. Benign lesions with rapid growth are easily misdiagnosed as malignant.

Zhi et al. [37] only studied masses with a diameter less than 20 mm, and they only discussed the role of elastography in BI-RADS. They showed that the combination of elastography and BI-RADS could give BI-RADS some help in the differentiation of benign and malignant breast small lesions.

This study had several limitations. First, it was a single-center study with a small sample, possibly resulting in some bias. Second, we did not perform a subgroup analysis for the association between various pathological types and MFI or SR. Given the few cases available for each subgroup, a larger sample is needed for such analysis. Third, as the same instrument acquired all US images used in this study, the adaptability of our findings to other devices could not be confirmed.

Conclusions

The multimodal diagnostic method combining US, S-Detect, MFI, and SR can effectively improve the diagnostic efficiency of breast masses, reduce unnecessary biopsies of BI-RADS 4A masses. And for small masses with a diameter less than 20 mm, malignant signs can be detected earlier to avoid delaying treatment. The multimodal diagnostic is recommended to be used as a routine examination for breast in future for better evaluation the benign and malignancy of breast masses.

Abbreviations

US	Ultrasonography
SR	Strain ratio
MFI	Microvascular flow index
BI-RADS	Breast Imaging Reporting and Data System
ROC	Receiver operating characteristic curve
AUC	Area under the curve
PPV	Positive predictive value
NPV	Negative predictive value
MVFI	Microvascular flow imaging
SE	Strain elastography

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Availability of data and materials
The authors can provide all raw data that support the conclusions of this paper.

Declarations

Ethics approval and consent to participate
In this study, all procedures abided by the protocol of The Second Affiliated Hospital of Anhui Medical University. The institutional review board approved this study. Ethical approval was approved by the Ethical Committee of the hospital, and obtained ethics approval in written (SL-YX2022-015). Written informed consent to participate was obtained from all the patients for publication of this study.

Consent for publication
All patients included in this research were above 18 years of age and gave written consent to publish the data included in the study.

Competing interests
The authors declare that they have no competing interest.

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