

Advantages of b-mode ultrasound combined with strain elastography in differentiation of idiopathic granulomatous mastitis from malignant breast lesions

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Background/aim: To evaluate the diagnostic performance of strain elastography (SE) combined with B-mode ultrasound in distinguishing between idiopathic granulomatous mastitis (IGM) and malignant breast lesions.

Materials and methods: Seventy-seven malignant breast lesions and 36 IGM were assessed using B-mode ultrasound and SE. Ultrasonographic findings for all the breast lesions were classified based on the 2013 American College of Radiology Breast Imaging Reporting and Data System (BI-RADS-US), and the SE findings were evaluated based on the strain ratio and a five-point scale. The diagnostic performances of B-mode ultrasonography, SE, and the combination of both methods were compared.

Results: Significant differences in strain ratio and elastography scores were found between IGM and malignant breast lesions. When the lesions were assessed with B-mode ultrasound alone, in order to distinguish between IGM and malignant breast lesions, sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were 94.8%, 66.7%, 85.9%, 85.7%, and 85.8%, respectively. However, when assessed with a combination of B-mode ultrasonography and SE, sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were 96.1%, 100%, 100%, 92.3%, and 97.3%, respectively.

Conclusion: The combination of SE and B-mode ultrasound has better diagnostic performance in the differentiation of IGM and malignant breast lesions than B-mode ultrasonography alone.

Key words: Idiopathic granulomatous mastitis, malignant, ultrasonography, elastography

1. Introduction

Idiopathic granulomatous mastitis (IGM) is a rare, benign breast disease that is accompanied by chronic, noncaseous, necrotizing granulomatous lobulitis with or without abscess formation (1). The clinical and radiologic findings observed in IGM can be confused with those of breast cancer, often leading to a delay in appropriate and well-timed treatment because of misdiagnosis (2). Conventional radiologic imaging methods, such as magnetic resonance imaging (MRI), ultrasound (US), and mammography, have yet to reach expected accuracy rates in distinguishing between IGM and malignant breast lesions (3–6).

The American College of Radiology Breast Imaging Reporting and Data System (BI-RADS) is widely used in the assessment of breast lesions (7). Several studies have reported that BI-RADS has high sensitivity and low specificity in the categorization of breast lesions (8). Strain elastography (SE) is another noninvasive US modality that is commonly used to determine tissue stiffness (9).

The aim of the present study is to determine the effectiveness of a combination of B-mode US and SE in the differentiation of IGM and malignant breast lesions.

2. Materials and methods

2.1. Subjects

This study was conducted after obtaining signed consent from the participants in accordance with the guidelines of the Declaration of Helsinki, and was approved by the local ethics committees. Two hundred and fourteen breast lesions that had been detected on B-mode US between August 2015 and May 2017, and for which SE had been performed, were retrospectively reviewed. One hundred and thirteen patients diagnosed with IGM (n = 36) or a malignant breast lesion (n = 77) were included in the study. Patients with non-IGM benign lesions, those with a history of radiotherapy and/or chemotherapy, and those who had undergone previous breast surgery were excluded.

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2.2. Conventional ultrasonography and strain elastography evaluations

B-mode US and SE imaging was performed using the Aplio 500 (Toshiba Medical Systems Corporation, Tokyo, Japan) and a high-frequency (12 MHz) linear array transducer. Descriptive ultrasonographic characteristics of the lesions, including margin, size, shape, echo pattern, posterior acoustic features, and distribution, were recorded during B-mode US examination. The US findings for the index lesions were classified according to the 2013 BI-RADS for Ultrasound criteria (7).

SE images were obtained after applying the probe to the breast and then focusing on the lesion in situ. Light vertical compression was applied and then removed using the probe in the manner described by Itoh et al. (10). Compression and decompression were performed approximately 5–7 times at a sustained frequency. We repeated this procedure until we obtained a stable still image that was suitable for diagnostic purposes using a correct elastography map. To obtain the best contrast, we selected an image obtained in the early phase of compression. For large lesions, the measurements were obtained by taking images of the lesions in sections from a few different points, and then we included the highest SE values in the assessment. The strain pattern in the resulting SE image was scored visually using the Tsukuba method, devised by Itoh et al. (10). According to this scoring method, lesions with an elastography score (ES) of 1, 2, or 3 were classified as benign, and lesions with an ES of 4 or 5 were classified as malignant. A cut-off value of 3 was accepted for ES in the differentiation of IGM from malignant breast lesions.

The strain ratio (SR) was assessed using the most appropriate relaxation curve. A first region of interest was placed in normal breast tissue as an internal reference, and a second region of interest was drawn by hand and adjusted to the lesion border so as to include the maximum lesion area on a B-mode US image. The SR values were automatically calculated with the software (Figure 1). The B-mode US and SE images were reviewed by two blinded radiologists, each with more than 6 years' experience in breast US, using a consensus method.

2.3. Combination of conventional ultrasonography and strain elastography

The B-mode US and SE methods were combined to reach the highest sensitivity, specificity, and accuracy for differentiation of IGM from malignant breast lesions. Using the combined technique, the values obtained from SR or ES may downgrade or upgrade the BI-RADS category of a lesion. If the SR or ES value of a target breast lesion is greater than the cut-off value, a BI-RADS Category of 3 for that lesion would increase to Category 4, but a BI-RADS Category of 4 or 5 would remain the same. If the SR or ES value of a target breast lesion is equivalent

or less than the cut-off value, a BI-RADS Category of 4 or 5 would decrease to Category 3, but a BI-RADS Category of 3 would remain the same.

2.4. Histopathology

A pathological diagnosis was obtained with US-guided core biopsy or surgical resection. A biopsy was performed for BI-RADS 3 lesions upon a clinician's request in patients who had been identified as at risk of breast cancer. All pathologic diagnoses were made by a single pathologist with more than 13 years' experience in breast pathology.

2.5. Statistical analysis

The statistical analyses were performed using SAS 9.4 (SAS Institute, Cary, NC, USA). Categorical variables are presented as frequencies and percentages. Independent samples t-test was used to assess differences between groups. Receiver-operating characteristic curve (ROC) analyses were performed to evaluate the predictive ability of the SR. The area under the ROC curve values was calculated using the optimal cut-off points. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy were calculated using these cut-off points. A P value of <0.05 was considered to be statistically significant.

3. Results

3.1. Subjects

The 113 breast lesions were histopathologically diagnosed as malignant breast lesions (n = 77) or IGM lesions (n = 36). The main characteristics of the patients and the breast lesions are presented in Table 1. The histological types of malignancy were as follows: invasive ductal carcinoma (n = 64), ductal carcinoma in situ (DCIS; n = 5), invasive lobular carcinoma (n = 4), mucinous carcinoma (n = 2), and medullary carcinoma (n = 2). In both groups, the most frequent clinical finding was a palpable mass. All the patients with IGM had a history of breastfeeding and none had a history of autoimmune disease, oral contraceptive use, or tuberculosis.

3.2. Conventional ultrasonography findings

In breasts with IGM, the most frequent B-mode US finding was multiple irregular heterogeneous hypoechoic masses with tubular extension (identified in 16 patients [44.4%], Figure 2). The second most frequent finding was focal hypoechoic mass-like lesions with an indistinct border (observed in 9 patients [25%], Figure 3). The B-mode US findings are summarized in Table 2.

In the 36 women with IGM, fistula and skin thickening were detected in 8 (22.2%) and 11 (30.5%), respectively. Seventeen women (47.2%) had moderately enlarged axillary nodes with mild cortical thickening and preservation of the hila. The 36 IGM lesions were categorized using BI-RADS criteria as Category 3 (n = 24) or as Category 4 or 5 (n = 12). In terms of differential diagnosis of IGM and

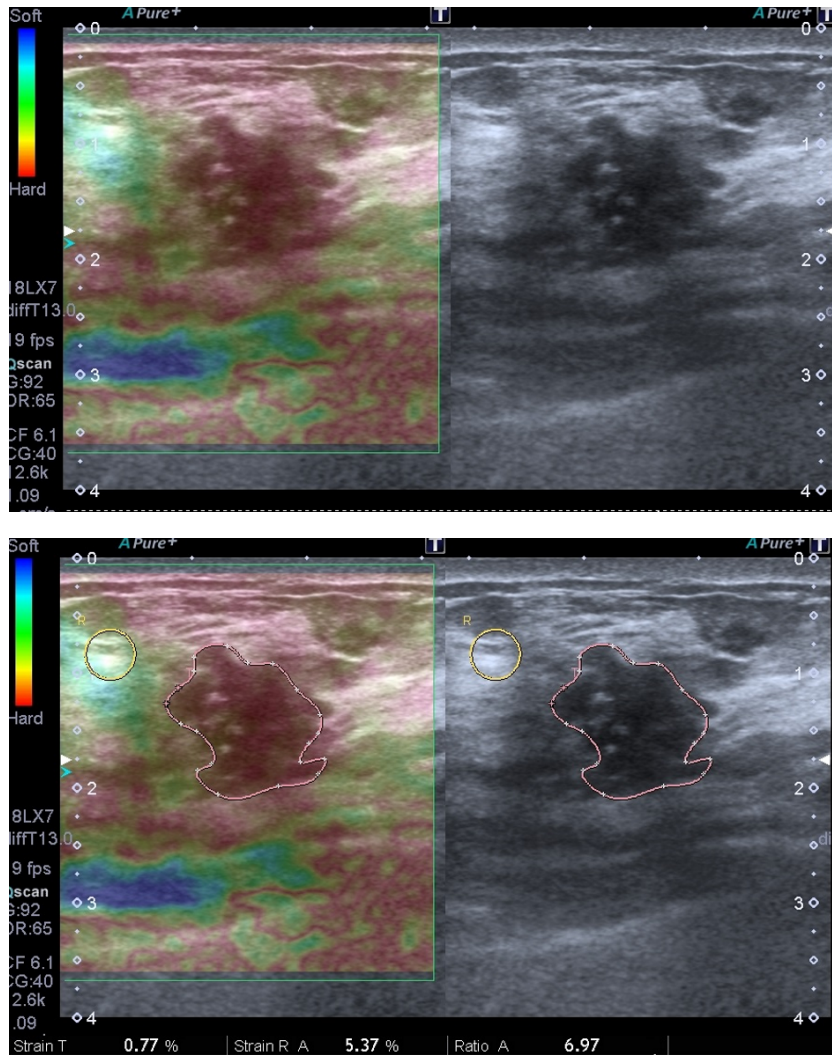


Figure 1. A 53-year-old patient with invasive ductal carcinoma. Grayscale image showing an irregular heterogeneous hypoechoic mass in BI-RADS Category 5. Elastography score (a) and strain ratio (b) values for the lesion were 5 and 6.97, respectively. BI-RADS: Breast Imaging Reporting and Data System.

malignant breast lesions, the sensitivity, specificity, PPV, NPV, and accuracy of B-mode US were 94.8%, 66.7%, 85.9%, 85.7%, and 85.8%, respectively.

3.3. Strain ratio and elastography score

The mean SR and ES values for malignant breast lesions were significantly higher than those for IGM, as seen in Table 2. SR values were drawn on the ROC curve to distinguish between IGM and malignant breast lesions. The SR cut-off value that maximized sensitivity and specificity was 2.71. Sensitivity, specificity, PPV, NPV, and accuracy were calculated as 87%, 100%, 100%, 78.3%, and 91.1% for SR and 83.1%, 100%, 100%, 73.5%, and 88.5% for ES, respectively. The mean SR and ES values for the IGM lesions were all below the cut-off value.

3.4. Combination of BI-RADS and strain elastography

By combining the SR and ES values with B-mode US, the same sensitivity, specificity, PPV, NPV, and accuracy rates were obtained. The diagnostic performances of B-mode US, SE, and a combination of these two methods are summarized in Table 3. Excellent specificity rates were achieved for differentiation of IGM and malignant breast lesions using the combined method. Increases in sensitivity, PPV, NPV, and accuracy were also observed.

4. Discussion

IGM is a rare benign inflammatory disease of unknown etiology, and its clinical and radiological findings are often confused with malignancy (11,12). Current theories

Table 1. Demographic and clinical patient characteristics.

Characteristics	IGM	Malignant lesion	P value
Patients			
Lesions, n (%)	36 (31.8)	77 (68.1)	
Age, years	35.6 ± 8.65 (24–56)	54.8 ± 11.8 (27–82)	<0.001
Symptoms			
Palpable mass, n (%)	28 (77.7)	34 (44.1)	
Breast pain, n (%)	26 (72.2)	24 (31.1)	
Erythema, n (%)	11 (30.5)	-	
Nipple change, n (%)	5 (13.8)	4 (5.1)	
Location of lesion			0.85
Right, n (%)	18 (50)	37 (48)	
Left, n (%)	18 (50)	40 (51.9)	
Lesions			
Nodule size, mm, (range)	31.2 ± 14.6 (11–75)	21.7 ± 13.9 (7–70)	0.002
Strain ratio (range)	1.08 ± 0.58 (0.32–2.70)	4.71 ± 1.56 (1.18–7.53)	<0.001
Elastography score (range)	1.36 ± 0.54 (1–3)	4.28 ± 1.01 (2–5)	<0.001

IGM: idiopathic granulomatous mastitis.

that explain the etiology of IGM favor an inflammatory response in the connective tissue of the breast stroma over glandular secretions leaked from damaged ductal epithelium (13). Other postulated reasons for this benign entity are the use of oral contraceptives and unidentified microorganisms as yet (14).

Common symptoms in patients with IGM include palpable lumps, localized or regional erythema, peau d'orange, and focal tenderness (15,16). Unilateral symptoms are most often reported, although both breasts may sometimes be involved (5). Most patients with IGM are premenopausal and report a history of breastfeeding (15). In our study, the most common symptom in patients with IGM or a malignant lesion was a palpable mass. The lesions were unilateral in all patients with IGM and on the same side as that used for breastfeeding.

The diagnostic accuracy of conventional radiographic imaging methods is still not optimal for diagnosis of IGM (2). Mammographic findings are nonspecific and reported in the literature as focal or regional asymmetry, a solitary mass or masses, skin thickening, skin and nipple retraction, and axillary lymphadenopathy (4,5,17). However, IGM is a disease encountered in the reproductive age group; therefore, the sensitivity of mammography is lower by virtue of the dense breast pattern in this age group (18,19).

MRI is another radiologic imaging technique used in the differentiation of IGM and malignant breast lesions. IGM-related MRI findings, including intensively and strongly enhancing masses, rim enhancement, and focal homogenous enhancing masses, may vary based on the severity of inflammation (3,20). In addition, larger fluid collections can be observed in an interspersed form within abnormal enhancement, with or without sinus tracts extending to the skin surface (5). However, the specificity of MRI is lower, and conventional MRI features, such as signal intensity and morphologic definition, have yet to achieve sufficient accuracy in distinguishing between IGM and malignant breast lesions (6,21). Furthermore, the apparent diffusion coefficient has been shown not to contribute to a diagnosis of IGM (21).

High-frequency US is the first-line modality in the evaluation of breast lesions. Based on the characteristics of B-mode US, the BI-RADS lexicon offers beneficial diagnostic features, in spite of its low specificity and PPV rates (8,22). In our study, even though we achieved high sensitivity rates in the differentiation between IGM and malignant breast lesions with B-mode US, our specificity rates were lower. The most important reason for the lower specificity rates was that the evaluation of morphological structure alone may be insufficient in the differentiation

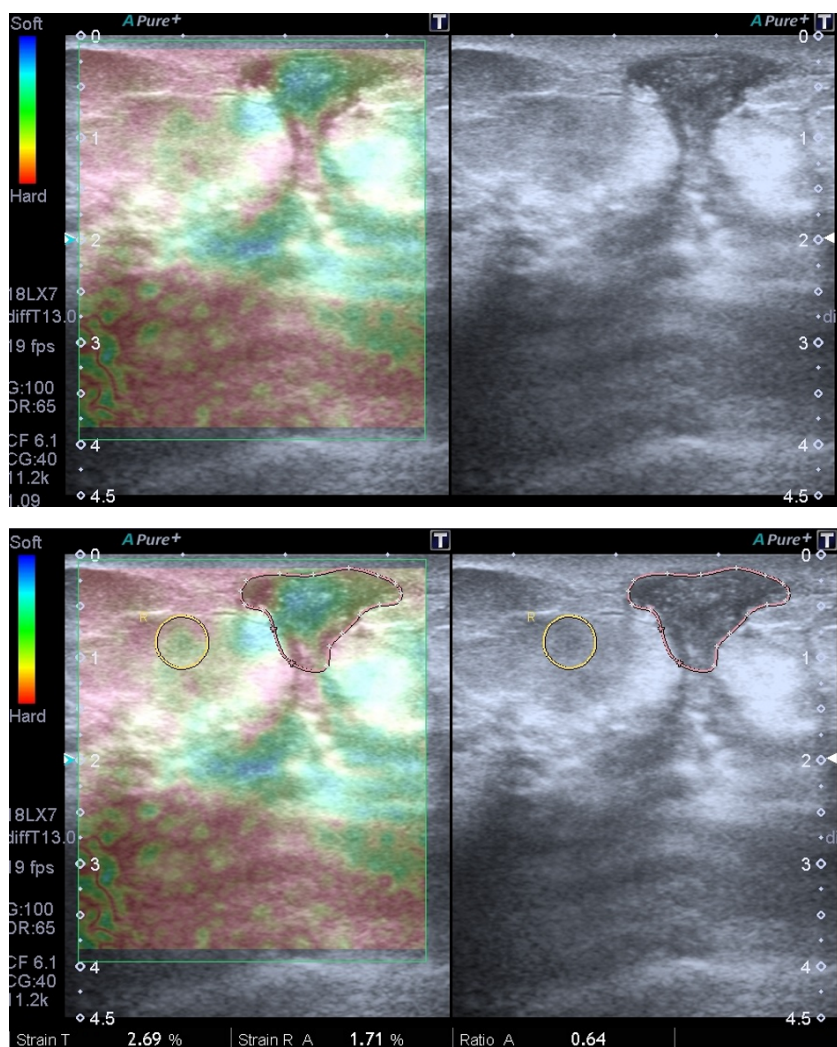


Figure 2. A 25-year-old patient with granulomatous mastitis. Grayscale image showing an irregular heterogeneous hypoechoic mass with tubular extension that was classified as BI-RADS Category 3. The elastography score (a) and strain ratio (b) values for the lesion were 2 and 0.64, respectively. BI-RADS: Breast Imaging Reporting and Data System.

of breast lesions. The US findings of IGM were reported to be confused with malignancy in several studies (14,18,23). The most common US findings are multiple irregular hypoechoic masses and collections with tubular connections and finger-like projections. Lesions with this morphologic structure are more easily diagnosed (18). Additionally, the presence of a fistula, abscess, or skin thickening is helpful for differential diagnosis (18,19,23). However, mass-like lesions with indistinct borders and lesions, taking the form of hypoechoic nodular areas in the millimeter range, are difficult to differentiate from malignant breast lesions on the basis of B-mode US findings alone (18,23). In our study, the most frequent finding in IGM lesions on B-mode US was multiple

irregular heterogeneous hypoechoic masses with tubular extension (44.4%). We classified these lesions as BI-RADS Category 3. Among all the malignant breast lesions in our study, a total of four lesions diagnosed as DCIS or mucinous carcinoma were classified as BI-RADS Category 3. DCIS and mucinous carcinomas are sometimes confused with benign lesions because they both appear as smooth-surfaced masses (24,25).

Additional modalities have been added to B-mode US in order to improve its diagnostic efficacy. Elastography is a commonly used ultrasonographic imaging technique that provides information on the stiffness of a lesion as well as its morphologic structure (10,23,26). In a study by Durur et al., using the SE method, IGM lesions were

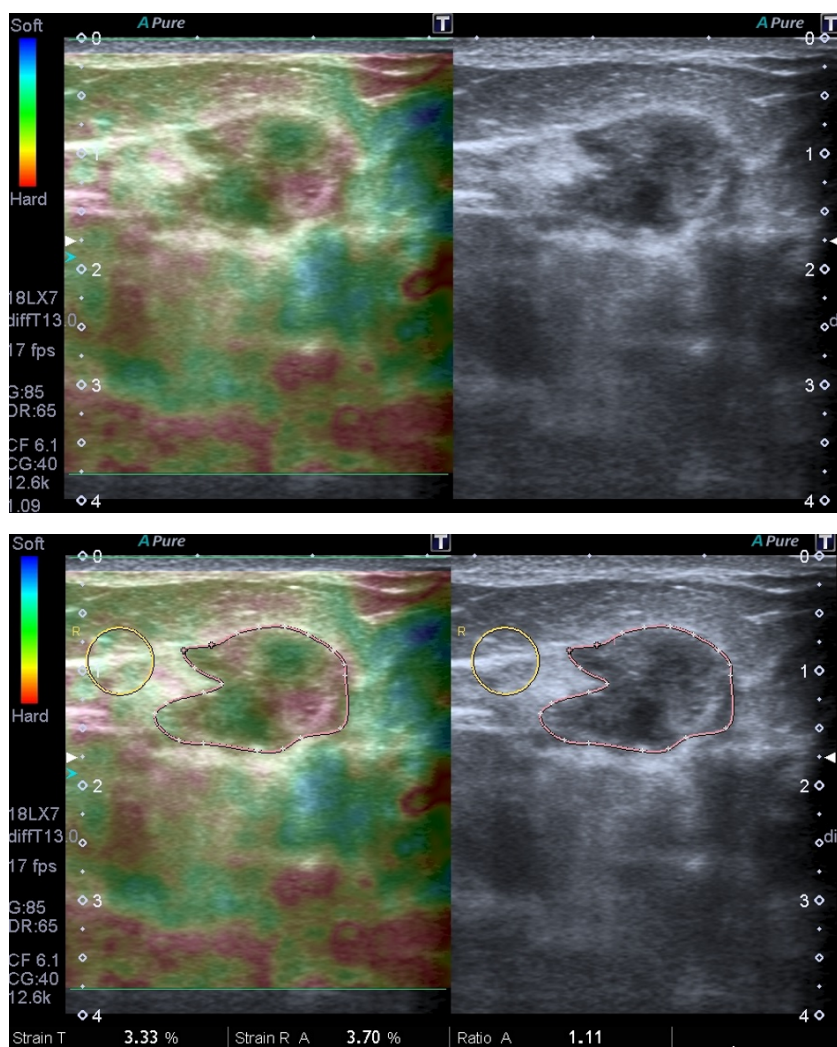


Figure 3. A 37-year-old patient with granulomatous mastitis. Grayscale image showing a mass-like lesion with an irregular and indistinct border in BI-RADS Category 4. The elastography score (a) and strain ratio (b) values for the lesion were 2 and 1.11, respectively. BI-RADS: Breast Imaging Reporting and Data System.

Table 2. B-mode ultrasonographic features of idiopathic granulomatous mastitis.

Ultrasonographic findings	n (%)
Multiple irregular heterogeneous hypoechoic masses with tubular extension	16 (44.4)
Mass-like lesions with indistinct borders	9 (25)
Collection areas with internal echoes consistent with abscess	5 (13.8)
Mass with distinct border of posterior enhancement	3 (8.3)
Millimetric hypoechoic nodular areas with indistinct border	3 (8.3)
Unilateral axillary adenopathy	17 (47.2)
Skin thickening	11 (30.5)
Fistulae	8 (22.2)

Table 3. Diagnostic performances for distinguishing between IGM and malignant breast lesions using B-mode ultrasonography, strain ratio, and elastography score alone, and a combination of these methods.

Groups	Cut-off	AUROC	Sen (%)	Spe (%)	PPV (%)	NPV (%)	Accuracy (%)
US	Category 3	0.80	94.8	66.7	85.9	85.7	85.8
ES	Score 3	0.91	83.1	100	100	73.5	88.5
SR	2.71	0.97	87	100	100	78.3	91.1
US + SR		0.98	96.1	100	100	92.3	97.3
US + ES		0.98	96.1	100	100	92.3	97.3

US: B-mode ultrasonography; ES: elastography score; SR: strain ratio; AUROC: area under the receiver-operating characteristic curve; Sen: sensitivity; Spe: specificity; PPV: positive predictive value; NPV: negative predictive value.

reported to have a lower SR (1.10 ± 0.79) and ES (1.66 ± 0.55); however, no comparison was made between IGM and malignant breast lesions (9). In another study that used an acoustic radiation force impulse imaging technique, Teke et al. obtained statistically significant marginal and internal shear wave velocity values when differentiating between IGM and malignant breast lesions (23). In that study, no accurate measurements were obtained from the centers of some of the larger heterogeneous IGM lesions due to absorption of US energy by the tissue. Although shear wave elastography and SE are different methods, both can yield similar results with regard to elasticity of lesions (26). However, SE requires more experience to perform. In our study, ES and SR values could be obtained from all lesions. A statistically significant difference in SR and ES was found between IGM and malignant breast lesions. We achieved excellent sensitivity, specificity, and

accuracy in the differentiation of IGM and malignant breast lesions by combining B-mode US and SE methods. We consider that IGM and malignant breast lesions can be differentiated more easily using the combined method, leading to a reduction in the number of unnecessary surgical procedures performed in patients with IGM. False negative findings were determined for invasive ductal cancer, mucinous cancer, medullary cancer, and DCIS lesions, as reported in the literature (10,24).

Our study had several limitations. Firstly, its design was retrospective. Secondly, no interobserver or intraobserver variability was present. Finally, the study findings were not compared to those obtained by mammography or MRI.

In conclusion, the combined use of B-mode US and SE is effective and easy to use for differentiation of IGM and malignant breast lesions with excellent sensitivity and specificity rates.

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