Comparison of Shear-Wave and Strain Ultrasound Elastography in the Differentiation of Benign and Malignant Breast Lesions

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OBJECTIVE. The purpose of this article is to compare the diagnostic performances of shear-wave and strain elastography for the differentiation of benign and malignant breast lesions.

SUBJECTS AMD METHODS. B-mode ultrasound and shear-wave and strain elastography were performed in 150 breast lesions; 71 were malignant. BI-RADS final assessment, elasticity values in kilopascals, and elasticity scores on a 5-point scale were assessed before biopsy. The results were compared using the area under the receiver operating characteristic curve (AUC).

RESULTS. The AUC for shear-wave elastography was similar to that of strain elastography (0.928 vs 0.943). The combined use of B-mode ultrasound and either elastography technique improved diagnostic performance in the differentiation of benign and malignant breast lesions compared with the use of B-mode ultrasound alone (B-mode alone, AUC = 0.851; B-mode plus shear-wave elastography, AUC = 0.964; B-mode plus strain elastography, AUC = 0.965; $p < 0.001$). With the best cutoff points of 80 kPa on shear-wave elastography and a score between 3 and 4 on strain elastography, the sensitivity was higher in shear-wave elastography, and specificity was higher in strain elastography (95.8% vs 81.7%, $p = 0.002$; 93.7% vs 84.8%, $p = 0.016$). In cases of infiltrating ductal carcinoma, mean elasticity scores were lower in grade 3 than in grade 1 and 2 cancers ($p = 0.017$) with strain elastography causing false-negative findings.

CONCLUSION. The diagnostic performance of shear-wave and strain elastography was similar. Either elastography technique can improve overall diagnostic performance in the differentiation of benign and malignant lesions when combined with B-mode ultrasound. However, the sensitivity and specificity of shear-wave and strain elastography were different according to lesion histologic profile, tumor grade, and breast thickness.

Keywords: breast cancer, elasticity imaging, shear-wave elastography, strain elastography, ultrasound

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In recent years, a variety of manufacturers have begun to incorporate elastography, a real-time tissue stiffness–measuring technique, in ultrasound equipment. The results have shown that elastography has the ability to yield accurate differentiation of benign from malignant breast lesions [1–3]. In the breast, cancers tend to be stiffer than benign lesions, and elastography has also been reported to improve the specificity for the diagnosis of solid masses at breast ultrasound [4–6].

The two most frequently used elastography techniques in the breast are compressive, or strain, elastography and shear-wave elastography. However, they are quite different in terms of the forces being measured and in their imaging methods. In strain elastography, stress is applied by repeated manual compression of the transducer, and the amount of lesion deformation relative to the surrounding normal tissue is measured and displayed in color. Thus, with this technique, data acquisition and interpretation of elasticity images are largely dependent on the examiner's experience, and significant interobserver variability has been found [2, 7]. In contrast to strain elastography, shear-wave elastography uses an acoustic radiation force impulse created by a focused ultrasound beam, which allows measurement of the propagation speed of shear waves within the tissue to locally quantify its stiffness in kilopascals or meters per second. Shear-wave elastography has been reported to be highly reproducible for assessing elastographic features of breast lesions within and across observers [3]. However, there is the potential for an increase in artifacts caused by reflection and refraction resulting from the large variation in shear wave velocity of normal and abnormal breast tissues [8].

The diagnostic performances of shear-wave and strain elastography in the differentiation of benign and malignant lesions have previously been reported [1, 4, 9–13]. However, to our knowledge, there have been no studies comparing the diagnostic performances of the two different techniques in the same study population. When the shear-wave and strain elastography techniques were applied in the same breast lesions, consistent or similar results are to be expected if the examination is performed by experienced operators. However, because each elastography technique has its own inherent drawbacks leading to false-positive or -negative results, variable outcomes depending on the techniques are applied used, as well as their diagnostic criteria, may be possible. Furthermore, breast thickness, lesion size, and histologic profile have been shown to affect the sensitivity and specificity of elastography for the differentiation of benign and malignant breast lesions [7]. Malignant lesions that are soft, such as mucinous carcinomas, necrotic tumors, and ductal carcinoma in situ (DCIS), may be misclassified as benign, and benign conditions that are stiff, such as scarring, fibrosis, and complex fibroadenomas, may be misinterpreted as malignant [1, 9, 12].

Thus, the purpose of this study was to compare the diagnostic performance of both shear-wave and strain elastography in the differentiation of benign and malignant breast lesions in the same breasts, using histologic analysis as the reference standard, and to evaluate factors that can affect the results of the two elastography techniques.

Subjects and Methods

Patients and Breast Lesions

This prospective study was conducted with institutional review board approval of Seoul National University Hospital, and informed consent was provided by all patients. In our institution, elastography has been used as a supplement to B-mode breast ultrasound in clinical practice since January 2008. Between February 2010 and June 2010, 153 breast lesions in 130 consecutive women who had been scheduled to undergo ultrasound-guided percutaneous needle biopsy or surgical excision were examined with B-mode ultrasound and both shear-wave and strain elastography. Among them, one patient with multifocal breast cancer was excluded because of difficulty in correlating the ultrasound-visible lesion and pathologic results because of multiplicity. Finally, 150 breast lesions in 129 consecutive women (mean age, 47.8 years; age range, 22–75 years) constituted our study population. Of these 129 women, 82 women were asymptomatic, 42 women presented with palpability, and five showed nipple discharge. On B-mode ultrasound, the final assessments of the 150 solid breast lesions determined before biopsy were BI-RADS category 3 (probably benign) for 15 lesions, category 4 (suspicious abnormality) for 87 lesions, and category 5 (highly suggestive of malignancy) for 48 lesions. Fifteen category 3 (probably benign) lesions were biopsied because of the patients' or surgeons' request.

Mammograms were available for 132 lesions in 113 women during the ultrasound examinations. Mammographic breast density was recorded according to the American College of Radiology's BI-RADS category [14]. The breast tissue densities on mammography were as follows: category 1, five patients; category 2, 17 patients; category 3, 74 patients; and category 4, 17 patients. Lesions were observed as a mass in 39 cases (30%), as a mass with microcalcifications in 24 cases (18%), as an architectural distortion in four cases (3%), and as focal asymmetry in 17 cases (13%). No mammographic abnormalities were found for 48 lesions (37%).

Of the 150 lesions, 79 (53%) were benign and 71 (47%) were malignant. All lesions were confirmed through ultrasound-guided core needle biopsy (14-gauge automated gun or 11-gauge vacuum-assisted). Among the lesions, 75 underwent subsequent surgical excision after ultrasound-guided needle localization. The duration of imaging follow-up with ultrasound for the lesions with benign biopsy histologic findings was 13–27 months, and lesion stability was confirmed in all cases.

Ultrasound Examinations

Conventional B-mode ultrasound and strain elastography images were obtained using a scanner (EUB-8500, Hitachi Medical) with a 6- to 14-MHz linear transducer, and shear-wave elastography images were obtained using an ultrasound system (Aixplorer, SuperSonic Imagine) with a 7.5- to 15-MHz linear transducer by one of three radiologists with 8–21 years of experience in breast ultrasound and 36–60 months of experience in ultrasound elastography. All radiologists were aware of the clinical and mammographic findings. After B-mode ultrasound, strain elastography images were acquired first, and then shear-wave elastography images were obtained by the same radiologist in the same imaging plane, without changing the position of the patient. Two elastography ultrasound units were installed in the same room, and the interval between shear-wave and strain elastography examinations was less than 1 minute.

For shear-wave elastography, elastographic images were generated without compression, as recommended elsewhere [12]. The lesions were located at the center of the elasticity boxes, and the shear-wave elastography images of the lesions were saved after a few seconds of immobilization to allow the shear-wave elastography image to stabilize. The size of each region of interest box was 2.5 × 1.5 cm by default, with a maximal size of 3 × 2.5 cm. Quantitative elasticity values were displayed as a color, and the default maximum display setting of 180 kPa (7.7 m/s) was used in this study. The red color represents a stiff lesion, and blue color represents a soft lesion on shear-wave elastography. The data acquisition procedure took approximately 2–3 minutes per case.

For strain elastography, the target lesion was vertically compressed by the transducer under light pressure [1]. The top of the region of interest on elastography images was set to include the subcutaneous fat, and the bottom of the region of interest was set to include the pectoral muscle; lateral borders were set more than 5 mm from the lesion's boundary. Real-time strain images were displayed through 256-color mapping according to the degree of displacement for all pixels within the region of interest, with a scale from red (greatest strain, softest component), to green (average strain, intermediate component), to blue (no strain, hardest component). The pressure and speed of manual compression were adjusted to reveal the subcutaneous fat layer as a mix of red and green and the pectoralis muscle layer as blue, to avoid interruption of color encoding. The data acquisition procedure also took approximately 2–3 minutes per case.

Image Evaluation

The radiologists who performed the B-mode and elastography examinations recorded the lesion size (maximal diameter as measured on ultrasound), lesion depth (measured as the vertical diameter from the skin to the center of the lesion), and breast thickness (measured as the vertical diameter from the skin to the pectoralis muscle in supine position) where the lesion was located. Measurements were performed by applying light pressure of the probe using the same method as done for elastography. BI-RADS final assessment on B-mode ultrasound was prospectively recorded by the radiologists who performed the B-mode ultrasound before elastography.

Quantitative elasticity values on shear-wave elastography were measured, without histologic information, at the area that showed maximum stiffness in the lesion on a color map provided by the shear-wave elastography system. The mean elasticity value in terms of the Young modulus (in kilopascals) and SD were measured and recorded in all cases by using a 2-mm^2 region of interest placed by a radiologist on the stiffest portion of the lesion, including immediately adjacent stiff tissue or halo [9].

Evaluation of elasticity score on strain elastography was performed by the radiologists at the same time when elasticity images were obtained. Elasticity scores on strain elastography (on a 5-point scale) were prospectively assigned when the images were obtained, according to the degree of strain in the hypoechoic lesion and without histologic information, as proposed by Itoh et al. [1]. A score of 1 indicated even strain for the entire hypoechoic lesion. A score of 2 indicated strain in most of the hypoechoic lesion with some strain-free areas. A score of 3 indicated strain at the periphery of the hypoechoic lesion and not in its center. A score of 4 indicated no strain in the entire hypoechoic lesion. A score of 5 indicated no strain in the entire hypoechoic lesion or in the surrounding area.

Pathologic Examinations

Of the 79 benign lesions, further surgical excision was performed for four intraductal papillomas at core needle biopsy. For all breast cancers at biopsy, mastectomy (n = 31) or breast-conserving surgery (n = 40) was performed in our institution. The histologic type, tumor grade, and invasive tumor size at pathologic examination were determined on the basis of the surgically resected specimen [15]. All diagnoses were made by a pathologist with 25 years of experience in breast pathologic examinations.

In all cases, imaging-histologic correlation was performed after surgery, and attention was given to investigating the differences in cellularity or composition between the central and peripheral portions of the tumor and surrounding marginal area. Findings of fibrosis and central necrosis in the tumor, as well as abnormalities in the surrounding marginal area, such as associated DCIS or benign lesions, were described. For cases showing discrepant results between shear-wave and strain elastography, histologic findings were reviewed with the radiologists who performed the elastography at an imaging-histologic conference.

Statistical Analysis

For statistical analysis, we examined the mean elasticity values on shear-wave elastography and elasticity scores on strain elastography of all benign and malignant lesions. The mean elasticity values or elasticity scores between benign and malignant lesions and those between histologic grades of infiltrating ductal carcinomas (IDCs) were also compared using the nonparametric Mann-Whitney test.

Receiver operating characteristic (ROC) curves for B-mode ultrasound and shear-wave and strain elastography images were analyzed to evaluate diagnostic performance and to compare the performances of established BI-RADS categories and elasticity values or scores. The best cutoff points yielding the maximal sum of sensitivity and specificity for B-mode ultrasound and for shear-wave and strain elastography were calculated. Sensitivity, specificity, positive predictive values (PPVs), and negative predictive values (NPVs) using the cutoff points were calculated, and sensitivity and specificity were compared between shear-wave and strain elastography using the McNemar test. After individual ROC analysis of each examination, the logistic regression model was used to perform ROC analysis of the combined data of B-mode and elastography images (B-mode vs B-mode with shear-wave elastography and B-mode vs B-mode with strain elastography). To summarize the overall performance, areas under the ROC curve (AUCs) were calculated and compared between these techniques. Because some patients had more than one breast lesion, the cluster effect was considered in ROC curve analysis. Statistically significant differences between AUC were reported as 95% CIs. The mean differences were regarded as being statistically significant at the 5% level when the corresponding CI did not encompass zero.

Using the best cutoff points of each elastography technique, we also compared the pathologic results with the elasticity values or scores of both techniques. To investigate which factors may have affected the result of the two techniques, lesions that showed discrepant results between shear-wave and strain elastography were analyzed according to patients' age, mean lesion size, lesion depth, breast thickness, and pathology. The results were compared between the two techniques using the Fisher exact test and Student t test. After identifying variables affecting discrepant results between shear-wave and strain elastography, we also divided lesions according to those variables in each technique, and diagnostic accuracies according to the variables were compared separately in each technique. The diagnostic accuracy of each group was estimated, and the method of the generalized estimating equation allowing cluster effects was used to determine whether there was a difference in diagnostic accuracy between the groups. Penalized maximum likelihood method in logistic regression was used when the zero cell exists. Because lesion variables showed significant differences between each group, the propensity score matching method was used to correct the difference in the distribution of lesion variables between the groups.

All statistical analyses were performed using commercially available software (SAS, version 9.1.3, SAS), with a p value of less than 0.05 indicating a statistically significant difference.

Results

Lesion Histologic Profiles and Comparison of Elasticity on Shear-Wave and Strain Elastography

Malignant lesions included IDC histologic grade 1 (well differentiated; n = 2), IDC grade 2 (moderately differentiated; n = 23), IDC grade 3 (poorly differentiated; n = 31), infiltrating lobular carcinoma (n = 6), mucinous carcinoma (n = 1), metaplastic carcinoma (n = 1), microinvasive ductal carcinoma (n = 2), and DCIS (n = 5). Benign lesions included fibroadenomas (n = 27), intraductal papillomas (n = 6), adenosis (n = 2), stromal fibrosis (n = 1), and fibrocystic changes (n = 43). On B-mode ultrasound, the mean (± SD) size of malignant lesions was 2.3 ± 1.3 cm (range, 0.5–6.2 cm) and that of benign lesions was 1.1 ± 0.8 cm (range, 0.4–2.9 cm). On shear-wave elastography, malignant lesions had a mean elasticity value of 150.0 ± 52.3 kPa, whereas benign lesions had a mean elasticity value of 47.3 ± 44.3 kPa (p < 0.0001). On strain elastography, the mean elasticity score for malignant lesions was 4.0 ± 0.8 and that for benign lesions was 1.9 ± 1.0 (p < 0.001). The difference was statistically significant in both techniques. The mean elasticity values and scores according to lesion size on B-mode ultrasound are shown in Table 1. The

TABLE 1: Elasticity Values and Elasticity Scores on B-Mode Ultrasound for Benign and Malignant Lesions, by Lesion Size

Lesion Size (mm)	Elasticity Value on Shear-Wave Elastography (kPa)		Elasticity Score on Strain Elastography	
	Benign	Malignant	Benign	Malignant
< 10 (n = 41)	42.89 ± 44.41 (3.3–172.4)	103.4 ± 19.30 (84.9–132.1)	1.64 ± 0.93 (1–4)	4.2 ± 0.45 (4–5)
10–20 (n = 71)	44.66 ± 41.50 (7.6–192.6)	204.4 ± 53.01 (59.1–273.8)	2.06 ± 0.98 (1–4)	4.9 ± 0.82 (2–5)
> 20 (n = 38)	83.68 ± 46.96 (29.2–149.5)	156.0 ± 52.3 (47.0–250.3)	2.43 ± 0.79 (1–3)	4.0 ± 0.68 (2–5)

Note—Data are mean ± SD (range).

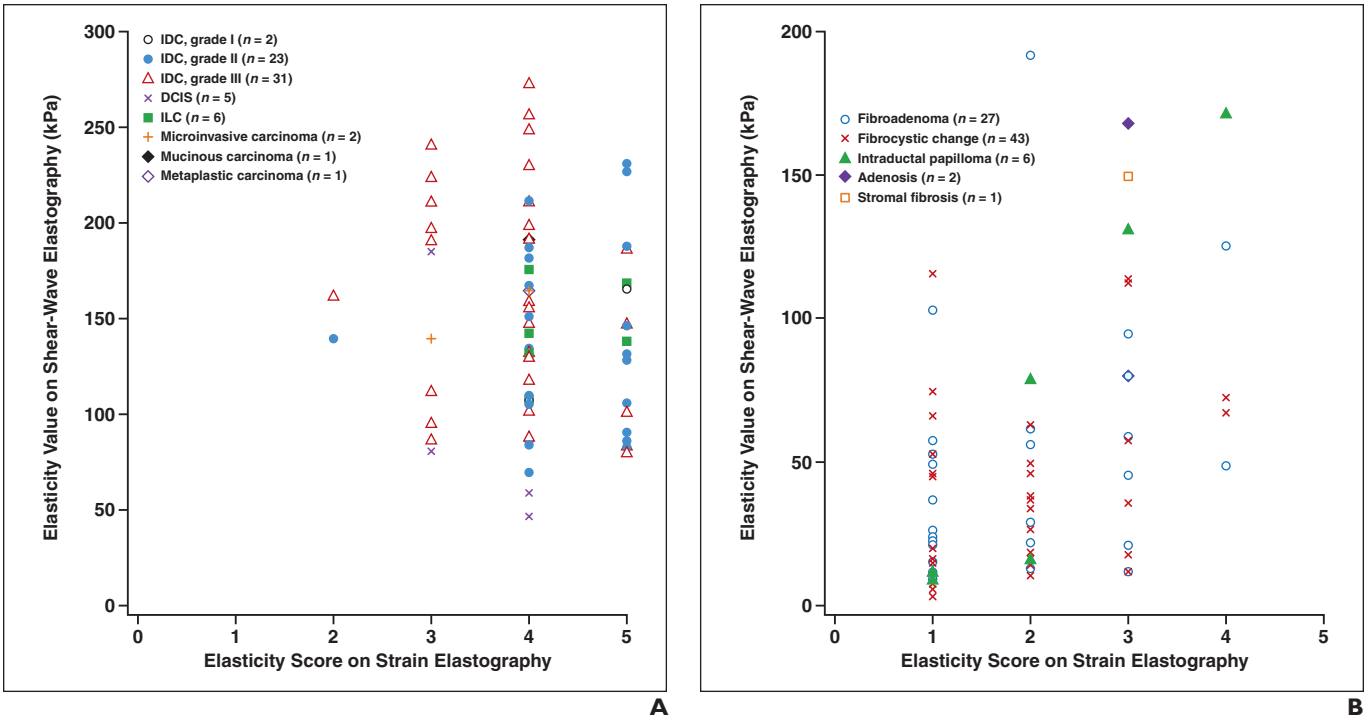


Fig. 1—Correlation between elasticity values on shear-wave elastography and elasticity scores on strain elastography.
A and **B,** Scatter diagrams show correlations for malignant (**A**) and benign (**B**) lesions. DCIS = ductal carcinoma in situ, IDC = infiltrating ductal carcinoma, ILC = infiltrating lobular carcinoma.

elasticity values and scores were higher in larger lesions for both benign and malignant lesions in general; however, for each size category, the mean value was still significantly higher for malignant lesions than for benign lesions ($p < 0.001$).

In cases of IDCs ($n = 56$), the mean elasticity values of histologic grade 3 cancers were higher than those of grade 1 and 2 cancers (165.9 ± 56.8 kPa vs 138.5 ± 47.0 kPa; $p = 0.059$) with shear-wave elastography, whereas the mean elasticity scores were lower in grade 3 cancers than those of grade 1 and 2 cancers (3.8 ± 0.8 vs 4.4 ± 0.7; $p = 0.017$) with strain elastography. Infiltrating lobular carcinomas ($n = 6$) had a mean elasticity value of 144.2 ± 24.97 kPa on shear-wave elastography, and the mean elasticity score was 4.3 ± 0.5 on strain elastography. DCIS ($n = 5$) had a mean elasticity value of 104.2 ± 60.0 kPa on shear-wave elastography and elasticity scores of 3.6 ± 0.5 on strain elastography. The elasticity values of malignant and benign lesions on shear-wave elastography and elasticity scores on strain elastography are plotted in Figure 1.

Sensitivity, Specificity, and ROC Analysis

The diagnostic performances of B-mode ultrasound and shear-wave and strain elastography at various cutoff points are shown in Table 2. B-mode ultrasound had 100% (71/71) sensitivity, 19.0% (15/79) specificity, 52.6% (71/135) PPV, and 100% (15/15) NPV when a cutoff point between categories 3 and 4 was used. For shear-wave elastography, the optimal cutoff point, yielding the maximal sum of sensitivity and specificity, was 80 kPa, and the sensitivity, specificity, PPV, and NPV of shear-wave elastography were 95.8% (68/71), 84.8% (67/79), 85.0% (68/80), and 95.7% (67/70), respectively. Additional cutoff points of 30, 50, 100, and 160 kPa used in other studies [8, 11] were also tested to compare their diagnostic performance. For strain elastography, the optimal cutoff point yielding the maximal sum of sensitivity and specificity was between elasticity scores of 3 and 4, and the sensitivity, specificity, PPV, and NPV of strain elastography were 81.7% (58/71), 93.7% (74/79), 92.1% (58/63), and 85.1% (74/87), respectively. Thus, with the best cutoff points, the sensitivity of shear-wave elastography was higher than that of strain elastography (95.8% [68/71] vs 81.7% [58/71]; $p = 0.002$), and the specificity of strain elastography was higher than that of shear-wave elastography (93.7% [74/79] vs 84.8% [67/79]; $p = 0.016$).

On ROC analysis, the AUC was 0.851 ± 0.03 (95% CI, 0.791–0.911) for B-mode ultrasound, 0.928 ± 0.02 (95% CI, 0.886–0.970) for shear-wave elastography, and 0.943 ± 0.02 (95% CI, 0.912–0.975) for strain elastography. The AUC of both elastography techniques showed higher values than B-mode ultrasound ($p = 0.044$ for shear-wave elastography, and $p = 0.012$ for strain elastography). In addition, there was no significant difference between shear-wave and strain elastography ($p = 0.503$). The combination of B-mode ultrasound and shear-wave elastography (AUC, 0.964 ± 0.013; range, 0.939–0.988) showed equal discriminating power to the combination of B-mode ultrasound and strain elastography (AUC, 0.965 ± 0.012; range, 0.941–0.989) for the detection of a malignancy, but significantly higher than B-mode ultrasound alone ($p < 0.001$ for B-mode vs B-mode plus shear-wave elastography; $p < 0.001$ for B-mode vs B-mode plus strain elastography).

Elasticity of Lesions According to BI-RADS Category on B-Mode Ultrasound

Malignancy rates for 150 breast lesions with their BI-RADS assessment and elasticity scores at shear-wave and strain elastography are listed in Table 3. There were 64 benign lesions that presented as BI-RADS category 4 lesions necessitating biopsy. Among them, 55 lesions (86%) showed elasticity values below 80 kPa, and 43 lesions (67%) showed elasticity values

TABLE 2: Diagnostic Performances of B-Mode Ultrasound, Shear-Wave Elastography, and Strain Elastography at Various Cutoff Points for the Diagnosis of Benign and Malignant Lesions

Cutoff Point	Sensitivity	Specificity	PPV	NPV
BI-RADS category on B-mode ultrasound[a]				
Between 2 and 3	71/71 (100)	0/79 (0)	71/150 (47.3)	NA
Between 3 and 4	71/71 (100)	15/79 (19.0)	71/135 (52.6)	15/15 (100)
Between 4 and 5	48/71 (67.6)	79/79 (100)	48/48 (100)	79/102 (77.5)
Elasticity value on shear-wave elastography				
30.0 kPa	71/71 (100)	40/79 (50.6)	71/110 (64.5)	40/40 (100)
50.0 kPa	70/71 (98.6)	52/79 (65.9)	70/97 (72.2)	52/53 (98.1)
80.0 kPa[b]	68/71 (95.8)	67/79 (84.8)	68/80 (85.0)	67/70 (95.7)
100.0 kPa	57/71 (80.3)	68/79 (86.1)	57/68 (83.8)	68/82 (82.9)
160.0 kPa	30/71 (42.3)	76/79 (96.2)	30/33 (90.9)	76/117 (65.0)
Elasticity score on strain elastography[c]				
Between 1 and 2	71/71 (100)	36/79 (45.6)	71/114 (62.3)	36/36 (100)
Between 2 and 3	69/71 (97.2)	56/79 (70.9)	69/92 (75.0)	56/58 (96.6)
Between 3 and 4[d]	58/71 (81.7)	74/79 (93.7)	58/63 (92.1)	74/87 (85.1)
Between 4 and 5	19/71 (26.8)	79/79 (100)	19/19 (100)	79/131 (60.3)

Note—Data are no. of lesions/total (%). NA = not applicable, NPV = negative predictive value, PPV = positive predictive value.
[a]Conventional ultrasound category was defined according to the BI-RADS classification for ultrasound.
[b]The optimal cutoff, yielding maximal sum of sensitivity and specificity in shear-wave elastography.
[c]Strain elastography score was defined according to the elasticity scoring system proposed by Itoh et al. [1].
[d]The optimal cutoff, yielding maximal sum of sensitivity and specificity in strain elastography.

below 50 kPa. On strain elastography, four lesions (6.3%) showed an elasticity score of 4, 13 (20.3%) showed an elasticity score of 3, 16 (25%) showed an elasticity score of 2, and 31 (48.4%) showed an elasticity score of 1.

When we used 80 kPa as a cutoff point of shear-wave elastography and elasticity scores of 1, 2, and 3 were considered to be test negative and scores of 4 and 5 were considered to be test positive on strain elastography, 64 of 79 (81.0%) benign lesions were true-negatives on both elastography techniques (Fig. 2), and 55 of 71 (77.5%) malignancies were true-positives on both elastography techniques (Fig. 3). Two (2.5%) benign lesions (one 0.6-cm papilloma and one 1.5-cm fibroadenoma) showed high elasticity values, leading to false-positive results; both lesions showed elasticity scores of 4 on strain elastography and elasticity values of 172.4 and 125.4 kPa on shear-wave elastography.

Analysis of Cases Showing Discrepant Findings Between the Shear-Wave and Strain Elastography

Twenty-nine of 150 lesions (19.3%; 13 benign and 16 malignant lesions) showed different results between the two techniques according to the cutoff points of 80 kPa on shear-wave elastography and an elasticity score between 3 and 4 on strain elastography. Sixteen lesions (13 malignant and three benign lesions)

TABLE 3: Malignancy Rates in BI-RADS Categories 3, 4, and 5 Lesions at B-Mode Ultrasound, by Lesion Elasticity

Elasticity	Malignancy Rate			
	Overall	BI-RADS Category 3	BI-RADS Category 4	BI-RADS Category 5
Elasticity values on shear-wave elastography				
≤ 30 kPa	0/40 (0)	0/6 (0)	0/34 (0)	NA
> 30 to ≤ 80 kPa	3/30 (10)	0/6 (0)	3/24 (12.5)	NA
> 80 to ≤ 160 kPa	38/47 (80.9)	0/3 (0)	14/20 (70.0)	24/24 (100)
> 160 kPa	30/33 (90.9)	NA	6/9 (66.7)	24/24 (100)
Elasticity scores on strain elastography				
1	0/36 (0)	0/5 (0)	0/31 (0)	NA
2	2/22 (9.1)	0/4 (0)	2/18 (11.1)	NA
3	11/29 (37.9)	0/5 (0)	5/18 (27.8)	6/6 (100)
4	39/44 (88.6)	0/1 (0)	13/17 (76.5)	26/26 (100)
5	19/19 (100)	NA	3/3 (100)	16/16 (100)
Total	71/150 (47.3)	0/15 (0)	23/87 (26.4)	48/48 (100)

Note—Data are no. of malignancies/no. of masses (%). NA = not applicable.

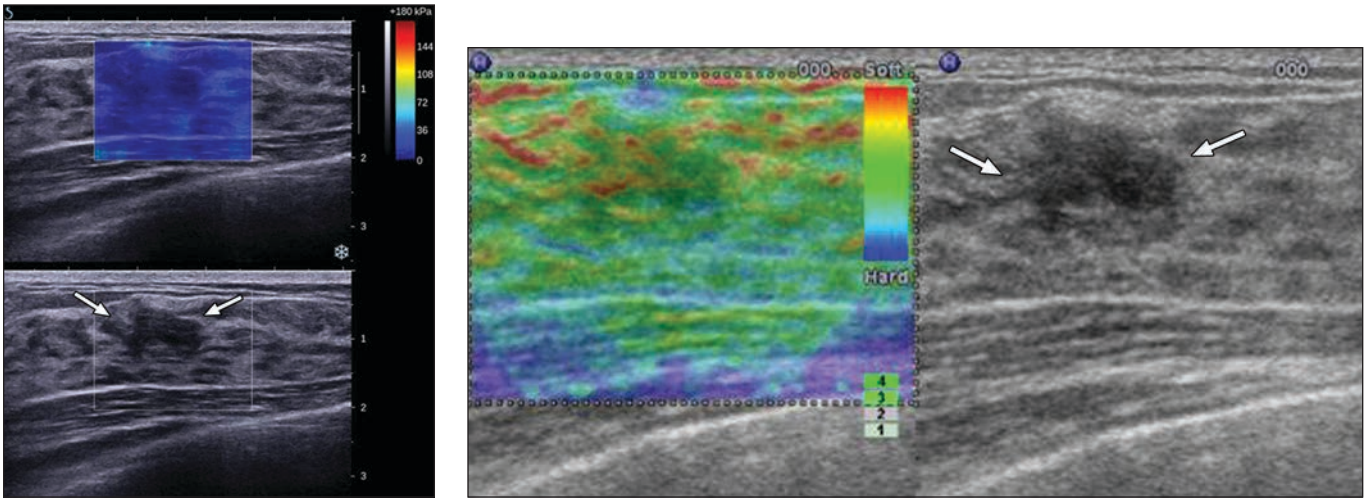


Fig. 2—41-year-old woman with fibroadenoma.
A, B-mode ultrasound (*bottom*) reveals ill-defined hypoechoic lesion (*arrows*), which was considered to be BI-RADS category 4. Shear-wave elastography (*top*) depicts homogeneous soft lesion, with elasticity value of 21.1 kPa. Color spectrum is at right, and maximum is set to 180 kPa (7.7 m/s). Red color represents stiff lesion, and blue color represents soft lesion on shear-wave elastography.
B, B-mode ultrasound (*right*) shows ill-defined hypoechoic lesion (*arrows*). With strain elastography (*left*), entire hypoechoic lesion was evenly shaded green, as was surrounding breast tissue, with elasticity score of 1. Color bar indicates degree of strain within region of interest box, and, in contrast to shear-wave elastography, blue color represents stiff lesion and red represents soft lesion on strain elastography. Number bar below color bar indicates speed of compression.

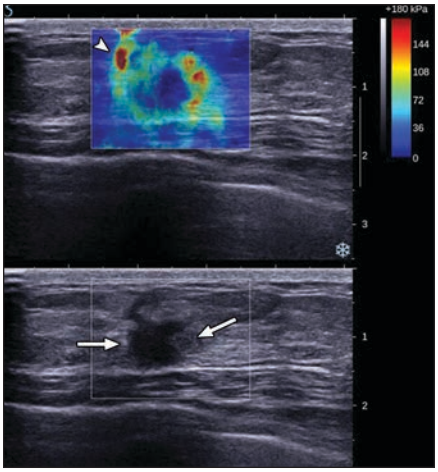
showed correct results only on shear-wave elastography, and 13 lesions (three malignant and 10 benign lesions) showed correct results only on strain elastography. These 29 lesions with discrepant results between shear-wave and strain elastography are listed in Table 4.

A higher malignancy rate (81.3% [13/16]: 10 IDCs, one microinvasive ductal carcinoma, and two DCISs) was noted in the lesions diagnosed correctly by shear-wave elastography only. Nine of the 10 IDCs were grade 3 cancers, and one was grade 2 cancer. Among the total of 31 grade 3 IDCs, nine grade 3 cancers in this group (29%) showed high elasticity values (mean, 166.6 kPa; range, 88–241 kPa) within the lesion, as well as the surrounding tissue on shear-wave elastography. On strain elastography, eight of nine grade 3 cancers showed an elasticity score of 3, and one grade 3 cancer showed an elasticity score of 2 (Fig. 4). On histologic analysis, five grade 3 cancers showed peripheral hypercellular and central hypocellular areas with some collagen formation and central necrosis. The other four grade 3 cancers showed no differences in cellularity or composition within the tumors. In contrast, a higher benign disease rate (76.9% [10/13]) was observed in the lesions diagnosed correctly by strain elastography only ($p = 0.003$). Three malignancies, including two DCISs and one grade 2 IDC, showed false-negative findings on shear-wave elastography but were true-positive on strain elastography, with an elasticity score of 4 in this group. The pathologic findings of the two DCISs showed the tumor cells filling the duct in the background of the preserved normal glandular structure or combined with sclerosing adenosis. The other IDC was a 1.0-cm grade 2 tumor in the background of sclerosing adenosis.

The breast thickness where the lesion was located was significantly thicker in the lesions diagnosed correctly by shear-wave elastography only, compared with the lesions diagnosed correctly by strain elastography only (2.33 ± 0.42 cm vs 1.71 ± 0.37 cm; $p = 0.0001$). In addition, lesion depth was significantly deeper in the lesions diagnosed correctly by shear-wave elastography only, compared with the lesions diagnosed correctly by strain elastography only (0.82 ± 0.31 cm vs 0.57 ± 0.28 cm; $p = 0.033$). In contrast, patient age (50.9 ± 11.7 years vs 45.3 ± 13.4 years; $p = 0.230$), and mean lesion size (2.0 ± 0.81 cm vs 1.64 ± 0.77 cm; $p = 0.236$) did not show significant differences between the two groups, which showed discrepant results between shear-wave and strain elastography. Therefore, because breast thickness and lesion depth showed significant differences between the two groups, we compared the accuracy between different breast thickness and lesion depth in both elastography techniques, adjusting all data for a propensity score. Higher accuracy was noted in evaluating lesions that were located in breasts equal to or thicker than 2 cm than in breasts not thicker than 2 cm (93.3% vs 76.7%; odds ratio [OR] = 4.261) on shear-wave elastography. In contrast, with strain elastography, lesions that were located in breasts equal to or thicker than 2 cm showed slightly lower accuracy compared with lesions located in breasts not thicker than 2 cm (80.0% vs 86.7%; OR = 0.615). However, no statistically significant differences were noted for both shear-wave elastography ($p = 0.081$) and strain elastography ($p = 0.486$). As for lesion depth, no statistically significant differences were noted between lesions located equal to or deeper than 1 cm and those shallower than 1 cm (shear-wave elastography, 95.2% vs 95.2%, OR = 1.000, and $p = 1.000$; strain elastography, 81% vs 76.2%, OR = 1.328, and $p = 0.709$).

Discussion

In our study, shear-wave and strain elastography showed similar overall diagnostic performance in the differentiation of benign from malignant lesions (AUC, 0.928 vs 0.943), even though discrepant findings were noted in some cases between the two techniques. When the best cutoff points (i.e., 80 kPa in shear-wave elastography and an elasticity score between 3 and 4 in strain elastography) were used, the sensitivity of shear-wave elastography was higher than that of strain elastography (95.8% vs 81.7%; $p = 0.002$), and the specific-



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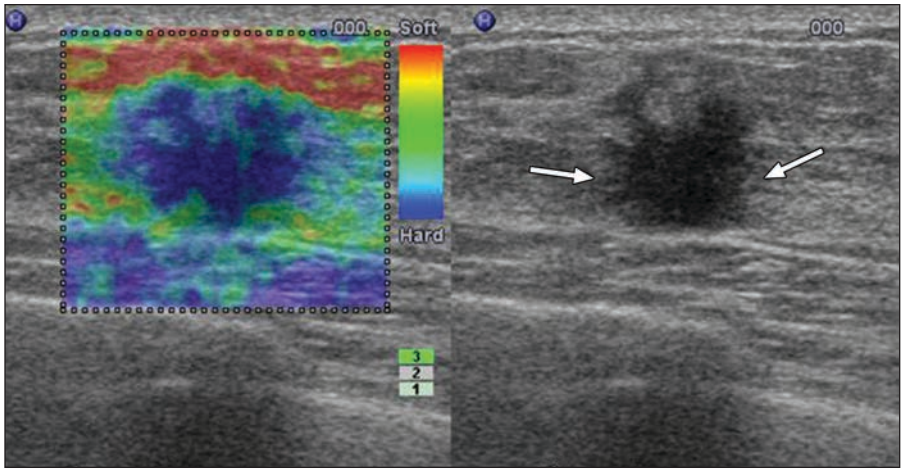

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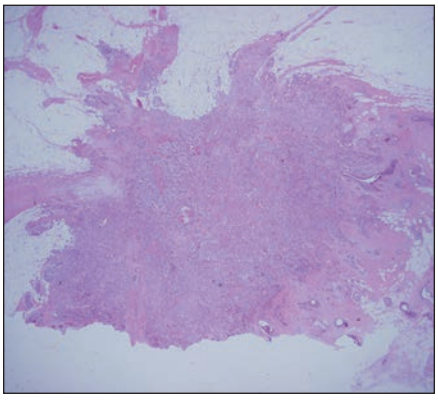


C

Fig. 3—51-year-old woman with grade 2 infiltrating ductal carcinoma.
A, B-mode ultrasound (*bottom*) reveals ill-defined hypoechoic BI-RADS category 5 lesion (*arrows*). Shear-wave elastography (*top*) depicts stiff lesion (*arrowhead*), with elasticity value of 163.9 kPa.
B, B-mode ultrasound (*right*) shows ill-defined hypoechoic lesion (*arrows*). With strain elastography (*left*), both entire hypoechoic lesion and its surrounding area were blue, with elasticity score of 5. Number bar below color bar indicates speed of compression in meters per second.
C, Photomicrograph (H and E, ×40) of surgical excision specimen shows homogeneous tumor cells in mass.

ity of strain elastography was higher than that of shear-wave elastography (93.7% vs 84.8%; $p = 0.016$). However, the combination of B-mode ultrasound and elastography regardless of the type (either shear-wave elastography or strain elastography) improved diagnostic performance in the differentiation of benign and malignant lesions compared with B-mode ultrasound alone (B-mode ultrasound alone, AUC = 0.851; B-mode ultrasound plus shear-wave elastography, AUC = 0.964; B-mode ultrasound plus strain elastography, AUC = 0.965). The best cutoff points found in this study, as well as the mean and range of elasticity values on shear-wave elastography and elasticity scores on strain elastography, were concordant with those in previous studies [1, 9, 12, 13].

In our study, most malignant lesions showed high elasticity values (> 80 kPa) and high elasticity scores (a score of 4 or 5) on both shear-wave and strain elastography, and most benign lesions showed low elasticity values and low elasticity scores. However, using our cutoff points, 13 of 87 (14.9%) cases evaluated with strain elastography were test negative but proved to be malignant, as did three of 70 (4.3%) cases with shear-wave elastography. These rates of false-negative findings are higher than the threshold of less than 2% for probably benign assessment. In a previous study [9], 28 of 289 malignancies showed maximum elasticity values less than or equal to 80 kPa, and it was recommended that elastographic features for BI-RADS category 3 or 4A lesions be used on B-mode ultrasound. Thus, using elastographic features alone without B-mode findings could misdirect patient management, and combined interpretation could improve the diagnostic performance.

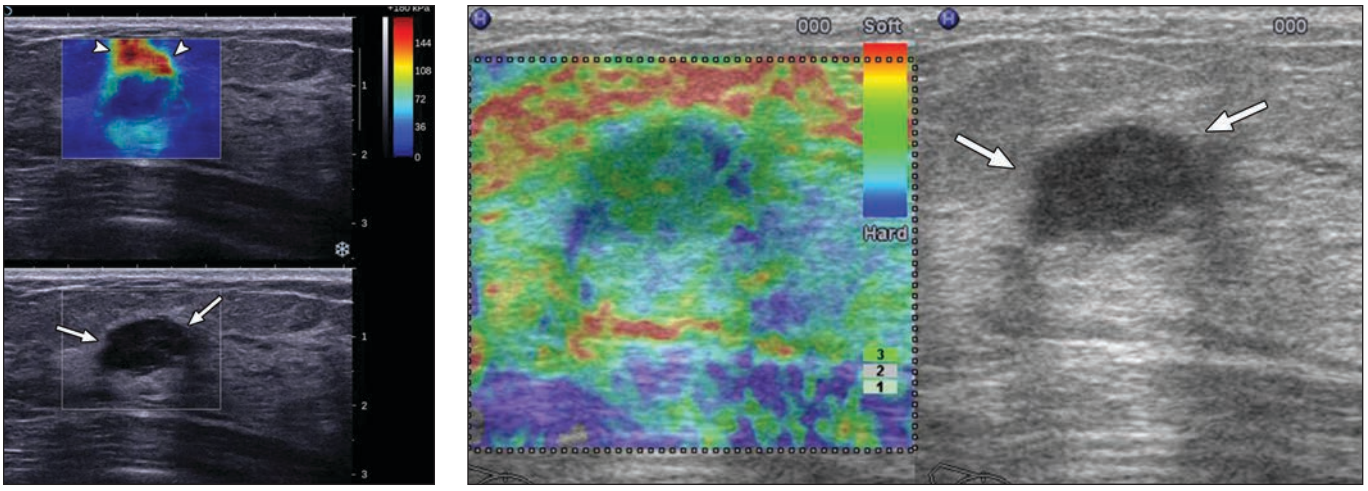
There were some malignant lesions, including grade 3 IDC and DCIS, that showed low elasticity values or elasticity scores in one of the elastography techniques and benign lesions, such as fibroadenomas or papillomas, that showed high elasticity values or elasticity scores in one of the elastography technique. Several explanations may be possible for the inconsistent results found between the two elastographic techniques, because they are quite different in terms of the forces being measured and in imaging methods. However, technical errors should be considered first, because elastographic images obtained using suboptimal techniques in one of the elastography methods can cause discrepant results between shear-wave and strain elastography. High intra- and interobserver variability associated with ultrasound probe compression has been previously emphasized as a potential shortcoming of strain elastography [16]. In contrast, shear-wave elastography is theoretically highly reproducible and less operator dependent because shear-wave elastography does not require external compression. Nonetheless, false-positive results can occur as a result of precompression of the tissue, increasing tissue stiffness values on shear-wave elastography [17, 18]. The radiologists in our study, as in previous studies, were instructed to avoid compression when obtaining shear-wave elastography images; however, artifactual vertical bands of stiffness, especially in superficially located lesions, may be difficult to avoid [9]. Misplacement of the region of interest due to slipping or movement of the ultrasound probe can occur during data acquisition and can also lead to false-negative or false-positive results on both shear-wave and strain elastography [9, 19, 20]. In addition, the user does need to subjectively or arbitrarily select one image in a complete image cine loop of the examinations, and this factor could affect the performance of strain elastography [2, 21, 22].

The most interesting finding of our study is that grade 3 IDCs showed higher mean elasticity values than did grade 1 and 2 cancers on shear-wave elastography, whereas grade 3 cancers showed significantly lower mean elasticity scores than did grade 1 and 2 cancers

TABLE 4: Breast Lesions That Showed Discrepant Results Between Shear-Wave and Strain Elastography

Case No.	Patient Age (y)	BI-RADS Category on B-Mode Ultrasound	Method of Correct Diagnosis	Elasticity Score on Strain Elastography	Elasticity Value on Shear-Wave Elastography (kPa)	Ultrasound Size (cm)	Lesion Depth (cm)	Breast Thickness (cm)	Pathologic Diagnosis
1[a]	64	4	Shear-wave elastography	3	212.1	1.5	1.1	2.1	IDC grade 3
2[a]	64	4	Shear-wave elastography	3	191.8	2.6	0.7	2.0	IDC grade 3
3	39	4	Shear-wave elastography	3	241.6	2	0.6	1.9	IDC grade 3
4	52	4	Shear-wave elastography	2	162.8	1.7	0.8	2.4	IDC grade 3
5	53	4	Shear-wave elastography	3	112.8	2	1.1	2.4	IDC grade 3
6	67	4	Shear-wave elastography	3	198.3	2.6	0.7	2.6	IDC grade 3 with DCIS
7	37	4	Shear-wave elastography	2	140.1	3.5	0.7	2.5	IDC grade 2 with DCIS
8[a]	62	5	Shear-wave elastography	3	224.9	2	0.3	2.8	IDC grade 3 with DCIS
9[a]	62	5	Shear-wave elastography	3	88.0	1.8	0.8	3.0	IDC grade 3 with DCIS
10	62	4	Shear-wave elastography	3	96.4	4	0.8	2.8	IDC grade 3 with DCIS
11	45	4	Shear-wave elastography	3	140.4	1.4	0.8	1.7	Microinvasive ductal carcinoma
12	40	4	Shear-wave elastography	3	185.5	1.6	0.5	2.2	DCIS low grade
13	57	4	Shear-wave elastography	3	81.2	2.1	1.6	2.4	DCIS low grade
14	47	4	Shear-wave elastography	4	72.3	1	1.2	2.9	Intraductal papilloma
15	48	4	Shear-wave elastography	4	67.2	0.9	0.8	2.4	Fibrocystic change
16	28	4	Shear-wave elastography	4	48.7	1.3	0.5	1.6	Fibroadenoma
17	68	4	Strain elastography	4	59.1	1.3	0.4	1.7	DCIS, low grade
18	44	4	Strain elastography	4	69.3	1.6	0.2	1.4	IDC grade 2 with DCIS
19	68	4	Strain elastography	4	47.0	2.1	1.2	1.7	DCIS, high grade
20	41	4	Strain elastography	3	94.7	2.8	0.2	1.2	Fibroadenoma
21	57	4	Strain elastography	3	131.3	1.4	0.9	2.3	Intraductal papilloma
22	40	3	Strain elastography	3	149.3	0.6	0.7	1.7	Fibrocystic change
23	32	4	Strain elastography	3	168	0.8	0.7	1.5	Adenosis
24	41	4	Strain elastography	1	116.0	0.6	0.4	1.2	Fibrocystic change
25	22	4	Strain elastography	2	192.6	1.7	0.4	1.7	Fibroadenoma
26	50	3	Strain elastography	3	149.5	2.9	0.5	1.9	Stromal fibrosis
27	33	4	Strain elastography	1	103	1.2	0.5	1.9	Fibroadenoma
28	42	4	Strain elastography	3	113.7	2.1	0.6	1.5	Fibrocystic change
29	51	4	Strain elastography	3	112.5	2.3	0.7	2.4	Fibrocystic change

Note—DCIS = ductal carcinoma in situ, IDC = infiltrating ductal carcinoma.
[a]Patient had multifocal breast cancer in the same breast.



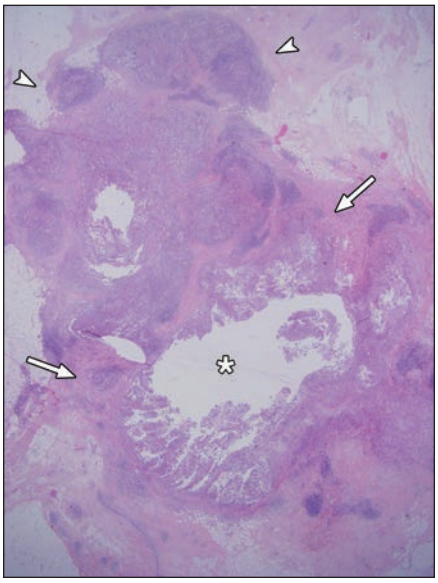


Fig. 4—52-year-old woman with grade 3 infiltrating ductal carcinoma.
A, B-mode ultrasound (*bottom*) reveals ill-defined hypoechoic BI-RADS category 4 lesion (*arrows*). Shear-wave elastography (*top*) depicts stiff area (*arrowheads*) in upper part of mass, with elasticity value of 162.8 kPa.
B, B-mode ultrasound (*right*) shows ill-defined hypoechoic lesion (*arrows*). With strain elastography (*left*), most of mass is soft, with elasticity score of 2. Breast thickness where lesion was located was 24 mm, and lesion depth from skin was 8 mm. Number bar below color bar indicates speed of compression.
C, Photomicrograph (H and E, ×40) of surgical excision specimen shows high-grade tumor cells and inflammatory cells (*arrowheads*) in upper and peripheral parts of mass, with central hypocellular area (*arrows*) and empty space caused by necrosis (*asterisk*).

on strain elastography, causing false-negative findings. In vitro biophysical studies have revealed that tumor stiffness is associated with tumor progression [23]. In a previous study of an animal model of colon cancer [24], mechanical properties of stiffness were correlated with tumor cellularity and microvessel density. The degree of fibrosis is also known to be correlated with stiffness values [25, 26]. The finding of higher mean stiffness on shear-wave elastography in high-grade cancers is important, considering that triple-negative high-grade tumors seen in *BRCA* carriers often manifest as ovoid-shaped benign-looking masses on B-mode ultrasound. We and other researchers found that invasive cancers with highly poor prognostic features have higher mean stiffness than do cancers with good prognostic features on shear-wave elastography [27]. In shear-wave elastography, however, improper color coding could occur in very hard and disorganized masses, such as invasive cancers, because the algorithm does not account for poor-quality shear waves [17]. Similarly, incident and reflected shear-waves, which propagate in the opposite direction, can cause artifacts in the estimation of shear velocity [8]. Further studies including in situ mapping of tissue stiffness and special staining for tissue fibrosis using surgical specimens are needed to confirm that quantitative elasticity values measured by shear-wave elastography reflect heterogeneous tissue stiffness in breast cancer.

In addition to tumor histologic features, breast thickness also can affect the discrepancy between two elastographic techniques. In this study, the breast where the lesion was located was significantly thicker in the lesions diagnosed correctly by shear-wave elastography only, compared with the lesions diagnosed correctly by strain elastography only. Even though adjustment with propensity score matching diminished the effect of breast thickness on the accuracy of both techniques, these findings are concordant with those of previous studies performed with the strain elastography technique. The diagnostic quality of strain elastography images has been shown to decrease substantially with increasing breast thickness [7, 28]. However, shear-wave propagation is also depth limited, and it is known that proper shear-wave velocity cannot be measured in lesions located deeper than 4 cm [17]. Because there was no lesion that was located deeper than 4 cm in our study, our results consistently showed no deterioration in accuracy of shear-wave elastography due to larger breast thickness and lesion depth. Complicated combinations of histopathologic features, including tumor grade, tumor size, location, and the breast thickness where the tumor is located, could possibly induce different findings in each elastographic techniques.

This study has several limitations. First, although there are many types of commercially available elastography techniques, each with their own vendor-specific elasticity algorithms, only one shear-wave elastography technique and one strain elastography technique were compared in this study. Second, our study included a cohort of women with a low prevalence of large breasts, which is the major technical limitation reported for strain elastography. Third, three breast radiologists assessed the elasticity images; however, inter- and intraobserver variability were not assessed in our study. In previous studies, significant observer variability was observed in reader studies using strain elastography images for the application of diagnostic scores of breast masses [2, 4]. Fourth, for differentiation of benign and malignant lesions, we used only one elastographic feature for each technique: mean elasticity value (measured in

kilopascals) for shear-wave elastography and elasticity score for strain elastography. A variety of features (e.g., shape, diameter, or area ratio relative to B-mode imaging; lesion-to-fat ratio; shape; and homogeneity) can be measured with both shear-wave and strain elastography [2, 9, 29]. In particular, in cases of discrepant findings, assessment of elasticity using other elastographic features could yield different results. Fifth, only one representative image was used in this study. It may be difficult to capture all the information on tumor stiffness with one elastographic image. Orthogonal plane images or 3D elastography may be useful to evaluate tumor heterogeneity. In addition, two orthogonal or 3D images of a breast mass may be more appropriate to reduce technical error by radiologists or inter- and intraobserver variability [30].

In conclusion, shear-wave and strain elastography showed similar overall diagnostic performance in the differentiation of benign from malignant lesions, and both elastography techniques when combined with B-mode ultrasound can improve diagnostic performance in differentiating benign from malignant lesions at breast ultrasound. However, the sensitivity and specificity of shear-wave and strain elastography were different according to lesion histologic profile, tumor grade, and breast thickness. This information can be used to optimize the use of elastography in clinical practice, and further studies are warranted to confirm these findings.

Acknowledgment

The shear-wave elastography data of our subjects have been used and published previously [12].

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