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FULL PAPER

Shear wave elastography for the diagnosis of small (≤ 2 cm) breast lesions: added value and factors associated with false results

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Objective: We compared the diagnostic performance of B-mode ultrasound, shear wave elastography (SWE), and combined B-mode ultrasound and SWE in small breast lesions (≤ 2 cm), and evaluated the factors associated with false SWE results.

Methods: A total of 428 small breast lesions (≤ 2 cm) of 415 consecutive patients between August 2013 and February 2017 were included. The diagnostic performance of each set was evaluated using the area under the receiver operating characteristic curve (AUC) analysis. Histologic diagnosis was used as reference standard. Multivariate logistic regression analyses identified the factors associated with false SWE results.

Results: Of 428 lesions, 142 (33.2%) were malignant and 286 (66.8%) were benign. The AUC of the combined modality was higher than that of B-mode ultrasound

(0.792 vs 0.572, $p < 0.001$) and that of SWE was higher than that of B-mode ultrasound (0.718 vs 0.572, $p < 0.001$). Multivariate analysis showed that the smaller lesion size and *in situ* cancer were associated with false negative, and patient's age, high-risk lesion, shorter distance from the skin or chest wall, and deeper breast thickness were associated with false positive (all $p < 0.05$).

Conclusions: The addition of SWE to B-mode ultrasound could improve the diagnostic performance in ≤ 2 cm lesions. However, ultrasound lesion size, pathology, and lesion location are likely to affect the SWE value and result in false results.

Advances in knowledge: Despite the diagnostic usefulness of SWE in small breast lesions (≤ 2 cm), ultrasound lesion size, pathology, and lesion location were associated with false results.

INTRODUCTION

The objective of breast screening is to detect occult small cancers at a stage that is early enough by which treatment will significantly reduce the risk of death.¹ Although mammography remains the gold standard in breast screening, high mammographic density may make it difficult to detect breast cancer.² Ultrasound is an invaluable tool in the detection of breast lesions, particularly in women with dense breasts.³ Most Asian females have relatively dense breast and small breast lesions are detected with increased frequency with the wide use of ultrasound screening.^{4,5} However, it is more difficult to characterize small lesions according to the Breast Imaging Reporting and Data System for Ultrasound (BI-RADS) than it is larger lesions.⁶

Ultrasound elastography is an imaging technique that evaluates tissue stiffness, and can be used in the evaluation and characterization of breast masses. The two most commonly

used elastography techniques are strain and shear-wave elastography.⁷ Prior studies suggest that strain elastography has a higher diagnostic performance than does conventional ultrasound for the characterization of small breast lesions.^{5,8,9} The strain elastography technique measures the relative strain between a lesion and the surrounding tissue by displacement of the tissue using manual compression. In contrast, shear wave elastography (SWE) quantitatively measures a lesion's stiffness; it is less operator-dependent, and has been shown to be highly reproducible.^{6,7} Several studies have found that SWE has improved the diagnostic performance of evaluating breast masses through its qualitative and quantitative parameters, including the color overlay pattern, maximum stiffness, mean stiffness, ratio of stiffness, and standard deviation.^{10–13} However, few studies have evaluated the diagnostic efficacy of the combination of SWE and conventional ultrasound for small breast lesions. Chang et al reported significant differences between the

SWE values of benign and malignant lesions when subcategorized by the lesion size.¹⁰ In contrast, Kim et al reported poorer diagnostic performance of SWE compared to conventional ultrasound in small breast lesions; however, there was no statistically significant difference in the SWE value in sub-centimeter lesions.¹⁴ In addition, although SWE provides objective and quantitative data regarding the intrinsic features of the target mass, prior studies found that SWE produced false positive and false negative findings that did not fit with the histopathological diagnosis. Clinical factors such as the lesion size, breast thickness, and lesion depth have been associated with false SWE results for breast masses.^{15,16}

Therefore, in this study, we evaluated and compared the diagnostic performances of B-mode ultrasound, SWE, and the combination of B-mode ultrasound and SWE in patients with small breast lesions (≤ 2 cm). We also aimed to evaluate the factors associated with false negative and false positive results.

METHODS AND MATERIALS

Patients

This retrospective study was approved by the Institutional Review Board of our institution, and informed consent was waived. Signed informed consent for biopsy or surgery was obtained from all patients before procedures. From August 2013 to February 2017, consecutive 451 patients with 473 breast lesions (that were ≤ 2 cm) underwent B-mode ultrasound with SWE before ultrasound-guided core needle biopsy or surgical excision. We excluded lesions that were adjacent to the previous surgical site ($n = 22$), lesions already diagnosed as breast cancer in another hospital ($n = 9$), lesions from patients who underwent mastoplasmy ($n = 1$), lesions in the axilla ($n = 8$), lesions that were lost to follow up ($n = 3$), and lesions that presented with calcifications without mass on ultrasound ($n = 2$). Finally, 428 breast lesions from 415 patients (mean age 49.5 ± 11.8 years, range 19–85) were included in this study. One patient had three breast lesions, and 11 females had two breast lesions. 99 (23.8%) of the patients were symptomatic on presentation. Symptoms included a palpable breast mass (79.8%, 79 of 99), breast pain (8.1%, 8 of 99) or nipple discharge (12.1%, 12 of 99). 396 patients underwent mammograms that were performed simultaneously with breast ultrasound. Of these, 116 patients (29.3%) had abnormal findings. The histopathologic findings were regarded as the reference standards in this study. Of the 428 breast lesions, 276 were confirmed via US-guided core needle biopsy, and 152 were confirmed via surgery.

B-mode ultrasound and SWE examination

Conventional B-mode ultrasound and SWE examinations were performed by one of two radiologists (Y.M.S. and M.S.), who were board-certified in breast imaging with 10 and 6 years of experience, respectively. B-mode ultrasound and SWE images were obtained using an Aixplorer system (SuperSonic Imagine, Aix en Provence, France) equipped with a 15–4 MHz linear array transducer. Bilateral whole breast B-mode ultrasound was performed first, with at least two orthogonal images of each lesion. The radiologists recorded the final assessment category according

to the American College of Radiology (ACR) BI-RADS before SWE.

After B-mode ultrasound, SWE was subsequently performed by the same radiologist. The transducer was applied without added pressure during the SWE examination. The qualitative and quantitative tissue elasticity values were measured with 2-mm- or 3-mm-diameter circular regions-of-interest (ROIs) (Q-box; SuperSonic Imagine). One was placed on the stiffest portion of the lesion, and the other on the surrounding normal fat tissue. The system automatically calculated the maximum elasticity (E_{max}), mean elasticity (E_{mean}), and minimum elasticity (E_{min}) values in kilopascals (kPa) for the mass. A qualitative SWE value was displayed using a color-coded map with the spectrum of colors ranging from 0 (blue; softer tissue) to 180 kPa (red; harder tissue).

Image analysis

All B-mode ultrasound and SWE images were reviewed in the Picture Archiving and Communication System (PACS) by two radiologists (M.S. and H.Y.C.) who were blinded to patient information. On the basis of the B-mode ultrasound image, the lesions were assessed and categorized according to the ACR BI-RADS. We also measured the lesion size (maximum diameter), distance from the skin, distance from the chest wall, breast thickness (distance from skin to pectoralis muscle), and distance from the nipple. Considering multiple quantitative SWE lesion features, E_{max} was selected because we used 2-mm- or 3-mm-diameter ROIs when measuring the elasticity value. In addition, the E_{max} has a higher sensitivity in detecting the focal stiff portion in heterogeneous breast masses.¹⁷ The effect of ROI size on the values of E_{max} is very limited.¹⁸

For 396 patients with 408 lesions who underwent mammography at the time of ultrasound examination, one radiologist retrospectively reviewed the mammographic breast density according to BI-RADS. Breast composition A (almost entirely fatty) and B (scattered areas of fibroglandular density) were categorized as 'fatty', while breast composition C (heterogeneously dense) and D (extremely dense) were categorized as 'dense'.

Histopathologic evaluation

We reviewed the histopathologic reports for malignant lesions ($n = 142$). Of the 142 malignant lesions, 74 were confirmed via breast-conserving surgery, 34 via total mastectomy, and 34 via ultrasound-guided core needle biopsy. In contrast, the 286 benign lesions included 43 high-risk lesions (26 intraductal papillomas, nine sclerosing adenosis lesions, six phyllodes tumors, one mucocoele-like lesion, and one radial scar), and 44 benign lesions that were surgically confirmed after ultrasound-guided core needle biopsy. The remaining 242 lesions with benign biopsy results were not surgically excised, but were followed using ultrasound. Lesion stability was confirmed for a duration of 12–66 months.

Data and statistical analysis

The histopathologic reports were regarded as the reference standard. The BI-RADS category on B-mode ultrasound,

pathology, and mammographic density of benign and malignant lesions were compared using the chi-squared test or Fisher's exact test as appropriate. The Kolmogorov–Smirnov test was used to check the normal distribution of all continuous data, including: patient age, ultrasound lesion size, Emax, distance from the skin, distance from the chest wall, breast thickness, and distance from the nipple. Because these data were not normally distributed, the Mann–Whitney U test was used to compare the continuous variables between benign and malignant groups.

To evaluate the diagnostic performances of B-mode ultrasound, SWE, and the combined set for distinguishing malignant from benign lesions, the area under the receiver operating characteristic curve (AUC) was obtained and compared among data sets. Using B-mode ultrasound, BI-RADS category 4a and higher was considered a positive result for a malignant lesion. In contrast, category 3 (and below) was considered a negative result.^{16,19} With the combined set of B-mode ultrasound with SWE, the AUC was obtained after reevaluating category 4a lesions for downgrading to category 3, and of category three lesions for upgrading to category 4a lesions (according to the cut-off for Emax from receiver operating characteristic (ROC) curves). The cut-off value was defined using Youden's index (Sensitivity + Specificity - 1). The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy using the cut-offs were calculated and compared using the McNemar test.

The optimal cut-off value of 85.3 kPa for Emax was calculated based on the ROC curve. We compared the SWE features with the final histopathological results. The 'true' and 'false' results were categorized as follows. For pathologically proven malignant lesions, the Emax >85.3 kPa was classified as 'true positive', while an Emax <85.3 kPa was classified as 'false negative.' For pathologically proven benign lesions, an Emax >85.3 kPa was classified as 'false positive,' while an Emax <85.3 kPa was classified as 'true negative.' The following parameters were compared between the true and false groups using the chi-squared test, Fisher's exact test, or the Mann–Whitney U test: patient age, ultrasound lesion size, pathology result, distance from the skin, distance from the chest wall, breast thickness, distance from the nipple, and mammographic density. Univariate and multivariate logistic regression analyses with odds ratio (OR) estimates and 95% confidence intervals (CI) were calculated to identify factors associated with false negative (malignant) and false positive results (benign). All factors in the univariate logistic regression analysis were adjusted in the multivariate logistic regression models. These factors included: patient age, ultrasound lesion size, pathology result, distance from the skin, distance from the chest wall, breast thickness, distance from the nipple, and mammographic density.

Statistical analyses were performed using SPSS® statistical software (SPSS Inc., Chicago, IL, ver. 22.0). *p* values < 0.05 were considered statistically significant.

RESULTS

Breast lesions

Of the 428 breast lesions, 142 (33.2%) were malignant and 286 (66.8%) were benign. The clinical, imaging, and pathology features of the 428 breast lesions are summarized in Table 1. The age of patients with malignant lesions was significantly higher than that of those with benign lesions (54 vs 46, *p* < 0.001). The malignant lesions were also statistically larger than were the benign masses (11 vs 9, *p* < 0.001). The BI-RADS categories using B-mode ultrasound were higher in malignant lesions than they were in benign lesions (*p* < 0.001). The Emax values on SWE were significantly higher were those in malignant lesions (141.8 vs 52.6, *p* < 0.001). The breast thickness and distance from the nipple were also significantly different between the benign and malignant groups (*p* < 0.050). A total of 396 patients with 408 lesions underwent mammography at the time of the ultrasound examination. The mammographic density differed between the two groups (*p* < 0.001).

Diagnostic performance of B-mode ultrasound and SWE

The AUC values for each modality are shown in Figure 1. The Emax value with a cut-off of 85.3 kPa had the highest AUC. The AUC of combined B-mode ultrasound with SWE was higher than that of B-mode ultrasound (0.792 vs 0.572, *p* < 0.001), and the AUC of SWE was higher than that of B-mode ultrasound (0.718 vs 0.572, *p* < 0.001). On B-mode ultrasound, the 428 lesions were categorized as follows: category 2 (*n* = 2), category 3 (*n* = 51), category 4a (*n* = 262), category 4b (*n* = 34), category 4c (*n* = 32), and category 5 (*n* = 47). The malignancy rates for each BI-RADS categories on B-mode ultrasound are as follows; 0.0% (0/2) for category 2, 7.8% (4/51) for category 3, 16.0% (42/262) for category 4a, 61.8% (21/34) for category 4b, 93.7% (30/32) for category 4c, and 95.7% (45/47) for category 5. Among the 51 category 3 lesions, 11 lesions (10 benign, one malignancy) with Emax over 85.3 kPa were upgraded to Category 4a on combined modality. Regarding 262 Category 4a lesions, 173 lesions (160 benign, 13 malignancy) with Emax less than 85.3 kPa were downgraded to Category 3 on combined modality. The malignancy rate for Category 3 and Category 4a in the revised BI-RADS categories on combined modality were 7.5% (16/213) and 30.0% (30/100), respectively.

In Table 2, the sensitivity was higher for B-mode ultrasound than for SWE or combined modality (B-mode ultrasound: 97.2% vs SWE: 71.1; *p* < 0.001, combined modality: 88.7; *p* = 0.005). However, the specificity was much higher for SWE or combined modality than for B-mode ultrasound (B-mode ultrasound: 17.1% vs SWE: 72.4; *p* < 0.001, combined modality: 69.6; *p* < 0.001). The accuracy and PPV increased in the combined modality compared to B-mode ultrasound (*p* < 0.001), as well as in SWE compared to B-mode ultrasound (*p* < 0.001).

False negative results of SWE

The characteristics of the false negative results for malignant lesions are summarized in Table 3. When applying 85.3 kPa of Emax as a cut-off value, 28.9% (41/142) were classified as false negatives, and 71.1% (101/142) were classified as true positives.

Table 1. Characteristics of 428 lesions

	Benign (<i>n</i> = 286)	Malignant (<i>n</i> = 142)	P
Age (year)	46 (41–52)	54 (46–63)	<0.001
B-mode ultrasound			
Lesion size (mm)	9 (7–13)	11 (8–16)	<0.001
BI-RADS category			<0.001
3 or 2	49 (17.2)	4 (2.8)	
4a	220 (76.9)	42 (29.6)	
4b	13 (4.5)	21 (14.8)	
4c	2 (0.7)	30 (21.1)	
5	2 (0.7)	45 (31.7)	
SWE			
Maximum elasticity (Emax, kPa)	52.6 (32.7–98.2)	141.8 (74.7–189.2)	<0.001
Pathology			N/A
Non-high-risk lesions	238 (83.2)		
High-risk lesions	48 (16.8)		
Cancer <i>in situ</i>		24 (16.9)	
Invasive cancer		118 (83.1)	
Distance from the skin (mm)	7 (5–9)	7 (4–10)	0.796
Distance from the chest wall (mm)	4 (2–6)	3 (2–6)	0.301
Breast thickness (mm)	18 (15–21)	19 (15–23)	0.023
Distance from the nipple (cm)	2 (1–4)	4 (2–5)	<0.001
Mammographic density			<0.001
Fatty	25 (9.4)	49 (34.8)	
Dense	242 (90.6)	92 (65.2)	

Continuous data are presented as median (interquartile range). Categorical data are presented as the number of lesions (percentage).

^aMammography was available for 408 lesions in 396 patients

Malignant breast lesions with false negative results had a smaller ultrasound lesion size, a lower proportion of invasive cancer and were farther from the skin than those with true positive results ($p < 0.001$, 0.005, and 0.008, respectively) (Figure 2). Multivariate analysis (Table 4) showed that the ultrasound lesion size (OR = 0.88, $p = 0.040$) and cancer *in situ* (OR = 3.17, $p = 0.029$) were important factors influencing the false negative results obtained by SWE.

False positive results of SWE

The characteristics of the false positive results for benign lesions are summarized in Table 3. When applying 85.3 kPa of Emax as a cut-off value, 27.6% (79/286) were classified as false positives, while 72.4% (207/286) were classified as true negatives. Benign breast lesions with false positive results had a higher proportion of high-risk lesions and were a shorter distance from the chest wall than were those with true negative results ($p = 0.022$ and 0.002, respectively) (Figure 3). Multivariate analysis (Table 4) found that the following were important factors that influenced the false positive results of SWE in benign breast lesions: patient age, non-high-risk lesion, distance from the skin, distance from

the chest wall, and breast thickness. Their ORs were 1.04 ($p = 0.043$), 0.34 ($p = 0.004$), 0.75 ($p = 0.001$), 0.72 ($p < 0.001$), and 1.17 ($p = 0.014$), respectively.

DISCUSSION

As expected, the Emax was significantly higher in malignant lesions than it was in benign lesions (141.8 kPa vs 52.6 kPa, $p < 0.001$), and these results are consistent with those of Kim et al. (average Emax of 123.3 kPa for malignancy and 45.6 kPa for benign).¹⁴ Unlike the previous study, after combining SWE with conventional B-mode ultrasound, using a cut-off value of 85.3 kPa on SWE, the AUC value significantly increased from 0.572 to 0.792 ($p < 0.001$). The accuracy also increased significantly (43.7 vs 75.9, $p < 0.001$). The specificity increased, while the sensitivity decreased significantly; these results were consistent with those of a previous study.¹⁴ Our results suggests that the additional use of SWE can reduce unnecessary biopsy differentiation of small breast lesions, and 160 (61.1%) benign lesions of 262 category 4a lesions were downgraded in this study. However, 13 BI-RADS category 4a malignant masses would also be downgraded and potentially missed by the SWE application. Similar findings were

Figure 1. Receiver operating characteristic curves for B-mode ultrasound, shear wave elastography (SWE), and combined B-mode ultrasound with SWE.

reported in the study of Kim et al.¹⁴ who proposed the application of conservative strategies for downgrading soft category 4a lesions for small (≤ 2 cm) breast cancers.

When applying 85.3 kPa of Emax as a cut-off value in this study, the false negative rate was 28.9% (41/142) and the false positive rate was 27.6% (79/286). Kim et al.¹⁴ used the Emax value with a cut-off of 87.5 kPa, which was slightly higher than our result, for 177 small (≤ 2 cm) breast lesions. This cutoff value may result in a slightly higher false negative rate and lower false positive rate compared to those in our study (31.7%, 12.9%, respectively). Yoon et al applied an Emax of 82.3 kPa as the cut-off value, and found a false negative rate of 12.8% (6/47) and false positive rate of 20.6% (36/175).¹⁶ In that study, breast lesions less than 2 cm in size accounted for approximately 80% of inclusion; therefore, we think that this results is comparable to ours. In our study, unlike the previous studies, the ROI size was not unified. Therefore, we only analyzed the Emax that was less affected by the

ROI size among the SWE values. This limitation is significant, but our findings are similar to those of previous studies. In the BE1 multinational study, the best performing quantitative SWE feature was the Emax of the lesions.¹² However, the false positives and negatives are affected by the cut-off value. Therefore, further studies are needed to establish a standard cut-off value.

In our study, 41 lesions (28.9%) were false negative and 101 lesions (71.1%) were true positive when 85.3 kPa of Emax was used as the cut-off value. In multivariate analysis, smaller ultrasound lesion size and cancer *in situ* were significantly associated with false negative results for malignant lesions. This finding was consistent those of previous studies.^{10,14,16,20} Yoon et al¹⁶ reported that malignant breast masses with false negative Emax were significantly smaller than were true positive lesions. Vinnicombe et al²¹ reported that pathologic lesion size was the most significant factor in obtaining a false negative result.²² In their study, only 2 of 18 false negative lesions were larger than 2 cm, and most were < 1 cm. The authors emphasized that importance should be given to the B-mode ultrasound findings without reliance on benign quantitative SWE findings in small screen-detected cancer. In our study, the specificity increased from 17.1% to 34.6% without decreasing the sensitivity when SWE was not applied to lesions < 1 cm. In addition, 15 of 16 missed cancers on combined modality were < 1 cm on breast ultrasound. Our results suggest that more research is needed to develop specific guidelines for the combination of the BI-RADS score and SWE values for small breast lesions.

In this study, 79 lesions (27.6%) were false positives and 207 lesions (72.4%) were true negatives when 85.3 kPa of Emax was used as the cut-off value. According to our multivariate analysis, high-risk lesions, a shorter distance from the skin or chest wall, and deep breast thickness were all significantly associated with false positive results of benign lesions. Previous studies have shown that intraductal papilloma and sclerosing adenosis, which accounted for most of the high-risk lesions in our study, tend to have high SWE values.^{10,14} In our study, the closer the lesion was to the skin or chest wall, the greater was the tendency for the SWE value to be a false positive. This result may be due to a rise in the SWE value due to precompression applied to the lesion. Breast elastography is very susceptible to precompression, because the chest wall or ultrasound probe is a hard surface that

Table 2. Diagnostic performances of B-mode ultrasound, shear wave elastography (SWE), and combined B-mode ultrasound with SWE

	B-mode	SWE	Combined	Pa	Pb	Pc
Sensitivity (%)	97.2	71.1	88.7	< 0.001	0.005	< 0.001
Specificity (%)	17.1	72.4	69.6	< 0.001	< 0.001	0.461
PPV (%)	36.8	56.1	59.2	< 0.001	< 0.001	0.543
NPV (%)	92.5	83.5	92.6	0.096	0.979	0.003
Accuracy (%)	43.7	72.0	75.9	< 0.001	< 0.001	0.186

NPV, negative predictive value; PPV, positive predictive value.

^aB-mode vs SWE

^bB-mode vs Combined

^cSWE vs Combined

Table 3. Comparisons between patient and lesion characteristics and combined B-mode ultrasound with shear wave elastography (SWE)

Malignant (n = 142)	True positive (n = 101)	False negative (n = 41)	P
Age (year)	53 (46–63)	58 (49–64.5)	0.264
Ultrasound lesion size (mm)	13 (9–17)	9 (7–12)	<0.001
Pathology			0.005
Cancer <i>in situ</i>	11 (10.9)	13 (31.7)	
Invasive cancer	90 (89.1)	28 (68.3)	
Distance from the skin (mm)	6 (3.5–9)	9 (5.5–11.5)	0.008
Distance from the chest wall (mm)	3 (1–5.5)	4 (2–6)	0.051
Breast thickness (mm)	19 (15–22.5)	19 (16–23)	0.445
Distance from the nipple (cm)	4 (2–5)	4 (2–4.5)	0.378
Mammographic density ^a			1.000
Fatty	35 (35)	14 (34.1)	
Dense	65 (65)	27 (65.9)	
Benign (n = 286)	True negative (n = 207)	False positive (n = 79)	
Age (year)	46 (41–52)	46 (42–52)	0.719
Ultrasound lesion size (mm)	9 (7–12)	10 (8–13)	0.062
Pathology			0.022
Non-high-risk lesion	179 (86.5)	59 (74.7)	
High-risk lesion	28 (13.5)	20 (25.3)	
Distance from the skin (mm)	7 (5–9)	6 (5–8)	0.058
Distance from the chest wall (mm)	4 (2–7)	3 (1–5)	0.002
Breast thickness (mm)	18 (15–21)	18 (15–21)	0.410
Distance from the nipple (cm)	2 (1–4)	2 (1–3)	0.116
Mammographic density ^b			0.634
Fatty	20 (10.2)	5 (7.0)	
Dense	176 (89.8)	66 (93.0)	

Continuous data are presented as median (interquartile range). Categorical data are presented as the number of lesions (percentage).

^aMammography was available for 141 lesions in 138 patients

^bMammography was available for 267 lesions in 259 patients

allows for substantial precompression.²⁰ During the SWE examination, compression of the probe should be minimized to obtain adequate image quality. Yoon et al reported that the larger breast thickness at the location of the target mass can have false SWE features, because the parenchymal tissue is known to attenuate the elasticity wave.¹⁶ We suggest that careful examination is needed, especially if the lesion is very close to the skin or chest wall, or if it is located in thick breast tissue. The lesion size was not significantly associated with the false positive results in our study. This result is unlike that of a previous study, which found that the lesion size was significantly associated with false SWE features among both benign and malignant masses.¹⁶ This result seems to be related to the small lesion size and narrow interquartile range of benign lesions compared with malignant lesions.

This study has several limitations. First, we did not evaluate the interobserver or intraobserver variability. Several previous studies have reported that the reproducibility of SWE was high^{6,23}. However, because the performance of the SWE may be influenced by the lesion's size or location, this limitation must be assessed in larger studies. A second limitation is that we used the E_{max} as the cut-off value for SWE in our study. In contrast, previous studies used various cut-off values, including other quantitative SWE features, such as E_{mean}, standard deviation, and elasticity ratio. However, there was no consensus for a standard cut-off value. In addition, a qualitative pattern color overlay map may also provide important information about the lesion. A larger study is required to establish a standard cut-off value. A third limitation is that although the diagnostic performance

Figure 2. A 58-year-old female with invasive ductal carcinoma at core needle biopsy (a) B-mode ultrasound showed a 7 mm hypo-echoic mass at the upper outer quadrant of the right breast, about 4 mm distant from the nipple. The final BI-RADS was category 4a. The distance of the cancer from the skin was 9 mm, from the chest wall it was 2 mm, and the breast thickness where the mass was located was 16 mm. (b) On the shear wave elastography (SWE) examination, the Emax was 35.0 kPa.

of combined B-mode ultrasound and SWE was evaluated, these results are limited to our study. The specific guideline for the combination of the BI-RADS score and SWE values was not provided. More studies are needed to address how best to combine the B-mode ultrasound and SWE for small breast lesions to enhance the benign and malignant differentiation. Another limitation is that the SWE was performed after B-mode ultrasound by the same radiologist. This set up may have influenced our results. A fifth limitation is that the 242 breast lesions

were confirmed via ultrasound-guided core needle biopsy. The false negative rate of the core needle biopsy is reported to be up to 12%, and could have affected our results²⁴. Our study may also have been subject to selection bias. In our hospital, breast ultrasound is performed when there is an abnormality on mammography, or when there is a specific patient- or clinician-request. Therefore, it is possible that the small cancers found on mammography of the fatty breast were more frequently included than they might be otherwise (Table 1).

Table 4. Univariate and multivariate analyses of variables and false results of the combined modality

	Univariate model		Multivariate model ^a	
False negative	OR (95% CI)	P	OR (95% CI)	P
Age (year)	1.01 (0.98,1.05)	0.384	1.02 (0.98,1.07)	0.356
Ultrasound lesion size (mm)	0.84 (0.77,0.93)	<0.001	0.88 (0.78,0.99)	0.040
Cancer <i>in situ</i> (vs invasive cancer)	3.80 (1.53,9.42)	0.004	3.17 (1.12,8.93)	0.029
Distance from the skin (mm)	1.11 (1.02,1.22)	0.021	1.13 (0.94,1.36)	0.191
Distance from the chest wall (mm)	1.09 (0.97,1.21)	0.149	1.14 (0.92,1.41)	0.237
Breast thickness (mm)	1.01 (0.95,1.07)	0.802	0.95 (0.81,1.11)	0.497
Distance from the nipple (cm)	0.93 (0.73,1.02)	0.377	0.96 (0.78,1.17)	0.649
Non-dense breast (vs dense breast)	0.96 (0.45,2.07)	0.923	0.71 (0.25,1.99)	0.512
False positive	OR (95% CI)	P	OR (95% CI)	P
Age (year)	1.00 (0.98,1.02)	0.999	1.04 (1.00,1.07)	0.043
Ultrasound lesion size (mm)	1.06 (0.99,1.13)	0.097	1.01 (0.93,1.10)	0.814
Non-high-risk lesion (vs high-risk lesion)	0.46 (0.24,0.88)	0.019	0.34 (0.16,0.70)	0.004
Distance from the skin (mm)	0.92 (0.78,1.10)	0.072	0.75 (0.63,0.88)	0.001
Distance from the chest wall (mm)	0.87 (0.80,0.95)	0.002	0.72 (0.62,0.84)	<0.001
Breast thickness (mm)	0.97 (0.92,1.03)	0.365	1.17 (1.03,1.32)	0.014
Distance from the nipple (cm)	0.87 (0.73,1.02)	0.090	0.84 (0.69,1.02)	0.077
Non-dense breast (vs dense breast)	0.67 (0.24,1.85)	0.436	0.55 (0.16,1.87)	0.340

CI, confidence interval.

^aAll effect estimates were adjusted for the other variable listed in the table

Figure 3. A 52-year-old female with intraductal papilloma at surgical excision (a) B-mode ultrasound showed a 10 mm hypoechoic mass at the upper outer quadrant of the left breast, approximately 3 mm from the nipple. The final BI-RADS was category 3. The distance of the mass from the skin was 10 mm, from the chest wall it was 2 mm, and the breast thickness where the mass was located was 18 mm. (b) On the shear wave elastography (SWE) examination, the Emax was 87.7 kPa.

In conclusion, adding SWE increased the diagnostic performance of B-mode ultrasound alone for small (≤ 2 cm) breast lesions. However, the ultrasound lesion size, pathology, and lesion location are likely to affect the SWE value and result in false results. Especially in small cancers, SWE may produce a false negative. If the lesion is located near the skin, the chest wall, or in thick breast tissue, there may be a false positive.

It is expected that the value of adding SWE will be higher when the SWE result is selectively combined with B-mode ultrasound on small breast lesions, avoiding the case where the SWE result is likely to be false. Further prospective study is needed to develop specific guideline for the combination of BI-RADS score and SWE values for small breast lesions.

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