

Diagnostic values of shear wave elastography and strain elastography for breast lesions

HUIWEN JIANG¹, XIAODAN YU², LINA ZHANG³,
LINXIAO SONG⁴, XIUHUA GAO⁵

ABSTRACT

Background: Strain elastography (SE) and shear wave elastography (SWE) have high diagnostic yield for breast lesions, but the optimal parameters remain elusive. **Aim:** To evaluate the diagnostic yield of SWE and SE for breast lesions by multivariate logistic regression analysis. **Material and Methods:** A total of 132 patients with 164 breast tumors were enrolled. Breast lesions were classified with the breast imaging reporting and data system (BI-RADS). Maximum (E_{max}), mean (E_{mean}) and standard deviation (E_{sd}) of elastic modulus, lesion/fat elasticity ratio and elastographic classification were obtained by SWE. Strain ratio (SR) and elastographic score were obtained by SE. A multivariate logistic regression analysis was performed. The diagnostic efficiencies of BI-RADS classification, SWE, SE and their combination were compared plotting ROC curves. **Results:** There were 110 benign and 54 malignant lesions which had significantly different SWE and SE parameters. The parameters included in the logistic regression were E_{sd} and elastographic classification obtained by SWE and the elastographic score obtained by SE. When combining SWE with SE, E_{sd}, SR and SWE classification were included in the equation. The areas under ROC curves for BI-RADS classification, SWE, SE and their combination were 0.75, 0.88, 0.79 and 0.89, respectively. **Conclusions:** The diagnostic value of SWE in combination with SE for breast lesions exceeded that of SE or SWE alone. E_{sd} showed a good diagnostic yield when SWE was used alone or combined with SE. (Rev Med Chile 2020; 148: 1239-1245)

Key words: Breast Diseases; Diagnosis; Elasticity Imaging Techniques.

Elastografía de deformación y de onda cortante para el diagnóstico de lesiones mamarias

Antecedentes: La elastografía de deformación (SE) y de onda cortante (SWE) son útiles para el diagnóstico de lesiones mamarias, pero falta definir los parámetros óptimos. **Objetivo:** Evaluar el valor diagnóstico de SE y SWE en lesiones mamarias usando una regresión logística multivariable. **Material y Métodos:** Ciento treinta y dos pacientes con 164 tumores mamarios fueron evaluados, los que se clasificaron usando el sistema BI-RADS (breast imaging reporting and data system). El módulo elástico máximo, promedio y su desviación estándar (E_{sd}), la razón entre la elasticidad de la lesión y de la grasa y la clasificación elastográfica se obtuvieron con SWE. La razón de deformación (SR) y el puntaje elastográfico se obtuvieron con SE. Se efectuó una regresión

¹Department of Ultrasonography, Weihai Central Hospital. Weihai, China.

²Blood Purification Center, Weihai Central Hospital. Weihai, China.

³Penglai People's Hospital, Penglai 265612. Shandong Province, China.

⁴Zhifu District Maternal and Child Health Family Planning Service Center. Yantai, China.

⁵Department of Breast Surgery, Weihai Central Hospital. Weihai, China.

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Correspondence to:
Xiuhua Gao

Department of Breast Surgery, Weihai Central Hospital, Weihai 264400. Shandong Province, China.

byronmccormickoup@yahoo.com

logística y las eficiencias diagnósticas de la clasificación BI-RADS, SWE and SE y su combinación se compararon usando curvas ROC (receiver operating characteristic curves). **Resultados:** Ciento diez lesiones fueron benignas y 54 malignas. Estas tenían parámetros SWE y SE significativamente diferentes. En la ecuación de regresión logística, se incluyeron la clasificación elastográfica y el Esd obtenidos por SWE y el puntaje elastográfico obtenido por SE. Cuando se combinó SWE y SE, se incluyeron en la ecuación el Esd, SR y la clasificación por SWE. Las áreas bajo la curva ROC para la clasificación BI-RADS, SWE y SE y la combinación de ambas fueron 0.75, 0.88, 0.79 y 0.89 respectivamente. **Conclusiones:** La combinación de SWE y SE tuvo un mejor rendimiento diagnóstico para lesiones mamarias que cada parámetro por separado. Esd tuvo un buen rendimiento diagnóstico cuando se utilizó SWE sola o combinada con SE. **Palabras clave:** Diagnóstico; Diagnóstico por Imagen; Elasticidad; Enfermedades de la Mama.

According to the data published by the International Agency for Research on Cancer, breast cancer has become the most common malignant tumor of females worldwide¹. Similarly, breast cancer has seriously endangered female psychological and physical health in China². The mortality rate can be reduced through preclinical prevention, so, early screening and diagnosis are of great significance.

In recent years, biomechanics-based ultrasonic elastography has been verified to play crucial roles in the differentiation and diagnosis of benign and malignant breast lesions³⁻⁷. Strain elastography (SE) and shear wave elastography (SWE) have high diagnostic values for breast lesions, but the optimal parameters remain unclear. In this study, multivariate logistic regression analysis was used to determine the optimal parameters of SE or SWE alone and their combination for diagnosing breast lesions, and to compare their diagnostic efficiencies.

Materials and Methods

Baseline clinical data

A total of 132 female patients with breast tumors treated from January 2017 to December 2018 in our hospital were enrolled. Inclusion criteria: Routine ultrasonography revealed solid breast masses. Exclusion criteria: history of surgery or aspiration biopsy of mammary glands on the same side as that of lesions; implants in breasts; cystic lesions; maximum lesion diameter > 3 cm. The 132 enrolled patients who were aged 15~81 years old (44.56 ± 8.76) on average) had 164 lesions. All

lesions were pathologically confirmed (140 were surgically resected and 24 received thick needle biopsy), including 110 benign and 54 malignant lesions. This study was approved by the ethics committee of our hospital, and written informed consents have been obtained from all patients.

Apparatus and Methods

SuperSonic AixPlorer ultrasound system (France) was used with a probe frequency of 4~15 MHz. Each patient was placed in the supine position, with the upper limbs lying flat on both sides to fully expose the breasts. Lesions were observed by two experienced sonographers in the gray-scale mode and classified by using the breast imaging reporting and data system (BI-RADS). After switching to the SWE mode, the probe was placed on the body surface and left still for 3 s to collect elastic images. Q-box was utilized to obtain the elastic modulus values of lesions: maximum (E_{max}), mean (E_{mean}), standard deviation (E_{sd}) and lesion/fat elasticity ratio (Eratio). During the measurement of E_{max}, E_{mean} and E_{sd}, the lesions were covered by Q-box as much as possible. To measure Eratio, two Q-boxes (2 mm²) were placed on the hardest part of the lesion and surrounding fat tissue, respectively. The elastic images of lesions were classified into four types according to the four-color overlay pattern⁸. Type I: Uniform blue image; type II: mostly blue image, with banded pseudo-color at the edge or inside; type III: local color change at the edge of lesion; type IV: uneven color changes inside tumor. Three frames of elastic images were collected from the same lesion and averaged.

SE was performed using Esaote My Lab Twice

color Doppler ultrasound system (Italy) with a probe frequency of 4~13 MHz. In the same body position, the SE mode was selected with the same tangent plane as that of SWE. The region of interest was selected centering on the nodule, and the probe was applied with an appropriate external force and gently shaken. When the “spring” icon on the screen was displayed in green and stabilized, elastic images were acquired. Lesions were scored according to the modified 5-point scale⁹. 1 point: Lesion is entirely or mostly green; 2 points: lesion is red at the center and green all around; 3 points: green and red colors have similar proportions in the lesion range; 4 points: lesion is red overall or slightly green inside; 5 points: lesion and surrounding tissues are red, with or without green inside. The strain ratio (SR) of lesion to normal surrounding breast tissue at the same depth was measured. Three frames of image were selected for each lesion and averaged.

Statistical analysis

All data were statistically analyzed by SPSS 17.0 software. The quantitative data were subjected to the K-S normality test. The normally distributed quantitative data were expressed as mean \pm standard deviation, and the non-normally distributed ones were represented as median. The Mann-Whitney test was performed to compare the elastic parameters of benign and malignant breast lesions. The pathological results were utilized as the golden diagnostic criteria. Multivariate logistic regression analysis was conducted through maximum likelihood estimation to screen the most valuable parameters of SWE or SE alone and their combination for diagnosing breast lesions. $P < 0.05$ was considered statistically significant. Receiver operating characteristic (ROC) curve was plotted to analyze the diagnostic efficiency of each mode. The area under curve (AUC) values were compared with the Z test.

Results

Pathological diagnosis and routine ultrasonography

Of the 164 lesions, 110 were benign, including 33 adenoses, 7 cystic hyperplasias, 45 fibroadenomas, 3 galactoceles accompanied by calcification, 8 intraductal papillomas, 9 interstitial collagen

fiber hyperplasias, 3 acute or chronic infiltrations of inflammatory cells and 2 hamartomas. There were 54 malignant lesions, including 31 invasive ductal carcinomas, 1 invasive lobular carcinoma, 10 intraductal carcinomas, 4 intraductal papillary carcinomas, 2 malignant lobulated tumors, 2 mucinous carcinomas, 3 invasive papillary carcinomas and 1 malignant lymphoma.

There were 42 lesions of BI-RADS category 3, 62 of category 4A, 21 of category 4B, 25 of category 4C and 14 of category 5. BI-RADS categories 3 and 4A were considered as benign masses, and categories 4B and 4C were determined as malignant masses. The diagnostic sensitivity of BI-RADS classification was 78.18%, the specificity was 70.37%, and the accuracy was 75.61% (Table 1).

SWE and SE parameters of benign and malignant lesions

The benign lesion group had significantly lower SWE parameters (E_{max}, E_{mean}, E_{sd}, E_{ratio} and SWE color pattern) and SE parameters (elastographic score and SR) than those of the malignant lesion group ($P < 0.001$) (Table 2).

Table 1. Prediction of breast lesion characteristics by SWE, SE and their combination

Prediction method	Pathological results	
	Benign	Malignant
BI-RADS category		
Benign	86	16
Malignant	24	38
SWE		
Benign	100	17
Malignant	10	37
SE		
Benign	95	16
Malignant	18	38
SWE + SE		
Benign	99	16
Malignant	11	38

BI-RADS categories 3 and 4A were considered as benign lesions, and categories 4B and 4C were determined as malignant lesions; SWE: malignant lesions were predicted by E_{sd} and elastographic classification; SE: malignant lesions were predicted by elastographic score; SWE + SE: malignant lesions were predicted by E_{sd}, SR and elastographic classification.

Multivariate logistic regression analysis results

Multivariate logistic regression analysis was performed for the five parameters (E_{max}, E_{mean}, E_{sd}, E_{ratio} and SWE color pattern) obtained by SWE (Table 3). E_{sd} (X1) and elastographic classification (X2) were derived into the multivariate logistic regression equation which was $y(P) = -3.786 + 0.324X1 + 0.526X2$. Then the likelihood ratio test revealed statistical significance ($\chi^2 = 35.182$, $P < 0.001$). The above mode was used to diagnose breast lesions, and a regression prediction probability of $P > 0.5$ for malignancy was assumed, giving 117 benign lesions (100 were pathologically benign) and 47 malignant ones (37 were pathologically malignant). The prediction sensitivity was 90.91%, the specificity was 68.52%, and the accuracy was 83.54%.

Multivariate logistic regression analysis was conducted for the two parameters (elastographic

score and SR) obtained by SE (Table 4). Elastographic score (X1) was derived into the multivariate logistic regression equation which was $y(P) = -5.489 + 1.343X1$. Then the likelihood ratio test revealed statistical significance ($\chi^2 = 31.276$, $P < 0.001$). The above mode was employed to diagnose breast lesions, and a regression prediction probability of $P > 0.5$ for malignancy was assumed, giving 111 benign lesions (95 were pathologically benign) and 56 malignant ones (38 were pathologically malignant). The prediction sensitivity was 85.59%, the specificity was 70.37%, and the accuracy was 81.10%.

Afterwards, multivariate logistic regression analysis was carried out for the five (E_{max}, E_{mean}, E_{sd}, E_{ratio} and SWE color pattern) and two parameters (elastographic score and SR) obtained by SWE and SE, respectively (Table 5). E_{sd} (X1), SR (X2) and elastographic classification (X3) were

Table 2. SWE and SE parameters of benign and malignant lesions

	Benign (n = 110)	Malignant (n = 54)	P
E _{max} (kPa)	26.28 (21.69-3.24)	60.39 (37.02-135.28)	< 0.001
E _{mean} (kPa)	14.36 (11.79-16.81)	25.26 (17.02-35.28)	< 0.001
E _{sd} (kPa)	3.87 (2.81-5.64)	11.08 (7.03-23.14)	< 0.001
E _{ratio}	2.59 (1.90-3.49)	6.54 (3.45-11.89)	< 0.001
SWE color pattern	1.54 ± 0.24	2.79 ± 0.48	< 0.001
SR	1.51 (1.13-1.80)	2.09 (1.53-2.41)	< 0.001
Elastographic score	2.85 ± 0.35	3.74 ± 0.42	< 0.001

Table 3. Logistic regression analysis results of SWE parameters

Variable	B	Sx	Wals	Df	Sig	Exp(B)
E _{sd}	0.219	0.058	13.219	1	0.000	1.232
SWE color pattern	0.463	0.218	4.318	1	0.031	1.576

Likelihood ratio revealed statistical significance ($\chi^2 = 35.182$, $P < 0.001$).

Table 4. Logistic regression analysis results of SE parameters

Variable	B	Sx	Wals	Df	Sig	Exp(B)
Elastographic score	1.298	0.267	22.198	1	0.000	3.281

Likelihood ratio revealed statistical significance ($\chi^2 = 31.276$, $P < 0.001$).

Table 5. Logistic regression analysis results of SWE + SE parameters

Variable	B	Sx	Wals	Df	Sig	Exp(B)
Esd	0.202	0.057	10.872	1	0.000	1.224
SR	0.961	0.391	5.927	1	0.014	2.598
SWE color pattern	0.453	0.229	4.013	1	0.041	1.578

Likelihood ratio revealed statistical significance ($\chi^2 = 75.428$, $P < 0.001$).

derived into the multivariate logistic regression equation which was $y(P) = -4.762 + 0.212X1 + 0.946X2 + 0.462X3$. The likelihood ratio test revealed statistical significance ($\chi^2 = 75.428$, $P < 0.001$). This mode was utilized to diagnose breast lesions, and a regression prediction probability of $P > 0.5$ for malignancy was assumed, giving 115 benign lesions (99 were pathologically benign) and 49 malignant ones (38 were pathologically malignant). The prediction sensitivity was 90.00%, the specificity was 70.37%, and the accuracy was 83.54%.

ROC curve analysis results

ROC curve was plotted by using the pathological results as the golden criteria, BI-RADS categories 3 and 4A as benign lesions, and categories 4B and 4C as malignant lesions. The resulting AUC was 0.751 (95% CI: 0.658~0.814). AUCs for SWE, SE and their combination were 0.875 (95% CI: 0.80~0.935), 0.785 (95% CI: 0.701~0.875) and 0.889 (95% CI: 0.83~0.951), respectively (Figure 1). AUC of SWE in combination with SE was significantly higher than that of SE alone ($P < 0.05$) and slightly higher than that of SWE alone ($P > 0.05$).

Discussion

Ultrasonic elastography, which was first proposed by Ophir et al. in 1991, has become a milestone in the field of ultrasonographic diagnosis⁵. Currently, SE and SWE are mainly employed to diagnose breast lesions. SE applies a constant pressure to the tissue for detection to cause deformation that is then calculated and displayed, which is static and semi-quantitative⁶. SWE generates an ultrasonic shear wave through transducer, continuously focuses at different depths of tissue, records the small displacement of tissue caused by wave propagation using ultra-hi-

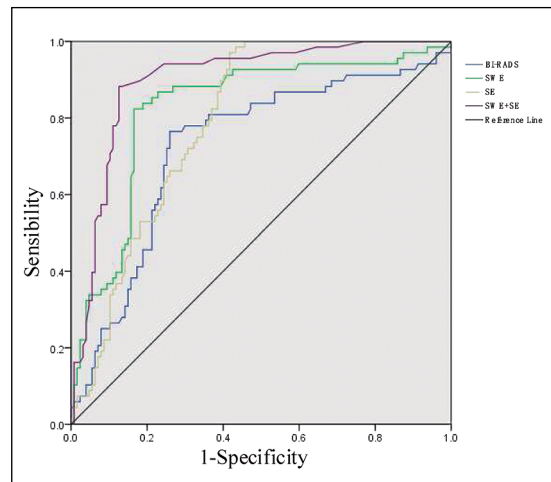


Figure 1. ROC curve analysis results for BI-RADS classification, SWE, SE and their combination.

gh speed imaging, and measures the speed of shear wave-induced spot movement by a quantitative analysis software, finally giving the absolute value of tissue elasticity^{4,7}.

Breast elastography is based on the close relationship between hardness of lesion and its internal pathological structure¹⁰. The SWE parameters (E_{max} , E_{mean} , E_{sd} , E_{ratio} and elastographic classification) and SE parameters (elastographic score and SR) of benign and malignant breast lesions were significantly different, suggesting that the lesions had significantly different hardnesses. SWE can predict the pathological type of breast cancer. When the cutoff value of average E_{max} is set at 70.7 kPa, the sensitivity for diagnosing invasive breast cancer is 72.0% and the specificity is 65.7%¹¹. However, SWE also gives false positive or negative results in identifying benign and malignant breast masses. Han et al. reported that when E_{max} was < 61.45 kPa, three cases of malignant

masses were misdiagnosed as benign ones, because lesion tissues cannot be completely penetrated by shear wave due to limited region of interest¹².

The hardness of breast mass can be obtained by both SWE and SE^{6,13}. Although the lesion elastographic parameters obtained by SWE and SE have diagnostic values, both of them have limitations^{6,7,13}. Esd represents the distribution of internal elastic modulus of a lesion in different regions, and a higher value means a less uniform distribution. For the differentiation of benign and malignant breast lesions, homogeneity may be more important than hardness¹⁴. SWE image is color-coded for the absolute value of tissue elastic modulus, which can visualize the hardness distribution and difference. Under standard conditions, the elastographic images of different lesions can be compared⁸. Our analyses showed that SWE classification reflected the overall characteristics of lesion elasticity, and had more diagnostic advantages than those of Emax and Emean. As to SE, the score was derived into the equation, verifying its high value in the differentiation of benign and malignant breast lesions. Until now, SWE has seldom been combined with SE to diagnose benign and malignant breast lesions. For SWE in combination with SE herein, Esd, SR and SWE classification were sequentially derived into the multivariate logistic regression equation, proving the diagnostic advantages of Esd and SWE classification. Notably, SR instead of SE score was derived into the equation, which may be attributed to the similar diagnostic value of the SE ratio method to that of the modified 5-point scale¹⁵. When combined with SWE, Esd and SWE classification can reflect the overall characteristics of lesion elasticity, and SR represents the relative hardnesses of lesion and surrounding tissue, so the diagnostic efficiency of SR is higher. ROC curve is commonly used to analyze the diagnostic efficiency of a detection method, and a larger AUC suggests a higher efficiency. In this study, the diagnostic efficiencies of SWE and SE for benign and malignant breast lesions both exceeded that of BI-RADS classification. The diagnostic efficiency of SWE in combination with SE was significantly higher than that of SE alone and slightly higher than that of SWE alone. Hence, diagnosis using SWE in combination with SE was not markedly superior to that using SWE alone.

Herein, the sensitivities of SWE, SE and their

combination for diagnosing breast lesions were all high, but their specificities were not high enough, possibly due to histopathological complexity and crossover between the hardnesses of benign and malignant lesions¹⁶. There were soft malignant lesions such as medullary, mucinous and necrotic invasive ductal carcinomas, and hard benign lesions such as hyaline fibroma and fat necrosis. In-depth studies with larger sample sizes involving other factors such as clinical characteristics of patients with lesions are still in need to increase the diagnostic efficiency.

Conclusions

In summary, the diagnostic value of SWE in combination with SE for breast lesion exceeded that of SE or SWE alone. Multivariate logistic regression analysis revealed that Esd showed diagnostic advantages for both SWE alone and SWE combined with SE.

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