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ORIGINAL ARTICLE

Quantitative differential diagnosis of breast tumors using shear wave velocity and different probe orientations*

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Abstract

Objective The aim of this study was to evaluate the additional benefit of the difference of maximum and minimum shear wave velocity (SWV) values obtained at different probe orientations (D-value) for the differential diagnosis of breast tumors.
Methods SWV (m/s) was measured in 123 breast tumors (92 benign, 31 malignant) in 76 female patients with the probe placed on the transverse, longitudinal, and 45° planes. The areas under the receiver operating characteristic (AUROC) curves were compared with respect to the maximum SWV, minimum SWV, D-value, maximum SWV combined with the D-value, and minimum SWV combined with the D-value.
Results There was a significant difference among the values of the maximum SWV, minimum SWV, and D-value for the 3 planes (P < 0.001). The AUROC curves for the maximum SWV, minimum SWV, and D-values of the 3 planes were 0.751 (P = 0.379), 0.486 (P = 0.863), and 0.603 (P = 0.204), respectively. The cutoff value for the maximum SWV for differentiating benign tumors from malignant tumors was 2.51 m/s (sensitivity 67%, specificity 50%). The cutoff value for the minimum SWV was 1.61 m/s (sensitivity 53%, specificity 50%). Adding the D-value increased the AUROC curve for the maximum SWV from 0.571 to 0.733 and the minimum SWV from 0.486 to 0.504 (P = 0.964), respectively.
Conclusion SWV differs in different planes of breast tumors. The D-value can provide a reference for the differential diagnosis of breast tumors.
Key words: shear wave; elastography; velocity; D-value; breast tumor; differential diagnosis

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Shear wave elastography has recently emerged as a novel method for quantitatively measuring tissue elasticity [1]. With this method, the probe produces an acoustic push pulse that induces a low-frequency shear wave that travels transverse to the axis of the probe in tissues [2]. Shear wave velocity (SWV) is positively correlated with tissue stiffness. The SWV increases as the tissue gets stiffer. This technology has been used in the differential diagnosis of benign and malignant breast lesions. By measuring the SWV of breast tumors, the properties of the breast lesions can be identified [3–4]. Past studies have shown that the SWV varies in myocardial [5–6] and skeletal muscles [7–8] with different orientations of the probe, suggesting that the cell and fiber orientations of the tissue may affect the SWV that travels through tissue. Thus, probe orientation should be considered when SWV is measured in such tissues. This study aimed to determine the impact of probe orientations on the SWV of breast tumors.

Materials and methods

Patients

We collected data from 76 female patients (mean age, 38 ± 14 years; range, 14–65 years) with breast lesions who were treated between May 2012 and January 2015. Ultrasonography (US) was performed among these 76 patients before Mammotome excision, and follow-up of the pathological results was performed. Overall, 123 breast tumors (size range, 0.4–14.3 cm; mean, 1.74 ± 1.39 cm) were assessed.

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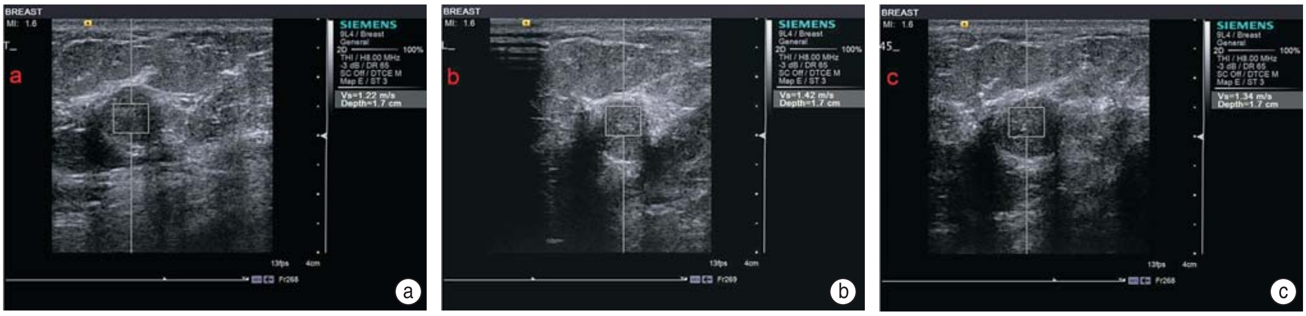

Fig. 1 SWV in 3 planes located in the same region of a breast fibroadenoma. (a) SWV measured in the transverse plane in 1.22 m/s; (b) SWV in the longitudinal plane is 1.47 m/s; (c) SWV in the 450 plane is 1.34 m/s. For this tumor, the SWV in the transverse plane was the smallest, while the SWV in the longitudinal plane was the largest.

Machine and methods

Breast US was performed using a Siemens S2000 ultrasound system equipped with a linear array transducer with a bandwidth of 4–9 MHz. First, conventional breast US was performed, and then quantitative implementation was used with the probe smoothly pressed at the center of the tumor. The patient was required to hold her breath, and the SWV was measured in 3 different planes (i.e., the transverse, longitudinal, and 45°; Fig. 1). For tumors in large breasts in which the region of interest (ROI) was deep in the tissue, we chose capillary vessels or tissue fiber as the reference to keep the ROI in the center of the tumor with the same depth. Measurements were repeated twice in each orientation and the mean SWV value was calculated. The mean value of the different orientations was compared, the maximum and minimum values were identified, and the difference of maximum and minimum SWV values (D-values) was calculated. We failed to obtain the SWV when it exceeded the measurable scale, the tissue in the ROI was heterogeneous, or when a liquid necrosis component was present [7], and their SWVs were displayed as X.XX m/s in Fig. 2.

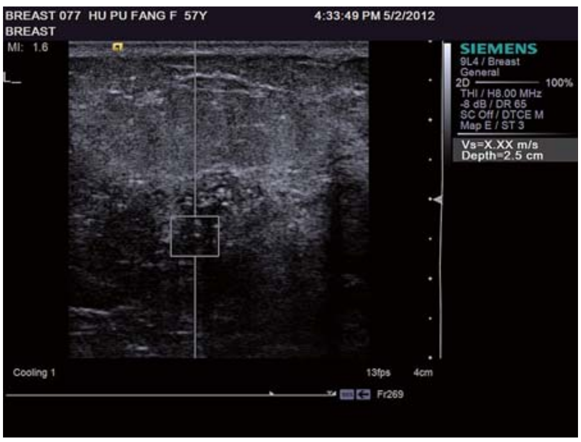

Fig. 2 Shear wave velocity in breast invasive duct cancer displayed as x.xx m/s. Rough calcium can be seen on B-mode ultrasonography.

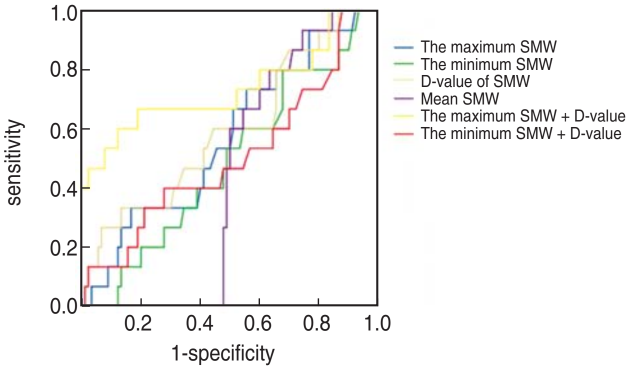

Fig. 3 Receiver operating characteristic (ROC) curves of the maximum SWV, the minimum SWV, mean value, D-value, and these variables combined with the D-value of SWV in breast tumors in the same region.

Statistical analysis

SPSS 17.0 software was used, and results were presented as mean ± SD. An analysis of variance was used to evaluate the differences between the maximum, medium, and minimum SWVs on different planes. Additionally, *t*-tests were used to differentiate between the different pathological types. The maximum SWV, minimum SWV, and D-value were obtained from receiver operating characteristic (ROC) curves, and the areas under the receiver operating characteristic (AUROC) curves were compared. *P*-values < 0.05 were considered significant.

Results

A total of 123 lesions from 76 patients were examined. There were 92 benign tumors in 48 patients (18 fibroadenoma, 16 mastopathy, and 58 mastopathy with fibroadenoma, respectively). Overall, the SWVs were successfully measured in 91 lesions, but there was one case (mastopathy with fibroadenoma) in which the SWV could not be assessed. There were 31 malignant tumors in 28 patients including 26 invasive breast duct carcinomas, 2 lobar cancers, 2 breast duct carcinomas in situ, and 1

Table 1 Comparison between the maximum and minimum SWV of the 3 planes of breast tumors (m ± s m/s)

Pathological types of breast tumors	n	Maximum SMW	Minimum SMW	D-value	P
Benign	92 (1)*	2.49 ± 0.73	2.09 ± 0.72	0.68 ± 0.47	< 0.001
Malignant	31 (16)*	2.67 ± 0.71	1.74 ± 0.54	0.93 ± 0.63	< 0.001
P	30	0.700	0.458	0.065	

mucoid cancer. Among the 31 malignant tumors, the SWVs in 15 breast tumors were measured, while those in 16 tumors (14 invasive breast duct carcinomas, 1 mucoid tumor, and 1 lobar tumor) were displayed as X.XX m/s.

Of the 106 successfully measured lesions, the maximum and minimum SWV values on the 3 planes were (2.51 ± 0.73) m/s and (1.79 ± 0.61) m/s, respectively. A t-test showed a significant difference between the maximum and minimum SWV, with a D-value of (0.72 ± 0.50) m/s (P < 0.001). For the 91 benign tumors, the maximum SWV, minimum SWV, and D-value were (2.49 ± 0.73) m/s, (2.09 ± 0.72) m/s, and (0.68 ± 0.47) m/s, respectively (P < 0.001). For the 15 malignant tumors, the maximum SWV, minimum SWV, and D-value were (2.67 ± 0.71) m/s, (1.74 ± 0.54) m/s, and (0.93 ± 0.63) m/s, respectively (P < 0.001), and the D-values of the SWV for benign and malignant tumors were (0.68 ±0.47) m/s and (0.93 ± 0.63) m/s, respectively (P = 0.056; Table 1). The AUROC curves of the maximum SWV, minimum SWV, and D-value were 0.571 (P = 0.379), 0.486 (P = 0.863), and 0.603 (P = 0.204), respectively (Fig. 3 and Table 2). The cutoff of the maximum SWV for the differential diagnosis of benign and malignant lesions was 2.51 m/s (sensitivity 67%, specificity 50%). The cutoff of the minimum SWV was 1.61 m/s (sensitivity 53%, specificity 50%). The cutoff of the D-value was 0.64 m/s (sensitivity 60%, specificity 56%). The maximum SWV and the D-value had similar AUROC curves, with no significant differences (Z = 0.29, P = 0.38). With the addition of the D-value, the AUROC curves of the maximum and minimum SWV increased from 0.571 to 0.733 (P = 0.004) and from 0.486 to 0.504 (P = 0.964), respectively (Table 2). The maximum SWV was associated with the maximum AUROC curve after being combined with the D-value (Fig. 3 and 4).

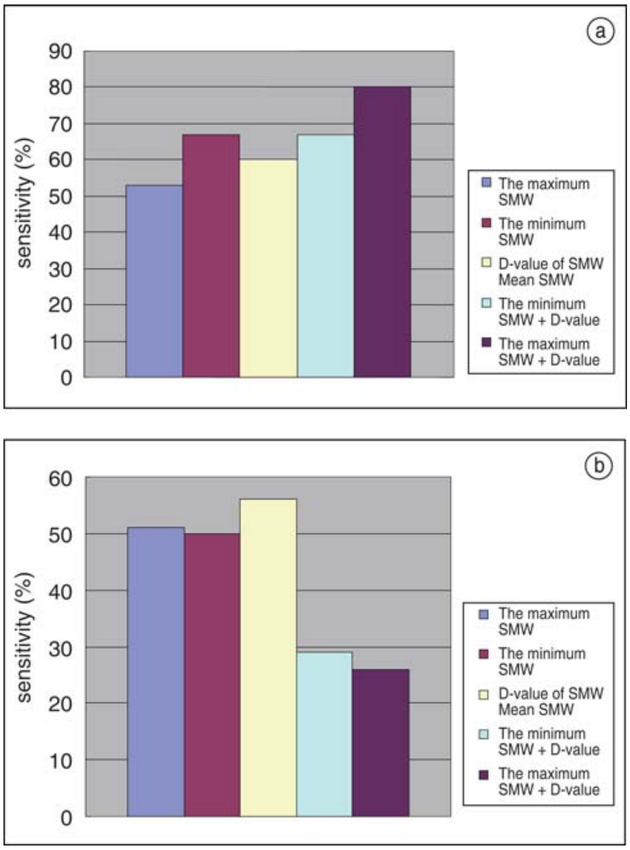

Fig. 4 Sensitivity and specificity of the minimum SWV, maximum SWV, and D-value and these variables combined with the D-value.

Discussion

The shear wave is produced by a normal linear array probe inducing regional movement that travels transverse across the tissue, vertically to the axis of the probe. An acoustic push pulse causes tissue movement and produces a shear wave, the velocity of which can reflect tissue stiffness. By measuring the SWV of the tissue, the stiffness

Table 2 Comparison of the maximum SWV, the minimum SWV, the D-value, and these combined with the D-value of SWV

Variable	Area	95% CI		Cutoff	Sensitivity (%)	Specificity (%)
		Down	Up			
The maximum SWV	0.571	0.421	0.721	2.51 (m/s)	67	50
The minimum SWV	0.486	0.337	0.635	1.61 (m/s)	53	51
Mean SWV	0.437	0.327	0.544	2.13 (m/s)	60	50
D-value of SWV	0.603	0.445	0.760	0.64 (m/s)	60	56
The maximum SWV + D-value	0.733	0.562	0.904	0.501	80	40
The minimum SWV + D-value	0.504	0.336	0.671	0.611	67	30

of the tissue in an ROI can be quantitatively assessed [9]. The shear modulus is a variable that reflects the tissue elasticity and can be calculated by the equation $\mu = \rho c2$, in which μ represents the shear modulus (i.e., the property of stiffness); shear wave has a velocity range of 1–10 m/s. According to the equation, SWV increases with regional stiffness [10].

It could be assumed that the shear wave travels in homogeneous tissue, SWV correlates with tissue elasticity, and that these should be constant in different orientations. Shear wave elastography has now been clinically used in breast tissue and other organs, such as the liver [11] and muscle [12]. In homogeneous tissues like liver, the SWV has high accuracy and repeatability [13]. However, the SWV varies as the fiber orientation of the muscle changes. Deffieux *et al*. investigated the biceps and found that the shear wave that is parallel to the fiber orientation of the muscle travels the fastest [7]. In striated muscle of healthy volunteers, the SWV tends to decrease as the angle across the muscle fiber orientation and the probe orientation increases [8]. Our previous study also showed that the shear modulus of different myocardial fiber layers changed when the probe was placed in different orientations [5]. This finding suggests that, in myocardial fiber, a shear wave travels faster in an orientation parallel to the fiber orientation.

This study showed that the value for the regional SWV of breast tumors changed as the probe orientation changed. It can be inferred that when the angle varies between the probe and fiber orientation in different planes, the probe orientation across the breast tumor will induce differences in the SWV on these different planes. The SWV was compared and analyzed in both benign and malignant tumors, and the value differed depending on the specific pathology. This difference may have been partly caused by the pathological tissue composition that varies at different orientations. Thus, the D-value of SWV should be considered when using SWV for quantitative differential diagnosis [14]. The AUROCs of the maximum SWV, minimum SWV, and D-value were investigated, and the results showed that the D-value between the maximum and the minimum SWV had a bigger area than did the SWV in a single plane, which suggested that the D-value of SWV can provide a reference for the differential diagnosis between benign and malignant tumors. Furthermore, after being combined with the D-value and the maximum SWV, the diagnostic utility of the minimum SWV improved and the AUROC curve increased. Some researchers insist that the maximum value rather than the average value should be chosen for the quantification of shear modulus in the differential diagnosis of breast lesions [15]. In our opinion, as a diagnostic reference, the maximum SWV is more suitable than the minimum SWV, and the D-value considerably valuable for diagnosis. We can choose a maximum SWV and a D-value in tumors to improve the identification of benign or malignant breast tumors. Scanning through multiple planes of a tumor can help improve the specificity of diagnosis in breast tumors.

Our study had some limitations. Most malignant breast tumors were excluded because the SWV could not be measured with shear wave elastography. With this system, numerical values of the SWV were too high or could not be obtained in some benign tumors that contained calcium or fibrosis composite. For such hard tissues, the ROI was set around the fibrotic region to make data analysis of the breast tumors feasible. Mucoid cancer with a soft pathological composite should have shown a low SWV value; however, when the SWV transversed through interfaces such as liquid necrotic tissues that cause faint vibration, it could not be detected [7]. In our study, one case of mucoid cancer was discovered in which SWV could not be measured. Now, shear wave elastography has been used to characterize breast tumors as well as fat and breast tissue glands. However, the malignant cases and pathological types in this study are limited, and many more samples are needed to verify the conclusion of the study. To date, shear wave elastography has been used in the diagnosis of many diseases, including breast tumors [16]. However, adding the D-value of different planes to the SWV may optimize the differential diagnosis of breast lesions.

In conclusion, the difference of the maximum and minimum SWV on different planes can provide a reference for the differential diagnosis of breast tumors.

Conflicts of interest

The authors indicated no potential conflicts of interest.

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