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Original Article

Role of strain elastography and virtual touch tissue quantification technique in the diagnosis of breast solid lesions

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Abstract: Objective: This study aimed to compare the diagnostic performance of the strain elastography and virtual touch tissue quantification (VTQ) technique in the differentiation of malignant and benign breast solid lesions, and determine which one is better than the other for a certain pathological type or a certain case. Materials and methods: 52 breast solid lesions (27 benign and 25 malignant) in 49 consecutive female patients (mean age, 46.7±11.8 years) were included in this study. Conventional ultrasound, subsequently strain elastography and VTQ examination were performed. The diagnostic performance were evaluated by receiver operating characteristic analysis. Results: There was significant difference in strain ratio (SR) (P < 0.001) and shear wave velocity (SWV) (P < 0.001) between benign and malignant lesions. For strain elastography, the optimal cutoff value of SR was 0.499 (AUC_{SR} = 0.919) with a sensitivity of 93.6%, specificity of 72.0%, PPV of 78.8%, NPV of 94.7% and accuracy of 84.6%. For VTQ technique, the optimal cutoff value of SWV was 2.90 m/s (AUC_{SWV} = 0.796) with a sensitivity of 68.0%, specificity of 92.6%, PPV of 89.5%, NPV of 75.8% and accuracy of 80.8%. *Z* test results showed that there was no significant difference in area under the curve (*P* = 0.057). Conclusions: Although the diagnostic performance of strain elastography and VTQ technique in the differentiation of breast solid lesions was almost equally. VTQ technique showed higher specificity but lower sensitivity than strain elastography. These two methods could be used to help to re-regulate the BI-RADS category of breast lesions, especially for equivocal BI-RADS category 3 and category 4 breast lesions.

Keywords: Elastography, strain ratio, virtual touch tissue quantification, breast tumor, ultrasonography

Introduction

Breast cancer threatens female's health seriously. The global prevalence of breast cancer is increasing in recent years. Breast cancer has been the leading cause of cancer-related mortality for women [1, 2]. Over the past years, ultrasonography has become an indispensable tool in breast imaging. It allows confident characterization of benign cysts and better evaluation of dense breast disease [3]. Ultrasonography has been commonly used in the diagnosis and follow-up of breast disease. With the expanded role of ultrasonography, the Breast Imaging Reporting and Data System (BI-RADS) ultrasound lexicon which were used to standardize terminology for description and management descriptions has been established by the American College of Radiology (ACR) [4]. The conventional ultrasound-based BI-RADS as-sessment is based on the morphologic features of the lesions [5]. However, the tissue stiffness or the elasticity which has been proven to be highly correlated with pathological tissue progression [6, 7] and couldn't be assessed.

Schaefer et al. [8] reported that elastography is a promising way to evaluate tissue stiffness or elasticity which was historically assessed manually by palpation. With the concept that harder lesions are more likely to be malignant, elastography has been regarded as an important complementary method for conventional ultrasound in tumor differential diagnosis [9, 10]. Currently, two principal elastography methods are mostly widely used in the diagnosis of breast lesions: strain elastography and virtual touch tissue quantification (VTQ) technique. Strain elastography is based on the application of a compressive force to the tissue and the measurement of the shape-deforming effect [11]. As Waki et al. [12] reported, sonographers could evaluate the stiffness by calculating strain ratio (SR) of the lesions to the healthy

Table 1. Performance of conventional ultrasound

		Pathological		Total
		Malignant	Benign	
BI-RADS category	4, 5 (Malignant)	22	9	31
	1-3 (Benign)	3	18	21
Total		25	27	52

BI-RADS, Breast Imaging Reporting and Data System. 1-3, 4, 5 is the type of BI-RADS category, such as BI-RADS category 1.

grandular tissue in the same depth. Compared with the 5-point scoring system the semi-quantitative assessment method might control the subjective bias [13]. Strain elastography is intuitive and easy to performed, but still with high operator dependency and obvious interobserver variability [14, 15]. For VTQ technique, an independent mechanical ultrasound beam is transmitted to generate perpendicular shear waves localized peripherally to the positioned region of interest (ROI) [11]. Tissue elasticity or stiffness could be assessed immediately by measurement of shear wave velocity (SWV) within the ROI. It has been reported that VTQ technique is highly repeatable and less operator dependent [16]. But there is the potential of large variation in SWV measurement in the case of high stiffness contrast between normal and abnormal tissues [17].

There are a large amount of studies about the diagnostic performance of strain elastography and VTQ technique in the differential diagnosis of breast lesions. However, as far as we are aware, there were few studies in which breast solid lesions were examined by both strain elastography and VTQ technique. Each technique has its own basic principle and inherent drawback leading to false-positive and false-negative results, the diagnostic performance of the two methods might be different when they are performed on the same breast lesions. Maybe for a certain type or a certain case, the evaluation accuracy of one technique could be better than the other one.

In this study, strain elastography and VTQ technique were performed on the same breast lesions. The purpose of this study was to compare the diagnostic performance of strain elastography and VTQ technique in the differentiation of malignant and benign breast solid lesions, and to determine which one is better than the other for a certain pathological type or a certain case.

Materials and methods

Patients and lesions

49 female patients (mean age, 46.7±11.8 years; age range, 22-81 years) who underwent surgery for breast lesions from May 2014 to October 2015 in our hospital were initially enrolled in this study. This study was approved by the institutional review board and ethics committee of our Hospital. Written informed consent was obtained from all the patients.

Breast lesion exclusion criteria were (1) lesions had been treated by neoadjuvant chemotherapy; (2) lesions with cystic portion more than 50%; (3) lesions with maximal diameter less than 5.0 mm or more than 45.0 mm, or depth more than 40.0 mm. Finally, a total of 52 breast solid lesions (mean maximal diameter, 17.7±10.9 mm; maximal diameter range, 4.0-41.0 mm) were included. Conventional ultrasound, subsequently strain elastography and VTQ examination were performed prior to the surgical procedure. All the ultrasound examinations were performed by the same two sonographers who have 8-10 years experience in breast ultrasonography. And all the decisions were made in consensus by them.

Ultrasound examination

Conventional ultrasound and strain elastography imaging were performed using a Philips iU22 (Philips Medical Systems, Bothell, WA, USA) sonography system with an L12-5 linear array probe.

For conventional ultrasonography, the maximal diameter, depth and characteristics of the lesions were recorded. The lesions were described by using BI-RADS Ultrasound lexicons: shape (oval, round, irregular), orientation (parallel, not parallel), boundary (abrupt interface, echogenic halo), margin (circumscribed, microlobulated, indistinct, angular, speculated), echo pattern (hyperechoic, isoechoic, hypoechoic, anechoic, complex) and posterior acoustic features (enhancement, shadowing, no posterior acoustic features, combined pattern). The lesions were assigned to 1-5 categories according to the ACR BI-RADS criteria [4]. BI-RADS categories 1-3 were taken as benign while BI-RADS categories 4-5 were regarded as malignant [18].

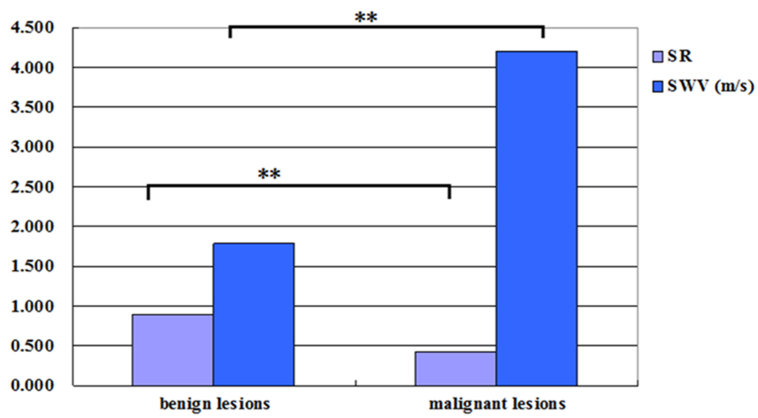

Figure 1. Strain ratio (SR) and shear wave velocity (SWV) of benign and malignant breast lesions (**P < 0.001).

For strain elastography, the lesions were repetitively compressed by the transducer under light pressure vertically on the skin. The elasticity box was set about two times of the targeted lesion area, including the targeted lesion (selected as A) and sufficient adjacent healthy glandular tissue (selected as B) in the same depth. The strain index was calculated automatically with the Qlab elastography analysis software as A/B ratio.

VTQ technique examination was performed on a Siemens S2000 (Siemens Medical Solutions, Mountain View, CA, USA) sonography system with a 9L4 linear array probe. The maximal cross section of the targeted lesion was selected. The probe was applied with minimal compression to the targeted lesion for several seconds until the image stabilized as recommended [19]. Then ROI box of VTQ (5.0 mm× 5.0 mm) was set to place in the center of the targeted lesion. Press 'update' button and then SWV of the targeted lesion was measured (maximum 9.00 m/s). When tissue inside the ROI was too stiff or heterogeneous, the SWV might be displayed with "X.XX m/s". In this case, we needed to further research the virtual touch tissue imaging (VTI) image. The stiffer the tissue, the darker the VTI image. The result was recorded as 9.00 m/s when the VTI image appeared dark [20].

Histology analysis

Histological diagnoses of the 52 lesions were made by a pathologist with 15 years of experience in breast pathology. All breast lesions were classified as benign and malignant, and furthermore divided into relevant subgroups. Histological results were used as reference standard.

Statistical analysis

The SPSS 17.0 software package (SPSS Inc, Chicago, IL) was used for all statistical analyses. All measurement data were expressed as mean ± standard. Student's t tests, one-way ANOVA tests and Fisher's exact tests were used for comparisons. Receiver operating characteristic (ROC) curves for strain elastography and VTQ technique were performed to evaluate the diagnostic performance. Z tests were used to compare the area under the curve (AUC) of BI-RADS categories and elasticity values. A P value < 0.05 was considered statistically significant.

Results

Patient and lesion characteristics

52 breast solid lesions in 49 consecutive female patients (mean age, 46.7±11.8 years; age range, 22-81 years) were analyzed in this study. Of these 49 female patients, 6 female patients were asymptomatic, 36 female patients presented palpability, and 7 female patients showed nipple discharge.

There were 25 malignant lesions: 18 invasive ductal carcinoma, 3 invasive lobular carcinoma, 3 ductal carcinoma in situ, and 1 micropapillary carcinoma. 27 lesions were benign and included: 10 fibroadenoma, 7 intraductal papilloma, 7 hyperplasia, 2 lipomyomas and 1 benign phyllodes tumor.

The mean maximal diameter of the malignant lesions and benign lesions were 14.1±10.5 mm and 21.6±10.3 mm, respectively. And there was no significant difference (P < 0.05).

Performance of conventional ultrasound examination

Table 1 presented the performance of conventional ultrasound in the differentiation of malignant and benign breast lesions. The sensitivity, specificity, positive predictive value (PPV), neg-

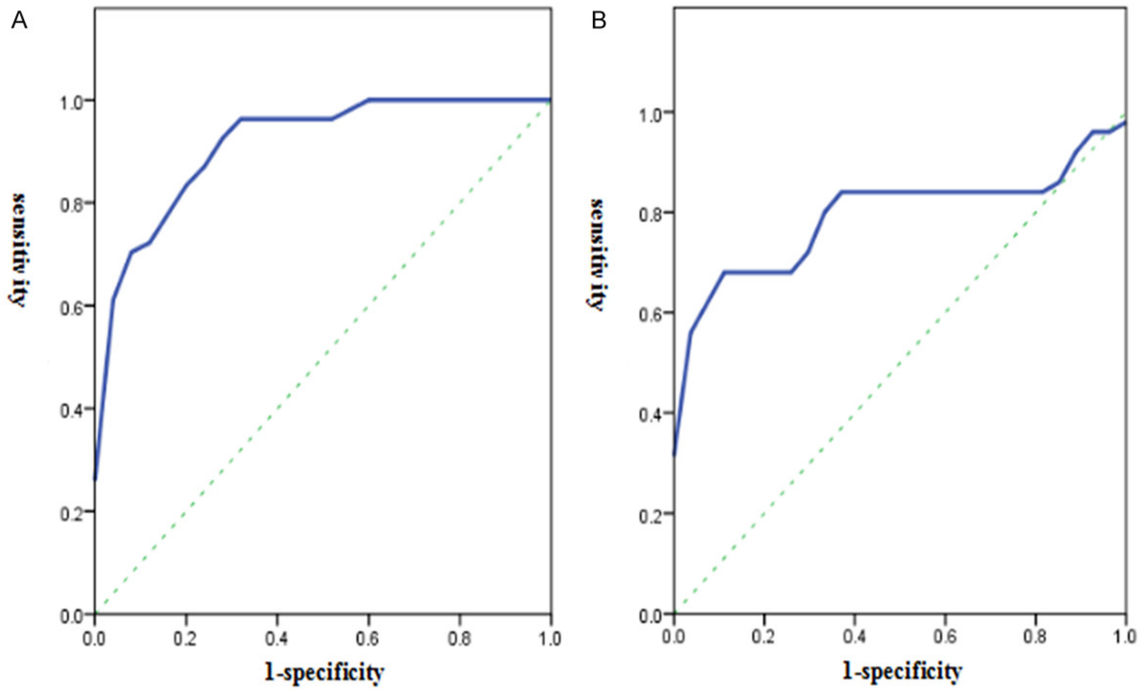

Figure 2. Receiver operating characteristic (ROC) curve of ultrasound elastography in the diagnosis of breast lesions. A: Strain elastography. B: Virtual touch tissue quantification technique.

ative predictive value (NPV) and accuracy was 88.0%, 66.7%, 71.0%, 85.7%, 76.9%, respectively. Among the 52 lesions, 3 malignant lesions were considered to be a BI-RADS category 3. They were 2 ductal carcinoma in situ and 1 micropapillary carcinoma. In addition, 9 benign lesions were classified as BI-RADS category 4 or 5, including 1 fibroadenoma with calcification, 5 intraductal papilloma, 2 hyperplasia and 1 benign phyllodes tumor.

Performance of ultrasound elastography

Strain elastography results show that the SR was 0.894±0.304 for benign lesions and 0.435±0.175 for malignant lesions. Check by VTQ technique, the SWV was 1.78±0.71 m/s for benign lesions and 4.19±2.51 m/s for malignant lesions. There was significant difference in SR ($P < 0.001$) and SWV ($P < 0.001$) between these two groups (**Figure 1**).

To compare the diagnostic performance of the two elastography methods in the diagnosis of breast lesions, the ROC analysis was performed, and their sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy were calculated. Results showed that the optimal cutoff value of SR was 0.499 (AUC_{SR} = 0.919) to differentiate benign and malignant breast lesions, with a sensitivity of 93.6%, specificity of 72.0%, PPV of 78.8%, NPV of 94.7% and accuracy of 84.6% (**Figure 2A**). And the optimal cutoff value of SWV was 2.90 m/s (AUC_{SWV} = 0.796) to differentiate benign and malignant breast lesions, with a sensitivity of 68.0%, specificity of 92.6%, PPV of 89.5%, NPV of 75.8% and accuracy of 80.8% (**Figure 2B**). Both strain elastography and VTQ technique could improve the specificity and accuracy of the conventional ultrasound-based BI-RADS assessment (**Table 2**). It's worth mentioning that strain elastography could enhance ultrasound specificity with maintained high sensitivity. When combining strain elastography with VTQ technique, the overall sensitivity increased up to 84.0%, specificity increased up to 88.9%.

Comparison of performance of strain elasography and VTQ technique

Z test results showed that there was no significant difference in AUC of ROC curves between these two elastography methods ($Z = 1.580$, $P = 0.057$). The diagnostic performance of the

Table 2. Performance of strain elastography, virtual touch tissue quantification technique and conventional ultrasound

Method	AUC	Cutoff point	Sensitivity	Specificity	PPV	NPV	Accuracy
Strain elastography	0.919	0.499	96.3%	72.0%	78.8%	94.7%	84.6%
VTQ technique	0.796	2.90 m/s	68.0%	92.6%	89.5%	75.8%	80.8%
BI-RADS category	-	-	88.0%	66.7%	71.0%	85.7%	76.9%

VTQ, Virtual touch tissue quantification; BI-RADS, Breast Imaging Reporting and Data System.

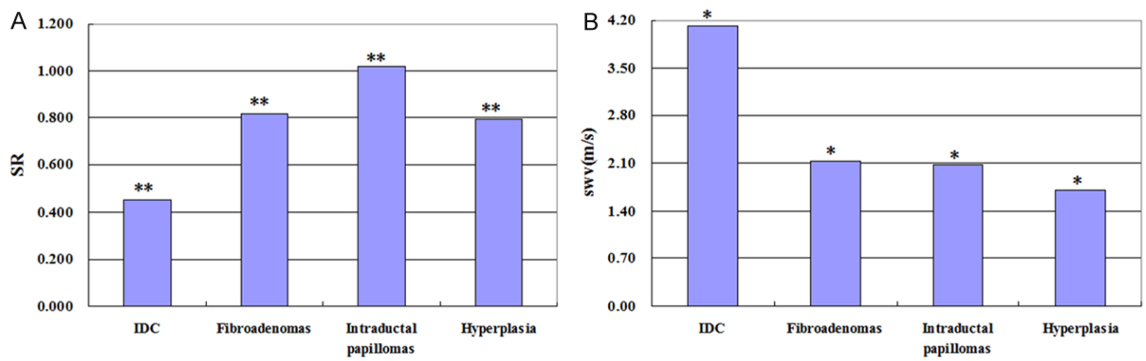

Figure 3. Elasticity values of different pathological subgroups (IDC = invasive ductal carcinomas) (***P* < 0.001, **P* < 0.05). A: Strain ratio. B: Shear wave velocity.

two methods to differentiate benign and malignant breast lesions was almost equal. Whereas, compared with strain elastography, VTQ technique was with higher specificity but lower sensitivity (**Table 2**).

Performance of strain elastography and VTQ technique in lesions of different pathological subgroups

There were significant differences ($P < 0.001$) in SR of invasive ductal carcinomas (0.455±0.193), fibroadenomas (0.818±0.376), intraductal papillomas (1.020±0.260) and hyperplasia (0.796±0.177) (**Figure 3A**).

There were significant differences ($P = 0.012$) in SWV among the above four groups (**Figure 3B**), and the SWV was 4.12±2.68 m/s, 2.13±0.65 m/s, 2.08±0.79 m/s, 1.71±0.77 m/s respectively.

Discussions

Conventional ultrasound plays an important role in the clinical practice of breast disease, such as creating a safety, noninvasive and cost-effective way for evaluation of suspected breast lesions. Though BI-RADS assessment standardizes the description terminology and has improved the diagnostic accuracy significantly, conventional ultrasound still has relatively low specificity. Concordant with other reports [21, 22], the sensitivity and specificity of conventional ultrasound was 88.0% and 66.7% respectively in the present study.

However, independent of morphological features and elastography depicts the mechanical tissue properties. Recent studies have shown that elastography is a promising complementary technique that enhances the conventional ultrasound specificity without too much loss of sensitivity, and it is able to reduce unnecessary biopsies therefore [21, 22]. With the optimal cutoff value of 0.499 for SR and 2.90 m/s for SWV, strain elastography and VTQ technique showed good diagnostic performance in the differentiation of benign and malignant breast lesions in this study. This is comparable with the reported studies [23, 24]. The specificity was 72.0% for strain elastography and 92.6% for VTQ technique. This suggested that both methods could improve the specificity and accuracy of the conventional ultrasound-based BI-RADS assessment. When combining the two elastography methods, the overall sensitivity increased up to 84.0%, and specificity increased up to 88.9%. The combination could

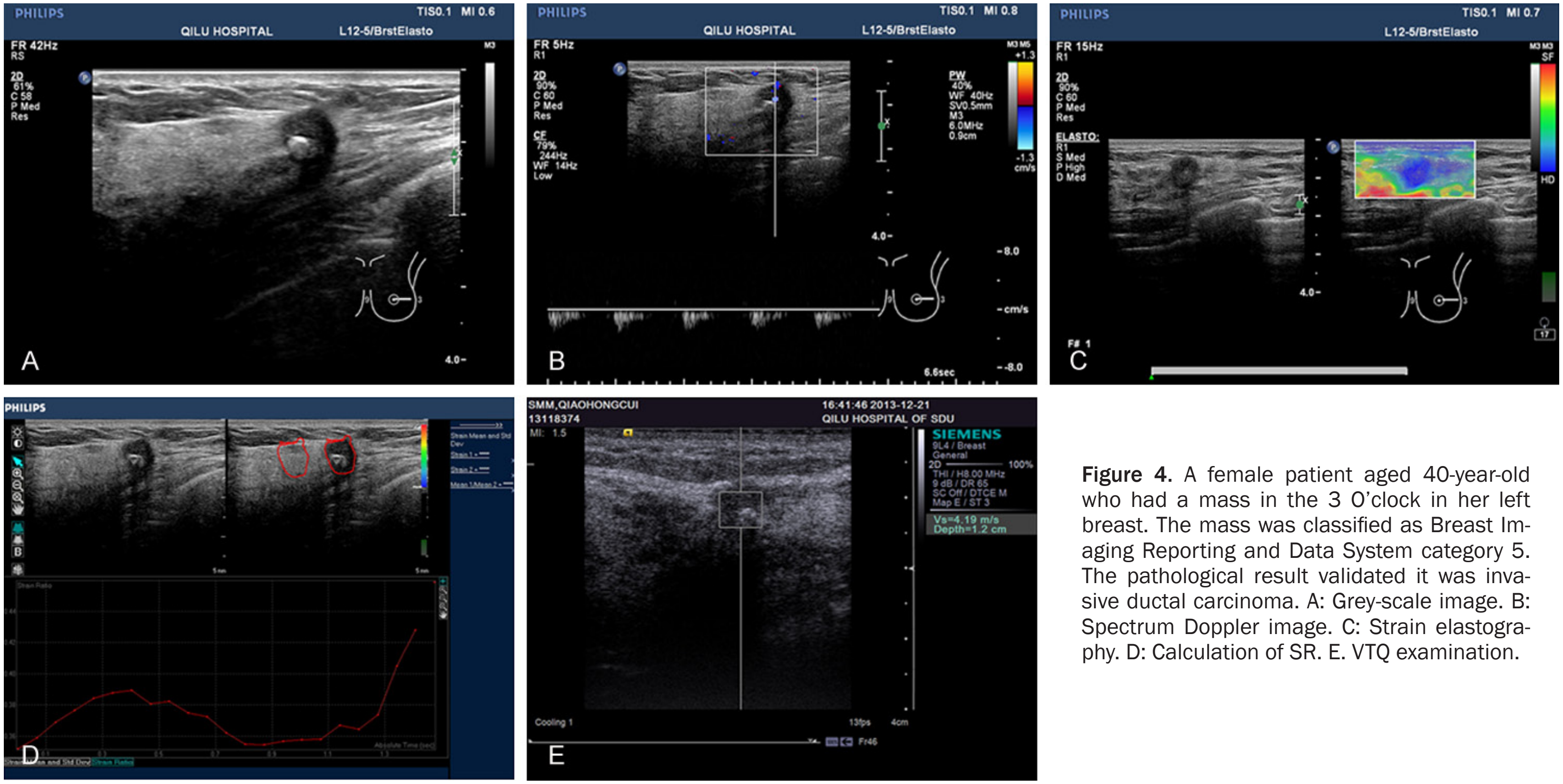

Figure 4. A female patient aged 40-year-old who had a mass in the 3 O'clock in her left breast. The mass was classified as Breast Imaging Reporting and Data System category 5. The pathological result validated it was invasive ductal carcinoma. A: Grey-scale image. B: Spectrum Doppler image. C: Strain elastography. D: Calculation of SR. E. VTQ examination.

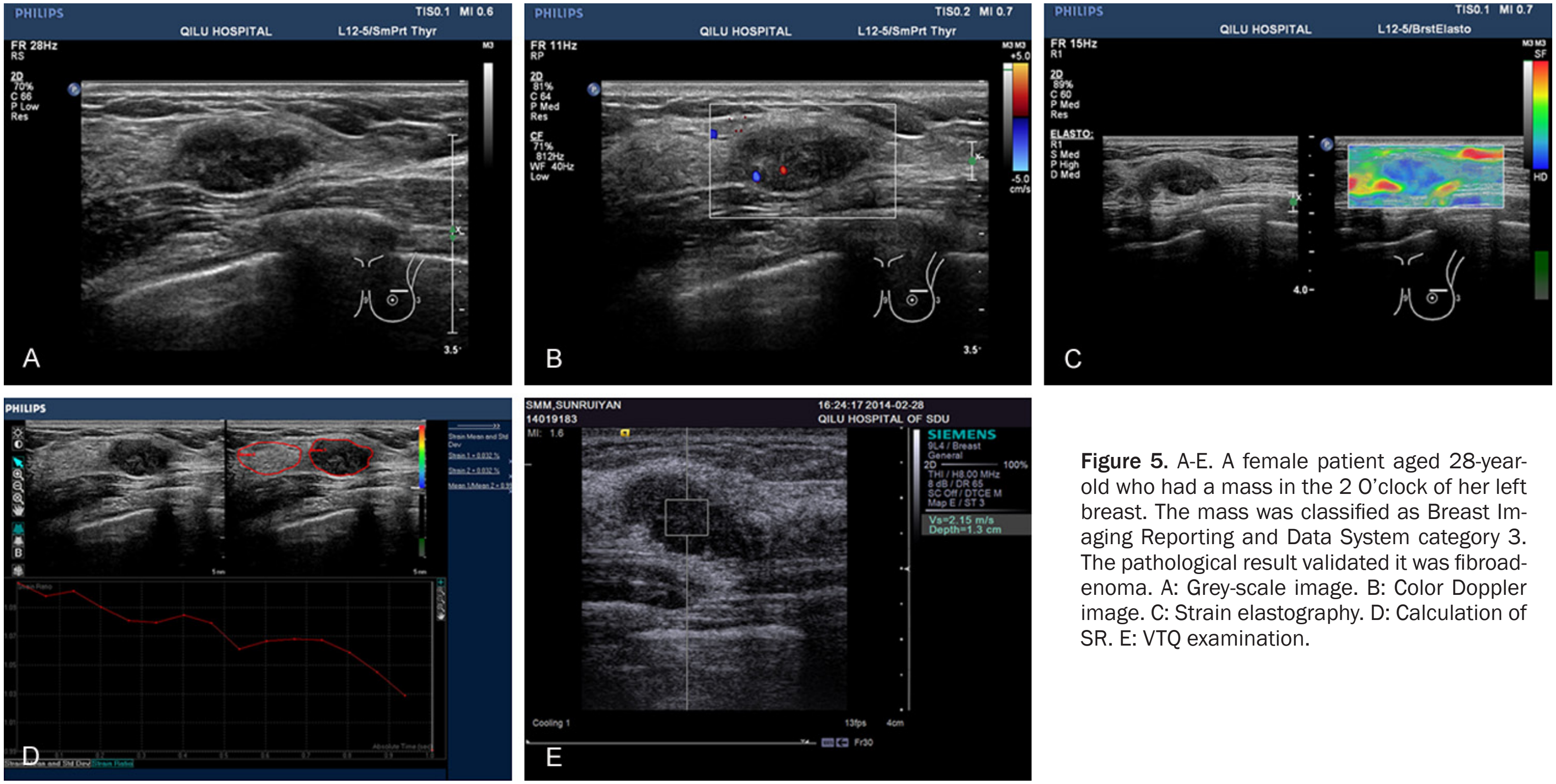

Figure 5. A-E. A female patient aged 28-year-old who had a mass in the 2 O'clock of her left breast. The mass was classified as Breast Imaging Reporting and Data System category 3. The pathological result validated it was fibroadenoma. A: Grey-scale image. B: Color Doppler image. C: Strain elastography. D: Calculation of SR. E: VTQ examination.

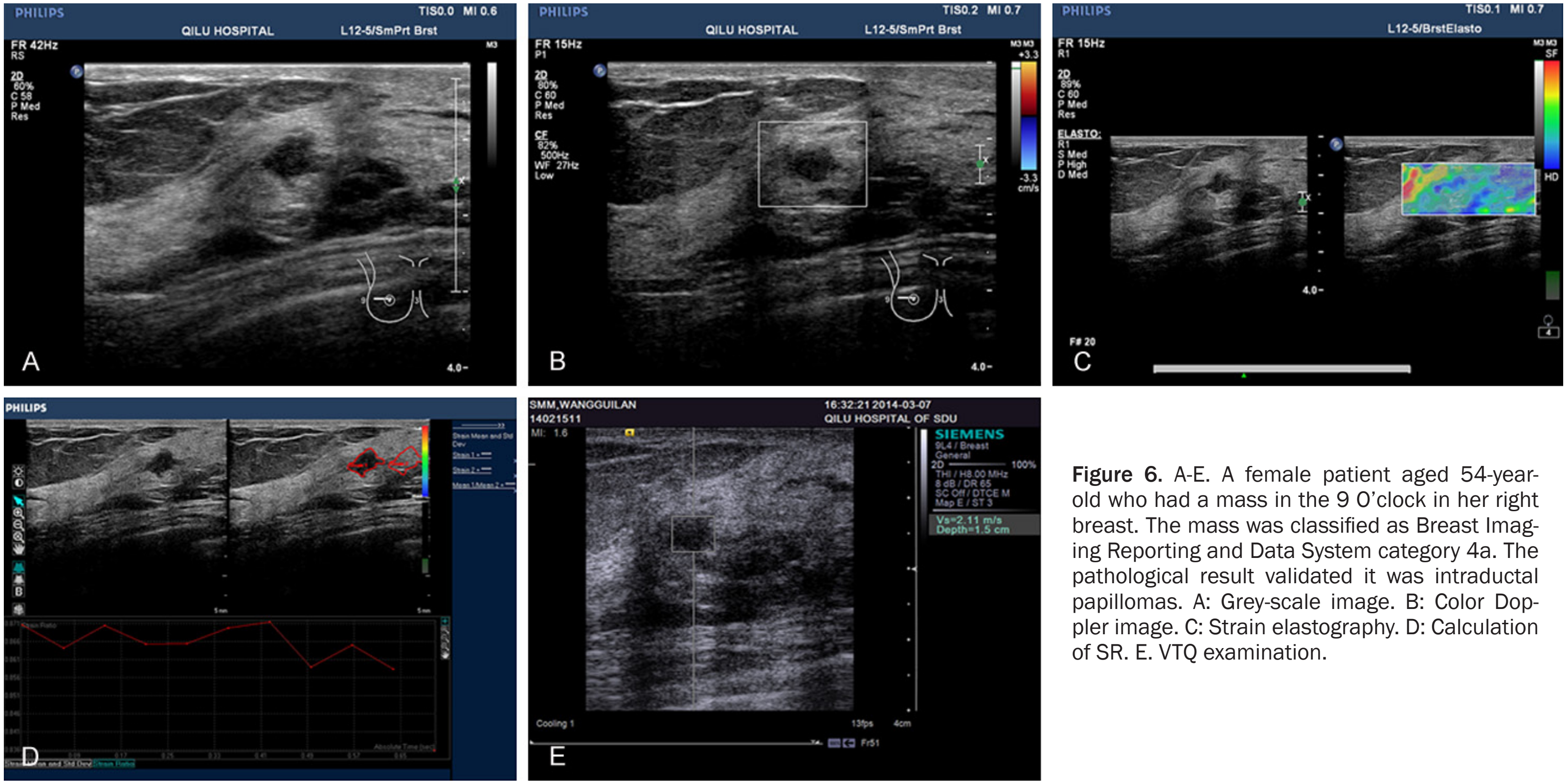

Figure 6. A-E. A female patient aged 54-year-old who had a mass in the 9 O'clock in her right breast. The mass was classified as Breast Imaging Reporting and Data System category 4a. The pathological result validated it was intraductal papillomas. A: Grey-scale image. B: Color Doppler image. C: Strain elastography. D: Calculation of SR. E. VTQ examination.

ensure the full utilization of the advantageous characteristics of both of the two methods. It could obviously contribute to the differentiation of benign and malignant breast lesions in the clinical practice.

In this study, the results displayed that the diagnostic performance of the two elastography methods in the differentiation of benign and malignant breast lesions were almost equal. When performed on the same breast lesions, the two elastography methods showed good consistency in the majority of the breast lesions, especially for the lesions classified as BI-RADS category 2 and category 5 (**Figure 4**). Whereas, we found that VTQ technique showed higher specificity but lower sensitivity than strain elastography. This phenomenon somewhat may be attributable to the technique itself as the two elastography methods have quite different basic principles and inherent drawbacks. This finding may provide useful information to the clinical sonographers when they characterize equivocal BI-RADS category 3 (**Figure 5**) and category 4 lesions (**Figure 6**). It suggested that the strain elastography and VTQ technique could be used to help re-regulate the BI-RADS category of breast lesions. With a higher sensitivity, strain elastography could reduce the false negative rate of malignant lesions. While VTQ technique could reduce the false positive rate of benign lesions and avoid unnecessary biopsies with a higher specificity.

As tumor tissue stiffness is recently regarded as a representative feature of tumor microenvironments, it is mainly regulated by interactions among tumor cells, stromal cells and extracellular matrix [7]. In this study, we also found that there were significant differences in SR and SWV in different pathological types. The stiffness were: invasive ductal carcinomas > intraductal papillomas > fibroadenomas. This finding suggested that maybe elastography methods could do help to characterize the pathological type of the breast lesions. But this hypothesis needs further validation with a large sample size study.

There were some limitations to the present study. Firstly, as a preliminary study, there were a relatively small sample size. Secondly, although our sonographers was experienced and had standardized the protocols of elastography examination, some differences (such as pressure applied, transducer position) still existed. Lastly, limited by the elastography modality, lesions larger than 45.0 mm and deeper than 40.0 mm couldn't be included.

Conclusions

In conclusion, both strain elastography and VTQ technique could improve the specificity and accuracy in the differentiation of benign and malignant breast lesions. The diagnostic performance of the two elastography methods were almost equal. But VTQ technique showed higher specificity but lower sensitivity than strain elastography. These two methods could be used to help to re-regulate the BI-RADS category of breast lesions, especially for equivocal BI-RADS category 3 and category 4 breast lesions.

Disclosure of conflict of interest

None.

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