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ORIGINAL ARTICLE

Breast Sonoelastography: Our Preliminary Experience in 155 Lesions

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ABSTRACT

Objectives: *To determine whether shear wave velocity is correlated with the ultrasound Breast Imaging–Reporting and Data System (BIRADS) grading and pathology result, and to establish a cutoff value to distinguish benign and malignant lesions.*

Methods: *This prospective study was conducted from November 2014 to March 2015 in a regional hospital in Hong Kong. Women with ultrasound-identified breast lesions were included. Ultrasound followed by sonoelastography was performed for all patients. Patient demographics, ultrasound findings, shear wave velocities, and cytology and histology results were analysed. Receiver operating characteristic curves were plotted to determine a cutoff value.*

Results: *Overall, 97 patients with 155 lesions were included. Pathology results were available for 61 benign and 27 malignant lesions. BIRADS grade 4 and 5 lesions had higher maximum (3.94 vs. 2.95 m/s; p = 0.029) and mean shear wave velocity (3.66 vs. 2.69 m/s; p = 0.023) than that of BIRADS 2 and 3 lesions. BIRADS grading had a moderate positive correlation with both maximum and mean shear wave velocity in sonoelastography (ϱ = 0.304 and 0.308; both p = 0.0001). Histologically proven malignant lesions had higher maximum (5.75 vs. 2.87 m/s; p < 0.0001) and mean shear wave velocity (5.36 vs. 2.62 m/s; p < 0.0001) than that of benign lesions. Based on the 88 lesions with pathology results, B-mode ultrasound BIRADS alone had a sensitivity of 100%, specificity of 42.6%, positive predictive value of 43.5%, and negative predictive value of 100%. With a cutoff velocity of 2.98 m/s, sonoelastography achieved a sensitivity of 88.9% and specificity of 60.7%. Applying this to BIRADS 4a lesions, specificity of BIRADS improved to 73.8% while sensitivity dropped to 88.9%.*

Conclusion: *Shear wave velocity is correlated with ultrasound BIRADS grading and final pathology. A cutoff at 2.98 m/s achieved a sensitivity of 88.9% and specificity of 60.7% for malignancy detection.*

Key Words: *Breast diseases; Breast neoplasms; Elasticity imaging techniques; Ultrasonography*

中文摘要

乳腺超聲彈性成像：155個病變的初步經驗

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目的：探討剪力波的波速是否與超聲乳腺影像報告和數據系統（BIRADS）的分級和病理結果相關，並設立截斷值用作鑒別良惡性病變。

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方法：這項前瞻性研究於2014年11月至2015年3月在香港一所分區醫院內進行。研究對象為經超聲成像證實有乳腺病變的婦女，於乳房超聲彈性成像之前，先行常規超聲檢查。分析患者人口學數據、超聲結果和剪力波的波速，以及細胞學和組織學結果。繪製ROC曲線以找出截斷值。

結果：總計97名患者的155例病變納入研究。當中61個良性和27個惡性病變有病理學結果。BIRADS 4級和5級病變的最大剪力波波速（3.94比2.95 m/s；p=0.029）和剪力波平均波速（3.66比2.69 m/s；p=0.023）均大於BIRADS 2級和3級病變。乳房超聲彈性成像方面，BIRADS分級與最大波速和平均波速呈中度正相關（ϱ=0.304和0.308，兩者皆為p=0.0001）。組織學證實的惡性病變最大波速（5.75比2.87 m/s；p<0.0001）和平均波速則更高（5.36比2.62 m/s；p<0.0001）。根據88例病理學結果，單獨運用乳房B-mode超聲BIRADS分級的靈敏度為100%，特異度42.6%，陽性預測值43.5%，陰性預測值100%。剪力波的波速截斷值為2.98 m/s時，乳腺超聲彈性成像的靈敏度可達88.9%，特異性為60.7%。將其應用於BIRADS 4a級乳腺病變，BIRADS的特異性提高至73.8%，靈敏度則降至88.9%。

結論：剪力波的波速與超聲BIRADS分級和最終病理學結果相關。剪力波的波速截斷值為2.98 m/s時，BIRADS對惡性腫瘤檢測的靈敏度為88.9%，特異性為60.7%。

INTRODUCTION

Ultrasound has a long established role in the assessment of breast lesions. With the use of the Breast Imaging–Reporting and Data System (BIRADS) criteria proposed by the American College of Radiology for lesion characterisation, ultrasound can achieve a high sensitivity in the detection of malignancy despite a low specificity.[1]

Sonoelastography is a newer development that measures the stiffness of tissue.[2,3] Malignant lesions often alter tissue stiffness and are usually stiffer than benign lesions. This constitutes the basic hypothesis of sonoelastography which can be used to differentiate benign and malignant lesions.[4,5]

There are two types of sonoelastography: strain elastography and shear wave elastography. Shear wave elastography measures propagation speed of shear wave within the tissue to quantify its stiffness in kilopascals (kPa) or metres per second (m/s).[1]

To our knowledge, there are currently no local data on the use of elastography in breast lesion characterisation. The aim of this study was to prospectively determine the correlation between shear wave velocity and ultrasound BIRADS grading and final pathology. Our secondary aim was to establish a cutoff value to distinguish benign and malignant lesions.

METHODS

Study Design and Study Population

This prospective study was approved by a local research ethics committee and was carried out in the Department of Diagnostic and Interventional Radiology at Kwong Wah Hospital, Hong Kong SAR, from 1 November 2014 to 31 March 2015. Patients older than 18 years with breast lesions identified on B-mode ultrasound were invited to take part. Patients with skin lesions, breast implants, or who were currently on chemotherapy or radiotherapy were excluded. The patients provided written informed consent, and approval was obtained from the local ethics committee.

B-mode Ultrasound and Sonoelastography

All ultrasound examinations were performed with an ultrasound unit ACUSON S3000 Ultrasound System (Siemens Medical Solutions, Inc., Mountain View [CA], USA). Standard B-mode ultrasound was first performed. Breast lesions were characterised according to BIRADS criteria and a BIRADS grading was assigned.

Sonoelastography was then performed with a 9-MHz linear transducer using the same ultrasound unit with Virtual Touch Imaging Quantification (VTIQ) software (Siemens Medical Solutions, Inc., Mountain View [CA], USA). VTIQ is an acoustic radiation force impulse imaging technique. The transducer generates a push pulse that travels through the tissue. This creates

displacement within the tissue and induces a shear wave that travels perpendicular to the initial push pulse. VTIQ measures the speed of the perpendicular shear wave by a detection pulse[6,7] that is proportional to the square root of tissue elasticity.[8] A single operator performed all sonoelastography examinations. Patients were instructed to hold their breath during the acquisition of elastogram. Shear wave velocities of the lesion were then measured by placing a fixed size (5 mm x 5 mm) region of interest over the stiffest part of the lesion. Five measurements were obtained.

Data Collection and Statistical Analysis

Patient demographic data and ultrasound lesion characteristics including BIRADS grading were recorded. Maximum and mean shear wave velocities of the lesions were noted. Cytology or histology examination results, if any, were retrieved from electronic patient records and analysed.

We broadly classified BIRADS 2 and BIRADS 3 lesions as BIRADS benign lesions and BIRADS 4 and BIRADS 5 lesions as BIRADS malignant lesions. Maximum and mean shear wave velocities of BIRADS benign lesions were compared with those of BIRADS malignant lesions. For lesions with cytology or histology results, maximum and mean shear wave velocities were compared between benign pathology lesions and malignant pathology lesions. The correlation between BIRADS grading and shear wave velocity was also analysed.

B-mode ultrasound BIRADS grading performance including sensitivity, specificity, positive predictive value, and negative predictive value was analysed based on lesions with cytology or histology results.

Diagnostic performance of maximum and mean shear wave velocities was analysed by plotting receiver operating characteristic (ROC) curves and obtaining the area under ROC curves. Based on the ROC curve for maximum shear wave velocity, we extrapolated a cutoff velocity that could help differentiate benign and malignant lesions. We then applied this cutoff velocity to all BIRADS 4a lesions and assessed the impact on overall B-mode ultrasound diagnostic performance.

Descriptive data are expressed as mean values. Student *t* test and Mann-Whitney *U* test were used for parametric and non-parametric data, respectively. Spearman's rank correlation was used to test correlation. All statistical analyses were performed with the Statistical Package for the Social Sciences (Windows version 22.0; SPSS Inc, Chicago [IL], USA). A 2-sided p value of <0.05 was considered statistically significant.

RESULTS

Patient Demographics and Ultrasound Lesion Characteristics

A total of 155 breast lesions in 97 female patients were included in the study. Their mean age was 51.3 years (range, 29-96 years). The mean value of maximum diameter of the breast lesions was 1.5 cm (range, 0.3-14.1 cm). BIRADS grading of the lesions are listed in Table 1.

Pathology results were available in 88 (56.8%) lesions that included 27 BIRADS 3 lesions, 49 BIRADS 4 lesions (42 BIRADS 4A, 4 BIRADS 4B, and 3 BIRADS 4C), and 12 BIRADS 5 lesions. Of these 88 lesions, 61 were benign and 27 were malignant in the final pathology. Patients with a malignant lesion were significantly older than those with a benign lesion (62.8 vs. 49.3 years; p = 0.0001). Malignant lesions were significantly larger than benign lesions (3.21 vs. 1.15 cm; p = 0.00005). Pathology results of the 27 malignant lesions are shown in Table 2.

Correlation between BIRADS Grading and Shear Wave Velocities

BIRADS grading and maximum and mean shear wave velocities had a significant moderate positive correlation (ρ=0.304 and 0.308; both p = 0.0001).

Table 1. BIRADS grading of all 155 lesions.

BIRADS grading	No. (%) of lesions
2	12 (7.7)
3	62 (40.0)
4	
A	60 (38.7)
B	6 (3.9)
C	3 (1.9)
5	12 (7.7)

Abbreviation: BIRADS = Breast Imaging–Reporting and Data System.

Table 2. Summary of pathology of 27 malignant lesions.

Pathology	No. (%) of lesions
Invasive ductal carcinoma, no special type	22 (81.5)
Cribriform carcinoma	1 (3.7)
Metaplastic carcinoma	1 (3.7)
Neuroendocrine carcinoma	1 (3.7)
Ductal carcinoma in-situ	2 (7.4)

BIRADS Benign Versus Malignant Lesions

The maximum and mean (± standard deviation) shear wave velocity in BIRADS benign lesions was 2.95 ± 1.20 m/s and 2.69 ± 1.04 m/s respectively, while those for BIRADS malignant lesions were 3.94 ± 2.43 m/s and 3.66 ± 2.36 m/s. The differences between maximum and mean shear wave velocities between groups were statistically significant ($p = 0.029$ and $p = 0.023$, respectively).

Benign Pathology Versus Malignant Pathology Lesions

The maximum and mean shear wave velocity in benign pathology lesions was 2.87 ± 1.44 m/s and 2.62 ± 1.26 m/s, respectively. Those for malignant pathology lesions were 5.75 ± 2.85 m/s and 5.36 ± 2.86 m/s, respectively. Again, the differences were statistically significant (both were $p < 0.0001$).

Diagnostic Performance

Based on the 88 lesions with pathology results, B-mode ultrasound BIRADS grading achieved a sensitivity of 100%, specificity of 42.6%, positive predictive value of 43.5%, and negative predictive value of 100%.

The Figure shows the ROC curves of maximum and mean shear wave velocities. Area under ROC curve was 0.849 for maximum shear wave velocity and 0.842 for mean shear wave velocity, suggesting good diagnostic performance.

Based on the ROC curve for maximum shear wave velocity, a cutoff velocity of 2.98 m/s was selected in order to achieve a reasonable sensitivity of 88.9% and specificity of 60.7%. We applied this cutoff value to the 42 BIRADS 4a lesions: 31 lesions were downgraded to BIRADS 3. Addition of shear wave velocity measurement to B-mode ultrasound BIRADS grading improved the specificity to 73.8% while sensitivity dropped to 88.9%.

DISCUSSION

In Hong Kong, breast cancer is the commonest cancer in females and ranked the third most common cause of cancer-related death in female patients.[9] Early detection of breast cancer can improve prognosis of patients.[10] Ultrasound is an appealing imaging modality with the advantages of low cost, no radiation, and being easy to perform and non-invasive. One major drawback is low specificity, however.[1]

Sonoelastography complements conventional B-mode ultrasound by providing information about lesion mechanical properties. Strain elastography requires continuous transducer compression or external mechanical compression through respiratory

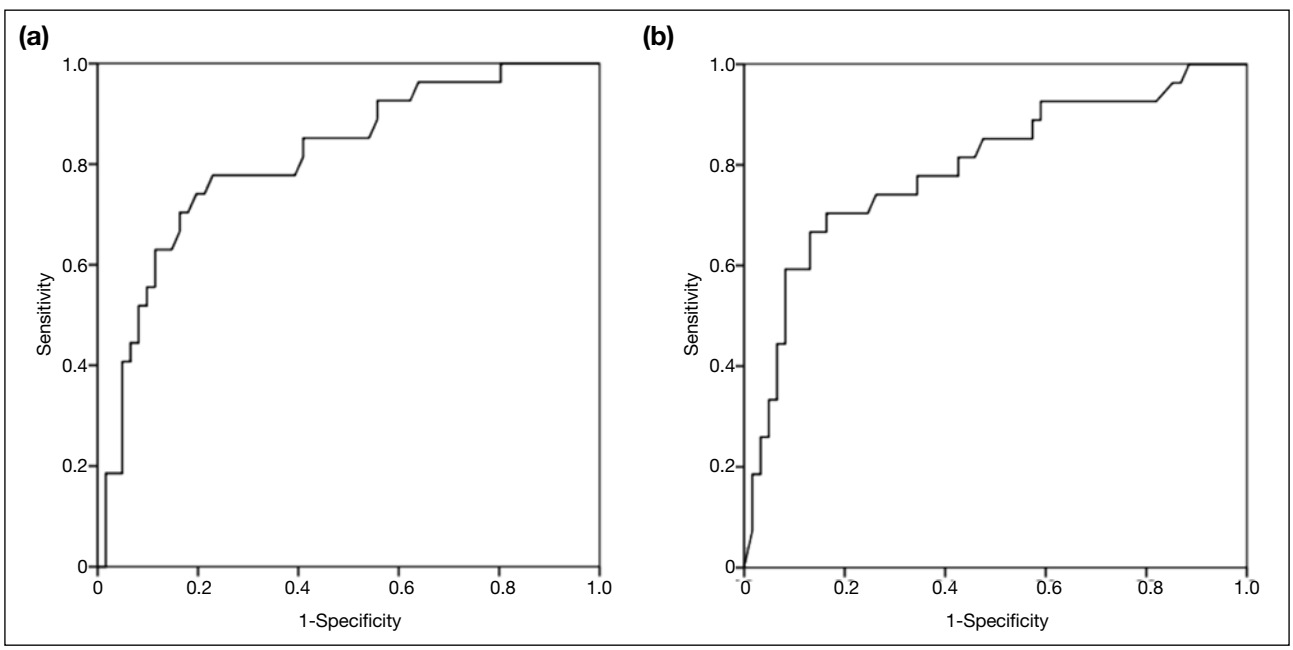

Figure. Receiver operating characteristic curves of (a) maximum and (b) mean shear wave velocity.

movements and cardiac pulsations.[6,11] Disadvantages of this technique are that compression cannot be quantified and the compression site cannot be restricted to the area of interest, leading to movement of the target and distortion of measured results. Shear wave elastography employs automatically generated impulses to induce shear waves within the area of interest[6] and therefore does not rely on the operator to apply appropriate manual pressure. Moreover, quantitative measurements such as shear wave speed measured in m/s are available in shear wave elastography.

In our study, a single operator performed all sonoelastography; hence reproducibility of shear wave velocity measurements was not examined. Tozaki et al[12] showed that shear wave elastography is highly reproducible with an intraclass correlation coefficient of 0.87. Several other studies have also confirmed the reproducibility of shear wave elastography.[4,13]

All sonoelastography techniques are based on the hypothesis that malignant lesions are stiffer than benign lesions.[4,5] Invasive ductal carcinoma, accounting for approximately 80% of all breast cancers, frequently elicits a desmoplastic reaction and fibrosis in the adjacent stroma. Chamming's et al[14] has shown that stiffness of breast cancer is positively correlated with tumour growth and proportion of fibrosis within the tumour and negatively correlated with necrotic components.

We applied the cutoff value of 2.98 m/s to all BIRADS 4a lesions. There were five false-positive cases (fibroadenoma) and three false-negative cases (invasive ductal carcinoma). Yoon et al[15] demonstrated that a false-positive result was associated with the size of the lesion and false positivity was more common in lesions of >2 cm. Nonetheless, only one false-positive case in our study had maximum dimension of >2 cm. We postulated that the false-positive cases of fibroadenoma in our study were more hyalinised and hence stiffer on elastography. Yoon et al[15] also found that false negativity was associated with smaller lesion size and farther distance from nipple. All the three missed cases had maximum diameter of <1 cm and two of them were 7 cm and 8 cm away from nipple. These factors could partly explain our false-negative results. Moreover, intrinsic soft tumour characteristics — such as those in early stage breast cancer, cancer with internal necrosis and mucinous carcinoma — could give rise to false-negative elastography results.[13,16,17] These might limit the use of shear wave elastography in breast lesion characterisation. We anticipate future large-scale studies on malignancy detection with shear wave elastography in lesions with less suspicious B-mode ultrasound features to address these issues.

There is a wide range of recommended cutoff values to differentiate benign from malignant lesions in the published literature, ranging from 2.89 m/s to 6.37 m/s.[4,12,18-20] This can probably be explained by the differences in the BIRADS categories and histological findings of lesions included in different studies. Our preliminary result of cutoff velocity of 2.98 m/s is in accordance with these studies. At present, elastography is mainly an investigational tool in breast lesion assessment. The latest version of BIRADS also includes 'elasticity assessment' in its ultrasound lexicon[21] in order to provide a framework for future research. Our preliminary results require further validation by future studies with longitudinal follow-up before application to clinical practice.

Our study has several limitations. First, size of malignant and benign lesions was different. This could be partly because we were just starting to use breast sonoelastography. Only a small number of eligible patients were available. We, however, do not believe that size of lesion alone could fully explain the difference in shear wave velocity results. Second, there were only 88 lesions with pathology results available and only 27 malignant lesions were included. Some patients opted for management in the private sector after the initial assessment and were lost to follow-up. Pathology results were not available in all BIRADS 2 lesions. These led to a small sample size that might affect the assessment of diagnostic performance of B-mode ultrasound BIRADS grading and shear wave velocities. In our centre, a 6-month follow-up ultrasound scan is recommended for BIRADS 3 lesions. Subjects with BIRADS 3 lesions were not due for follow-up scan at the time of data analysis. Some lesions might be upgraded during follow-up scanning and this would affect the assessment of diagnostic performance of B-mode ultrasound BIRADS grading. Last, we included a heterogeneous spectrum of breast cancers with different histological subtypes and grading. This might have some bearing on the diagnostic performance of shear wave velocity as well as the final extrapolated cutoff value. Future studies with more patients and lesions will be helpful to validate our results.

CONCLUSION

This is the first local study of the use of elastography in breast lesion characterisation. Our preliminary results show that shear wave velocity is correlated with BIRADS grading and final pathology. A cutoff velocity of 2.98 m/s can achieve a sensitivity of 88.9% and specificity of 60.7% in malignancy detection. Sonoelastography can potentially be used to improve ultrasound specificity.

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