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● *Original Contribution*

# QUANTIFICATION OF ACOUSTIC RADIATION FORCE IMPULSE IN DIFFERENTIATING BETWEEN MALIGNANT AND BENIGN BREAST LESIONS

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**Abstract—The aim of this study was to evaluate the use of gray-level quantification (GLQ) in virtual touch tissue imaging (VTI) in the differential diagnosis of breast lesions. GLQ values of 153 lesions (101 benign, 52 malignant) were analyzed with matrix laboratory software (MATLAB, The MathWorks, Natick, MA, USA), with gray levels ranging from 0 (pure black) to 255 (pure white). The diagnostic performance of GLQ was also evaluated using receiver operating characteristic curve analysis. The mean GLQ value for benign lesions (103.27 ± 39.44) differed significantly from that for malignant lesions (44.57 ± 13.61) ($p < 0.001$). At a cutoff value of 52.31, the sensitivity, specificity, accuracy, positive predictive value and negative predictive value were 86.5%, 93.1%, 90.8%, 86.5% and 93.1%, respectively. In conclusion, we have proposed a method for quantification of gray levels in VTI for the differential diagnosis of breast lesions. Our results indicate that this method has the potential to aid in the classification of benign and malignant breast masses. (E-mail: ultra304@sina.com) Crown Copyright © 2014 Published by Elsevier Inc. on behalf of World Federation for Ultrasound in Medicine & Biology**

***Key Words:*** **Breast lesion, Acoustic radiation force impulse, Quantification, Gray level, Ultrasound, Strain elastography.**

## INTRODUCTION

Ultrasonography (US) has emerged as the most important adjunct to mammography in the diagnosis of breast lesions (Flobbe et al. 2002). Two-dimensional US can be used to obtain morphologic information on the breast, but cannot determine tissue stiffness. In general, benign lesions of the breast tend to be softer than malignant lesions (Sewell 1995).

Breast elastography is a new technique that can be used to determine the stiffness of targeted areas and has been found to be of clinical value in characterizing breast lesions as benign or malignant (Alhabshi et al. 2013; Barr and Zhang 2012; Barr et al. 2012; Parajuly et al. 2012). In strain elastography imaging (EI), a compressive force is applied to the tissue, and the shape-deforming effect on the tissue is measured, yielding a qualitative value for the stiffness of the lesion. The compressive force can be applied manually or with a "push" ultrasound force (acoustic radiation force impulse) (Barr et al. 2012; Jin et al. 2012).

In acoustic radiation force impulse (ARFI) imaging, tissue stiffness is evaluated by using short-duration acoustic pulses to generate small (1–10 $\mu$m) localized tissue displacements instead of external compression (Nightingale et al. 2002). The tissue's response to this radiation force is observed using conventional B-mode US imaging pulses to track tissue displacement, which correlates with local stiffness of the tissue. The waves generated can produce either a qualitative response (gray-scale map) by virtual touch tissue imaging (VTI) or a quantitative response by virtual touch tissue quantification (VTQ), depending on how they interact with the transducer (Palmeri et al. 2008; Zhai et al. 2008). In VTI, tissue stiffness is expressed using gray-level imaging, which should not be affected by equipment gain. The greater the stiffness, the darker is the gray level (Tozaki et al. 2011a, 2011b). Tissue stiffness for VTQ is expressed as shear wave velocity (m/s). Measurement of the time to peak displacement at each lateral location is used to calculate the shear wave velocity of VTQ within the tissue (D'Onofrio et al. 2010).

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Because the gray level of virtual touch images is correlated with tissue stiffness, we hypothesized that gray-level quantification (GLQ) can be used to differentiate benign from malignant lesions. To the best of our knowledge, previous studies of VTI have focused mainly on area ratio (EI/B-mode) and semi-quantification of gray levels (Barr 2010; Meng et al. 2011; Tozaki et al. 2011a, 2011b). Classification of benign and malignant breast tumors using GLQ in VTI has not been reported. The main purpose of this study, therefore, was to assess the potential of GLQ in such classification.

## METHODS

### *Patients*

The study was approved by the ethics committee of our hospital, and all the patients gave informed consent. Between December 2010 and June 2013, ARFI imaging was performed after conventional B-mode US in 151 consecutive women with breast lesions. Four patients were excluded from the study group for a lack of pathologic results. The final study group consisted of 147 patients (mean age: 45.3 y, range: 21–80 y) with a total of 153 breast lesions (101 benign, 52 malignant).

### *Pathologic diagnoses*

All breast lesions were confirmed histologically by means of surgery or biopsy. Lesions were first classified as malignant or benign and then were divided into subgroups as described in Table 1. All diagnoses were made by a pathologist with 15 y of experience in breast pathologic examination.

### *Data acquisition*

Virtual touch images were obtained with the Acuson S2000 US system (Siemens Medical Solutions, Mountain View, CA, USA) with a linear array transducer (9 L4, 7–9 MHz) by one sonographer with 25 y of experience in the performance of breast ultrasound. For data acquisition, conventional US scanning was performed with patients in the supine position with both breasts fully exposed. When a clear image of the target lesion appeared on the screen, the VTI button was pressed and a region of interest (ROI) was delineated around the lesion, making sure that the ROI included sufficient surrounding breast tissue. For good imaging results, the probe should be applied with slight pressure and the patient should hold her breath; the virtual touch image appears to the right of the corresponding B-mode US image on the monitor. After each examination, the sonographer who performed elastography selected one representative image of the lesion. The image was sent to a picture archiving and communication system and saved as bit-map file on hard disk for further quantitative analysis.

Table 1. Histologic results for malignant and benign breast lesions*

| Benign lesions (n = 101) | | Malignant lesions (n = 52) | |
|---|---|---|---|
| Histopathologic diagnosis | n | Histopathologic diagnosis | n |
| Fibroadenoma | 76 | Invasive ductal carcinoma | 43 |
| Mastitis | 9 | Ductal carcinoma *in situ* | 4 |
| Fibrocystic mastopathy | 7 | Medullary carcinoma | 5 |
| Lobular hyperplasia | 9 | | |

* Sensitivity = 86.5%, specificity = 93.1%, accuracy = 90.8%, positive predictive value = 86.5%, negative predictive value = 93.1%, true positives = 45, false positives = 7, true negatives = 94, false negatives = 7.

### *Computer-aided quantification*

Images were analyzed using matrix laboratory software (MATLAB, The MathWorks, Natick, MA, USA). The processing procedure was programmed, and the mask and histogram tools of this software were used. The details of the operating procedure are as follows: First, the virtual touch image is opened using MATLAB. Second, the cursor is placed over the area of the lesion, the enter key is pressed once and the cursor is moved continuously in the lesion area until this area is completely red. The left key of the mouse is then pressed once, and the mean gray level value of the lesion is automatically displayed on the monitor (Woo et al. 2010).

### *Intra- and inter-observer reproducibility of method*

To determine intra-observer reproducibility, two GLQs were performed for each lesion, for all patients, by the same operator. Inter-observer reproducibility was also assessed independently by two operators, who performed GLQs for every lesion in all patients.

### *Statistical analysis*

Statistical analyses were carried out using professional statistical software (SPSS for Microsoft Windows, Version 19.0, Chicago, IL, USA). A $p$-value $< 0.05$ was considered to indicate a statistically significant difference. Means and standard deviations of GLQ values were calculated for the malignant and benign lesions. Significant differences in values between malignant and benign lesions were evaluated with an independent-sample Student $t$-test. Intra- and inter-observer reproducibility was assessed using correlation coefficient analysis. Receiver operating characteristic (ROC) curve analysis was adopted to evaluate the ability of the GLQ value to distinguish between malignant and benign lesions. The best cutoff point was obtained from ROC curve analysis using Youden's index.