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● *Original Contribution*

ANISOTROPIC PROPERTIES OF BREAST TISSUE MEASURED BY ACOUSTIC RADIATION FORCE IMPULSE QUANTIFICATION

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Abstract—The goal of our study was to investigate the anisotropy of normal breast glandular and fatty tissue with acoustic radiation force impulse (ARFI) quantification. A total of 137 breasts in 137 women were enrolled. These breasts were divided into the duct-apparent group and the duct-inapparent group, divided into the ligament-apparent group and the ligament-inapparent group. Shear wave velocity (SWV) in the radial (SWV^r) and anti-radial (SWV^{a-r}) directions was measured. The elastic anisotropy of glandular tissue and fatty tissue was evaluated as the ratio between SWV^r and SWV^{a-r}. The SWV ratio was 1.30 ± 0.45 for glandular tissue and 1.27 ± 0.53 for fatty tissue in the total group. In glandular tissue, the SWV ratio of the duct-apparent group was higher than that of the duct-inapparent group ($p = 0.011$). In both glandular and fatty tissue, the SWV ratio was higher in the ligament-apparent group than in the ligament-inapparent group ($p < 0.05$ for both). SWV^r was higher than SWV^{a-r} in both glandular tissue and fatty tissue in all groups ($p < 0.05$ for all) except in breast fatty tissue in the ligament-inapparent group ($p = 0.913$). It is concluded that both breast glandular tissue and fatty tissue exhibited anisotropy of elastic behavior. To improve the diagnostic power of elastography in breast lesions, the elastic anisotropy of glandular tissue and fatty tissue should be taken into account in calculating strain ratio or elasticity ratio. (E-mail: shanghairuijin@126.com) © 2016 World Federation for Ultrasound in Medicine & Biology.

Key Words: **Breast imaging, Ultrasound, Elastography, Acoustic radiation force impulse, Shear wave speed, Anisotropy.**

INTRODUCTION

Ultrasound plays a very important role in breast lesion characterization (Hooley et al. 2013). Breast ultrasound elastography, a new ultrasound imaging technique providing information on stiffness, has become a routine tool in addition to conventional ultrasound in clinical practice (Barr et al. 2015; Cosgrove et al. 2013; Hooley et al. 2013; Li et al. 2013; Sadigh et al. 2012). Strain elastography and shear wave elastography are the two types of elastography currently available. In strain elastography, in addition to qualitative elasticity score, the semiquantitative strain ratio is employed to discriminate benign and malignant breast lesions. The strain ratio is calculated by comparing the strain of the lesion with that of the adjacent normal glandular tissue or fatty tissue (Zhi et al. 2008). Similarly, in some studies using shear wave elastography, glandular tissue or fatty tissue is used as the reference normal tissue to calculate the shear wave velocity (SWV) ratio (Jin et al. 2012) or the elastic modulus ratio (Youk et al. 2013).

The aforementioned studies, however, do not take into account the possibility of anisotropy (*i.e.,* the tissue's material properties are orientation dependent) in breast glandular tissue or fatty tissue. It is commonly known that anisotropy in biological tissue is a rule more than an exception (Gennisson et al. 2003; Levinson 1987). This anisotropy is a consequence of the orientation of the tissue fibers (Bouchard et al. 2009; Gennisson et al. 2010; Mace et al. 2011). The breast is composed of glandular and fatty tissue fixed by fibrous bands known as Cooper's ligaments. The glandular tissue is drained by ducts that are arranged in a radial fashion (Going 2011; Love and Barsky 2004). Similarly, Cooper's ligaments are distributed in a radial orientation in the whole breast (Oliveira et al. 2012). Therefore, we hypothesized that breast glandular and fatty tissue might exhibit an anisotropic elasticity distribution, which might have an effect on the diagnostic performance of elastography using strain ratio or elasticity ratio.

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To the best of our knowledge, to date there has been no research exploring the anisotropic property of normal breast tissue using ultrasound shear wave elastography. Few studies have investigated the elastic anisotropy of breast tissue using ultrasound, and all were focused on detecting the anisotropy of only breast lesions, not normal breast tissue (Skerl et al. 2013, 2016). These studies indicated that malignant breast lesions are more anisotropic than benign lesions. Therefore, anisotropy has the potential to be used to differentiate benign from malignant solid breast masses using shear wave elastography. The aim of this study was to investigate the anisotropy of normal breast glandular and fatty tissue with acoustic radiation force impulse (ARFI) quantification technology.

METHODS

Patients and study design

This prospective study was carried out from July 2013 to September 2013. Our institutional ethics committee approved this study, and all participants were provided with written informed consent. All participants were women and recruited prospectively from the outpatient center at the Comprehensive Breast Center of our hospital. These patients were referred to the breast clinic because of symptoms and/or screen-detected abnormalities. The enrollment criteria were as follows: (i) female, at least 18 y old; (ii) non-lactating; (iii) no current pregnancy; (iv) no breast implants; (v) no history of breast surgery. A total of 230 consecutive women were initially enrolled in this study based on these criteria.

All 230 participants were examined with gray-scale ultrasound followed by ARFI quantification technology (Virtual Touch tissue quantification [VTQ]) using the ACUSON S2000 ultrasound scanner system (Siemens Medical Solutions, Mountain View, CA, USA). Both breasts were carefully scanned with a 9 L4 linear probe. In addition to examination of the suspicious area in the breast, particular attention was paid to evaluation of the breast ducts in the glandular tissue and Cooper's ligaments in the subcutaneous fatty tissue. Both the ducts and Cooper ligaments were classified as apparent or inapparent based on their ultrasound appearance (Figs. 1 and 2). Because the region of interest (ROI) of VTQ has a fixed size of 5 mm $\times$ 6 mm width, 25 women with either breast glandular tissue or fatty tissue thickness $<$5 mm on gray-scale ultrasound were excluded from the study. Of the remaining 205 woman, 68 with bilateral breast masses were excluded. Thus, 137 women underwent the following ARFI examination. For 78 women with unilateral breast masses on gray-scale ultrasound, the breast tissues of the mass-free breast were selected for ARFI examination; for 59 women with no mass in either breast, the tissues of randomly selected breasts were assessed. Finally, 137 breasts in 137 women (mean age, 44.28 $\pm$ 12.03 y; age range, 18–74 y) were enrolled in this study. Both gray-scale ultrasound and ARFI examinations were performed by one radiologist (J.Q.Z.) with 15 y of experience in breast ultrasound.

These 137 breasts were divided into the duct-apparent group and the duct-inapparent group on the basis of ultrasound appearance of the breast ducts, divided into the ligament-apparent group and the ligament-inapparent group based on the ultrasound appearance of Cooper's ligaments. Moreover, four subgroups were further established based on different combinations: group A, breasts with apparent ducts and apparent Cooper's ligaments; group B, breasts with apparent ducts and inapparent Cooper's ligaments; group C, breasts with inapparent ducts and apparent Cooper's ligaments; group D, breasts with inapparent ducts and inapparent Cooper's ligaments.

In the ARFI examination, VTQ was performed to measure the SWV (m/s), which increases with tissue stiffness, of breast glandular and fatty tissue by moving the ROI (5 $\times$ 6 mm) within the field of the gray-scale ultrasound image. The elastic anisotropy of glandular tissue and fatty tissue was evaluated by calculating the SWV ratio, the ratio between the SWV in the radial direction (SWV^{r}) and SWV in the anti-radial direction ($SWV^{a\text{-}r}$).

In measuring the SWV ratio of glandular tissue, the ROI was moved to ensure that at least one duct was included in the ROI for the duct-apparent group (Fig. 1); the ROI was placed in a random area of the glandular tissue for the duct-inapparent group (Fig. 2). The SWV of glandular tissue was measured by placing the ROI in the target glandular tissue first in the radial plane and then in the anti-radial plane. The SWV ratio of fatty tissue was measured using a similar procedure, in which fatty SWV was measured by placing the ROI in the target fatty tissue in both the radial and anti-radial planes. For the ligament-apparent group, special care was taken to ensure that Cooper's ligaments were included in the ROI (Fig. 2); for the ligament-inapparent group, the ROI was placed in random area of the fatty tissue (Fig. 1).

During ARFI examination, patients were asked to hold their breath, and the transducer was gently applied to breast skin using as little pressure as possible. SWV was measured three times at each sampling, and the mean value was recorded for statistical analysis.

Statistical analyses

SWV^{r} and $SWV^{a\text{-}r}$, in both glandular and fatty tissue, do not follow a normal distribution. The Wilcoxon signed-rank test was used to assess the difference between SWV^{r} and $SWV^{a\text{-}r}$ in both glandular and fatty tissue, to compare SWV^{r} and $SWV^{a\text{-}r}$ between glandular