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● *Original Contribution*

PRE-OPERATIVE EVALUATION OF AXILLARY LYMPH NODE STATUS IN PATIENTS WITH SUSPECTED BREAST CANCER USING SHEAR WAVE ELASTOGRAPHY

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Abstract—The aim of this study was to evaluate shear wave elastography (SWE) for pre-operative evaluation of axillary lymph node (LN) status in patients with suspected breast cancer. A total of 130 axillary LNs in 130 patients who underwent SWE before fine-needle aspiration, core biopsy or surgery were analyzed. On gray-scale images, long and short axes, shape (elliptical or round), border (sharp or unsharp) and cortical thickening (concentric, eccentric or no fatty hilum) of LNs were assessed. On SWE, mean, maximum, minimum, standard deviation and the lesion-to-fat ratio (E_{ratio}) values of elasticity were collected. Gray-scale and SWE features were compared statistically between metastatic and benign LNs using the χ^2-test and independent *t*-test. Diagnostic performance of each feature was evaluated using the area under the receiver operating characteristic curve (AUC). Logistic regression analysis was used to determine gray-scale or SWE features independently associated with metastatic LNs. Of the 130 LNs, 65 (50%) were metastatic and 65 (50%) were benign after surgery. Metastatic LNs were significantly larger ($p = 0.018$); had higher elasticity indexes at SWE ($p < 0.0001$); and had higher proportions of round shape ($p = 0.033$), unsharp border ($p = 0.048$) and eccentric cortical thickening or no fatty hilum ($p = 0.005$) compared with benign LNs. On multivariate analysis, E_{ratio} was independently associated with metastatic LNs (odds ratio = 3.312, $p = 0.008$). E_{ratio} had the highest AUC among gray-scale (0.582–0.719) and SWE (0.900–0.950) variables. SWE had good diagnostic performance in metastatic axillary LNs, and E_{ratio} was independently associated with metastatic LNs. (E-mail: jhyouk@yuhs.ac) © 2017 World Federation for Ultrasound in Medicine & Biology.

Key Words: **Ultrasonography, Sonoelastography, Shear wave elastography, Axilla, Lymph node.**

INTRODUCTION

In patients with newly diagnosed breast cancer, pre-operative evaluation of axillary lymph node status is critical as an integral component of breast cancer management, including staging, treatment plan and prognosis (Fisher et al. 1983; Humphrey et al. 2014). Ultrasound has been performed for non-invasive pre-operative evaluation of the axillary nodal basin because it is widely available and easily incorporated into the standard workup for breast cancer patients (Moorman et al. 2015). Sonographic criteria based on size (>5 mm) or morphologic characteristics (round, hypo-echoic, with loss of central hilum, eccentric cortical hypertrophy) have exhibited varied diagnostic performance for metastatic lymph nodes (Alvarez et al. 2006). To enhance the diagnostic performance, other ultrasound techniques for axillary lymph nodes have been studied, for example, contrast-enhanced ultrasound, which provides microvascular information on lymph nodes (Ahmed et al. 2014; Matsuzawa et al. 2015). However, this technique has the limitations: it involves the intravenous or intradermal injection of microbubble contrast agent and examination times up to 10 min (Xie et al. 2015).

Ultrasound elastography is an imaging technique used to estimate tissue stiffness by measurement of the degree of distortion under application of external pressure (Chiorean et al. 2016). Elastography in breast ultrasound, either strain elastography or shear wave elastography (SWE), has been used to improve diagnostic confidence and, in particular, to increase the specificity of ultrasound interpretation (Comstock 2011; Youk et al. 2014a, 2014b). For axillary lymph nodes in patients with breast cancer, two previous studies, one *in vivo* and the other *ex vivo*, investigated SWE of sentinel lymph nodes.

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However, ultrasound examinations were not performed on the axillary basin as a pre-operative workup for breast cancer patients in these studies (Kilic et al. 2016; Tourasse et al. 2012). Therefore, the present study was performed to evaluate SWE for pre-operative evaluation of axillary lymph node status in patients with suspected breast cancer.

METHODS

The present retrospective study was conducted with institutional review board approval and a waiver of the need for written informed consent from participants. All patient records and information were made anonymous and de-identified before analysis.

From May 2011 through August 2013, 171 women who had suspected breast cancer or were scheduled for breast cancer surgery were examined by SWE as pre-operative workup for axillary lymph nodes. Among these patients, 130 axillary lymph nodes in 130 women aged 18–84 y (mean, 49.4 ± 11.2 y) were enrolled in the present study. The remaining 43 women were excluded from the study because they had undergone neoadjuvant chemotherapy at the time of SWE (n = 29), had lymph nodes located deeper than 30 mm (there is signal loss with SWE at this depth, n = 7) or underwent SWE for lymph nodes of 30 mm or greater in size that were not fully included in the maximum range of SWE color overlay (n = 7) (Lee et al. 2014).

Ultrasound examinations

Ultrasound examinations were performed using the Aixplorer ultrasound system (SuperSonic Imagine, Aix-en-Provence, France) equipped with a 4- to 15-MHz linear-array transducer, by one of four radiologists with 5–15 y of experience in breast and axillary ultrasound. The investigators knew the results of the clinical examination and mammography at the time of the ultrasound examination. After gray-scale ultrasound images were obtained, SWE images from at least two longitudinal planes were obtained by applying minimal scanning pressure with generous amounts of contact jelly to avoid artefactual stiffness for the most suspicious axillary lymph node when two or more axillary lymph nodes were identified on gray-scale ultrasound. Lymph nodes exhibiting loss of the fatty hilum, a round shape or eccentric cortical thickening were considered suspicious. The loss of fatty hilum was considered the most suspicious, and eccentric cortical thickening was considered the least suspicious. The transducer was kept still for 10–20 s, allowing the SWE image to stabilize. Measurements were performed along the longitudinal axes of lymph nodes to reduce an anisotropic phenomenon yielding different stiffness values depending on the how they were measured, on either the long axis or the short axis (Kilic et al. 2016; Tourasse et al. 2012). The representative image with adequate quality and the fewest artifacts was selected and saved. The built-in region-of-interest (ROI) box (Q-box, SuperSonic Imagine) of the system was set to include the lesion and surrounding normal tissue. Overlain on the gray-scale image was a semi-transparent color map of tissue stiffness with a range from dark blue, indicating the lowest stiffness, to red, indicating the highest stiffness (0–180 kPa). An investigator placed a fixed 2-mm circular ROI over the stiffest part of the lymph node, including the immediate adjacent stiff tissue. Like malignant breast lesions at SWE, malignant lymph nodes can exhibit the "stiff rim sign," that is, increased stiffness at the lesion margin and adjacent tissue on the color elastic map, a well-known sign of malignancy, and the ROI can be set over the stiffest part of the immediate adjacent stiff tissue (Zhou et al. 2014). A second ROI of the same size was placed in the axillary fatty tissue. This allowed calculation of elasticity ratio (E_{ratio}), the ratio between the mean elasticity value in the lymph node and that in fat tissue. The system automatically calculated the mean (E_{mean}), maximum (E_{max}), minimum (E_{min}), and standard deviation (E_{SD}) values of elasticity, in kilopascals, as well as the E_{ratio} for the lymph node.

Image evaluation

Each gray-scale ultrasound image was reviewed by a single radiologist with 10 y of experience in breast ultrasound. During the review session, the radiologist was blinded to clinical and pathologic findings. With respect to gray-scale ultrasound features, the size, shape (elliptical or round), border (sharp or unsharp) and cortical thickening (concentric, eccentric or no fatty hilum) of the lymph node were assessed. Nodal size was defined as length along the longest axis as measured on the images. Shape was determined as the shortest axis/longest axis ratio; a ratio <0.5 indicated an elliptical node, and a ratio ≥ 0.5 indicated a round node. The nodal border was classified as sharp or unsharp compared with surrounding fatty tissue. For evaluation of cortical thickening, the cortex was considered thickened when the thickness at its broadest point was half the transverse diameter of the hilum or greater in the longitudinal plane. Nodes that exhibited focal cortical widening of at least 100% (*i.e.,* the thickness of the cortex at one site was at least double that at its narrowest point) were classified as having eccentric cortical thickening. If the nodal hilum was absent, cortical thickening could not be assessed (Vassallo et al. 1992; Youk et al. 2008). For SWE, E_{mean}, E_{max}, E_{min}, E_{SD} and E_{ratio} of the lymph node were collected.