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● *Original Contribution*

SHEAR WAVE ELASTOGRAPHY AND CERVICAL LYMPH NODES: PREDICTING MALIGNANCY

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Abstract—This prospective study evaluates the accuracy of virtual touch imaging quantification (VTIQ), a non-invasive shear wave elastography method for measuring cervical lymph nodes (LN) stiffness in differentiating benign from malignant LN. The study evaluated 270 LN in 236 patients with both conventional B-mode ultrasound and VTIQ shear wave elastography before fine-needle aspiration biopsy (FNAB). LN stiffness was measured as shear wave velocity (SWV) in m/s. Surgical resection was advised for FNAB results that were not clearly benign. Surgical pathology confirmed 54 malignant LN. The receiver operating curve (ROC) identified a single cut-off value of 2.93 m/s as the maximum SWV for predicting a malignant cervical LN. The sensitivity and specificity were 92.59% and 75.46%, respectively. Positive predictive value (PPV) was 48.54% and negative predictive value (NPV) was 97.60%. LN stiffness measured by VTIQ–generated shear wave elastography is an independent predictor of malignancy. (E-mail: azizi@wilmingonendo.com) **© 2016 The Authors. Published by Elsevier Inc. on behalf of World Federation for Ultrasound in Medicine & Biology. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).**

Key Words: **Lymph node, Malignancy, Shear wave elastography, Fine-needle aspiration biopsy, Ultrasound.**

INTRODUCTION

Assessment of cervical lymph nodes (LN) is essential in patients with head and neck cancer because it predicts prognosis and helps in selection of treatment options (Ishii et al. 1991; Vassallo et al. 1992). B-mode ultrasound (US) imaging is widely used for pre-operative imaging of head and neck cancer (Choi et al. 2013).

Sonographic features of malignant LN include cystic content, spherical shape, central vascularity and calcification. Presence of fatty hilum suggests a benign LN (Ahuja and Ying 2003; Ying and Ahuja 2003).

Papillary thyroid carcinoma (PTC) recurs most frequently at the cervical LN, with a reported recurrence rate of up to 31% in patients. Recent studies revealed that regional LN metastasis predicts lower survival rates (Jung et al. 2015).

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Strain and shear wave elastography investigate differences in the mechanical properties of structures by applying an external force and monitoring the deformation response. Low relative displacement is linked to decreased elasticity and malignancy. This technology has been integrated into conventional US machines (Ianculescu et al. 2014; Krouskop et al. 1998).

Shear wave can quantify velocity and indirectly measure tissue stiffness. Virtual touch imaging quantification (VTIQ) is capable of creating shear wave images and subsequent tissue quantification in one display and allows for identification of regions for measurement of tissue stiffness (Benson and Fan 2012). The use of VTIQ software in the United States was approved by the FDA in June of 2013 (Bell 2013). For this manuscript we decided to use the term VTIQ instead of a generic shear wave term because of some specific features unique to this technology.

Principle of acoustic radiation force impulse elastography

VTIQ is based on the principle of acoustic radiation force impulse (ARFI) technology (Benson and Fan 2012).

Tissue is compressed using an acoustic push beam that is focused at the region of interest (ROI) to maximize the local displacement of tissue *via* the acoustic impulse. In tissue, shear waves travel at a velocity of around 1–10 m/s (Benson and Fan 2012). Using image-based localization and proprietary implementation of ARFI technology, the shear wave speed may be quantified in a precise anatomic region focused on a ROI with a pre-defined 1.5 mm size provided by the system (Sporea et al. 2011).

The VTIQ image is a color-coded display of relative shear wave velocities within the user-defined ROI superimposed onto a conventional B-mode US image. VTIQ is capable of four discrete shear wave display maps: velocity, quality, travel time and displacement (Benson and Fan 2012). The quality map is particularly important to make sure that the VTIQ image quality is appropriate. Several publications have shown that certain disease processes, including malignancy, can alter the elastic properties of tissue (Benson and Fan 2012; Rosen et al. 2008; Wellman et al. 1999).

OBJECTIVE

The purpose of this study was to assess the effectiveness of shear wave elastography with VTIQ, alone and in combination with other B-mode characteristics, in evaluating the risk of malignancy in cervical LN in the setting of a clinical endocrine practice specializing in thyroid disorders.

METHODS

We prospectively evaluated 270 LN in 231 consecutive patients from March 28, 2013 to November 12, 2014. Patients were referred for the following reasons: enlarged cervical LN (90 LN in 76 patients); thyroid nodule (TN) management where LN were found during US exam before FNAB (97 LN in 86 patients); or a history of thyroid carcinoma (TC) when enlarged LN were diagnosed during routine post-operative US exam (83 LN in 69 patients). All patients were evaluated clinically and with US by a single practitioner with more than 16 y of experience in thyroid and neck US, 8 mo experience using SWE routinely before study and whose practice is enriched in thyroid disorders. We selected LN based on US features suspicious for malignancy, and if LN did not have worrisome features, the largest LN was selected for analysis. All LN ≥15 mm in maximal dimension were sampled regardless of B-mode US features and when worrisome B-mode features were present, LN ≥5 mm were biopsied. Our reference standard was the FNAB cytology result or surgical pathology result when FNAB was unable to make a definitive diagnosis.

The *Health Insurance Portability and Accountability Act* compliant study protocol was approved by the Institutional Review Board and patients were studied both before and after the VTIQ technology was approved by the FDA. The FNAB cytopathology result or surgical result when available was considered the reference standard. The inclusion criteria were the presence of LN greater than 5 mm requiring FNAB to exclude malignancy and age 18 y or older. All patients gave written informed consent. The exclusion criteria were non-diagnostic biopsy sample who refused repeat FNAB, atypical/inconclusive FNAB result without definitive diagnosis of cancer or when patient refused recommended surgical resection to have final diagnosis.

Gender, age, and number of US determined LN were noted at the time of initial US examination.

The LN were evaluated for the following B-mode characteristics: size (length and height), cystic content, presence of a fatty hilum, calcifications and location in the neck. The axis ratio is defined as the shortest measurement divided by the longest measurement of the LN. LN were placed into two groups based on an axis ratio ≥0.5 and <0.5.

For power Doppler vascular patterns LN were divided into three groups: group 1 had no blood flow; group 2 had peripheral blood flow only; and group 3 had central blood flow (with or without peripheral vascularity). LN locations in the neck were classified as anatomic levels 2, 3, 4, 5 and 6. Figure 1 shows neck level classification based on American Joint Committee on Cancer recommendations (Som et al. 2000).

Shear wave elastography

Conventional US exam and shear wave elastography were performed with Siemens ACUSON S3000 US system (Siemens Medical Solution, Mountain View, CA, USA). The B-mode features were recorded with an 18 LHD probe. Based on the location of the LN and anatomy of the neck, we used a frequency between 8–17 MHz to assess B-mode and vascularity features. The majority of LN were assessed with a frequency between 12–15 MHz. The shear wave image was created and reproduced twice with a 9 L4 Multi-D probe. Shear wave velocity (SWV) measurement was performed using VTIQ software (Siemens Medical Solution, Mountain View, CA, USA). A small ROI box was used to measure LN tissue velocity. The stiffest area within the LN was measured twice, read 1 and 2, because the ROI box is relatively small (1.5 mm in diameter). The highest velocity was reported as the maximum SWV. Velocity mean was defined as the average of the two LN velocity measurements. The elastography exam was the last part of the US exam before FNAB.

Fine-needle aspiration biopsy procedure

Consent was obtained before performing the procedure. FNAB was performed under sterile conditions with