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● *Original Contribution*

VIRTUAL TOUCH TISSUE IMAGING QUANTIFICATION SHEAR WAVE ELASTOGRAPHY: PROSPECTIVE ASSESSMENT OF CERVICAL LYMPH NODES

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Abstract—The goal of this study was to prospectively evaluate the diagnostic performance of Virtual Touch tissue imaging quantification (VTIQ) shear wave elastography in the discrimination of benign and malignant cervical lymph nodes in routine clinical practice. Shear wave velocity was analyzed using VTIQ in 100 patients with 100 histologically proven cervical lymph nodes. Diagnostic performance was evaluated using receiver operating characteristic curve analysis and leave-one-out cross-validation. Agreement between measurements was assessed with intra-class correlation coefficients. The mean shear wave velocity was significantly higher in metastatic lymphadenopathy (4.46 ± 1.46 m/s) than in benign lymphadenopathy (2.71 ± 0.85 m/s) ($p < 0.001$) at a cutoff level of 3.34 m/s. The cross-validated accuracy, sensitivity and specificity were 77%, 78.9% and 74.4%, respectively. Agreement of measurements with VTIQ was excellent (intra-class correlation coefficient = 0.961). VTIQ shear wave elastography may be a feasible quantitative imaging method for differentiating benign and malignant cervical lymph nodes. (E-mail: jehee23@gmail.com)   © 2015 World Federation for Ultrasound in Medicine & Biology.

Key Words: **Head and neck, Malignant, Lymph nodes, Ultrasound, Shear wave elastography, Virtual Touch tissue imaging quantification.**

INTRODUCTION

Assessment of nodal metastases is the most important clinical aspect of oncologic staging because it predicts prognosis and helps in the selection of treatment. Different imaging modalities such as gray-scale ultrasonography (US), US-guided fine-needle aspiration cytology, computed tomography (CT) and magnetic resonance imaging have been used to evaluate cervical lymph nodes (Atula et al. 1997; de Bondt et al. 2007; Sumi et al. 2003). Recently, US elastography has emerged as a complementary tool for the detection of metastatic cervical lymph nodes with promising results (Choi et al. 2013, 2015; Lo et al. 2013; Tan et al. 2010).

Strain elastography (Ophir et al. 1991), the first commercialized elastography technique, uses unquantifiable freehand compression, which requires continuous transducer compression or external mechanical compression and displays qualitative results of tissue stiffness (Bhatia et al. 2010). Acoustic stress elasticity imaging, such as acoustic radiation force impulse (ARFI) imaging, is a new elastography technique that reduces operator dependency and improves reproducibility because of the addition of automated tissue compression (Fujiwara et al. 2013; Meng et al. 2013; Nightingale et al. 2002). This technique uses focused high-intensity, short-duration acoustic pulses from a US transducer and makes localized tissue displacements producing shear waves in the region of interest (ROI), providing quantitative assessment of tissue stiffness based on tracking of the shear wave propagation caused by the pushing pulse (Balleyguier et al. 2013; Sarvazyan et al. 1998). The more stiff a tissue is, the more shear wave velocity it produces. Virtual Touch tissue imaging quantification (VTIQ) is a new measurement technique that uses ARFI imaging technology to gently displace tissue for qualitative visualization and quantitative evaluation of tissue stiffness. The VTIQ shear wave technique uses multiple push pulses across the transducer face at multiple depths and provides an

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elastogram of tissue stiffness based on shear wave speed. Multiple ROIs can be placed on the elastogram, which detects pulse sequences that can measure localized shear wave velocity from 0.5 to 10 m/s in multiple locations (Matsuzuka et al. 2015).

In addition to detecting shear wave velocity, VTIQ can also display shear wave quality. This is useful in interpreting whether the shear wave was of sufficient magnitude with an adequate signal-to-noise ratio to accurately estimate shear wave velocity in the shear wave velocity display, and is also valuable in understanding whether the shear wave was adequately formed (Tozaki et al. 2013). VTIQ shear wave elastography has been widely used for the assessment of breast diseases (Golatta et al. 2013; Ianculescu et al. 2014; Tozaki et al. 2013), testicular lesions (Trottmann et al. 2014), liver disease (Leschied et al. 2015) and bowel wall fibrosis (Dillman et al. 2014) and has been found to be effective in differentiating between benign and malignant lesions and in evaluating tissue hardness. However, to our knowledge, VTIQ shear wave elastography has not been used in the discrimination of benign and malignant cervical lymph nodes. The purpose of this study was to prospectively determine the diagnostic performance of VTIQ shear wave elastography in differentiating between benign and malignant cervical lymph nodes.

METHODS

This prospective study protocol was reviewed and approved by the institutional review board of our hospital. Written informed consent for routine US was obtained from all patients before each US examination.

Study patients

This study was conducted at a single tertiary referral center between July 2014 and February 2015. We enrolled consecutive patients who were referred for US-guided biopsy based on the following criteria: (i) neck lymph nodes undergoing US-guided fine-needle aspiration for cytology (FNAC) or US-guided core needle biopsy (CNB) in routine clinical practice; (ii) neck lymph nodes >5 mm in minimal axial diameter; and (iii) cytopathologically confirmed benign or metastatic lymph nodes. Criteria for a referral US-guided biopsy were as follows: (i) discomfort and palpable symptoms in the cervical region suspicious for lymphadenopathy, or a lymph node detected on CT or [^{18} F]fluorodeoxyglucose positron emission tomography ([^{18} F]FDG PET) in an underlying malignancy when diagnosis by CT or PET is inconclusive, and (ii) a need for pathologic diagnosis. Exclusion criteria were as follows: Failure to undergo FNAC or CNB, lymph nodes with inadequate cytopathologic results and low VTIQ image quality were the exclusion criteria.

VTIQ examinations

During routine clinical practice, each study patient underwent VTIQ shear wave elastography using the Acuson S3000 ultrasound system (Siemens Medical Solutions, Erlangen, Germany) equipped with a linear array transducer (Siemens Medical Solutions) with a bandwidth of 4–9 MHz. The detection pulse transmits at 6.15 MHz with a pulse repetition frequency in the range 7 to 10 kHz depending on depth. The total tracking duration was around 10 ms for each shear wave excitation. All US examinations were performed by a radiologist with 4 y of experience who had been trained by a VTIQ applications specialist.

Each patient was placed in a supine position with the neck slightly extended over a pillow. The radiologist located the probe vertical to the skin and applied the probe with minimal pressure to create complete contact with the cervical lymph node while letting the patient hold his or her breath. Elastography color maps were displayed on the box, and a ROI was identified in the cortex, avoiding cystic and calcified components. A ROI was determined in the target area on the color-coded 2-D maps to obtain the shear wave velocity, which was quantitatively measured in meters per second (m/s). The shear wave quality map was obtained before measuring shear wave velocity. On VTIQ, high-quality regions are displayed as green, low-quality regions as orange and marginal-quality regions as yellow (Tozaki et al. 2013). VTIQ shear wave elastography was performed twice in a single session by one observer, was blind to the velocity measurement value during the examination. The shear wave velocity value was defined as the average of two-time measurements.

For analysis of patients with multiple lymph nodes, we selected a target lymph node that exhibited at least one of the following criteria: (i) increased uptake on [^{18}F] FDG PET and/or (ii) malignant US or CT findings, including loss of hilar fat, cortical heterogeneous echogenicity, echogenic dots or calcification, cystic or necrotic area, long-to-short axis diameter ratio <2.0 and peripheral cortical vascularity (Choi et al. 2013; Meng et al. 2013; Teng et al. 2012; Yoon et al. 2009). When none of these criteria was met, the largest lymph node was selected as a target lymph node.

Final diagnosis

After US elastography, all lymph nodes underwent US-guided FNAC or CNB. The final diagnosis was based on adequate cytopathology results. US-Guided FNACs were performed routinely with a disposable 23-guage needle. Capillary or aspiration technique was used according to the characteristics of each nodule. US-Guided CNBs were performed with a 1.1- or 1.6-cm excursion, disposable, 18-gauge, double-action, spring-activated needle