European Journal of Radiology 82 (2013) 1788–1792

Contents lists available at ScienceDirect

European Journal of Radiology

journal homepage: www.elsevier.com/locate/ejrad

Initial experience of acoustic radiation force impulse ultrasound imaging of cervical lymph nodes

Wei Meng, Ping Xing, Qi Chen, Changjun Wu*

Ultrasound Department, The First Affiliated Hospital of Harbin Medical University, 23 Youzheng Street, Harbin, Heilongjiang 150000, China

ARTICLE INFO

Article history:
Received 27 November 2012
Received in revised form 3 April 2013
Accepted 18 May 2013

Keywords:
Cervical lymph nodes
Acoustic radiation force impulse
ARFI imaging
Ultrasound

ABSTRACT

The aim of this study was to evaluate acoustic radiation force impulse imaging for cervical lymphadenopathy in routine clinical practice and to correlate the acoustic radiation force impulse values with the morphological signs and the pathological results, which were used as the reference standard. The virtual touch tissue quantification values were analyzed in 123 patients (mean age 40.8 years, range 1–81 years) with 181 cervical lymph nodes (87 benign, 94 malignant). The diagnostic performance of acoustic radiation force impulse values were evaluated with respect to sensitivity, specificity, and area under the curve using a receiver operating characteristic curve analysis. The mean virtual touch tissue quantification values of the benign lesions (2.01 ± 0.95 m/s) differed from that of the malignant lesions (4.61 ± 2.56 m/s; $P < 0.001$). The cutoff level for virtual touch tissue quantification value for malignancy was estimated to be 2.595 m/s. Using the receiver operating characteristic curve curves with the cutoff value, the virtual touch tissue quantification value predicted malignancy with a sensitivity of 82.9%, specificity of 93.1% and gave an areas under the curve of 0.906 (95% CI 0.857–0.954). Acoustic radiation force impulse is feasible for cervical lymph nodes and provides quantitative elasticity measurements, which may complement B-mode ultrasound and potentially improve the characterization of cervical lymph nodes.

1. Introduction

Differentiation between benign and malignant cervical lymphadenopathy is an important procedure for patient because the results influence the choice of therapy and the prognosis, and one of the differentiating criteria is elasticity of the lymph node. However, there are certain disadvantages with the conventional ultrasound (US) and the conventional elastography [1–3].

Acoustic radiation force impulse (ARFI) imaging is a new method that could quantify the mechanical properties of a tissue. Without any need for external compression, it evaluates tissues, providing complementary informations to conventional US, potentially improving the characterization of tissues and focal lesions [4–8]. ARFI imaging uses commercially available ultrasound scanners to generate short-duration (<100 μs), high-intensity, acoustic pulses to generate localized, micron-scale displacements in tissue, the response, monitored with US, is mainly related to the viscoelastic properties of tissues: the more elastic a tissue is, the more displacements it experiences [9].

Relying on the interactions with the transducer, the generated waves can provide qualitative (gray scale map) or quantitative (wave velocity values, measured in m/s) responses, by virtual touch tissue imaging (VTI) and virtual touch tissue quantification (VTQ), respectively [10,11]. VTI, ARFI induced displacement of tissue within the ROI is detected and presented as a gray scale image. This image visualizes the relative stiffness in the selected ROI with a gray scale picture. The harder a tissue, the darker the image. VTQ tracks a shear wave within the ROI that travels perpendicular to the transmitted longitudinal push pulse. Time to peak analysis computes a numerical value of the shear wave speed [8] obtained over the ROI, expressed in the unit "meters/second" (m/s). The shear wave velocity tracked with ultrasonic correlation-based methods is proportional to the square root of tissue elasticity [8,12]. The stiffer a tissue, the greater the shear wave velocity. Thus it provides numerical measurements that give quantitative information about tissue elasticity properties.

ARFI has been evaluated in various tissues using both the gray scale map and the shear wave speed [13–17]. Our recent study results showed that ARFI is a promising imaging technique that can provide assistance in the differentiation of benign and malignant breast lesions [16]. However, to our knowledge, ARFI has not been applied to cervical lymph node characterization. The purpose of our pilot study is to estimate the accuracy of ARFI in

* Corresponding author. Tel.: +86 0451 85555286; fax: +86 0451 85555286.
E-mail address: changjunwu234@163.com (C. Wu).

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http://dx.doi.org/10.1016/j.ejrad.2013.05.039

the differentiation of benign and malignant cervical lymph nodes with the pathological results as the reference standard.

2. Materials and methods

2.1. Study population

The study was approved by the ethics committee of our hospital, and all patients gave informed consent. ARFI was performed following conventional B-mode US in 131 consecutive patients who underwent evaluation of cervical lymph nodes at our center between March 12, 2012 and August 20, 2012. Eight patients were excluded from the study group because of lack of pathologic results. The final study group therefore consisted of 123 patients (mean age 40.8 years, range 1–81 years).

2.2. Imaging techniques

The examination started with a conventional US followed by ARFI. Both of them were performed on an ACUSON S2000 ultrasound system (Siemens Medical Solutions, Mountain View, CA, USA), with linear probes (9L4) by two experienced radiologists together. The positioning of the patients for imaging was identical to that used for standard clinical neck US: The patient was positioned on his or her back with neck slightly extended over a pillow. All cervical lymph nodes included in this study had at least one conventional US feature of abnormality including increased size, round shape, intra-nodal necrosis or calcifications, disordered vascularity, abnormal parenchymal echogenicity and architecture. These criteria included nodes considered to be benign or malignant on conventional US.

ARFI measurements were made in the "virtual touch tissue Imaging mode" and "virtual touch tissue quantification mode". In the VTI mode, the target lymph node was displayed in B-mode and then the region of interest (ROI) was placed around the node. Special care was taken to ensure that sufficient surrounding tissue was included in the ROI. In order to obtain appropriate images, the probe was applied with minimizing pressure to make complete contact with the cervical lymph node but to let the patient in breath-hold. The VTI button was then pressed, and the VTI image (gray-scale image) was produced on the right of the corresponding B-mode scan. In the VTQ mode, ARFI technology uses short-duration acoustic radiation forces to generate localized tissue displacement which results in shear-wave propagation [7]. For ARFI measuring during real-time B-mode imaging, the ROI, characterized by a box with fixed dimension of 0.5 cm × 0.6 cm and a maximum depth of 5.5 cm. The shear waves produced propagate perpendicular to the acoustic pulse away from the target ROI. The calculation of the shear wave speed is expressed in m/s. The ROI box was entirely included into the cervical lymph node when the node was small, while for the big node, the ROI box was positioned on the location where was the darkest in the corresponding VTI image (avoiding both macro and microcalcification). In such a way, we got the highest shear wave speed (VTQ value) of the cervical lymph node. In each node 5 VTQ values were made in breath-hold and the arithmetic mean of these 5 measurements was used for statistical analysis. The limits for measurement of the VTQ values (shear wave speed) for this machine were 0–9 m/s. Values outside these limits were displayed as "X.XX m/s"; the result was recorded as 0 m/s when the VTI image appeared bright, 9 m/s when the VTI image appeared dark.

2.3. Pathological diagnoses

All cervical lymph nodes were confirmed histologically by means of surgery, biopsy, or fine needle aspiration (FNA), according to clinical indication or the intention of patient. Of the 87 benign lymph nodes, 12 were diagnosed at surgery, 49 at US-guided needle biopsy, and 26 at FNA, while of the 94 malignant nodes, 46 were diagnosed at surgery, 39 at US-guided needle biopsy, and 9 at FNA. Nodes were first classified as malignant or benign, then were divided into subgroups .All diagnoses were made by a pathologist with many years of experience in pathological examination.

2.4. Statistical analysis

For all the cervical lymph nodes, the role of the ARFI values in discriminating malignant from benign lesions was analyzed as follows.

The mean VTQ values of malignant and benign nodes were compared by Student's *t* test. All tests were two-sided. $P < 0.05$ indicated a significant correlation or difference. The ability of the VTQ values to differentiate malignant from benign nodes was evaluated using receiver-operating characteristic (ROC) curve analysis. The best cutoff point were obtained using Youden's index (sensitivity + specificity − 1) from the ROC curve analysis. Sensitivity and specificity values and their respective 95% confidence intervals (CI) were estimated. All data were analyzed using SAS version 9.2.1 software (SAS Inc., Cary, NC, USA).

3. Results

3.1. Final diagnosis

Of 181 lymph nodes, 94 were malignant (lymphomatous infiltration, 8; castleman's disease, 1; metastatic nodes, 85. metastatic nodes comprised as follows; 4 adenocarcinoma of the lung, 9 small cell carcinoma of the lung, 24 squamous cell carcinoma of the lung, 11 squamous cell carcinoma of the esophagus, 4 breast carcinoma, 3 nasopharyngeal cancer, 21 papillary thyroid cancer, 1 pancreatic carcinoma, 1 brain glioma, 2 ovarian adenocarcinoma, 3 squamous cell carcinoma of the tongue, 2 poorly differentiated cancer) and 87 were benign (63 reactive, 11 tuberculous nodes, 13 necrotizing granulomatous lymphadenitis).

3.2. Acoustic radiation force impulse imaging

3.2.1. VTI mode

Although no freehand compression was required to perform ARFI, meticulous care was required in terms of minimizing pressure of the transducer on the neck. When displayed as VTI images, 6.4% of the malignant cervical lymph nodes,as well as 71.6% of the benign nodes, were slightly darker or the same in brightness compared with the surrounding tissue or muscles, while, 93.6% of the malignant cervical lymph nodes and 28.4% of the benign nodes were substantially darker (stiffer) than the surrounding tissues (Table 1). Benign nodes tended to appear spatially and temporally homogeneous with slightly dark or gray hue equating to low stiffness on VTI images (Fig. 1a). By contrast, malignant nodes were either homogeneously dark or markedly heterogeneous in terms of very high and low stiffness (Fig. 2a).

3.2.2. VTQ mode

The mean VTQ value of the benign lymph nodes (2.01 ± 0.95 m/s) (Fig. 1b) was statistically lower than that of the malignant lymph nodes (4.61 ± 2.56 m/s; $P < 0.001$) (Fig. 2b). The cutoff level for VTQ value for malignancy was estimated to be 2.595 m/s. Using the ROC curves with this cutoff value, the VTQ value predicted malignancy with a sensitivity of 82.9%, specificity of 93.1% (Table 1) and gave an areas under the curve (AUC) of 0.906 (95% CI 0.857–0.954) (Fig. 3).