



The value of virtual touch tissue image (VTI) and virtual touch tissue quantification (VTQ) in the differential diagnosis of thyroid nodules



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ABSTRACT

Objectives: To explore the value of virtual touch tissue image (VTI) and virtual touch tissue quantification (VTQ) in the differential diagnosis of thyroid nodules.

Methods: One-hundred and seven patients with 113 thyroid nodules were performed conventional ultrasound and acoustic radiation force impulse (ARFI) elastography. The stiffness of the nodules on virtual touch tissue image (VTI) was graded, and the area ratios (AR) of nodules on VTI images versus on B-mode images were calculated. Shear wave velocity (SWV) within the thyroid nodules were measured using virtual touch tissue quantification (VTQ) technique. The pathological diagnosis as the gold standard draws the receiver-operating characteristic curve (ROC) to find the cut-off point of VTI grades, AR and SWV to predict thyroid cancer.

Results: The difference in VTI grades of malignant and benign nodules was statistically significant ($P < 0.05$), as well as in AR and SWV. There was no significant difference in the AR of nodules or the SWV of nodules in benign group or in malignant group. The sensitivity, specificity, accuracy, positive predictive value (PPV), and negative predictive value (NPV) of VTI grades, AR, and SWV in the differential diagnosis of thyroid nodules were calculated. There was no significant difference in diagnostic accuracy among the three methods.

Conclusion: VTI grades, AR of nodules on VTI images versus on B-mode images and SWV within the nodules can help the differential diagnosis of thyroid nodules.

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1. Introduction

Acoustic radiation force impulse (ARFI) imaging is a new elastic imaging technology which can analyze the stiffness of tissue qualitatively and quantitatively [1,2]. ARFI evaluates the stiffness of tissue, provides complementary information for conventional ultrasound (US), so potentially improves the characterization of tissues and focal lesions [3]. Previous external pressure elastography is a semi-quantitative method for tissue elasticity. The external pressure elasticity obtained is highly dependent on the extent of the tissue compression applied [4], the skill impacts the reproducibility of the elastography [5], and reliability is questioned [6].

ARFI is currently the newest imaging mode for detection of mechanical properties of tissue without external compression. ARFI technology includes virtual touch tissue imaging (VTI) and virtual touch tissue quantification (VTQ). Micro-displacement is generated in a tissue within the region of interest (ROI) when the commercially available ultrasound transducer launches short-duration ($< 100 \mu\text{s}$), high-intensity acoustic pulses to the tissue. The displacement of the tissue depends on its elasticity. The more elastic the tissue is, the more displacement it experiences [1]. The displacement of the tissue within the ROI induced by ARFI is detected and presented as a grey-scale image which is called virtual touch tissue imaging (VTI). The harder the tissue is, the darker the image is. The tissue within the ROI generates horizontal shear wave when it is pushed by the longitudinal pulse generated from the transducer. The shear wave velocity is calculated and expressed in the unit “meters/second” (m/s), which is called virtual touch tissue quantification (VTQ). The stiffer the tissue is, the faster the shear wave propagates. The wave propagation speed is an intrinsic and reproducible property of the tissue, so ARFI tissue quantification generates objective and reproducible data [7]. VTQ can provide shear wave velocity numerical measurements and the shear wave

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propagation velocity is proportional to the square root of the tissue elasticity [3,8], therefore, VTQ can quantitate the tissue elasticity.

ARFI technology has been applied in the diagnosis of abdominal diseases [9–11] and breast diseases [4,12]. Reports about the application of ARFI technology in thyroid, especially using a linear array transducer, are not many and it still needs further studies [13–19]. Those studies explored the imaging types of VTI and the VTQ values and compared the diagnostic accuracy between VTQ and qualitative real-time elastography (RTE). The present study focusing on VTI grades, the area ratio (AR) of nodules on VTI, and on B-mode and shear wave velocity (SWV) evaluates the diagnostic performance of the above methods in the differential diagnosis of thyroid nodules. The diagnosis was confirmed by histology.

2. Materials and methods

2.1. Study population

This study was approved by the Ethics Committee of the Fourth Hospital of Hebei Medical University. Between July 2012 and January 2013, 185 patients referred for ultrasound examinations were recruited for this study. All of the participants signed the informed consents required by the human study committee before enrollment. Seventy eight of them were lost during following up (50 patients with obviously benign ultrasound-character nodules chose yearly ultrasound observation instead of fine needle aspiration biopsy, and 28 did surgery in other hospitals whose pathological results were suspicious). The enrollment criteria of patients were as follows: (1) the images of the nodules on two dimension (2D) were stable when the patients hold their breath; (2) the size of the nodules ranged from 0.6 to 2.0 cm; (3) solid or almost solid (<20% cystic) nodules on ultrasound (US); (4) enough thyroid tissue surrounding the nodule at the same depth; and (5) thyroid surgery performed after US examination. Not every nodule can be included for the patients with multiple nodules in this study because of the size and component of nodules restrictions. In the study, many patients had multiple nodules, but only one or two satisfied the inclusion criteria. Finally, 107 patients (mean age 35.56 ± 10.34 years, range 21–75 years) with 113 nodules (mean size 1.5 ± 0.3 cm, range 0.5–2.0 cm) met the inclusion criteria, and these nodules were resected and the pathological results were acquired.

2.2. Imaging techniques

Both conventional US and ARFI examinations were performed with an Acuson S2000 ultrasound system (Siemens Medical Solutions) equipped with 9L4 linear array transducer (bandwidth frequency of 4–9 MHz) and ARFI software. Patients were in a supine position with a fully exposed neck. The nodule's morphology characteristics, size, boundary, echoes, and color Doppler feature were observed by conventional US. Then, switching to VTI model, the probe touched the skin lightly, adjusted the size of ROI, ensured the nodule, and enough surrounding gland were included in the ROI. Make the maximum longitudinal section of the nodules displayed in the center of the screen, and then ask the patients to hold their breath, at the same time trigger the update button. Then, the VTI image was produced on the right of the corresponding B-mode scan. Perform five times consecutively and choose three images with clear boundary to save as research data. The areas of the nodule on VTI and on B-mode US were measured. The area of thyroid nodule on VTI was selected as A1 and the corresponding area on B-mode US as A2, and the area ratio (AR) was calculated accordingly. The average of three AR measurements from each nodule was used for further statistical analysis. All of the examinations were

Table 1
Virtual touch tissue image scoring of benign and malignant thyroid nodules.

Pathology outcome	Virtual touch tissue image score			
	I(n)	II(n)	III(n)	IV(n)
Adenomatous hyperplasia nodules	22	31	4	3
Adenoma	3	4	0	0
Papillary carcinoma	0	1	27	6
Follicular-type papillary adenocarcinoma	0	1	4	5
Medullary carcinoma	0	0	2	0

conducted by a sonographer with more than 10 years of experience in conventional sonography and 3 years of experience in ARFI, who was blinded to the histopathological results.

Referring to the VTI classification method of Tian et al. [20], the VTI images of thyroid nodules were divided into four grades according to the gray scale. Grade I: images were white or white honeycomb; grade II: images were gray or light gray, similar to surrounding tissues; grade III: images were dark grey or with a small amount of white dots, very different from surrounding color; grade IV: images were absolute black. The harder the tissue is, the darker the images are.

In the VTQ mode, the region of interest (ROI) with fixed dimension of 6 mm × 5 mm was placed inside nodules when the nodules had similar size with ROI. The nodules were measured five times and the mean of five-time measurements was calculated and used for further analysis. The movement range of the ROI was small in the nodule when the size of the nodule was similar to the ROI. The repeatability of five-time sampling was very high, and the results were in good agreement. The movement range of the ROI was bigger in a bigger nodule; the tissue could be completely different for each measurement, and measurements were not consistent. So the large nodule was divided into four parts, each part was measured twice, the mean of eight measurements was more reliable than the mean of five-time measurements for bigger nodules. The range for measurement of the VTQ values (shear wave velocity) for this machine was 0–9 m/s. Values outside this range were displayed as “X.XX m/s” and the result was recorded as 9 m/s when the nodule was solid [4,21].

2.3. Pathological diagnoses

Thyroid surgery was performed for all patients enrolled in the present study. All nodules were confirmed by histology. All pathological diagnoses were made by a pathologist with many years of experience in thyroid pathological examination. Nodules were first classified as benign or malignant, and then they were divided into subgroups as described in Table 1.

2.4. Statistical analysis

Values of AR and VTQ were not normally distributed and therefore expressed as median values. The AR and SWV differences between the benign group and malignant group; comparisons within benign group or within malignant group, and the VTI grades analysis were performed using the non-parametric Mann–Whitney *U*-test. The Kruskal–Wallis non-parametric test was used to compare whether there were significant differences in the AR or in the SWV among different pathologic types of malignant nodules. The abilities of VTI grades, AR, and VTQ values (SWV) to differentiate malignant from benign nodules were evaluated by receiver-operating characteristic (ROC) curve analysis. The best cutoff points for VTI grades, AR, and VTQ values were obtained using Youden index (sensitivity + specificity – 1) from the ROC curve analysis. Sensitivity, specificity, accuracy, positive predictive value (PPV), and negative predictive value (NPV) were calculated with the

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