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● *Original Contribution*

REAL-TIME ELASTOGRAPHY IN THE EVALUATION OF DIFFUSE THYROID DISEASE: A STUDY BASED ON ELASTOGRAPHY HISTOGRAM PARAMETERS

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Abstract—The purpose of this study was to evaluate the diagnostic performance of quantitative histogram parameters using real-time tissue elastography (RTE) in the diagnosis of patients with diffuse thyroid disease. One hundred and sixteen patients (mean age, 43.7 ± 10.97 y) who had undergone pre-operative staging ultrasonography and RTE were included. For each patient, 11 parameters were obtained from RTE images, from which the "elastic index" was calculated. Diagnostic performance of the elastic index and that of the 11 parameters on RTE were calculated and compared. Of the 116 patients, 31 had diffuse thyroid disease and 85 had normal thyroid parenchyma. Area under the receiver operating characteristic curve (A_z) of MEAN (average relative value) elasticity was high (0.737), without significant differences from other elasticity values. Diagnostic performance of the elastic index was higher than the MEAN, A_z = 0.753, without significance (p = 0.802). In conclusion, RTE using the elastic index was found to have good diagnostic performance and may be useful in the diagnosis and management of patients with diffuse thyroid disease. (E-mail: Docjin@yuhs.ac) © 2014 World Federation for Ultrasound in Medicine & Biology.

Key Words: **Thyroid, Ultrasound, Real-time elastography, Diffuse thyroid disease, Thyroiditis.**

INTRODUCTION

Ultrasonography (US) is a tolerable and easily applicable diagnostic method that has been used worldwide in the differential diagnosis of thyroid nodules. US mostly represents the morphologic features of the targeted thyroid mass, and studies have reported high levels of performance with combinations of gray-scale US features in the diagnosis of thyroid nodules (Kim et al. 2002; Moon et al. 2008; Papini et al. 2002). In addition to gray-scale US, there has recently emerged elastography, which provides an estimate of tissue stiffness by measuring the degree of displacement secondary to external compression applied (Asteria et al. 2008; Itoh et al. 2006; Rago et al. 2007). Based on the concept that malignant masses are relatively stiff compared with the adjacent normal parenchyma (Itoh et al. 2006; Yoon et al. 2011), elastography has been used mostly in the differentiation between benign and malignant nodules within the thyroid (Asteria et al. 2008; Dighe et al. 2008; Ding et al. 2012; Hong et al. 2009; Moon et al. 2012; Rago et al. 2007). In addition to evaluation of masses, elastography has been reported to have a role in evaluating the extent of inflammatory infiltrations and fibrosis within the diseased parenchyma (Friedrich-Rust et al. 2007; Sandrin et al. 2003; Wang et al. 2012).

Real-time elastography (RTE) visualizes the elasticity of the target area by capturing echo signals derived secondary to repetitive compressions applied with a free-hand technique (Kanamoto et al. 2009; Wang et al. 2012; Yoon et al. 2011). A quantitative analysis method based on RTE has been developed that can be used on diffuse pathologic lesions, such as liver fibrosis, as reported in

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several studies (Friedrich-Rust et al. 2007; Kanamoto et al. 2009; Wang et al. 2012). Results of these studies have proved that the quantitative data obtained from RTE constitute a useful, non-invasive imaging method with promising results in the assessment of liver fibrosis in patients with chronic hepatitis. Similarly, thyroid stiffness assessment has been used in the diagnosis of diffuse thyroid gland pathology with acoustic radiation force impulse elastography (Sporea et al. 2011b) or shear wave elastography (Kim et al. 2014) in several recent studies, with promising results. Quantitative parameters obtained from RTE may also be helpful in the diagnosis and management of patients with diffuse thyroid disease (DTD). The 11 elastography parameters used in RTE, which are calculated by maneuvering the ultrasound unit, each display characteristics related to the elastography image, factors related to the elastography histogram and factors related to the gray-scale co-occurrence matrix. Also, the "elastic index," calculated on the basis of the 11 parameters derived from RTE by principal component analysis used in the diagnosis of liver fibrosis (Wang et al. 2012), may be applied to the thyroid gland. Although RTE parameters, including elastic index, have been used to evaluate fibrosis in liver parenchyma, to our knowledge, there are no other studies reporting the application of quantitative RTE parameters and the elastic index to the diagnosis of DTD. On this basis, we evaluated the diagnostic performance of quantitative histogram parameters using high-technology RTE in the diagnosis of patients with DTD.

METHODS

Informed written consent was obtained from all patients. The study was performed in accordance with the ethics guidelines of the Helsinki Declaration and was approved by the institutional review board of Severance Hospital, Seoul, Korea.

Study population

From September to November 2012, this study was performed at our institution, a referral center. Since 2006, pre-operative staging US has been performed in patients diagnosed with a thyroid malignancy, patients suspicious for papillary thyroid carcinoma or patients diagnosed with a follicular neoplasm on US-guided fine-needle aspiration at our institution (Choi et al. 2011). During the study period, 119 patients underwent pre-operative staging US and subsequent elastography. Of these patients, 2 were excluded because they had not undergone surgery after staging US. Another patient was excluded because of the lack of a sufficient amount of thyroid parenchyma surrounding the target mass when the elastography images were obtained, as the patient had presented with multiple thyroid nodules involving nearly the entire thyroid gland. In total, 116 patients were included in this study. Ninety-five (81.9%) were women and 21 (18.1%) were men. Mean age was 43.7 ± 10.97 y (range, 23–66 y) for the 95 women and 42.8 ± 9.4 y for the 21 men (range, 26–60 y).

Gray-scale US and elastography imaging

Real-time US examinations of the neck area were performed with a 5- to 13-MHz linear array transducer (HI VISION Ascendus, Hitachi Aloka Medical, Tokyo, Japan). Pre-operative US staging was performed by one of three board-certified radiologists (H.J.M., J.Y.K., E.K.K) with 7 to 15 y of experience in thyroid imaging.

After gray-scale US, RTE was performed by the same radiologist. All RTE images were obtained in the longitudinal plane, with the neck slightly extended. During RTE, the probe was positioned perpendicular to the skin while light, repetitive compression was applied to the skin above the thyroid. Elastography images were displayed in split-screen mode on the left, superimposed to the corresponding gray-scale US image displayed on the right. Each pixel of the elastography image was displayed in 1 of 256 colors, ranging from blue, indicating no strain, to red, indicating the greatest strain. For optimal elastography image acquisition, elastography images showing color homogeneity or the pressure indicator ranging between the numbers 2 and 3 were recorded (Friedrich-Rust et al. 2007; Yoon et al. 2011). Patients were asked to refrain from swallowing or talking during the examination. A region of interest (ROI), set by the radiologist, included a sufficient amount of the thyroid parenchyma, consisting of more than one-third of a thyroid lobe, carefully excluding thyroid nodules. For each patient, a total of six elastography measurements were made: three measurements of the right thyroid within the same area and three of the left thyroid. Measurement area, tissue elasticity and RTE parameters were automatically calculated and displayed by the US machine. Data were recorded and entered into a computer database for analysis. The measurement area was 34-372 mm (mean ± standard deviation: 162 ± 63.9 mm^2).

Eleven histogram parameters were obtained from RTE, including average relative value (MEAN on US), standard deviation of relative strain (SD on US), area ratio of low-strain region (%AREA on US), complexity (COMP on US), kurtosis (KURT on US), skewness (SKEW on US), contrast (CONT on US), entropy (ENT on US), inverse difference moment (IDM on US), angular second moment (ASM on US) and correlation (CORR on US image) (Fig. 1) (Wang et al. 2012). Of these, the factors related to the elastography image were as follows: MEAN was defined as the average relative value of strain within the ROI; SD as the standard deviation of the