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● *Original Contribution*

QUANTITATIVE ANALYSIS OF DYNAMIC POWER DOPPLER SONOGRAMS FOR PATIENTS WITH THYROID NODULES

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Abstract—To clarify and determine whether power Doppler sonograms are useful for the detection of malignant thyroid nodules, a computerized quantification method was used to evaluate the vascular density of a thyroid nodule in a prospective setting. Sonographic power Doppler images were collected in consecutive frames (45 frames of images), and a proprietary program (AmCAD-UV) was implemented using methods proposed in this article automatically calculated a quantified power Doppler vascular index (PDVI). The minimum PDVI value ($PDVI_{min}$) was suggested as a measure of the vascular density of the nodule. The vascular densities of the peripheral and central areas of the nodule, referred to as central $PDVI_{min}$ and Ring $PDVI_{min}$, respectively, were also evaluated. For 238 tumors (79 malignant and 159 benign) from 208 patients, all of the proposed indices of benign lesions were significantly higher than those of the malignant lesions. The area under the receiver operating characteristic curve (AUC) reaches 71% with the $PDVI_{min}$. When the vascular patterns were further classified into intra-nodular and peripheral vascularity types, no vascularity type was observed significantly more frequently in malignant nodules than in benign nodules. These proposed computerized vascular indices provide a quantification method to objectively evaluate thyroid nodules and have potential as predictors of thyroid malignancy. The conventional vascular characterizations of malign nodules, that is, more vessels are observed in malignant nodules than in benign nodules, are shown to be unreliable in our study. Instead, a higher value of the quantified power Doppler vascular density was observed in benign nodules. (E-mail: achen@ntu.edu.tw) © 2013 World Federation for Ultrasound in Medicine & Biology.

Key Words: **Vascularity, Vascular index, Power Doppler, Thyroid cancer, Computer-aided detection.**

INTRODUCTION

Thyroid nodules occur frequently and are discovered by palpation in 3% to 7%, by ultrasonography (US) in 20% to 76% and by autopsy in approximately 50% of the general population (Brander et al. 1991; Filetti et al. 2006; Hegedus 2004; Mazzaferri 1992, 1993; Mortensen et al. 1955; Tan and Gharib 1997; Vander et al. 1968). Thyroid nodules are clinically important primarily because thyroid cancer occurs in approximately 5% of all thyroid nodules, regardless of size (Hegedus 2004; Nam-Goong et al. 2004; Papini et al. 2002). Because of the high prevalence of nodular thyroid disease, it is not economically feasible or clinically necessary to perform a complete structural and functional assessment for all or even most thyroid nodules. Therefore, it is essential to develop and follow a systematic, cost-effective strategy for the diagnosis of thyroid nodules.

The current primary method for the diagnosis of thyroid nodules is fine-needle aspiration cytology (FNAC). According to a 2007 study reviewing published literature from 1966 to 2005, FNAC is trusted as a front-line test in the diagnosis of thyroid cancer because of its reported high specificity (0.74–0.92). Its sensitivity, however, can be much lower than what is reported in the literature, as most patients (>75%) with negative FNAC results do not undergo surgery and are not included in the calculations of sensitivity. It is estimated that the sensitivity could be as low as 0.66 after adjustment of the calculation base (Tee et al. 2007). Diagnosis using US images can thus complement the FNAC result

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for the diagnosis of thyroid malignancy and provide guidance to physicians regarding patient selection for thyroidectomy. The superficial location and the distinctive echogenic pattern of the thyroid make it an ideal organ for study by sonography. The increasing availability and use of high-resolution US images have facilitated and improved the management of thyroid nodules. On the basis of the various US characteristics of the thyroid, it is now possible to distinguish thyroid tumors and predict their prognosis (Frates et al. 2006; Mandel 2004; Papini et al. 2002). However, few of the characteristics are currently quantitative or objective and, thus, are not easily universally defined or clinically applied (Chan et al. 1998).

The application of power Doppler has made obvious progress in the study of tumors (Chan et al. 2003). Some studies claim that vascular patterns are useful in predicting thyroid malignancy (Frates et al. 2003; Papini et al. 2002; Yuan et al. 2006), whereas others report that these patterns are not useful (Bannier et al. 2010; Frates et al. 2005; Rago et al. 1998). A serious concern is that the vascular patterns (no vascularity, intranodular vascularity or peripheral vascularity) have been described qualitatively and are thus potentially subject to intra-observer and inter-observer variability (Wienke et al. 2003). Quantitative analysis of tumor vascularity has therefore been investigated (Lyshchik et al. 2007). However, only static power Doppler images were subjectively chosen and used in the aforementioned study, without consideration of the dynamic changes caused by the vascular perfusion.

To overcome the shortcomings of subjective judgment of the sonographic characteristics used in diagnosis, we have proposed a computerized quantification method to characterize the calcifications and make the diagnosis more objective (Chen et al. 2011). The aim in this study was to collect and quantify more US information than the static gray-scale echoic images. We propose the use of novel quantitative thyroid vascular indices (VIs) to study the hemodynamics of thyroid vascular perfusion.

The purpose of our study was to prospectively evaluate the diagnostic performance of these quantitative thyroid VIs from power Doppler US images and to determine which, if any, of these new VI parameters are useful in predicting thyroid malignancy.

METHODS

Patients

The institutional review board of the National Taiwan University Hospital approved this prospective study, and informed consent was obtained from all patients recruited for this study. From 1 December 2007 to 31 May 2009 (18 mo), a total of 305 patients with thyroid tumors were recruited and assessed by ultrasonography in the National Taiwan University Hospital. Patients who refused to or otherwise did not undergo fine-needle aspiration cytology or pathologic examinations were excluded from further software analysis because of uncertain diagnosis results. Patients whose multinodular goiters could not be differentiated from one another and those who had previously undergone goiter biopsies were excluded from the study on the grounds that these issues would potentially degrade the ultrasound images. A total of 208 patients (166 women and 42 men; median age, 49.57 y) with euthyroidism defined to be within normal limits by laboratory data (free thyroxine [FT4] and hormone-sensitive thyroid-stimulating hormone [hsTSH]) were included in the prospective study. Final diagnosis was based on the cytologic results with more than 2 y of follow-up and/or histopathology results. The doctors who actually treated and diagnosed the patients were blind to all software analysis data, and therefore, the data did not influence their clinical decisions.

Equipment and sonographic procedures

Examinations were performed with a Philips HDI 5000 device (Philips Healthcare, Bothell, WA, USA; manufactured in 2000) with a 5- to 12-MHz linear multi-frequency probe (L12–5).

The sonographic study was performed with the patient in dorsal decubitus position, with a cushion under the shoulders and with the neck hyperextended. The probe was lightly positioned on the skin without any compression to ensure correct estimation of vascularization intensity. The images were obtained using power Doppler. Settings of the power Doppler ultrasound were standardized by using a medium wall filter, a pulse repetition frequency of 1000 Hz, a consistent focusing depth of 4.8 cm and 82% color power angio (CPA). The vascularity pattern was evaluated using transverse scans performed along the maximum diameter of the nodules.

As seen in Figure 1, the power Doppler vascular density of a thyroid tumor dynamically changed over consecutive frames. Figure 1a is the frame with minimal vascularity density, likely indicating a state of low perfusion. Figure 1b is the frame with maximal vascularity density, indicating a probable high perfusion state. To collect information from these frames using a method other than subjectively choosing only one or a few, all scanned images were analyzed off-line through dicom format, which contains forty-five 24-bit frames of consecutive images 640 $\times$ 476 pixels in size. The quantification of vascular parameters was automatically computed by the proprietary software AmCAD-UV (AmCad BioMed, Taipei City, Taiwan).