Ultrasound in Med. & Biol., Vol. ■, No. ■, pp. 1–7, 2015

0301-5629/$ - see front matter

ELSEVIER

http://dx.doi.org/10.1016/j.ultrasmedbio.2015.01.001

● *Original Contribution*

VASCULARITY ASSESSMENT OF THYROID NODULES BY QUANTITATIVE COLOR DOPPLER ULTRASOUND

Laith R. Sultan, Hui Xiong, Hanna M. Zafar, Susan M. Schultz, Jill E. Langer, and Chandra M. Sehgal
Department of Radiology, University of Pennsylvania, Philadelphia, Pennsylvania, USA

(*Received* 23 *May* 2014; *revised* 25 *November* 2014; *in final form* 1 *January* 2015)

Abstract—Our objective was to assess the role of quantitative Doppler vascularity in differentiating malignant and benign thyroid nodules. Color Doppler images of 100 nodules were analyzed for three metrics: vascular fraction area, mean flow velocity index and flow volume index in three regions (nodule center, nodule rim and surrounding parenchyma). Vascular fraction area and flow volume index were higher in malignant than benign nodules in both the central and rim regions, whereas flow velocity index was equivalent in both regions. Of the three vascularity metrics studied, the vascular fraction area of the central region was most effective in predicting malignancy, with a sensitivity of 0.90 ± 0.05, specificity of 0.88 ± 0.13, positive predictive value of 0.84 ± 0.14, negative predictive value of 0.92 ± 0.03 and accuracy of 0.89 ± 0.08. Quantitative Doppler vascularity of the nodule center yielded a high level of discrimination between benign and malignant nodules and, thus, has the greatest potential to contribute to gray-scale assessment of thyroid cancer. (E-mail: Chandra.sehgal@uphs.upenn.edu) © 2015 World Federation for Ultrasound in Medicine & Biology.

Key Words: **Quantitative Doppler ultrasound, Thyroid cancer, Cancer diagnosis.**

INTRODUCTION

Thyroid cancer is the most common endocrine cancer and the fastest growing incident cancer diagnosis among all cancer diagnoses in both men and women. In 2013, the American Cancer Society estimated that approximately 60,220 new thyroid cancers were diagnosed, the majority through biopsy. Currently, high-resolution sonography is the modality of choice for evaluating thyroid nodules; its use has evolved beyond simple differentiation between solid and cystic thyroid lesions to playing an important role in differentiating benign nodules from those with indeterminate or probable malignant features warranting biopsy (Cheng et al. 2013).

Although the use of color Doppler sonography has grown increasingly significant in the diagnosis of malignant tumors of various organs, such as the liver, breast, ovary and prostate, as well as in the differential diagnosis of lymphadenopathy (Kidron et al. 1999; Martinoli et al. 1998; Schick et al. 1998; Sehgal et al. 2000; Shigeno et al. 2000; Sohn et al. 1997; Tanaka et al. 1998), its role in the management of thyroid nodules remains limited and not well established.

In general, the distribution of blood vessels in Doppler images of thyroid nodules is characterized subjectively as either central (intranodular) or peripheral (perinodular) (Sofferman and Ahuja 2012). Most benign nodules have either absent vascularity (type 1) or perinodular vascularity greater than intranodular vascularity (type 2). In contrast, malignant nodules generally exhibit intranodular vascularity that is greater than peripheral vascularity (*i.e.*, type 3) (Fig. 1). Accordingly, various studies have exploited differences in regional vascularity by Doppler sonography for thyroid cancer diagnosis (Appetecchia and Solivetti 2006; Brunese et al. 2008; Chan et al. 2003; Frates et al. 2003; Papini et al. 2002; Varverakis et al. 2007). However, results from these studies have been mixed, and currently there is no unanimity on the value of Doppler imaging in differentiating malignant and benign nodules. Although these studies have indicated that the presence of central vascularity assessed by Doppler imaging enhances the sensitivity and specificity of the diagnosis (Frates et al. 2003; Papini et al. 2002; Varverakis et al. 2007), the same studies also found that not all malignant nodules have central vascularity (Papini et al. 2002) and up to

Address correspondence to: Chandra M. Sehgal, Department of Radiology, University of Pennsylvania, 1 Silverstein, 3400 Spruce Street, Philadelphia, PA 19104, USA. E-mail: Chandra.sehgal@uphs.upenn.edu

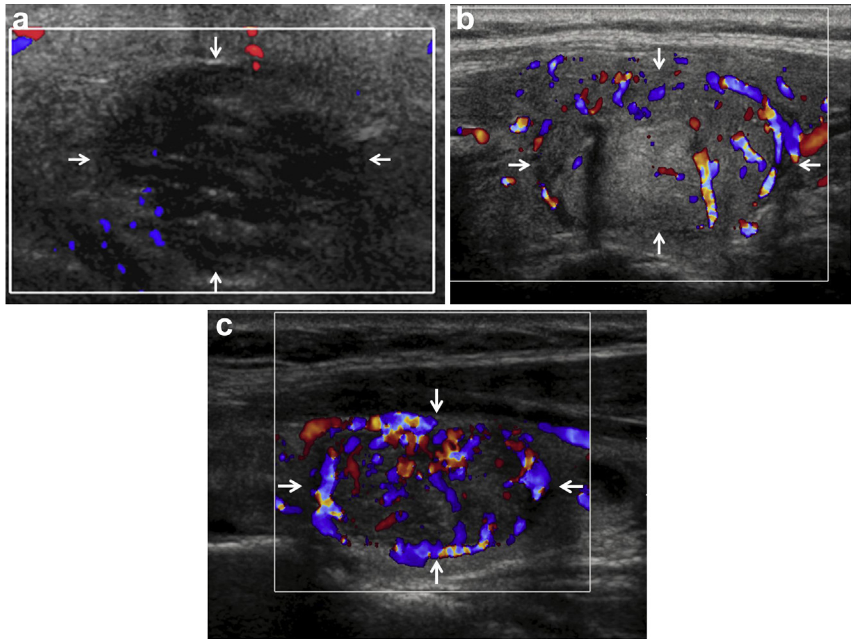

Fig. 1. Color Doppler images of thyroid nodules. (a) Benign thyroid nodule with absent vascularity (type I vascularity pattern). (b) Benign nodule with more peripheral than central vascularity (type II vascularity pattern). (c) Malignant nodule with higher vascularity particularly in the central region (type III vascularity pattern). The *arrows* point to the lesion in the three images.

50% of hypervascular nodules are benign (Frates et al. 2003). Such discrepancies can potentially arise from the subjective and qualitative nature of Doppler image evaluation, as well as the histologic subtypes of the cancers in the studied populations. To address these issues, we evaluated a quantitative approach to studying the Doppler vascularity of thyroid tumors, as previously recommended (Lyshchick et al. 2007). Instead of subjectively dividing nodules into intra- and perinodular regions, we used an automated approach that divides the lesion into concentric regions of equal area. The use of Doppler ultrasound to differentiate malignant from benign nodules was optimized by the learning and testing methodology commonly used in machine learning-based decisions.

METHODS

Image acquisition

The institutional review board approved this retrospective study and waived the need for informed consent. Images of 100 thyroid nodules from 99 patients were acquired from the institutional clinical database for the years 2002–2012. All nodules selected for analysis had a diagnostic fine-needle aspiration (FNA) result of either benign or malignant; nodules with other cytologic results (*e.g.*, follicular lesion of uncertain significance) were excluded. Included images were drawn from routine clinical examinations performed by multiple sonographers using a variety of ultrasound scanners including the Philips HDI 5000 (68 cases), Philips iu22 (30 cases), GE LOGIC E9 (1 case) and GE LOGIC 9 (1 case). All sonographers were board certified by the American Registry for Diagnostic Medical Sonography, which includes testing on thyroid imaging, and during the study period, technologists averaged 7 y in clinical practice. Thyroid examinations included in this study were performed using practice guidelines established by the American Institute of Ultrasound in Medicine (AIUM). With the use of standardized clinical procedures, color Doppler gain was maximized until disappearance of noise. Similarly, pulse repetition frequency (PRF) was increased to a level just below aliasing. Furthermore, a radiologist reviewed all studies before patient discharge. Included nodules consisted of 58 cytology-proven benign nodules and 42 surgically confirmed malignant tumors. No specific inclusion or exclusion criteria were used to select the images in the study. Images of one patient acquired with a Phillips iu22 scanner were found to be of inadequate quality and were not included in the study. For each patient, date of birth, race and gender were recorded.

Qualitative analysis

Vascularity patterns of the thyroid lesions were first analyzed qualitatively. A physician with 3 y of general radiology training, blinded to the histologic diagnosis, classified the cases as absent vascularity (type 1), perinodular vascularity greater than intranodular vascularity (type 2) or intranodular vascularity greater than