Ultrasound in Med. & Biol., Vol. 35, No. 10, pp. 1607–1614, 2009

0301-5629/09/$–see front matter

doi:10.1016/j.ultrasmedbio.2009.05.014

● *Original Contribution*

COMPUTER-AIDED DIAGNOSIS FOR BREAST TUMORS BY USING VASCULARIZATION OF 3-D POWER DOPPLER ULTRASOUND

YU-LEN HUANG,* SHOU-JEN KUO,† CHIA-CHIA HSU,* HSIN-SHUN TSENG,† YI-HSUAN HSIAO,† and DAR-REN CHEN†

*Department of Computer Science and Information Engineering, Tunghai University, Taichung, Taiwan; and †Comprehensive Breast Cancer Center, Cancer Research Center, Changhua Christian Hospital, Changhua, Taiwan

(*Received* 16 *May* 2008, *revised* 12 *May* 2009, *in final form* 18 *May* 2009)

Abstract—This study assessed the accuracy of three-dimensional (3-D) power Doppler ultrasound in differentiating between benign and malignant breast tumors by using a support vector machine (SVM). A 3-D power Doppler ultrasonography was performed on 164 patients with 86 benign and 78 malignant breast tumors. The volume-of-interest (VOI) in 3-D ultrasound images was automatically generated from three rectangular regions-of-interest (ROI). The vascularization index (VI), flow index (FI) and vascularization-flow index (VFI) on 3-D power-Doppler ultrasound images were evaluated for the entire volume area, computer extracted VOI area and the area outside the VOI. Furthermore, patient's age and VOI volume were also applied for breast tumor classifications. Each ultrasonography in this study was classified as benign or malignant based on the features using the SVM model. All the tumors were sampled using k-fold cross-validation (k = 10) to evaluate the diagnostic performance with receiver operating characteristic (ROC) curves. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy of SVM for classifying malignancies were 94%, 69%, 73%, 92% and 81%, respectively. The classification performance in terms of A*z* value for the ROC curve of the features derived from 3-D power Doppler is 0.91. This study indicates that combining 3-D power Doppler vascularity with patient's age and tumor size offers a good method for differentiating benign andmalignant breast tumors. (E-mail: ylhuang@thu.edu.tw (Y.-L.H.); darren_chen@cch.org.tw (D.-R.C.)) © 2009 World Federation for Ultrasound in Medicine & Biology.

Key Words: **Three-dimensional power Doppler, Tumor vascularity, Volume-of-interest, Computer-aided diagnosis, Support vector machine.**

INTRODUCTION

Tumor vascularity has been demonstrated to be an important factor correlated with tumor malignancy (Folkman 1985, 1990). Angiogenesis is widely accepted as a fundamental process involved in tumor establishment, growth and dissemination. The growth of breast cancer is related to angiogenesis during the development of the tumor. Compared with benign tumors, breast cancers are expected to exhibit increased vascularity (Sehgal et al. 2000). Various investigations have reported the vascularity of breast tumors and distinguished between benign and malignant lesions using color Doppler ultrasound (Cosgrove et al. 1990; McNicholas et al. 1993; Madjar et al. 1997). Color Doppler sonography characterizes blood flow velocities and the calculation of resistance indices using the mean Doppler frequency shift at a specific position. The heterogeneous vascularity of breast malignancies is the major problem in flow assessment with color Doppler (Madjar 1992). Color Doppler performs poorly in detecting the vessels perpendicular to the beam direction. A study dealing with preoperative assessment of breast lesions showed that color Doppler sonography did not outperform other diagnostic methods because it was vulnerable to being affected by changes in probe direction (Blohmer et al. 1999).

Power Doppler was developed to enhance small vessel visualization using a different measurement of the strength of the Doppler signal, which essentially depends on the amount of blood. Power Doppler ultrasound offers a clearer means of detecting the course of tumor vessels due to its being less angle-dependent, as well as being independent of velocity above the cut off threshold. Power Doppler imaging, thus, outperformed color Doppler imaging in classifying benign and malignant breast

Address correspondence to: Yu-Len Huang, Department of Computer Science and Information Engineering, Tunghai University, 181, Taichung-Kang Road, Sec. 3, Taichung 407, Taiwan. E-mail: ylhuang@thu.edu.tw; Dar-Ren Chen, Comprehensive Breast Cancer Center, Laboratory of Cancer Research, Changhua Christian Hospital, 135 Nanhsiao Street, Changhua 500, Taiwan. E-mail: darren_chen@cch.org.tw

masses based on assessment of tumor vascularity (Wright et al. 1998; Lee et al. 2002). These studies have demonstrated that power Doppler ultrasound has higher diagnostic accuracy than color Doppler ultrasound. Particularly, three-dimensional (3-D) power Doppler ultrasound can quantify the power Doppler signal and detect total vascularity within the entire breast tumor volume (Carson et al. 1997; Chang et al. 2006).

Volume information is important for physicians in making diagnosis because malignancy tends to be associated with larger tumor size. Due to malignant tumors frequently being large, volume data, thus, has been considered a useful characteristic for differentiating benign and malignant breast tumors (Riccabona et al. 1996; Chen et al. 2003b; Hsiao et al. 2008). Moreover, statistics from American Cancer Society (2005) have indicated that breast cancer usually occurs in females over 40 years old and, moreover, there is a positive relationship between increasing age and tumor malignancy. Recently, there has been interest in the associations between patient's age and breast cancer vascularity by 3-D power Doppler ultrasound (Hsiao et al. 2008). The authors state that age and tumor volume are two of important factors in the differentiating between malignant and benign tumors. Owing to relationship between age of patients and volume of breast tumors with the potential malignancy of the tumor, they added age and tumor volume as two of the classification factors in vascularity analysis. The investigation also demonstrates advanced patient age and larger tumor volume are significant factors that predict malignancy in patients with breast tumor.

This study utilized computer-aided diagnosis (CAD) for power Doppler imaging to assist physicians in diagnosis and improve the prevision accuracy. The proposed CAD classified breast tumors as benign or malignant using a support vector machine (SVM). The SVM model has become extremely popular as a method of classification and prediction (Christianini and Shawe-Taylor 2000; Kim et al. 2002; Song et al. 2002). This technique, which is capable of exceptional and rapid classification, was widely applied not only to classification but also to image recognition and bioinformatics (El Naqa et al. 2002; Song et al. 2002; Sun et al. 2003; Huang et al. 2006, 2008). This study considered vascular features, tumor volume and patient age as features for differentiating benign and malignant breast tumors. Furthermore, the SVM model was employed as a classifier to assess the capabilities of 3-D power Doppler ultrasonographic technology for differential diagnosis of solid breast tumors.

MATERIALS AND METHODS

Patients

The study was approved by the institutional review board and ethics committee at Changhua Christian Hospital, Taiwan. Informed consent was obtained from all patients. If the patient had multiple breast lesions, the biggest lesion was included in the study.

Data acquisition

During the period of January to December 2003, there were 86 benign and 78 malignant breast tumors in 164 patients whose ages ranged from 17 to 80 years (mean age, 44 years) were collected. All these identified solid tumors had undergone fine needle aspiration cytology, core biopsy or/and excisional biopsy. Informed consent was obtained from all patients. All of the 3-D ultrasound imaging and 3-D power Doppler ultrasound imaging was performed with a scanner (Voluson730; GE Healthcare, Zipf, Austria, equipped with RSP 6-12 transducer). The transducer was a linear-array broadband probe with a frequency of 6 to 12 MHz, has a scan width of 37.5 mm and a sweep angle of 5 to 29 to obtain 3-D volume scanning. A preinstalled 20° sweep angle and power Doppler settings with mid frequency, 0.9 kHz pulse repetition frequency, -0.6 gain, and ''low 1'' wall motion filter were fixed for all women in this study. If patient's chest wall movement was prominent on scanning (each scanning takes about 10–15 seconds) excessive artifact is created. The operator also held the large 3-D probe as steady as possible to lessen the artifact on scanning.

To avoid the variations, such as intensity of power Doppler color gain, body habitus, and wall filter, settings were maintained throughout the whole study. Each 3-D volume had 199 two-dimensional (2-D) ultrasound images with corresponding power Doppler ultrasound images. Figure 1 presents the ultrasound image and its corresponding power Doppler ultrasound image.

VOI extraction

To extract the volume-of-interest (VOI) in 3-D ultrasound imaging, a physician with experience in breast ultrasound examination defined and manually selected a rectangular region-of-interest (ROI) including the tumor border in the specific three slices, *i.e.*, the first, middle and last slices in 3-D ultrasound imaging (Chen et al. 2003a). The first, middle and last slices were the slice on which tumor tissue appeared, the slice on which the tumor diameter was largest and the slice on which the tumor was disappearing, respectively. Figure 2 presents an example of the ROI for the three slices that were manually selected by the physician. After defining the ROIs in the three slices, the VOI area was automatically extracted from the 3-D volume. Figure 3 illustrates generation of the VOI area in 3-D power Doppler ultrasound imaging. The selected VOIs were outlined to include the entire extent of the tumor margin. The VOI extraction procedure is the easiest way to derive an approximate tumor volume.