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Role of 3D power Doppler ultrasound in the further characterization of suspicious breast masses

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ABSTRACT

Purpose: To investigate effectiveness of vascular indices obtained with 3D power Doppler ultrasound in the further characterization of breast masses and prevention of unnecessary biopsies.

Materials and methods: Between April 2013 and March 2014, 109 patients (age range, 17–85 years; mean age, 47 years) with 117 radiologically or clinically suspicious breast masses were prospectively evaluated with 3DPDUS before biopsy. Mass volume (MV), vascularization index (VI), flow index (FI) and vascularization flow index (VFI) were calculated using Virtual Organ Computer-aided Analysis (VOCAL) software and they were correlated with the final diagnosis. Cutoff values of vascular indices were determined and diagnostic efficacy was calculated with receiver operating curve (ROC) analysis.

Results: All vascular indices, age of patients and tumor volume were significantly lower in benign masses compared with malignant ones ($p < 0.001$). AUCs were 0.872, 0.867 and 0.789 for VI, VFI and FI, respectively. The diagnostic efficacy of VI (for cutoff 1.1; 83% sensitivity, 82% specificity and 82% accuracy) and VFI (for cutoff 0.4; 80% sensitivity, 83% specificity and 80% accuracy) were significantly higher than FI (for cutoff 33,9; 73% sensitivity, 69% specificity and 71% accuracy). It was found that with the use of vascular indices of 3DPDUS in the further characterization of suspicious breast masses between 24% to 37% of unnecessary biopsies could have been avoided.

Conclusion: The vascular indices obtained with 3DPDUS seem reliable in the further characterization of suspicious breast masses and might be used to decrease unnecessary biopsies.

1. Introduction

Breast cancer is the most frequently diagnosed cancer in women and there is an increase in its incidence. Mammography and ultrasound are most widely used radiological methods for the diagnosis of breast cancer [1,2]. They have high sensitivity but low specificity. Because of this, approximately 40–60% of the breast biopsies performed based on mammographic and ultrasonographic findings result in benign diagnosis [3,4]. These negative biopsies load unnecessary fear, anxiety, discomfort, pain and financial cost to the patients. Therefore, reliable techniques are needed to be able to reduce the negative biopsy rates in breast.

Many imaging techniques and interpretation strategies had been developed and used to increase the specificity and positive predictive value (PPV) in breast imaging. One of these techniques is three dimensional (3D) power Doppler ultrasoud.

Increased vascularity plays an important role in uncontrolled growth invasion and metastasis of the malignant tumors [5,6]. Vascularity is evaluated with many techniques to be able to characterize tumors as either benign or malignant. Color or power Doppler ultrasound is used in many studies to evaluate vascularity of breast tumors. Power Doppler US is shown to be superior to color Doppler US in the differentiation of benign from malignant breast tumors [7]. Because it has higher sensitivity to low flow rates, independent from the Doppler angle and has not aliasing artifact [8].

Three-dimensional power Doppler US is a newly developed technology. This noninvasive technology has the potential to eveluate and quantify blood flow within tissues, organs and tumors [9,10]. In studies of 3D power Doppler US, virtual organ computer-aided Analysis (VOCAL) software is used to calculate volume and vascularity [11–14]. Three vascular indices are obtained with this software; vascularization index (VI), flow index (FI) and vascularization flow index (VFI) [14]. VI is the ratio of color voxels to all voxels in the interested volume and shows the density of vessels.

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FI is the mean value of all color voxels in the studied volume and represents average color intensity. VFI is the combination of two and sum of weighted color voxels divided by all voxels and shows vascularization and perfusion [13].

There are studies that used 3DPDUS in clinical fields of obstetrics, oncology and breast [15,16]. In the breast there are some studies showed that malignant masses had significantly higher vascular indices than benign ones [17–19]. Hovewer there are conflicting result about which vascularity parameter is more effective and it is not known how much we could prevent unnecessary biopsies with the use of 3DPDUS in the breast.

In this study, we aimed to determine the role of 3DPDUS in further characterization of suspicious solid breast masses and prevention of unnecessary biopsies.

2. Materials and methods

2.1. Study population

Between April 2013 and March 2014, 109 patients (age range, 17–85 years; mean age, 47 years) with 117 radiologically or clinically suspicious breast masses were prospectively evaluated by using 3DPDUS before biopsy. Simple cysts and new biopsied masses were excluded from the study. Because it was not possible to include whole lesion into one 3D acquisition, masses larger than 5 cm were not also included in the study. Final diagnoses were obtained with histopathologic analysis of core and/or excisionally biopsied masses. Patients with a benign diagnosis at core biopsy were followed up for at least 1 year with mammography and/or ultrasound to ensure the stability of the lesions. The study was approved by the Institutional Ethics Committee, and written informed consent was obtained from all patients before 3DPDUS exam.

2.2. 3DPDUS examination

All examinations were performed by using Voluson 730 Expert (General Electric, Waukesha, Wisconsin) with a volumetric lineer probe. This transducer is a broad-based linear-array probe with a frequency of 6–12 MHz, has 50 mm scanning width and a sweep angle of 5–29° to allow for the performance of a 3D volume scan. All examinations were performed in supine position with the arm extended overhead. The transducer was held with enough jelly to contact the skin and care was given not to compress breast tissue too much. During performing 3D volume scan, all women were asked to hold their breath approximately 20 s. In order to standardize our assessment of breast vascularization, following power Doppler settings were used; pulse repetition frequency, 0.9 kHz; wall motion filter, low 1; quality, normal; frequency, low; harmonic frequency, middle; smooth, 5/5, line density, 7; balance gray >170; artifact on. After the mass was localized in the 2D view, 3D static power Doppler scanning was performed by using the widest scanning angle (29°) including the whole breast mass (Fig. 1). Firstly, the highest gain was set and then gain reduced until all artefacts were disappeared. After the examination, the obtained volume datasets were analyzed by using the VOCAL software. The rotation angle was set to 30°. Thereby, six different consecutive mass sections were obtained. Whole contours of the mass had been drawn manually in those six different sections (Fig. 2). After than that, volume and three vascular indices of vascularization index (VI), flow index (FI), and vascularization flow index (VFI) parameters belong to mass were calculated automatically by histogram facility in the VOCAL software (Fig. 3). Of the complex cystic lesions, just the solid components were evaluated.

2.3. Statistical analysis

All the data were analyzed using the Statistical Package for the Social Sciences (SPSS 13.0 Statistical Software, SPSS Inc., Chicago, IL, USA). The medians and ranges of patient age, tumour size, volume, and vascularization indices of benign and malignant breast tumors were calculated. The Kolmogorov–Smirnov test was used to show deviation from normal distribution. The non-parametric Mann–Whitney *U* test for volume, VI, VFI and the parametric Student's *t* test for FI were used to compare volume and vascular indices of benign and malignant breast lesions. Also, the non-parametric Mann–Whitney *U* test was used to compare vascular indices of different histologic types. Optimal cutoff points of vascular indices for the differentiation of malignant and benign lesions were found with receiver operating characteristic (ROC) analysis. If the obtained vascular index value which was less than the given cut-off value were considered as benign, if not considered as malignant. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy of vascular indices were calculated. To determine the effect of the tumor volume on diagnostic performances, volume was classified in to two groups as larger than or equal to 2 cm^3 or smaller than 2 cm^3. ROC analysis was performed to assess the diagnostic performances of vascular indices. The area beneath the fitted binormal ROC curve (AUC) was used as a measure of diagnostic efficacy. The AUC values were calculated and were compared. A p value of less than 0.05 was considered to indicate a significant difference.

3. Results

In the present study, 63 (53.8%) of the 117 suspicious breast masses were malignant. Histopathologic diagnosis were 53 invasive ductal carcinomas (IDCs), five invasive lobular carcinomas (ILCs), three papillary carcinomas, one mucinous carcinoma and one ductal carcinoma in situ. Fifty-four (46.2%) of the 117 suspicious breast masses were diagnosed as benign. Those were 21 fibroadenomas, five papillomas, four fibrocystic changes, two mastitis, one fat necrosis, one benign epithelial hyperplasia, one sclerosing adenosis and 19 benign histopathology. Of the 117 biopsied masses; 9 (7.6%) had been classified prospectively as BI-RADS 3, 57 (48.7%) as BI-RADS 4 and 51 (43.5%) as BI-RADS 5. Biopsies in category 3 masses were performed due to clinical suspicious findings or patient preferences

The median ages of patients were 42 years (range 17–58) and 50 years (range 26–85) for benign and malignant groups, respectively. Patient ages, tumor volumes and vascular indices for benign and malignant tumors were given in Table 1. All vascular indices, age of patients and tumor volume were significantly lower in benign masses compared with malignant ones ($p < 0.001$). The median values of VI, FI and VFI in two biggest histologic type of IDCs and ILCs were 3.58, 36.8, 1.40 and 2.46, 36.1, 0.9, respectively. There were not significant differences between the vascular indices of these two histologic group ($p = 0.357$).

Table 1
The comparison of age, mass volume (MV) and vascular indices between benign and malignant breast masses.

	Benign	Malignant	p Value
Age	42 ± 1.3	50 ± 1.3	<0.001
MV	1.1 ± 0.2	2.8 ± 0.5	<0.001
VI	0.2 ± 0.2	3.8 ± 0.5	<0.001
FI	30.4 ± 0.8	36.9 ± 0.7	<0.001
VFI	0.1 ± 0.1	1.5 ± 0.2	<0.001

MV: Mass Volume; Values are mean values ± SD; p: significance level for all pairs