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● *Original Contribution*

# NON-MASS BREAST LESIONS ON ULTRASOUND: FEATURE EXPLORATION AND MULTIMODE ULTRASONIC DIAGNOSIS

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**Abstract—The aim of this study was to analyze the features of non-mass breast lesions (NMLs) on B-mode ultrasound (US), color Doppler US, strain elastography (SE) and contrast-enhanced ultrasound (CEUS) and to develop a multimode ultrasonic method for NML differentiation. Seventy-one NMLs were included in this retrospective study. Binary logistic regression was used to identify the independent risk factors. Pathology results were used as the standard criterion. Microcalcification on US, high stiffness on SE and hyper-enhanced intensity on CEUS were identified as features correlated with malignancy. A multimode method to evaluate NMLs based on the logistic regression was developed. The sensitivity and specificity for US, US + Doppler, US + SE, US + CEUS and the multimode method were 100% and 29%, 92.5% and 41.9%, 97.5% and 58.1%, 90.0% and 58.1% and 95.0% and 77.4%, respectively. The accuracy of these methods was 69.0%, 70.4%, 80.2%, 76.1% and 87.3%, respectively. The multimode ultrasonic method is simple and exhibited high diagnostic performance, which might be helpful for predicting the potential malignancy of NMLs. (E-mail: Luobm@mail.sysu.edu.cn, bmluo2005@126.com)** **© 2018 World Federation for Ultrasound in Medicine & Biology. All rights reserved.**

*Key Words:* **Breast diseases, Ultrasonography, Elasticity, Contrast media, Diagnosis, Non-mass breast lesions on ultrasound, Feature exploration, Multimode ultrasonic diagnosis.**

## INTRODUCTION

Due to its technical development, ultrasound (US) has become an important screening tool for Chinese women with dense breasts. Most abnormalities found by US are mass-like lesions that can be outlined and standardized by the American College of Radiology Breast Imaging Reporting and Data System atlas (ACR BI-RADS) (American College of Radiology 2013). However, some lesions still lack typical features of masses and present as ill-defined geographic hypo-echoic, tubular hypo-echoic duct-like structural or architectural distortions, which were defined as NMLs by radiologists (Ko et al. 2015). NMLs have been reported to constitute 9.21% (95% confidence interval [CI]: 9.09%–9.33%) of breast abnormalities (Choi et al. 2016; Ko et al. 2012, 2014; Wang et al. 2015). Calcification and architectural distortions have been reported to be common features of NMLs (Ko et al. 2015). A previous review (de Paula and Campos 2017) of nipple discharge found that the most common characteristic on magnetic resonance imaging was non-mass enhancement, whereas on ultrasound imaging, the usual findings were ductal ectasia, subareolar nodules and acoustic shadowing, which would fulfill most of the criteria of NMLs. Ko et al. (2015) classified the B-mode presentations of NMLs into four categories: type I for ductal NML pattern (Ib with calcification, Ia without); type II for non-ductal NML pattern (IIb with calcification. IIa without); type III for NMLs with architectural distortion; and type IV for NMLs with posterior acoustic shadowing. Then the four NML types were correlated with different BI-RADS categories 4a (types IIa), 4b (types Ia, III and IV) and 4c (types Ib and IIb). According to their positive predictive values, the four types were found to be helpful in the differentiation of benign from malignant lesions. However, the differentiation of NMLs by B-mode US remained ambiguous, and further exploration was needed.

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Ultrasound imaging technologies were commonly used in the diagnosis of breast disease, such as elastography and contrast-enhanced ultrasound (CEUS), which have been applied in clinical practice for decades (Guo et al. 2018). Both techniques have unique advantages. The mechanical index of tissue (elasticity) can be evaluated *via* elastography. Strain elastography (SE) and shear wave elastography (SWE) are the two main elasticity techniques routinely used. SE is both qualitative (5-point scoring system) and semiquantitative (strain ratio) based on color maps imposed on 2-D images, whereas SWE is both qualitative and quantitative based on color maps and numerical values. Elastography is useful in the differentiation between malignant and benign breast lesions, and after intensive research, the value of elastography is well-established in cases of breast masses (Burnside et al. 2007; Itoh et al. 2006; Parajuly et al. 2010; Zhi et al. 2013). With respect to NMLs, benign NMLs were reported to be soft with lower quantitative values ($E_{mean}$ and $E_{max}$) on SWE (Choi et al. 2016; Ko et al. 2014), whereas malignant lesions were harder (Ko et al. 2014). With the use of contrast agents, CEUS can depict the microcirculation of breast masses and provide qualitative and quantitative analysis for characterizing breast lesions (Guo et al. 2018), which has been reported to be beneficial for breast tumor differentiation (Wan et al. 2012; Wang et al. 2016; Xia et al. 2014; Xiao et al. 2014, 2017). Whether CEUS could be helpful in the differentiation of NMLs remained uncertain.

Multimode ultrasound diagnosis is a diagnostic method combining B-mode US, elastography and CEUS. Additional information regarding the elasticity and vascularity of breast lesions could improve the low specificity of B-mode US. To our knowledge, no study has evaluated NMLs by B-mode US combined with elastography and CEUS so far. Therefore, the aims of our study were to (i) explore significant features of NMLs based on B-mode US, SE and CEUS; (ii) perform multivariate logistic regression analysis to identify risk factors of NMLs; and (iii) develop a multimode ultrasound method for differentiation of NMLs that could be used in practice and that, we supposed, would perform better than any single modality.

## METHODS

*Patient enrollment*

This retrospective study was approved by the institutional review board. Patient approval and informed consent were waived because of strict maintenance of patient anonymity. From December 2014 to November 2016, 928 consecutive patients were referred to our department for breast US. Among the lesions detected, 82 lesions in 79 patients fulfilled the criteria for NMLs, as they exhibited distortion of normal breast tissue or layered duct-like structures with no space occupation on two different projections. Meanwhile, no previous surgery or biopsy had been performed in the region of the lesion. Five of the 82 lesions were excluded for unavailable pathology result, and 6 were excluded for the lack of CEUS data. And finally, 71 lesions in 68 patients underwent thorough CDFI (color Doppler flow Imagine (CDFI), SE and CEUS and were included in our study. The maximal diameter of the lesions ranged from 0.47 to 5.62 cm (mean diameter: 2.25 ± 1.30 cm). Patients ranged from 23 to 79 y of age (mean age: 46.32 ± 9.96 y). Among these 68 patients, 49 patients complained of palpable mass, 12 patients complained of nipple discharge, 8 patients complained of pain and 2 patients found an enlarged axillary lymph node without breast uncomfortable. Finally, 70 lesions underwent surgical excision, and 1 lesion underwent core-needle biopsy. The pathology results were used as the reference standard.

In total, 40 women with 43 lesions underwent mammography. Architecture distortion was observed in 1 lesion (malignant). Calcification alone was found in 15 lesions (10 malignant, 5 benign). Anomalous density alone was observed in 8 lesions (5 malignant, 3 benign), and both anomalous density and calcification were found in 9 lesions (6 malignant, 3 benign). Hyperplasia without any other features on mammography was observed in 10 lesions and was categorized as BI-RADS 2 (3 malignant, 7 benign).

*Ultrasound examination*

B-Mode US, CDFI, SE and CEUS were performed for each lesion. All examinations were performed by two sonographers with 12 and 20 y of experience in breast US. The sonographers were blinded to the clinical information and other imaging results. US and SE were performed with a HV900 (Hitachi Medical, Tokyo, Japan) equipped with a 13.5-MHz linear transducer, and CEUS was performed with an iU22 ultrasound system (Philips Medical Systems, Andover, MA, USA) equipped with 9.3-MHz linear transducer; the contrast agent was SonoVue (Bracco Imaging B.V., Geneva, Switzerland).

Bilateral whole-breast US was first used to detect the lesions. When an NML was detected, 2-D and CDFI images were recorded. Subsequently, the elasticity of the lesion was evaluated by SE, and CEUS was performed to assess the microvascularity of the lesion. The probe should be positioned perpendicular to the skin, and minimal compression is important during the entire procedure. For SE, the square region of interest (ROI) should include the whole lesion and the surrounding tissue. The superior and inferior boundaries were set to include subcutaneous fat and the pectoral muscle. Because the margins of NMLs are difficult to define clearly, the lateral boundaries were set as the entire scanning interface. To improve the quality of the elasticity image, it should be kept stable for at least