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Breast lesions diagnosed by ultrasound-guided core needle biopsy: Can shearwave elastography predict histologic upgrade after surgery or vaccuum assisted excision?

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ABSTRACT

Purpose: To compare breast stiffness based on shear-wave elastography (SWE) quantitative parameters with histopathologic results diagnosed by ultrasound (US)-guided core needle biopsy (CNB) to determine their association with upgrade rates after surgical excision or follow-up US as well as clinico-radiologic differences between upgrade and non-upgrade groups.

Materials and methods: This retrospective study enrolled 225 breast lesions from 225 patients, including 159 benign lesions, 38 high risk lesions and 28 ductal carcinoma in situ (DCIS) diagnosed by US-guided CNB. Quantitative SWE parameters of breast lesions were measured before CNB and compared according to histopathologic results (benign, high risk and DCIS) and lesion size (< 20 mm and > 20 mm). Clinico-radiologic and pathologic factors were compared between upgrade and non-upgrade groups after surgical excision or follow-up US.

Results: After surgical excision or follow-up US after more than one year, 29 lesions were upgraded for an overall upgrade rate of 12.9% (29/225). There were significant differences between upgrade and non-upgrade groups in age, mammographic category, US category, and sonographic features, including shape, margin, orientation, imaging-histologic correlation and E ratio. Patients with lesion upgrade were much older and had lesions characterized by significantly higher mammographic and US category (> 4b), irregular shape, nonparallel orientation, microlobulated or angular margin, calcification in a mass, larger size on US (> 20 mm) and greater imaging-histologic discordance. Multivariate analysis showed only mean and minimum elasticity values displayed a borderline association with histologic underestimation.

Conclusion: Upgrade of breast lesions diagnosed by US-guided CNB can be predicted using E_{mean} and E_{min} among quantitative SWE parameters.

1. Introduction

Percutaneous ultrasound-guided core needle biopsy (US-CNB) is used as an accurate, less invasive, cost-effective alternative to surgery for diagnosis of breast lesions on ultrasound (US). However, sampling error or limited sampling can lead to histologic underestimation or false negative diagnosis of breast cancer [1,2]. Histologic underestimation is reported in 17–42.7% of cases using 14- gauge core needle biopsy device [1–3], and more often occurs in high risk lesions or in ductal carcinoma in situ (DCIS), which may be upgraded to invasive cancer after surgical excision or vacuum-assisted excision (VAE) [3]. Such outcomes decrease the useful benefit of percutaneous biopsy and complicate treatment planning. Therefore, prediction of histologic underestimation in CNB is crucial for diagnosis of breast lesions.

Breast US elastography is a new technique that uses lesion stiffness, strain or shearwave elastography (SWE) as an adjunctive tool to B-mode US [4–14]. Both techniques are reported to be valuable for differentiating benign and malignant lesions. However, SWE is less operator dependent and reproducible than strain elastography [8,15]. Several studies have reported that quantitative SWE stiffness correlates with histopathologic results of breast lesions and that invasive cancer has higher stiffness than DCIS and benign lesions [16–21]. In addition, malignant lesions with higher stiffness show larger tumor size, positive lymph node status and higher histologic grade [22]. Our institution has performed SWE as an additional tool to B-mode US in patients for US-CNB since August 2013. We hypothesized that high risk lesions or DCIS

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at CNB with the possibility of histologic upgrade after surgery would have a higher stiffness than benign lesions or those without upgrade. Therefore, the purpose of our study was to investigate whether SWE could predict histologic upgrade of benign or high risk lesions and DCIS as confirmed by US-CNB after surgery or VAE.

2. Materials and methods

This retrospective study was conducted with our Institutional Review Board approval and the requirement for informed consent was waived.

2.1. Patients

Initially, 571 consecutive women who underwent SWE before US-guided core needle biopsy (CNB) between August 2013 and March 2016 were included in this study. Among them (n = 571), invasive cancers (n = 176) were excluded. High risk lesions were defined as atypical ductal hyperplasia (ADH), phyllodes tumor, radial scar, sclerosing lesion, papillary lesion and columnar cell change [1,23]. Among these lesions, 148 benign lesions were excluded because SWE was not performed (n = 102) or there was no follow-up US for at least 12 months (n = 46), and 15 high risk lesions and 7 DCIS were excluded due to the absence of SWE images or transfer to other hospital. Benign lesions were included only if excised using surgery and VAE or followed for > 12 months. Ultimately, a total of 225 lesions in 225 patients (159 benign lesions, 38 high risk lesions and 28 DCIS) were included in the current study.

2.2. US examination

Breast US examination including the axillary area was performed with a high-resolution sonographic unit using 5-10-MHz or 5-12-MHz linear-array transducers (ATL HDI 5000, Philips Healthcare-Advanced Technology Laboratories, Bothell, WA, USA; Logic 9, GE Healthcare, Milwaukee, WI, USA). After B-mode US, SWE images were obtained using a 4–15 MHz linear array transducer (Aixplorer system, Supersonic Imagine, Aix en Provence, France) by two radiologists with nine years and five years of experience, respectively, in breast imaging before biopsy. SWE images of the masses were saved after a few seconds of stabilization. The built-in region of interest (ROI) was set to include the lesion and surrounding breast tissue. The ROI was placed by the investigator at the stiffest part of the lesion including adjacent stiff tissue and the second ROI in adjacent fat layer. Lesion stiffness was represented by a color-coded map with a color range from dark blue (soft) to red (hard) indicating the highest stiffness (0–180 kilopascal (kPa)). An automatic system calculated the maximum (E_{max}), mean (E_{mean}) and minimum (E_{min}) stiffness value in kPa and the elasticity ratio (E_{ratio}).

2.3. Biopsy procedures and histopathologic evaluation

US-guided core biopsy was performed using a free hand technique with a 14-gauge dual-action semiautomatic core biopsy needle (Stericut with coaxial; TSK Laboratory, Tochigi, Japan). The throw of the biopsy needle was 2.2 cm. Each biopsy was performed by one of two specially trained radiologists dedicated to breast imaging with nine or five years of experience, respectively, under US-guidance. Four or five core samples per lesion were obtained.

After obtaining the pathologic results, imaging-histologic correlation was performed. Discordant benign lesions were recommended for larger sampling such as VAE or surgical excision. High risk lesions and DCIS underwent subsequent surgery.

2.4. Data and statistical analyses

Medical records were reviewed for clinical variables such as patient age and symptoms (palpable masses, bloody nipple discharge and pain) and interval day from CNB to surgery or VAE. Radiologic features were reviewed, including mammographic density and mammographic BI-RADS category, and US features were based on the Breast Imaging and Reporting and Data Systems (BI-RADS) lexicon [24] and included shape, margin, orientation, echo pattern, posterior acoustic features and the presence of calcification. We used the BI-RADS final assessment of the imaging study for categorical classification of the original radiology reports. Lesion size was recorded using US images divided into lesions < 20 mm and > 20 mm. For SWE, quantitative values of E_{max}, E_{mean}, E_{min} and E_{ratio} were recorded.

Histologic upgrade was defined after surgery or VAE compared with CNB results when lesions were initially diagnosed as benign, high risk or DCIS by CNB, but later diagnosed as high risk or DCIS and invasive cancer at surgical excision. The upgrade rate was determined by dividing the number of upgraded cases by the total number of CNBs performed. Upgrade and non-upgrade groups were compared using SWE parameters and clinical and radiologic features.

Histopathologic factors after surgery were reviewed, including histologic cancer type and hormonal receptor status [Estrogen receptor (ER), Progesterone receptor (PR), Human epidermal growth factor receptor-2(HER2)].

Statistical analyses were performed using the Chi-square test or Fisher's exact test for categorical variables and the Mann-Whitney U test for continuous variables. A P-value < 0.05 indicated statistical significance. All statistical analyses were performed with statistical software (SAS, version 9.4, SAS Institute Inc., Cary, NC, USA).

3. Results

Among the 225 included lesions, 159 were benign, 38 were high risk [intraductal papilloma (n = 19), ADH (n = 4), sclerosing adenosis (n = 5), phyllodes tumor (n = 4), columnar cell lesion (n = 2), radial scar (n = 2), mucocele-like lesion (n = 1), atypical lobular hyperplasia (n = 1)] and 28 were DCIS based on CNB results. Some benign lesions were excised due to imaging histologic discordance (n = 8), size increment (n = 2) and patient request (n = 3).

After surgical excision or follow-up US, 29 lesions were upgraded, for an overall upgrade rate of 12.9% (29/225) from benign to high risk (53.8%, 7/13) or benign to invasive cancer (46.2%, 6/13), high risk to DCIS or invasive cancer (100%, 6/6) or DCIS to invasive cancer (100%, 10/10).

Results of the univariate analyses are listed in Table 1. The median age was 53 (range, 32–76) years for the upgrade group (Fig. 1) and 46

Table 1
Univariate analysis of clinical and pathologic factors of histologic upgrade.

Variables	Non-upgrade (n = 196)	Upgrade (n = 29)	Upgrade rate (%)	P value
Clinical Factors				
Age (years) Median (range)	46 (17–76)	53 (32–76)		**0.0058**
Sx				0.8262
Palp	27 (62.8%)	6 (66.7%)	18.2[6/33]	
Non-Palpable	16 (37.2%)	3 (33.3%)	15.8[3/19]	
Pathologic Factors				
ER				0.8028
Negative	6 (33.3%)	5 (29.4%)	45.5[5/11]	
Positive	12 (66.7%)	12 (70.6%)	0.5[12/24]	
PR				0.1926
Negative	8 (44.4%)	4 (23.5%)	33.3[4/12]	
Positive	10 (55.6%)	13 (76.5%)	56.5[13/23]	
HER 2				0.8812
Negative	7 (43.8%)	7 (41.2%)	0.5[7/14]	
Positive	9 (56.2%)	10 (58.8%)	52.6[10/19]	

ER: Estrogen receptor. PR: Progesterone receptor. HER 2: Human epidermal growth factor receptor-2. Sx: Symptom. There were 35 patients with pathologic factors.