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Research article

Dual-modal computer-assisted evaluation of axillary lymph node metastasis in breast cancer patients on both real-time elastography and B-mode ultrasound

Qi Zhang[a,b,*], Jingfeng Suo[a], Wanying Chang[c], Jun Shi[a], Man Chen[c,**]

[a] Institute of Biomedical Engineering, Shanghai University, Shanghai, China
[b] Fujian Provincial Key Laboratory of Information Processing and Intelligent Control (Minjiang University), Fuzhou, China
[c] Department of Ultrasound, Ruijin Hospital, School of Medicine, Shanghai Jiaotong University, Shanghai, China

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ABSTRACT

Purpose: To propose a computer-assisted method for quantifying the hardness of an axillary lymph node on real-time elastography (RTE) and its morphology on B-mode ultrasound; and to combine the dual-modal features for differentiation of metastatic and benign axillary lymph nodes in breast cancer patients.

Materials and methods: A total of 161 axillary lymph nodes (benign, $n = 69$; metastatic, $n = 92$) from 158 patients with breast cancer were examined with both B-mode ultrasound and RTE. With computer assistance, five morphological features describing the hilum, size, shape, and echogenic uniformity of a lymph node were extracted from B-mode, and three hardness features were extracted from RTE. Single-modal and dual-modal features were used to classify benign and metastatic nodes with two computerized classification approaches, i.e., a scoring approach and a support vector machine (SVM) approach. The computerized approaches were also compared with a visual evaluation approach.

Results: All features exhibited significant differences between benign and metastatic nodes ($p < 0.001$), with the highest area under the receiver operating characteristic curve (AUC) of 0.803 and the highest accuracy (ACC) of 75.2% for a single feature. The SVM on dual-modal features achieved the largest AUC (0.895) and ACC (85.7%) among all methods, exceeding the scoring (AUC = 0.881; ACC = 83.6%) and the visual evaluation methods (AUC = 0.830; ACC = 84.5%). With the leave-one-out cross validation, the SVM on dual-modal features still obtained an ACC as high as 84.5%.

Conclusion: Dual-modal features can be extracted from RTE and B-mode ultrasound with computer assistance, which are valuable for discrimination between benign and metastatic lymph nodes. The SVM on dual-modal features outperforms the scoring and visual evaluation methods, as well as all methods using single-modal features. The computer-assisted dual-modal evaluation of lymph nodes could be potentially used in daily clinical practice for assessing axillary metastasis in breast cancer patients.

1. Introduction

Axillary nodal status is one of the most powerful prognostic factors of breast cancer and is crucial for breast cancer management [1–3]. The gold standard for evaluating axillary metastasis is the pathological findings of lymph nodes dissected. Axillary lymph node dissection (ALND) has been an important step in the treatment of invasive breast cancer. However, for most patients with early breast cancer, the node dissection may not exert therapeutic effect but can increase the post-operative complications [4]. In recent years, the sentinel lymph node biopsy (SLNB) is increasingly used and has become the standard for axillary staging in patients with clinically node negative axilla [5,6]. However, the SLNB is expensive and invasive and has a risk of stain allergy and false negative results. Lymphedema secondary to node dissection, whether full node dissection or SLNB, is a complication that may be encountered and ideally would be desirable to avoid. Therefore,

Abbreviations: RTE, real-time elastography; US, ultrasound; SLNB, sentinel lymph node biopsy; ALND, axillary lymph node dissection; FNA, fine-needle aspiration; S/L axis ratio, ratio of the short-axis diameter to the long-axis diameter; GLCM, gray level co-occurrence matrix; SVM, support vector machine; SD, standard deviation; SEN, sensitivity; SPC, specificity; ACC, accuracy; YI, Youden's index; AUC, area under the receiver operating characteristic curve; LOOCV, leave-one-out cross validation

* Corresponding author at: Room 803, Xiangying Building, Shanghai University, No. 333, Nanchen Rd, Shanghai 200444, China.
** Corresponding author at: 197 Rui Jin Er Rd, Shanghai 200025, China.
E-mail addresses: zhangq@t.shu.edu.cn (Q. Zhang), maggiech_1221@163.com (M. Chen).

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there is a need to develop a noninvasive, accurate and feasible system for detection of axillary metastasis.

Conventional ultrasound (US) imaging including B-mode and color Doppler can provide valuable information on the number, size, shape, boundary, internal echogenicity, and lymphatic and blood flow characteristics of lymph nodes [7,8]. Recently, real-time elastography (RTE) has been applied to assessing tissue elasticity, which involves manual compression of tissues with the hand-held transducer to generate tissue strains (deformations) [9–12]. Compared with conventional US, the RTE provides additional information with regard to the biomechanical properties of lymph nodes.

The RTE has shown to be effective in identifying metastatic lymph nodes [9,13]. In clinical practice of RTE, several grading systems including Alam [9], Tsukuba [14], Furukawa [15], Bhatia [16], Choi [17], Taylor [18] and Park [19] systems, are used for qualitative assessment of a lymph node, which are multiple-point scales that visually grade the hardness of a node. However, the grading methods suffer from considerable inter-observer variability because of their subjectiveness [16], and no standard grading protocol has been established [19]. Quantitative assessment of RTE with computer assistance is potentially valuable for more objective measurement of lymph node hardness.

The RTE imaging system often provides dual-modal visualization of lymph nodes consisting of both a B-mode image and an elastogram. However, the current evaluation methods for differentiating metastatic and benign lymph nodes are mainly focused on single-modal images, either B-mode or elastograms, and the combination of dual modalities for evaluation is limited [17,18,20,21].

The purpose of this study was two-fold: (1) to propose a computer-assisted method for quantifying nodal hardness on RTE and nodal morphology on B-mode; (2) to combine the dual-modal quantitative features with two computerized classification approaches, i.e., a computerized scoring approach and a support vector machine (SVM) approach, so as to differentiate metastatic and benign lymph nodes.

2. Methods

2.1. Image acquisition

From December 2013 to December 2014, 161 lymph nodes (92 metastatic and 69 benign) from 158 consecutive breast cancer patients (55.20 ± 5.20 years old; age range, 21–81 years), who underwent axilla conventional US and RTE simultaneously and did not take neoadjuvant therapy before SLNB or ALND, were included in this study. Ethical approval was obtained and written informed consents were received from all patients.

The pathology results of SLNB or ALND were used as the reference standard. In our hospital, fine-needle aspiration (FNA) and SLNB were recommended respectively for the clinically positive and negative lymph nodes. If the result of FNA was negative, SLNB was recommended subsequently. Axillary lymph nodes dissection (ALND) could be avoided if the result of SLNB was negative. If the result of FNA or SLNB was positive, ALND was recommended.

The L523 probe with a frequency of 4–13 MHz was used in the Mylab 90 system (Esaote, Genoa, Italy). The patient was in the supine position. The entire axilla was scanned by one radiologist with more than 5 y of experience in axillary US and 3 y in RTE. The target lymph node was selected on the conventional US and subsequently examined with the RTE. During RTE examination, the radiologist manually applied slight axial compression to a lymph node with the ultrasound probe until the pressure indicator depicted a sinus curve with 4–5 cycles and stably lasted for 2 or 3 s (bottom right in Fig. 1a). The RTE imaging system provides dual-modal visualisation in a full screen (Fig. 1a), where the left part is a grayscale B-mode image, and the right part is a composite color image displayed as a translucent color elastogram superimposed on the grayscale B-mode image.

Static images of conventional US (i.e., B-mode and Doppler) and elastograms were selected and saved for radiologists' visual evaluation of lymph nodes. For each lymph node, if a hilum was absent, static images of conventional US were obtained in the largest section of the lymph node; if a hilum was present, the static images were obtained in the largest section which included the hilum. A static elastogram (with dual-modal visualisation of both RTE and B-mode) was selected in the section where the hardest stiffness within a lymph node was found. Computer-assisted evaluation of lymph nodes was performed on the same elastograms (with B-mode side-by-side) as used in the radiologists' visual evaluation, but not on Doppler US images.

2.2. Visual evaluation of lymph nodes

Two radiologists with more than 5 y of experience in axillary US and 3 y in RTE visually interpreted and evaluated the dual-modal images, blind to patient clinical information and histopathological results of lymph nodes. Discordance was solved by consensus.

2.2.1. Visual evaluation on B-mode and Doppler US

With visual observation and manual measurement by radiologists, five features of B-mode and Doppler US were extracted to represent lymph node size, shape, hilum presence, cortical thickness, and vascular pattern, as shown in Table 1. The size of a lymph node was quantified as its short-axis diameter (in cm). The shape was evaluated as the ratio of the short-axis diameter to the long-axis diameter (S/L axis ratio), and a higher ratio means a more circular shape and a lower ratio means more elliptical shape. The vascular pattern was assessed on Doppler US and was rated as absent pattern, central pattern, peripheral pattern, or mixed pattern.

The following evaluation criteria were adopted: short-axis diameter ≥ 0.7 cm; S/L axis ratio ≥ 0.5; cortical thickness ≥ 0.4 cm; absence of a fatty hilum; peripheral or mixed disordered vascular pattern. The lymph nodes meeting three or more of the criteria were considered to have a tumor metastasis.

The visual evaluation method on B-mode and Doppler US was denoted as "B-doctor".

2.2.2. Visual evaluation on elastography

The hard area ratio was defined as the ratio of the hard area within a lymph node to the entire nodal area and was assessed visually (Table 1). If the ratio was visually estimated to be more than 50%, the lymph node was classified as metastatic. Otherwise, it was considered to be benign. The visual evaluation method on elastography was denoted as "E-doctor".

During the visual evaluation, the conventional US (B-mode plus Doppler) and elastography were also combined as follows (denoted as "C_doctor"): if a lymph node on either conventional US or RTE was evaluated as metastatic, the node was finally classified as metastatic.

2.3. Computer-assisted evaluation of lymph nodes

With computer assistance, the hardness values of a lymph node were first retrieved from the RTE image, and then five features were extracted from B-mode US and three features were extracted from RTE. Finally, two computerized classification approaches, i.e., a scoring approach and a support vector machine (SVM) approach, were used on single-modal or dual-modal features to classify benign and metastatic nodes.

2.3.1. Hardness retrieval

In the Mylab 90 system, the color bar (right in Figs. 1 a; 2 b) indicates tissue elasticity, where green, purple, and red represent soft, medium, and hard tissues, respectively. Colors in each row of the color bar represent the same elasticity but different underlying B-mode grayscales. The color elastogram was converted to a softness map