Sonoelastography of breast lesions: a prospective study of 215 cases with histopathological correlation

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Abstract

Background: Elastography is an imaging technique, which displays the hardness of soft tissue, by showing the behavior of tissue when subjected to mechanical stress. The purpose of this study was to assess the role of ultrasound elastography in differential diagnosis of breast lesions. Materials and Methods: A prospective study was conducted in our Research Centre, University of Medicine and Pharmacy of Craiova. We introduced in this prospective study 215 patients diagnosed with breast lesions between January 2009 and January 2011. The patients were examined in the supine position and a ductal exploration was made over the breast. The final diagnose was cytology (FNA – fine needle aspiration), histology after excision or follow-up for six months. For obtaining the elastography images, we used a EUS Hitachi EUB 8500 and Siemens ultrasound systems with elastography modules incorporated. For assessment of ultrasound elastography role in differential diagnosis of breast lesions, we performed ROC analysis.

Results: The elasticity score for benign lesions was on average 1.95±1.1, and for malignant lesions was 4.21±0.9. The mean diameter of malignant lesions was 27.3 mm, which was higher than the average diameter of benign lesions (19.9 mm). The most common histology of the benign nodules was fibroadenomas, cysts, and fibrocystic change. Of the malignant nodules, the most common lesion was infiltrative ductal carcinoma. We obtained a sensitivity of 85.3%, and a specificity of 90% (area under the ROC curve=0.908, 95%CI=0.856–0.945 and \(p=0.0001\)) when a cut-off point of 3 was used. Conclusions: Elastography is a method which can complement conventional ultrasound by improving the diagnostic performance. The introduction of ductal ultrasound combined with elastography increased the sensitivity and specificity, the radial technique allowing the precise localization of lesions regarding the breast gland.

Keywords: ultrasound elastography, breast lesions, ROC analysis.

Introduction

Breast cancer is the most common type of cancer in women. Advances in imaging techniques have improved the sensitivity of breast cancer detection and diagnosis [1].

The recent introduction of elastography increased the ultrasound specificity and early diagnose of breast cancer. Elastography can be thought of as an imaging technique that quantifies the hardness of a breast lesion in relation to the surrounding tissue, being useful in differentiating between benign and malignant lesions [2, 3]. Malignant tumors have a reduced elasticity, deform less and display larger dimensions on elastography [4, 5]. The benign lesions appear similar to the surrounding tissue and deform to a higher degree when compressed [6, 7]. But, the elastography data analysis is still qualitative and not quantitative, and the only possible measurements are those of strain ratio, which compares the strain of the target lesion with the fatty tissue in the breast [6].

The purpose of this study was to assess the role of ultrasound elastography in diagnosis different breast lesions with histopathology correlation.

Materials and Methods

Our study group included a prospective trial of 215 patients presenting with a breast lesions for whom ultrasound and elastography imaging was performed. An informed consent was obtained before the examination. The patients were examined in the supine position with the arm on the examination side placed behind the head. The ultrasound probe lubricated with gel was placed on the breast, and a radial, ductal, exploration was made. The breast lesion was localized using the B-mode ultrasound and then the elastography images were alongside displayed to ensure the assessment was made in the area of interest.

The technical equipment consisted in ultrasound systems provided by Hitachi Medical and Siemens with elastography modules, Doppler and SieScape techniques incorporated. One physician evaluated all ultrasound images of each lesion. Images obtained on conventional US were scored according to the Breast Imaging Recording and Data System (BI-RADS) criteria for US (grade 1 – negative for malignancy; grade 2 – benign; grade 3 – probably benign; grade 4 – lesion suspicious...
for malignancy; grade 5 – lesion highly suggestive of malignancy) [8]. The characteristics considered were shape, margin, orientation, echo pattern posterior acoustic feature and the presence of calcifications within a mass.

Elasticity images were obtained after evaluating the lesions in conventional ultrasound and the area of interest was set to include the lesion and also the subcutaneous layers and pectoralis muscle, without costal arches. The pressure was set between scores 1 to 6 (score 1 indicates the lowest pressure, score 6 indicates highest pressure). We applied a maximal pressure of 3 or 4 because strong pressure produces strain even in hard tissue, providing false information. The images were acquired in ductal, radial way and the elastography strain images were scored according to the Tsukuba elasticity score developed by Itoh A and Ueno E [3].

The use of ductal ultrasound combined with elastography is defined as full breast elastography, which is a new concept after Amy, one of the initiators of the method [9].

The elasticity of tissues was visualized on color-coded mode on Siemens, with non-elastic areas displayed as red and elastic tissue coded as green and blue. On Hitachi module, the stiffer tissue structures are displayed in blue, while the more easily deformed tissues are in red.

Five scores were used for evaluating the elastography lesions: score 1 for lesions with elasticity similar to the surrounding breast tissue, with the same strain over the entire lesion (Figure 1), score 2 were lesions with mosaic elasticity (Figure 2). Score 3 was used for lesions with elastic green periphery and stiff centre (Figure 3). Score 4 was used for nodules that were entirely stiff, excepting the echoic halo. Score 5 was reserved for cases which had no strain over the whole lesion and the adjacent tissue (Figure 4).

The strain ratio for all lesions obtained with Hitachi system was calculated with a strain ratio under 3, suggestive for a benign lesion while a strain index over 4 was suggestive for malignancy. We used fine needle aspiration cytology (FNAC) or excision biopsy for histopathologic and immunohistochemical analysis of the lesions. The lesions were divided in benign and malignant. The benign lesions were followed-up for a period of six months. The malignant lesions were classified in ductal carcinoma in situ (DCIS) and invasive carcinoma. The most common histology of the benign nodules was fibroadenomas, cysts and fibrocystic change. From the malignant nodules, the most common lesion was invasive ductal carcinoma.

Figure 1 – Ultrasound elastography performed in a 39-year-old patient reveals a hypoechoic lesion, which is green on elastography images, with a strain ratio 1.13 (A). On histopathology, the lesion was invasive ductal carcinoma, low grading G1, HE stain, 200× (B).

Figure 2 – A fibroadenoma with elasticity score 2, and strain ratio 1.03 (A), with positive immunostaining for actin in myoepithelial cells, LSAB technique, 200× (B).
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The diameter of malignant lesions was between 10–43 mm, with an average of 27.3 mm, which was higher than the benign lesions diameter (mean 19.9 mm, range between 1–39 mm). The breast cancers were confirmed by cytopathology and excision biopsy with histopathology analysis. The benign lesions were diagnosed by FNAC (41 patients), excision biopsy (49 patients) and follow-up for six months (51 patients) in which no changes were observed.

We evaluated the elasticity score for benign and malignant lesions (Table 3).

Table 3 – Distribution of elasticity score for benign and malignant breast lesions

<table>
<thead>
<tr>
<th>Elasticity score</th>
<th>Benign</th>
<th>Malignant</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>48</td>
<td>3</td>
<td>51</td>
</tr>
<tr>
<td>2</td>
<td>38</td>
<td>2</td>
<td>40</td>
</tr>
<tr>
<td>3</td>
<td>13</td>
<td>6</td>
<td>19</td>
</tr>
<tr>
<td>4</td>
<td>6</td>
<td>28</td>
<td>34</td>
</tr>
<tr>
<td>5</td>
<td>6</td>
<td>35</td>
<td>41</td>
</tr>
<tr>
<td>BGR</td>
<td>30</td>
<td>0</td>
<td>30</td>
</tr>
<tr>
<td>Total</td>
<td>141</td>
<td>74</td>
<td>215</td>
</tr>
</tbody>
</table>

BGR: Blue-green-red.

Among malignant lesions, 28 (37.8%) had an elasticity score of 4 and 35 (47.2%) had an elasticity score of 5. Six lesions (8.1%) with elasticity score 3, two lesions (2.72%) with score 2 (Figure 5) and three lesions (4.05%) with score 1 were found malignant. From 141 benign lesion, 86 lesions (60.9%) were scored 1 or 2 and 30 (21.2%) were classified as blue-green-red lesions (Figure 6). 13/141 patients (10.6%) with elasticity score of 3, six lesions scored 4 (4.2%) (Figure 7), and...
six lesions scored 5 (4.2%) turned out to be benign lesions after FNAC or excision biopsy. The elasticity score for benign lesions was on average 1.95±1.1, which was significantly lower than for malignant lesions (4.21±0.9).

The role of elastography in diagnosing breast lesions was assessed by performing ROC analysis, and we obtained a sensitivity of 85.3%, and a specificity of 90% (area under the ROC curve=0.908, 95%CI=0.856–0.945 and \( p=0.0001 \)) (Figure 8).

**Figure 5** – An hypoechoic lesion which was shaded in green and blue, Ueno score 2, and strain ratio 1.22 (A). On histopathology the lesion was invasive ductal carcinoma, intermediate grading G2, HE stain, 200× (B).

**Figure 6** – A typical blue-green-red elastographic appearance of a cyst.

**Figure 7** – Elastographic image of a calcified fibroadenoma with elasticity score 4 in a 57-year-old female (A) and diffuse positive estrogen receptors on immunohistopathology (B).

**Figure 8** – Sensitivity, specificity values on ROC analysis for elastography (MedCalc Software 9, 2008, Mariakerke, Belgium).

### Discussion

The major role of breast ultrasound is to diagnose early breast cancers. The interpretation of breast nodules detected on B-mode ultrasound (US) depends on morphological criteria. Tumor type, grade, and the presence of biological markers had a significant importance on the ultrasound characteristics. Invasive
cancers had more frequent an irregular shape, a not parallel orientation and a hypoechoic or complex echo pattern [10, 11]. Ductal carcinoma in situ has less of these typically malignant features, thus the imagist may misinterpret the lesion [12].

Thus, additional ultrasonographic criteria were developed to improve the accuracy of US including Doppler and harmonic imaging [13, 14]. US elastography is useful for differentiation between benign and malignant lesions based on their firmness. The lesions contour, the dimensions, color or strain ratio and appearance on the elastography are some of the multiple criteria used for differentiating benign and malignant lesions. The strain ratio is applied for displaying the relative compliance stiffness of lesions compared with surrounding tissues. The malignant lesions which are very stiff deform less and are displayed in blue on the elastography images compared with benign lesions which deform much more easily and are depicted as green color [15–17]. The first clinical results about elastography were published in 1997–2001, but only in 2003–2005 there was developed ultrasound equipment which had incorporated software for real time processing of elastography images and routine US examinations [17, 18]. For characterization of breast lesion, two elasticity scores are proposed: Tsukuba score developed by Itoh A and Ueno E [3, 16] and a second one, designed by the Italian Research Group after Locatelli M, Rizzatto G et al. [15]. Strain ratio is useful because it compares lesion deformability with the elasticity and compressibility of normal neighboring tissue. A ratio above 5 is considered suspicious for malignancy, but there is ongoing research for establishing the correct values for better differentiation of benign and malignant lesions.

The primary objective of our study was to evaluate the diagnostic performance of real-time freehand elastography in different breast masses with histopathology or cytopathology correlation. As results, we reported that when a cut-off point of 3 was used, elastography had a sensitivity of 85.3%, and a specificity of 90%, results that can concurred to other published data on the use of real-time ultrasound elastography. A sensitivity of 77.6% and 79.6% and specificity of 91.5% and 84.5% were the results of examination of 108 breast lesions by two examiners in a study published by Thomas A et al. [19]. Zhi H et al. [20], in a recent study, demonstrated that ultrasound elastography was the most specific, with specificity of 95.7% and with the lowest false positive rate of 4.3%.

Fibroadenomas appeared softer or with the same elasticity as adjacent glandular tissue with elasticity grade of 1 or 2, and a strain ratio suggestive for a benign lesion. Breast cysts had a characteristic three layer aspect: blue-green-red (BGR), blue being the superficial color and red the deep one, with an elasticity grade of 1, even in large dimension lesions and the fibro-cystic nodules had an elasticity aspect similar to surrounding parenchyma. In our study five cases with elasticity, one or two were malignant lesions. An explanation could be that non-scarrhous carcinomas appear softer at elastography because it contain more cellular tissue than do scirrhous carcinomas, and the five cases were carcinomas of non-scarrhous type with low and intermediate grading [21]. Also, some breast cancers may display benign features, as mucinous cancer, and we found one case with this pathology. We found six cases with elasticity score 3 and we needed cytopathologic or histopathologic confirmation for correct diagnosis. Breast carcinomas had elasticity grades of 4 or 5 and they appeared larger on the elastography image because of better visualization of the surrounding desmoplastic reaction. The strain ratio for most of the malignant lesions was over 3. False positive results for breast cancer were determined by calcified fibro-adenomas with 3 or 4 elasticity score, complicated cysts or fibro-cystic dysplasia.

Routine ultrasound examination detects many non-palpable lesions and it is not very specific for screening [22]. The advantages of ductal ultrasound consists in standardized anatomic examination of breast, with precise localization of lesions, and the visualization of connections with epithelial/parenchymatous breast structures, generally in the area of specific ducto-lobular units described by histologists. On mammography, only the micro calcifications appear as indirect signs, because the ducto-lobular epithelium cannot be visualized, the lesions spreading on intraductal or lymphatic way, lengthwise Cooper ligament. The recent introduction of elastography increased the ultrasound specificity and early diagnoses of infracentimetric breast cancer, especially quantitative elastography with FLR index, which improves the diagnosis in the stages 3 and 4 BI-RADS, decreasing the number of biopsies [23]. This imaging method allows the diagnosis and precise localization of lesions, ultrasound becoming a technique with sensitivity comparable with MRI. In clinical situations, elastography may be useful in deciding the imaging follow-up of patients or determining whether to apply interventional method [24]. Sometimes, it is difficult to differentiate between scores 2 and 3 on elastography images, but it is very easy to diagnose a lesions as having score 1, because no blue area is observed. Ultrasound elastography is less sensitive than standard US when dealing with non-focal anomalies and is not indicated for the evaluation of postoperative changes, diffuse lesions or large ones, which exceed the probe length or its field of view (FOV) [25]. Elastography is also limited in very dense, fibrous parenchyma, in case of hematomas or breast implants. Some studies demonstrate the value of elastography in benign-malignant differentiation of lymph nodes [26].

The introduction and validation of the concept of full breast ultrasonography will permit the increase of elastography sensitivity, by systematic diagnose of lesions using ductal technique, without being operator-dependent, and also the increase of diagnose specificity, the ductal ultrasound allowing the precise localization of lesions regarding the breast gland (galactophore ducts, lobules and ducto-lobular terminal units).
Conclusions

Breast elastography is a very simple and rapid method that can improve the sensitivity and specificity of ultrasound, especially when we are dealing with elastography score 3 or 4. The use of ductal ultrasound combined with elastography represents the fastest technique, with lowest cost/efficiency ratio, the most un–invasive and accessible imaging method, which can lead to a decreased rate of unnecessary biopsies. Elastography is a method which will not replace conventional B-mode US for the detection of breast cancer, but can complement conventional US by improving the diagnostic performance.

References


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