Real-time elastography – an advanced method of ultrasound: first results in 108 patients with breast lesions


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KEYWORDS: breast lesion; real-time elastography; ultrasound

ABSTRACT

Objectives To evaluate whether real-time elastography, a new, non-invasive method for the diagnosis of breast cancer, improves the differentiation and characterization of benign and malignant breast lesions.

Methods Real-time elastography was carried out in 108 potential breast tumor patients with cytologically or histologically confirmed focal breast lesions (59 benign, 49 malignant; median age, 53.9 years; range, 16–84 years). Tumor and healthy tissue were differentiated by measurement of elasticity based on the correlation between tissue properties and elasticity modulus. Evaluation was performed using the three-dimensional (3D) finite element method, in which the information is color-coded and superimposed on the B-mode ultrasound image. A second observer evaluated the elastography images, in order to improve the objectivity of the method. The results of B-mode scan and elastography were compared with those of histology and previous sonographic findings. Sensitivities and specificities were calculated, taking histology as the gold standard.

Results B-mode ultrasound had a sensitivity of 91.8% and a specificity of 78%, compared with sensitivities of 77.6% and 79.6% and specificities of 91.5% and 84.7%, respectively, for the two observers evaluating elastography. Agreement between B-mode ultrasound and elastography was good, yielding a weighted kappa of 0.67.

Conclusions Our initial clinical results suggest that real-time elastography improves the specificity of breast lesion diagnosis and is a promising new approach for the diagnosis of breast cancer. Elastography provides additional information for differentiating malignant BI-RADS (breast imaging reporting and data system) category IV lesions. Copyright © 2006 ISUOG. Published by John Wiley & Sons, Ltd.

INTRODUCTION

In the last 10 years, different sonographic methods have been developed to determine the relationship between different structures and their tissue elasticity as well as the potential use of this relationship for diagnosing malignant tumors1–3. Elastography, which involves the visual display of tissue mechanical properties’ data, is a method for detecting pathological tissue alterations in realtime4,5. This method determines compressibility parameters of a tissue under external pressure. To this end, the stretching changes of tissue displacement are recorded with the help of a high-frequency ultrasound scanner and are evaluated by correlation methods. These changes are differentiated according to static compression, dynamic oscillation and pulsed oscillation excitation6–9. Elastography evaluates elasticity by extrapolating tissue characteristics from ultrasound wave reflections from normal tissue compared with tumor tissue. The modulus of elasticity is the relationship between the tension (pressure) needed to achieve a relative change of length (extension). Thus, healthy soft tissue has higher coefficients of extension than does hard or tumorous tissue10. The investigations of the ‘Kompetenzzentrum Medizintechnik Ruhr KMR’ in Bochum, where the method of elastography was
developed in 1991, yielded the first promising results in the diagnosis of prostate carcinoma using high-frequency ultrasound in 2001. Recent publications have described the use of elastography in the diagnosis of liver lesions and in women with breast cancer.

Although conventional ultrasound and Doppler allow characterization of focal lesions, histological confirmation remains indispensable in inconclusive cases. Based on the assumption that tumor tissue is harder compared with normal tissue and is therefore less deformable, elasticity measurements might improve sensitivity in the diagnosis of breast cancer.

The aim of this study was to evaluate whether the new method of real-time elastography improves the differentiation and characterization of benign and malignant breast lesions, especially in patients with inconclusive findings or potentially malignant lesions of malignant breast lesions, especially in patients with the new method of real-time elastography improves

METHODS

A total of 150 consecutive women referred over an 8-month period to the outpatient ultrasound service with specific diagnostic queries (focal breast lesion, pain, follow-up) underwent routine diagnostic assessment. Of these, a total of 108 patients in whom B-mode ultrasound demonstrated a focal lesion were included in the study, while the other 42 patients with normal B-mode ultrasound findings were excluded. The patients included in the study had an average age of 53.9 (range, 16–84) years.

The 108 study patients underwent a further B-mode ultrasound examination using the high-end Hitachi EUB-8500 (Hitachi Medical Systems GmbH, Wiesbaden, Germany) ultrasound system, equipped with a 13-MHz linear transducer. In addition, a power Doppler examination was performed at a pulse repetition frequency of 800–1000 Hz.

Real-time elastography was performed at the same time as the second B-mode ultrasound examination, and consisted of two steps. First, we measured the echo reflected from the target tissue before and after compression; second, we reconstructed a three-dimensional image from the data obtained and evaluated mathematically the deformation as a result of compression using the finite element method. The elasticity values of the tissue structure examined with this method are determined by a so-called ‘extended combined autocorrelation’ method, which allows calculation of the stretched state of tissue in realtime. The method takes into account, and compensates for, possible lateral tissue displacement.

In the device used in this study, the sonoelastography unit is integrated completely into the system platform (Hitachi Medical Systems GmbH, Wiesbaden, Germany). With this unit, the amplitude characteristics of the echo signals are recorded during pressure induction in realtime in a region of interest. Elasticity values are calculated, color-coded and superimposed on the conventional B-mode scan. This was performed in axial as well as in lateral planes, in order to achieve higher spatial resolution and to capture the possible lateral movement of hardened regions. The induced pressure was thus very small.

A total of 324 representative ultrasound scans, consisting of two B-mode scans (one in conjunction with elastography) and a power Doppler scan for each patient, were stored on the hard disk of the ultrasound unit. For each case the observer evaluated these three standardized images, which were displayed on the monitor of the ultrasound unit; in each case they evaluated the original B-mode scan first, and then the B-mode scan in combination with the power Doppler scan. The observer was then presented all 108 elastography images for evaluation, while being blinded to the clinical data, all other imaging modalities and the final histological diagnosis. All elastography images were evaluated by a second experienced observer, who was likewise blinded.

On the B-mode scans, lesions were characterized using BI-RADS criteria; lesions of BI-RADS categories II and III were classified as benign and those of categories IV and V as malignant. The degree of vascularization determined by power Doppler was assessed on a semiquantitative analog scale as being low (1), moderate (2), or high (3). The elastography images were analyzed using a standardized color scale, with blue indicating regions with low elasticity (harder tissue areas) and red regions with high elasticity (soft tissue) (Figures 1 and 2). They were evaluated using the scoring system proposed by Matsumura et al., which distinguishes the following scores. Score 1: elasticity extending across the whole lesion (e.g. cyst); Score 2: elasticity over the largest part with individual solid structures (e.g. fibroadenoma); Score 3: elasticity in the peripheral region/solid in the center of the lesion (unclear sign); Score 4: absence of elasticity over the whole lesion (suspicion of carcinoma); Score 5: absence of elasticity over the whole lesion and vicinity (infiltrating carcinoma). In addition, both observers gave a subjective assessment of the new method of elastography.

For comparison of techniques, elastography scores were matched with the BI-RADS categories, with a BI-RADS II lesion corresponding to elastography Scores of 1 and 2, and one to one correspondence for the other categories.

Cytology and histology served as the gold standard for comparison of B-mode ultrasound and elastography. After scanning and elastography, all 108 focal lesions were examined histologically. For solid tumors jet biopsy with removal of five representative core specimens and documentation of the needle position in two planes was used. Cysts were punctured for release of pressure. Routine hematoxylin and eosin staining and immunohistological examinations were performed. All 108 aspirated specimens were examined cytologically.

Statistics

We used statistical software packages StatXact, SAS, SPFC, and SPSS (Chicago, IL, USA). To assess the accuracy...
of the elastography measurements compared with the histological results, logical (true/false) tests were carried out. The diagnostic sensitivity, specificity and positive and negative predictive values were calculated based on histology as the gold standard. A separate analysis of the sensitivity and specificity with respect to identification of BI-RADS IV tumors was performed.

RESULTS

All 108 specimens obtained were adequate for cytological and histological examinations. We diagnosed 59 benign and 49 malignant focal breast lesions. The histological diagnoses are summarized in Table 1. The mean tumor diameter was $2.3 \pm 1.2$ cm. In 48% of the patients, the
Table 1 Histological diagnoses of benign and malignant breast lesions in 108 patients with breast lesions

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Benign lesions (n = 59)</th>
<th>Malignant lesions (n = 49)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyst</td>
<td>21</td>
<td>Invasive ductal</td>
</tr>
<tr>
<td>Fibroadenoma</td>
<td>15</td>
<td>Invasive lobular</td>
</tr>
<tr>
<td>Fibrosis</td>
<td>6</td>
<td>Invasive ductal and lobular</td>
</tr>
<tr>
<td>Fibrocystic mastopathy</td>
<td>4</td>
<td>Tubular adenocarcinoma</td>
</tr>
<tr>
<td>Nonpuerperal mastitis</td>
<td>2</td>
<td>Invasive mucinous</td>
</tr>
<tr>
<td>Chronic inflammation</td>
<td>1</td>
<td>Invasive cribriform</td>
</tr>
<tr>
<td>Adenomatous hyperplasia</td>
<td>2</td>
<td>Cystic carcinoma</td>
</tr>
<tr>
<td>Papilloma</td>
<td>2</td>
<td>Ductal carcinoma in situ</td>
</tr>
<tr>
<td>Seroma</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Scar</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Hamartoma</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Adenomyoepithelioma</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

Table 2 Comparison of sensitivity, specificity and positive and negative predictive values for B-mode ultrasound and elastography in the differentiation of benign from malignant breast cancer

<table>
<thead>
<tr>
<th>Method</th>
<th>B-mode</th>
<th>Observer 1</th>
<th>Observer 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity (%)</td>
<td>91.8</td>
<td>77.6</td>
<td>79.6</td>
</tr>
<tr>
<td>Specificity (%)</td>
<td>78</td>
<td>91.5</td>
<td>84.7</td>
</tr>
<tr>
<td>Positive pred.</td>
<td>77.6</td>
<td>88.4</td>
<td>81.3</td>
</tr>
<tr>
<td>Negative pred.</td>
<td>92</td>
<td>83.1</td>
<td>83.3</td>
</tr>
</tbody>
</table>

focal lesions were <2 cm in size and were located at depths of up to 1 cm in 86% of patients.

Of the 59 benign lesions, 46 were identified correctly using B-mode, while 13 benign focal lesions were classified as BI-RADS IV or V lesions. Using elastography, the first observer identified 54 of the 59 benign lesions correctly, compared with 50 benign focal lesions identified correctly by the second observer.

Of the 49 malignant lesions, 45 were classified as definitely malignant using B-mode, while the remaining four lesions were classified as BI-RADS II or III. Using elastography, the first and second observers diagnosed correctly 38 and 39 of 49 malignant lesions, respectively. The resulting sensitivity for B-mode scanning was 91.8%, with a specificity of 78%. Elastography had a sensitivity of 77.6% and a specificity of 91.5%, for the first observer, compared with 79.6% and 84.7%, respectively, for the second observer. The results are summarized in Table 2.

In 28 of 49 malignant lesions, vascularization scores were 2–3. The power Doppler findings did not change the BI-RADS categories determined on B-mode scanning in any case. Twelve of 49 malignancies showed no vascularization and nine had a low vascularization value of 1. The two observers agreed on power Doppler findings.

Of the 17 lesions classified as BI-RADS IV by B-mode ultrasound, 11 (65%) turned out on histology to be benign. Of the lesions classified as BI-RADS IV by elastography, four of 22 (18%, Observer 1) and eight of 32 (25%, Observer 2) were diagnosed histologically as benign lesions.

There was good agreement between B-mode ultrasound and elastography, with a weighted kappa value of 0.67. The kappa was weighted following Fleiss, with weights restricted to lie in the interval between 0 and 1. Furthermore, there was good agreement between Observers 1 and 2 in the interpretation of the elastography images (weighted kappa, 0.73).

There was agreement in the subjective assessment of both observers concerning deeper focal lesions. Both concluded independently that lesions located deeper than 1 cm cannot be evaluated adequately by elastography.

**DISCUSSION**

To our knowledge, this is the first study to use elastography in realtime. Earlier studies investigating tissue elasticity relied on complicated experimental set-ups that are not feasible in the routine clinical setting.

With the equipment used here, we have shown for the first time that B-mode ultrasound and elastography can be performed in the same session. We evaluated this new approach in 108 patients undergoing routine diagnostic assessment of breast lesions.

In our experience, elastography can be performed clinically without problems and superimposition of the elastography data on the B-mode scan is not more time consuming than is a power Doppler examination. Elastography scores of Matsumura et al. can be matched with BI-RADS categories in a straightforward manner and this is recommended for further standardization of the method.

The sensitivity in our study for B-mode ultrasound of 91.8% corresponds to results reported in the literature, 28.29. The specificity (78%) was rather poor, but this was increased to up to 91.5% by the use of realtime elastography. The results are comparable to those of Matsumura et al., who reported a sensitivity of 86.8% and a specificity of 92%; other studies had a sensitivity of 85% and a specificity of 87.5%. 27,28

Our results suggest that elastography in conjunction with B-mode sonography is a reliable method for the confirmation of benign breast lesions and that the differentiation of malignancy categories with elastography is comparable to that of conventional ultrasound. In fact, based on the excellent results obtained in gelatine models, we might expect elastography to have a much higher sensitivity than does ultrasound; a possible explanation for our elastography and ultrasound results being comparable is the clinician’s greater experience with the interpretation of ultrasound scans. One must also be aware that measurements in a living subject rather than a model are more susceptible to various types of errors. One such potential source of error is patient movement (e.g. respiratory motion or slight changes in position), which may change areas of tissue shift, resulting in errors in the calculated elasticities. Such
errors would affect primarily ‘harder’ tissue, making it appear ‘softer’. As a result, tumors may be identified less accurately, being calculated as false negative. The differences in the interpretation of the elastography images between the two observers were small (weighted kappa of 0.73).

In the diagnostic evaluation of benign lesions, elastography improves diagnostic confidence and may in the future help to reduce the number of core biopsies. Real-time elastography was beneficial with regard to BI-RADS category IV lesions, which pose most diagnostic problems from a clinical perspective. In this case, elastography reduced the rate of false-positive findings. No diagnostic improvement was seen for BI-RADS category V malignancies. This may be due to the scoring system of Matsumura et al.27, according to which a lesion is assigned a score of 5 only if there is definitive evidence of infiltration of surrounding tissue. On the other hand, the presence of a central necrosis may also impair the diagnostic assessment in elastography.

The use of Doppler ultrasound did not yield additional information and the findings had no effect on the final BI-RADS classification of the lesion. Only 57% of the malignant lesions showed increased vascularization. These findings are in accordance with numerous other studies that reported a sensitivity of only 64% for power Doppler31–33.

This study did have some limitations. Both observers concluded independently that lesions located deeper than 1 cm cannot be evaluated adequately by elastography. The findings indicate that elastography is beneficial in the discrimination of benign from malignant breast lesions. The concordance analysis (kappa value) is likely to affect the prevalence of malignant lesions and by the way the agreement is weighted.

Our initial clinical results obtained with real-time elastography in the diagnostic evaluation of breast cancer suggest that this is a promising new approach for the differentiation of benign from malignant breast lesions. The findings indicate that elastography is beneficial in the identification of typical benign features of BI-RADS category II–III lesions and in the differentiation of category IV malignancies.

REFERENCES


