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# Differential diagnosis of breast lesions using ultrasound elastography

Ioana Andreea Gheonea, Zoia Stoica, Simona Bondari
Department of Radiology and Imaging, University of Medicine and Pharmacy Craiova, Romania

**Correspondence:** Dr. Ioana Andreea Gheonea, Petru Rares Street, No 2, Craiova – 200349, Romania. E-mail: iagheonea@gmail.com

## Abstract

**Context:** The recent introduction of elastography has increased the specificity of USG and enabled early diagnosis of breast cancer. Quantitative elastography, especially with strain ratio (SR) index, improves diagnostic accuracy and decreased number of biopsies. **Aims:** The purpose of this study was to assess the role of USG elastography in the differential diagnosis of breast lesions. **Settings and Design:** This prospective study was conducted in the University of Medicine and Pharmacy Research Centre of Craiova. **Materials and Methods:** Fifty-eight patients diagnosed with breast lesions between January 2009 and January 2010 were included in this prospective study. All the patients were examined in the supine position, and the B-mode USG image was displayed alongside the elastography strain image. For obtaining the elastography images we used a EUS Hitachi EUB 8500 ultrasound system with a 6.5-MHz linear probe. The elastography strain images were scored according to the Tsukuba elasticity score. **Statistical Analysis:** We performed receiver operator characteristic (ROC) analysis for assessment of the role of USG elastography in the diagnosis of breast lesions. **Results:** We obtained a sensitivity of 86.7% and a specificity of 92.9% for elasticity score and a sensitivity of 93.3% and a specificity of 92.9% for SR (when a cutoff point of 3.67 was used). There was very good correlation between SR and elasticity score (Spearman coefficient of 0.911). **Conclusions:** Elastography is a fast, simple method that can complement conventional USG examination. This method has the lowest cost/efficiency ratio and it is also the most noninvasive and accessible imaging method, with an accuracy comparable to MRI.

**Key words:** Breast lesions; receiver operator characteristic analysis; ultrasound elastography

## Introduction

The high incidence of breast cancer and its slow evolution before diagnosis have led to research on new diagnostic techniques.[1–3] The recent introduction of elastography has increased the specificity of USG and enabled earlier diagnosis of breast cancer. The use of quantitative elastography with strain ratio (SR) improves diagnostic accuracy in cases with equivocal Stavros criteria (stages 3 and 4 BI-RADS).

USG elastography (SE) differentiates between benign and malignant lesions on the basis of their elasticity: benign lesions have an elasticity similar to the surrounding tissue, while malignant lesions are harder than adjacent tissue.[4]

The purpose of this study was to assess the role of SE in the diagnosis of breast lesions. Malignant tumors have reduced elasticity and also display larger dimensions on elastography due to the accompanying desmoplastic reaction.[5,6] Benign lesions appear similar to the adjacent tissues and have a smaller diameter than on B-mode USG images.[7,8]

## Materials and Methods

In this prospective study, consecutive patients presenting with palpable breast lesions were assessed with conventional B-mode USG. Those confirmed to have a breast lesion were then assessed with SE after informed consent was obtained. SE was performed by a single experienced physician who was not aware of the results of previous investigations. The operator was not blinded at conventional USG because the lesion was localized first with conventional B-mode USG

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and then SE was done. The patients were examined in the supine position with the arm placed behind the head. The USG probe, lubricated with gel, was placed on the breast and a radial, ductal exploration was made as follows: the transducer was placed perpendicularly to the skin and radially on the breast, with one end overlapping on the areola and the other end directed toward the periphery. The orientation of the transducer was such that the nipple appeared at the left-hand side of the image. The transducer was then rotated around the areola. When a duct was identified, the rotation of the transducer was halted and it was moved back and forth laterally for thorough evaluation of the duct and its branches and the lobules. The transducer was then rotated again until the next ducto-lobular complex was found. This procedure was repeated until all the ductal structures were evaluated. A second rotating sweep was performed over the upper outer peripheral part of each breast. The B-mode US image was displayed alongside the elastography strain image to ensure that the assessment was made in the area of interest. We included in the area of interest the lesion and also the subcutaneous layers and the pectoralis muscle, without the costal cartilages.

A EUS Hitachi EUB 8500 US system (Hitachi Medical, Tokyo, Japan) with an elastography module and a 6.5 MHz linear probe was used to obtain the B-mode and elastography strain images. The images were acquired in a ductal, radial manner as described above and the elastography strain images were scored according to the Tsukuba elasticity score developed by Itoh and Ueno.[4] Ductal USG combined with SE is defined as full-breast elastography, a new concept initiated by Amy D[9] We used five scores for characterizing the lesions: score 1 for lesions with elasticity similar to the surrounding breast tissue, displayed in green color on elastography; score 2 for lesions with inhomogeneous elasticity, with green and blue elastography appearance; score 3 for lesions with an elastic green periphery and a stiff blue centre; score 4 for nodules that were entirely stiff, showing no deformation; score 5 for cases where the whole lesion and the adjacent tissue showed a blue appearance on the elasticity image.

For all lesions we calculated the strain ratio (SR). The average strain of the lesion was determined by selecting a region of interest (ROI) from the lesion and a corresponding ROI of the adjacent adipose tissue. Using specific software, the SR value was displayed on a static image as the ratio of tumor-adjusted ROI and the ROI placed in the adjacent fatty tissue. We used fine needle aspiration cytology (FNAC) ($n$=12) or excision biopsy ($n$=18) for histopathological analysis of the malignant lesions. The benign lesions were diagnosed by a combination of FNAC ($n$=10), excision biopsy ($n$=7), and follow-up for 6 months ($n$=11).

## Results

In this study we included 58 patients with breast lesions confirmed on US. The average age of the women was 45.3 years. There were 28 (48.27%) benign and 30 (51.73%) malignant lesions. Among the benign nodules the common lesions were fibroadenoma, cyst, and fibrocystic change. Among the malignant nodules, the most common lesion was infiltrative ductal carcinoma. Ductal carcinoma *in situ* was diagnosed in 10 cases [Table 1].

Fibroadenomas appeared either softer than or had the same elasticity as adjacent glandular tissue [Figures 1 and 2]. Breast cysts had an elasticity score of 1 with a characteristic three-layered appearance: blue-green-red (BGR), blue being the superficial color and red the deep one, even in large dimension lesions [Figure 3]. Fibrocystic nodules had elasticity similar to surrounding parenchyma [Figure 4]. The mean elasticity score for benign lesions was 1.92±1.01. Breast carcinomas showed an average elasticity score of 4.23±0.89; they appeared larger on the elastography image because of better visualization of the surrounding desmoplastic reaction [Figures 5 and 6; Table 2].

After FNAC and excision biopsy, four lesions (14.28%) with elasticity score 3, one lesion (3.57%) with elasticity score 4 [Figure 7], and one lesion (3.57%) with elasticity score 5 were found to be benign; also, one lesion (3.33%) with elasticity score 1 and three lesions (10.72%) with elasticity score 3 [Figure 8] turned out to be malignant lesions.

The average SR for benign lesions was 2.08, which was significantly lower than that for malignant lesions (mean SR: 6.28). To calculate the sensitivity and specificity of elastography, lesions with elasticity scores 1–3 were classified as benign, while those with scores of 4 or 5 were classified as malignant. For assessment of the role of SE in the differential diagnosis of breast lesions, we performed a receiver operator characteristic (ROC) analysis. We obtained a sensitivity of 86.7% and a specificity of 92.9% [Figure 9A] for elasticity score (area under the ROC curve=0.928; 95% CI=0.829 to 0.979; $P$=0.0001) and a sensitivity of 93.3% and a specificity of 92.9% for SR, when a cutoff point of 3.67 was used (area under the ROC curve=0.965, 95% CI=0.880 to 0.995; $P$=0.0001) [Figure 9B]. Furthermore, the Spearman coefficient of rank correlation for SR values and elasticity score was 0.911 (95% CI 0.853 to 0.946; $P$<0.0001), showing that there was very good agreement between the two methods.

**Table 1: Final pathology diagnosis of all lesions**

| Pathology diagnosis | Number of lesions (%) |
|---|---|
| Fibroadenoma | 10 (17.3) |
| Cysts | 8 (13.8) |
| Fibrocystic disease | 10 (17.3) |
| Invasive ductal carcinoma | 20 (34.9) |
| *In situ* ductal carcinoma | 10 (17.3) |

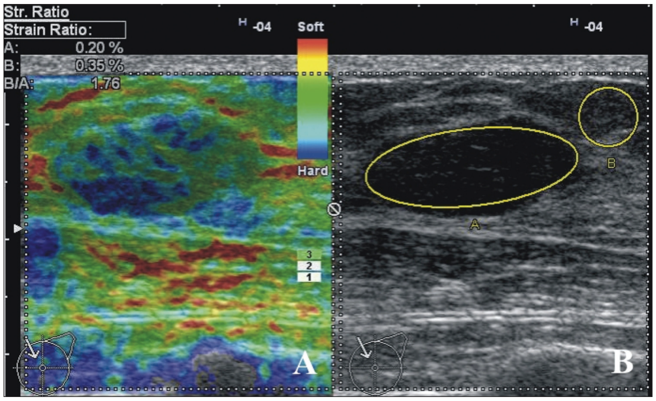


**Figure 1 (A, B):** SE image (A) and B-mode USG image (B) show a hypoechoic circumscribed lesion that is predominantly elastic, displaying a mosaic pattern of green and blue. This was a fibroadenoma with a Tsukuba elasticity score of 2 and an SR of 1.76

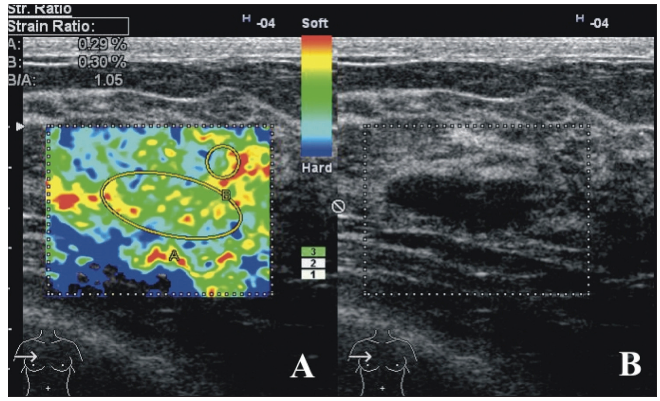


**Figure 2 (A, B):** SE image (A) and B-mode USG image (B) reveal a fibroadenoma-like lesion that is predominantly green, with an SR of 1.05; this is typical of a benign lesion

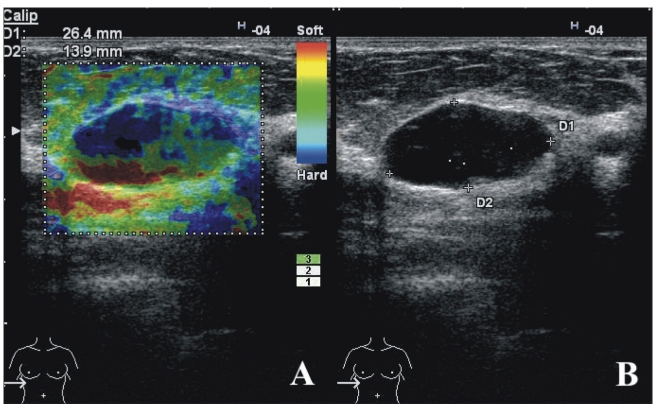


**Figure 3 (A, B):** SE image (A) and B-mode USG image (B) show the typical elastographic appearance (blue, green, red) of a cyst. This was a cyst of 26.4 mm diameter in a 23-year-old patient

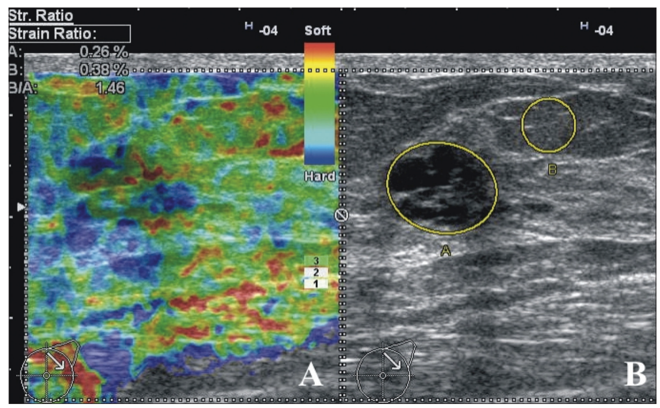


**Figure 4 (A, B):** SE image (A) and B-mode USG image (B) reveal an image of fibrocystic dysplasia with a Tsukuba elasticity score of 1 and an SR of 1.46, suggestive of a benign lesion

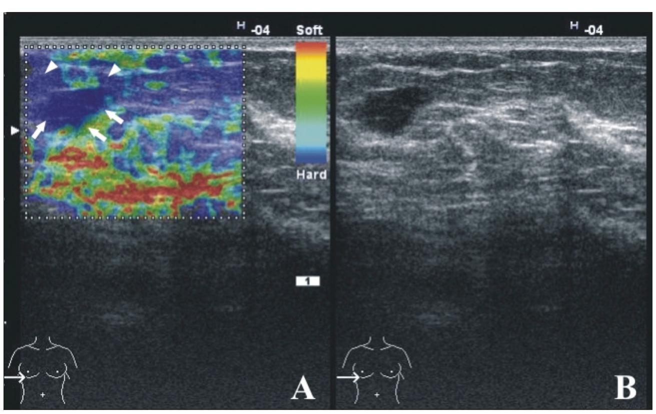


**Figure 5 (A, B):** SE image (A) and B-mode USG image (B) -- the lesion (arrows) and the surrounding tissue (arrowhead) were colored blue, with an elasticity score of 5. Pathology revealed an invasive ductal carcinoma

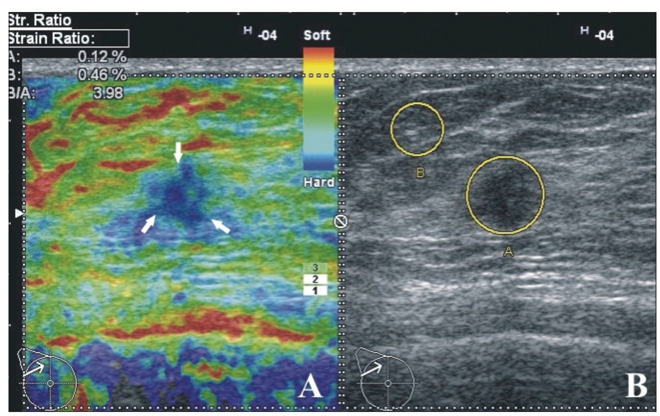


**Figure 6 (A, B):** SE image (A) and B-mode USG image (B) reveal a small, suspicious, stiff lesion (arrows). The lesion appears to be larger on the elastographic image due to the accompanying desmoplastic reaction with a Tsukuba elasticity score of 5 and an SR of 3.98. Pathology revealed ductal invasive carcinoma

## Discussion

The interpretation of breast nodules detected on B-mode US relies mainly on morphological criteria. To improve the accuracy of USG, additional techniques can be used, including Doppler and harmonic imaging.[10,11] Over the last

**Table 2: The elasticity score for benign and malignant lesions**

| Final diagnosis/elasticity score | 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|
| Benign lesions (n) | 11 | 11 | 4 | 1 | 1 |
| Malignant lesions (n) | 1 | 0 | 3 | 13 | 13 |

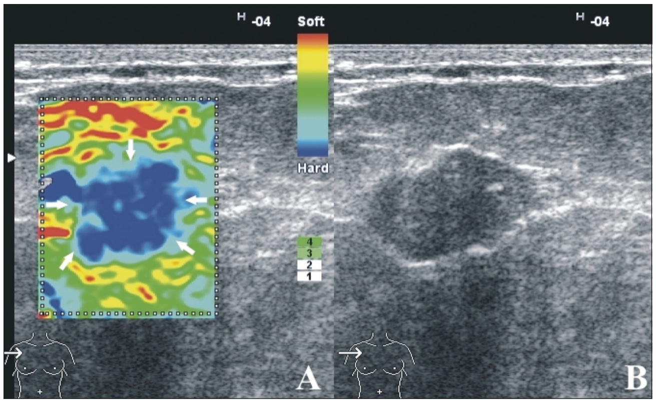


**Figure 7 (A,B):** SE image (A) and B-mode USG image (B) show a hypoechoic lesion in the right breast, with small foci of calcification (arrows) predominantly blue on elastography, with an elasticity score of 4. It was a calcified fibroadenoma

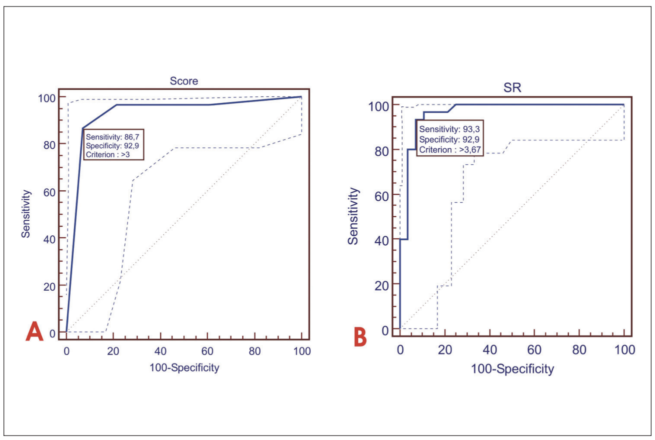


**Figure 9:** Sensitivity and specificity values on ROC analysis for elasticity score (A) and for SR (B) (MedCalc® software v. 9, 2008, Mariakerke, Belgium)

decade, there has been increasing interest in imaging the elasticity of biological tissues to complement information from standard anatomical imaging. SE can differentiate between benign and malignant lesions on the basis of their firmness. The lesion's contours, dimensions, color, SR, and appearance on elastography are some of the criteria used for differentiating benign from malignant lesions. The SR represents the relative compliance stiffness of lesions compared with surrounding tissues. Malignant lesions, which are very stiff, deform less and are displayed in blue on the elastography images, whereas benign lesions deform much more easily and are depicted in green color.[12,13]

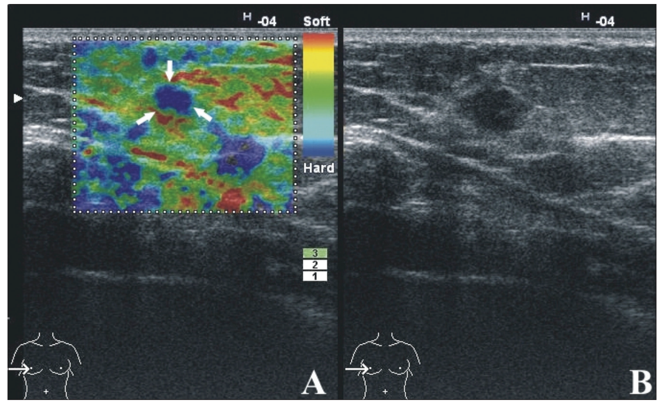


**Figure 8 (A,B):** SE image (A) and B-mode USG image (B) performed in a patient with fibrocystic dysplasia reveals a hypoechoic lesion with irregular boundaries (arrows). Tsukuba elasticity score was 3. Pathology showed in situ ductal carcinoma

Results of the clinical use of SE were initially published in 1997–2001,[13] but it was only in 2003–2004 that US equipment was developed that had incorporated software for real-time processing of elastography images and routine US examinations.[14] For characterization of breast lesions, two elasticity scoring systems have been proposed: the Tsukuba score developed by Itoh and Ueno[4] and another designed by the Italian Research Group after Locatelli, Rizzatto *et al*.[10]

In this study, when a cutoff point of 3 was used, we found a sensitivity of 86.7% and a specificity of 92.9%, results that are consistent with other published data on the use of real-time US elastography.[4,15] A sensitivity of 77.6% and 79.6% and specificity of 91.5% and 84.5% were reported by Thomas *et al*., in a study where 108 breast lesions were examined by two examiners separately.[15] Another study of 111 lesions reported higher values: sensitivity of 89.3% and 83.3% and specificity of 93.1% and 86.7%.[4]

As the SR ratio of >3 is generally considered suspicious for malignancy,[16] there is ongoing research for establishing the correct values for better differentiation of benign and malignant lesions. In our study, the mean SR for benign lesions was 2.08 and for malignant lesions it was 6.28, with the cutoff point being 3.67. In comparison, the critical SR value for diagnosing breast cancer was 3.08 in a study by Zhi *et al*.[17]

Routine USG examination detects many nonpalpable lesions and it is not very specific for screening cases.[18] The advantages of ductal USG is that standardized anatomic examination of the breast is possible, 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. Ductal USG is an anatomical method of breast investigation that allows the correct assessment of the internal structures of the breast. The recent introduction of SE, especially quantitative elastography with SR, has increased the specificity of USG and enabled early diagnoses of subcentimeter breast cancer and decreased the need for biopsies.[19]

In the clinical setting SE is useful for deciding whether to follow-up patients with imaging or to intervene.[19] Sometimes it is difficult to differentiate between scores 2 and 3 on SE images, but it is very easy to diagnose a lesion as having score 1, because no blue area is observed.[20] Our study showed that there was good correlation (Spearman coefficient=0.911) between qualitative and quantitative elastography methods (elasticity score and SR) and we suggest that by performing both techniques a more confident diagnosis can be made. SE is less sensitive than standard USG when dealing with nonfocal anomalies and is not indicated for the evaluation of postoperative changes, diffuse lesions, or large ones that exceed the probe length or its field of view (FOV).[21] SE is also of limited usefulness in very dense fibrous parenchyma and in the case of hematomas or breast implants.[11] Some studies have also demonstrated the value of elastography in the benign–malignant differentiation of lymph nodes.[22]

The introduction and validation of the concept of full-breast USG have increased the sensitivity of SE.[9] Full-breast USG allows the systematic diagnosis of lesions using the ductal technique; it is not operator dependent, has high specificity, and allows the precise localization of lesions within the breast gland (galactophore ducts, lobules, and ducto-lobular terminal units).[9] Also the use of Doppler and elastography techniques permits evaluation of the risk of neoplastic transformation, with a specificity of over 90%.[4,11]

In conclusion, breast SE is a very simple and rapid method that can improve the sensitivity and specificity of USG, especially when dealing with BI-RADS 3 or 4 lesions. Ductal USG combined with SE is a rapid technique, with the lowest cost/efficiency ratio of all the modalities; it is the most noninvasive and accessible imaging method, with accuracy comparable with MRI, and can decrease the rate of unnecessary biopsies.

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