ORIGINAL ARTICLE

Real-time ultrasound elastography: Does it improve B-mode ultrasound characterization of solid breast lesions?

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Abstract *Introduction:* Elastography is a non-invasive medical imaging technique that detects tumors based on their stiffness (elasticity). Strain images display the relative stiffness of lesions compared with the stiffness of surrounding tissue as cancerous tumors tend to be many times stiffer than the normal tissue, which "gives" under compression. An image in which different degrees of stiffness show as different shades of light and dark is called an elastogram.

Purpose: To prospectively evaluate the sensitivity and specificity of the real-time sonoelastography as compared with B-mode US for distinguishing between benign and malignant solid breast masses. The density of the glandular breast tissue was taken in consideration in addition to the Breast Imaging Reporting and Data System (BI-RADS) categories of the lesions, with biopsy results as the reference standard.

Methods: A total of 216 candidate solid lesions (123 benign and 93 malignant) in 188 patients were examined with 2-dimensional ultrasonography, elastosonography and mammography (for 147 patients). The lesions were classified according to the density of the glandular breast tissue into low density group (D1) and a high density group (D2) and were categorized with the BIRADS score. Elastographic images were assigned an elasticity score of 1 to 5 (1–3, benign; 4 and 5, malignant) according to the Multi-Center Team of Study and the strain ratios of the lesions were measured. Concordance between the imaging findings and histopathologic results was documented.

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Statistical analysis was performed and sensitivity, specificity and positive and negative predictive values for both elastography and conventional sonography were calculated.

Results: Elastography showed less sensitivity but higher specificity than conventional sonography in the differentiation of benign from malignant solid lesions: B-mode sonography had sensitivity of 85.1%, specificity of 93.9%, a positive predictive value of 92.5% and a negative predictive value of 87.8%, compared with the sensitivity of 80.1%, specificity of 97.1%, a positive predictive value of 96.8% and a negative predictive value of 82.1% for elastography. Elastography was superior to B-mode US in diagnosing solid lesions in the low density group (D1) (96.6% vs. 92.4% specificity) and less in the dense glandular tissue (97.8% vs. 95.9% specificity).

Conclusions: Real-time sonoelastography is an useful technique for the characterization of benign and malignant solid lesions as it increases the diagnostic specificity comparable to B-mode ultrasound, particularly in both ACR 1 and 2, thus reducing the false-positive rate.

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1. Introduction

Breast ultrasonography (US) has become an invaluable tool for the detection of breast lesions: a decade ago, physicians found that the imaging features on ultrasonographic images could be used to classify benign and malignant solid breast masses and thus decrease the numbers of biopsies performed (1). US, however, is still strongly operator-dependant, and a correct diagnosis may be sometimes difficult because of the overlapping between the features of malignant and benign breast lesions, although they have been described (2–4) and categorized (5). Conventional ultrasound can distinguish benign from malignant breast lesions based on the appearance of the lesion: margin irregularity, shape, echogenicity and shadowing (2) (Table 1).

Compressibility has also been used to assess a lesion (6). Soft benign lesions will flatten more upon compression than hard malignant ones. However, this may be subjective and operator-dependent. Consequently, the diagnostic confirmation may often require image-guided biopsy procedures.

Recently, sonoelastography (SE), looking at the mechanical properties of tissues (relative stiffness) as opposed to conventional ultrasound, which looks at the backscatter of transmitted ultrasound waves through tissues (7). Elastography is the technique of imaging the hardness of soft tissue. Strain images display the relative stiffness of lesions compared with the stiffness of surrounding tissue. Stiffer areas deform less easily than do their surroundings and are depicted as dark on strain images, whereas softer areas deform more easily than do their surroundings and are depicted as light. Malignant masses typ-

ically appear dark and have high contrast with background breast tissue during deformation. Benign masses typically appear lighter and have lower contrast with background breast tissue during deformation (8). The interpretation criteria in elastography consist of the qualitative parameter elasticity score (ES) and the quantitative parameter strain ratio (SR). Various qualitative classifications that differentiate between 3 and 5 patterns have been reported for real-time elastography (RTE); the most frequently used one being that differentiates five RTE patterns, where patterns 4 and 5 indicate malignant breast lesions and patterns 1–3 indicate benign breast lesions (9). A semiquantitative method of lesion assessment, referred to as strain ratio measurement, has also been developed. Calculation of the SR value is based on determining the average strain measured in a lesion and comparing it to the average strain of a similar area of fatty tissue in the adjacent breast tissue. The SR reflects the relative stiffness of the lesion. Probability of malignancy increases as the SR value increases (10).

Tissue elasticity imaging is performed with a conventional ultrasound probe and does not require additional equipment. The calculation of tissue elasticity is in real-time and the resultant strain image is represented in color over the conventional B mode ultrasound. In addition, the B mode image can be displayed at the same time as the elastography strain image. This method combines the added information from elastography with the flexible manipulation of a free-hand probe (11).

The aim of the study was to prospectively evaluate the sensitivity and specificity of the real-time sonoelastography as compared with B-mode US for distinguishing between benign and malignant solid breast masses, taking into consideration the density of the glandular breast tissue and the Breast Imaging Reporting and Data System (BI-RADS) categories of the lesions (5), with biopsy results as the reference standard.

2. Materials and methods

Two hundred forty-three patients who underwent imaging of 292 solid focal lesions were enrolled between December 2009 and June 2010. Only pathologically proved lesions, 216 in 188 patients, were included in the study. Their ages were ranging between 18 and 72 years (mean age of 45 years). One hundred thirty-eight lesions were palpable (63.9%) and the remaining 78 lesions (36.1%) were nonpalpable. The inclusion criterion was demonstration of a solid focal lesion by ultrasound. This number represents the set of eligible cases,

Table 1 Stavros criteria of benign versus malignant breast masses (2).

Criteria associated with benign lesion	Criteria associated with malignant lesion
Smooth shape (rounded, oval)	Irregular shape
Linear well defined margin	Ill defined/spiculated
Homogenous echotexture	Heterogenous echotexture
Iso, hypoechoic	Distorted architecture
Distal/edge shadowing	Central shadowing
Width to AP diameter $\geqslant 1.4$	Width to AP diameter $\leqslant 1.4$
Gentle lobulation	Micro-lobulation
Dilated ducts	Microcalcification

after the exclusion of 16 cases because of unsatisfactory image quality.

Histopathologic results of percutaneous or excisional biopsy were considered the reference standard. Concordance between the imaging and histopathologic results was documented for each lesion to minimize the chance of sampling error.

2.1. Mammography

Mammographies were available in 147 of 188 study patients. Mammographic examinations were performed with a dedicated mammography unit Mammomat 1000 (Siemens). The results included in our report were based on the standard craniocaudal and mediolateral oblique projections of each breast; some patients needed cone down views with or without markers. No mammographies were performed in 41 patients (21.8%), for the following reasons: benign lesions and the patients' young age ($\leqslant$35 years) in 29 cases, 5 patients had a mammography within less than 12 months, 2 patients had refused mammography and outside films that were not available in 5 cases.

2.1.1. Assessment criteria
Mammographies were evaluated for the glandular density according to the American College of Radiology (ACR) classification that identified four major groups for classifying breast density (Kopans [12]): (1) predominantly fat; (2) fat with some fibroglandular tissue; (3) heterogeneously dense; (4) extremely dense.

2.2. US technique

After the clinical examination (inspection, palpation), all 188 patients underwent ultrasonography using a high-end US device (HITACHI EUB-7500) with the integrated elastography software and a linear transducer ranging from 7 to 12 MHz, depending on lesion depth and breast thickness. On US, both breasts were scanned as well as the area of the expected abnormality. The patients were put in a supine position with the ipsilateral arm behind the head, and then rolled to the contralateral posterior oblique position (to flatten the breast tissue over chest wall and maximizing the high frequency probe scanning characteristics). The protocol included scanning in both transverse and longitudinal real-time imaging, examining the whole breasts circularly and then targeting on the region of complaint. The lesions were described according to number, location, greatest diameter, shape, orientation, echogenicity, echo-texture, margin, acoustic transmission and the presence of calcification.

Following conventional US B mode scanning, Power Doppler study US was done to majority of the patients. The scanning plan was selected for optimal visualization of vascularity. Tissue velocities were encoded in red and blue depending on direction and superimposed on the lesion.

2.2.1. Assessment criteria
Lesion characterization on the B-mode images was done using the BI-RADS criteria of the American College of Radiology [5]. In absence of mammography, the US scans were also evaluated using the American College of Radiology criteria and—analogous to the mammography densities—categories I–IV

were assigned according to the sonographic density of the breast tissue. Patients with indices of I and II were assigned to group D1, those with III or IV to group D2. Lesions with BI-RADS categories II and III were classified as benign and those with BI-RADS IV and V as malignant.

In Power Doppler US study, the vascularity of the lesions and distribution were analyzed and then were classified into two categories: avascular and vascular either hypovascular (less than 20% color flow) or hypervascular (more than 20% color flow).

2.3. Elastographic method

After B-mode US detection of the lesion of interest, the patient remains in the supine position, and a stabilizer device is mounted on the probe to hold a homogeneous pressure on a wider area of the skin's surface by minimizing lateral movements of the probe. Then the dual elastographic program starts, with the US monitor showing in real time the B-mode US image of the lesion on the right side and the same image with color-coded elasticity features superimposed on the left side and motion images are obtained by applying a light constant pressure with the probe in contact with the skin perpendicular to the chest wall. In order to obtain correct elastographic images, attention must be paid to the definition of the ROI, which has to be sufficiently wide to include enough breast tissue surrounding the lesion so that data about the average strain of the tissue inside the region are available. The ROI usually must extend from the subcutaneous fat at the top to the anterior profile of the pectoral muscle at the bottom, with lateral borders set more than 5 mm from the lesion's boundary. The exam is correctly performed checking the 1–5 LED scale that appears laterally to the right of the elastographic image that is indicative of proportionality between pressure and tissue strain. The color-coded image must be consistently overlapped with the B-mode US image, with a smooth appearance and without color flashes. The elasticity images are obtained according to a 256-color scale ranging from red, indicative of the softest tissues that show the greatest strain, to blue for the hardest components that do not exhibit any strain, with green corresponding to the average strain observed in the ROI. Strain imaging allowed analysis of the strain ratio values that were also calculated. The examination took approximately 10–15 min.

2.3.1. Assessment criteria
To classify elastographic images, the 5-score system proposed by Ueno and co-workers [13] was considered; however, a slight adjustment of Ueno scoring descriptors was undertaken according to the panel assessment of an Italian Multi-Centric Team of Study for Sonoelastography Evaluation [14]. It differs mainly for the score 1 lesions, which exhibit a typical three-layer feature (blue–green–red from the surface to the bottom) usually indicative of cystic lesions.

In our classification, score 2 is a benign-like lesion almost entirely green with random blue points. A score 3 is a lesion predominantly green showing some blue spots, consistent with benignity. Score 4 is an almost entirely blue lesion with minimal green points at the periphery, suspect for malignancy. Score 5 is the same as in the Ueno classification, with an entirely blue lesion surrounded by a blue halo, consistent with malignancy (Fig. 1).

Fig. 1 Sonoelastographic classification by the Italian Multi-Center Team of Study (14).

The SRs were calculated from a tumor-adjusted region of interest and a comparable region of interest placed in the lateral fatty tissue. According to Cohn (15), we assumed a mean strain ratio of 1.83 for benign lesions and 8.38 for malignant lesions with a cutoff point of 3.05.

According to both RTE patterns and SR measurement, the lesions were categorized with the BI-RADS score into benign and malignant. Among the 216 solid breast lesions, the relationship between US and SE scores is shown in Table 2.

3. Results

Histologic examinations yielded 93 malignant (43%) and 123 benign lesions (57%). The mean tumor diameter was 2.1 cm (range 0.7–3.5 cm). The histologic diagnosis of all 216 lesions is listed in Table 3.

3.1. Grouping according to breast density

Mammographies were available for 147 of our 188 patients with histologically proven focal lesions (78.2%). In these 147 patients, the glandular tissue was assigned a density index of ACR 1 or 2, (involuted, partially involuted glandular tissue) in 87 (59.2%) cases based on mammography and in 19 of the remaining 41 cases (46.3%) based on B-mode US with a total of 106 patients (56.4%) with 125 lesions (58%). These lesions were set as low density group (D1) while the 91 lesions (42%) in the 82 patients with prominent breast density (ACR 3 and 4) were set as high group density (D2).

3.2. B-mode US

Evaluation of the B-mode images correctly diagnosed 108 of 123 benign lesions, whereas 15 benign lesions were assigned BI-RADS 4 or 5. Reliably identified were 86 of 93 malignant lesions, whereas the remaining 7 lesions were classified as BI-RADS 2 or 3. B-mode US thus had a sensitivity of 85.1% and a specificity of 93.9% (Table 4).

Table 2 Relationships between US and SE scores in 216 breast lesions.

US scores (BI-RADS)	Sonoelastographic scores				Total
	2	3	4	5	
2	38	17	1	Nil	56
3	14	35	9	1	59
4	Nil	Nil	51	26	77
5	Nil	Nil	9	15	24
Total	52	52	70	42	216

Table 3 Histologic diagnosis in 216 solid breast lesions.

Pathologic diagnosis	No. of cases	Percent
Malignant lesions	93	33.8
-Ductal invasive carcinoma	71	32.9
-Lobular invasive carcinoma	13	6
-Mucinous carcinoma	1	0.5
-Tubular carcinoma	2	0.9
-DCIS	6	2.8
Benign lesions	123	66.2
-Fibroadenoma	101	46.8
-Fat necrosis	9	4.2
-Itraductal papilloma	4	1.9
-Fibrocytic changes	3	1.4
-Atypical hyperplasia	1	0.5
-Intramammary lymph node	2	0.9
-Hamartoma	2	0.9
-Tubular adenoma	1	0.5

For lesions in patients with pronounced involution of glandular breast tissue (group D1), B-mode US reliably diagnosed 51 of the 56 malignant lesions and 61 of the 69 benign lesions; while in group D2, 35 malignant lesions were identified of the 37 and 47 of the 54 benign ones. Thus a lower breast tissue density is associated with a lower specificity (92.4%) and increased sensitivity (86.4%) compared to group D2 (Table 5).

Table 4 Sensitivity, specificity, positive and negative predictive values of B-mode ultrasound and elastography.

	B-mode (%)	Elastography (%)
Sensitivity	85	80
Specificity	94	97
Positive predictive value	92.5	97
Negative predictive value	88	82

Table 5 Sensitivity, specificity, positive and negative predictive values in relation to density indices I–II (group D1) and III–IV (group D2).

	B-mode		Elastography	
	D1 (%)	D2 (%)	D1 (%)	D2 (%)
Sensitivity	86	83	82	78
Specificity	92	96	97	98
Positive predictive value	91	95	96	97
Negative predictive value	88	87	83	81.5

3.3. Elastography

101 of the 123 benign lesions were diagnosed correctly as well as 90 of the 93 malignant tumors. Elastography had a sensitivity of 80.1% and a specificity of 97.1% (Table 4).

For 125 patients with a density index of ACR 1 or 2 (group D1), elastography correctly diagnosed 57 out of 69 benign lesions and 54 of the 56 malignant lesions. This resulted in a sensitivity and specificity of elastography in group D1 of 81.8% and 96.6%, respectively, as opposed to 78.3% and 97.8% in group D2 (Table 5). The distribution of ultrasound and elastographic classifications for malignant and benign lesions is represented in Fig. 2.

Figs. 3 and 4 are lesions of elastographic score 4 and high strain ratio values; while Figs. 5–7 are for lesions yielding scores 2 or 3 with low SR values.

4. Discussion

The advances in ultrasound technology over the past two decades have transformed this diagnostic modality into a
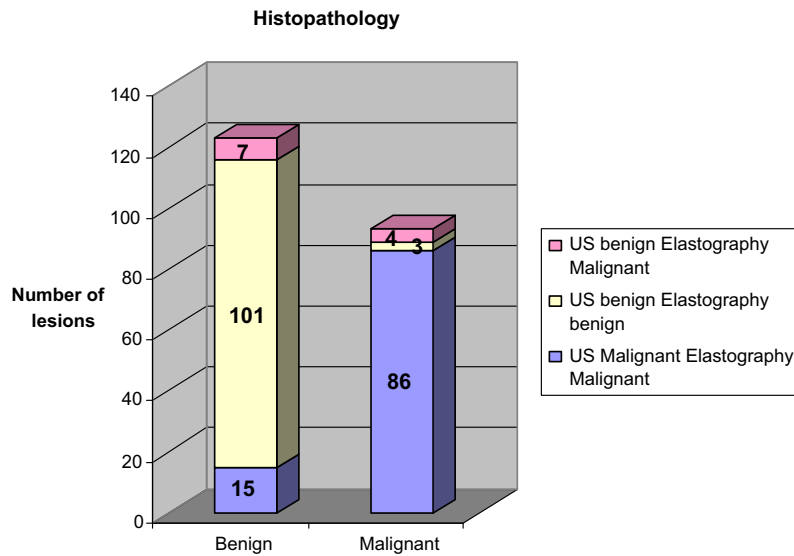

Fig. 2 Bar graph demonstrating the distribution of ultrasound and elastographic classifications for malignant and benign lesions.
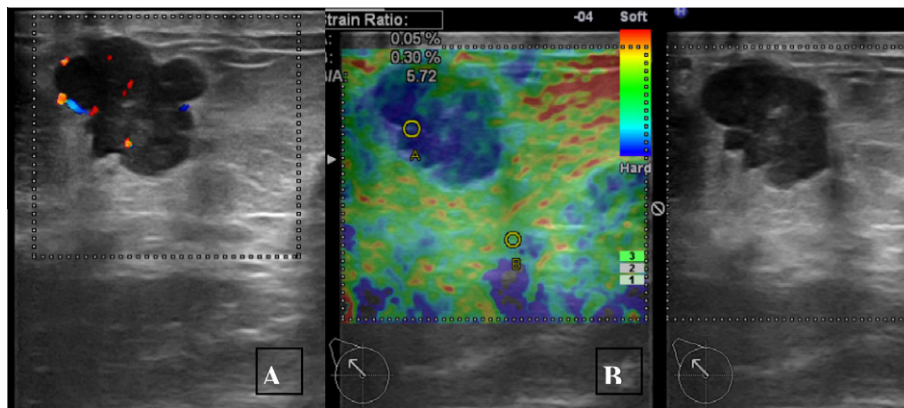

Fig. 3 A 47-year-old lady having her Routine Screening Mammogram. US revealed a micro lobulated hypoechoic solid lesion. Color Doppler (A) revealed abnormal internal vascularity. Elastography (B) revealed score 4 and the SR yielded the value 5.72 between the mass and the surrounding tissue. It was categorized as BIRADS 4c. Biopsy demonstrated invasive duct carcinoma.
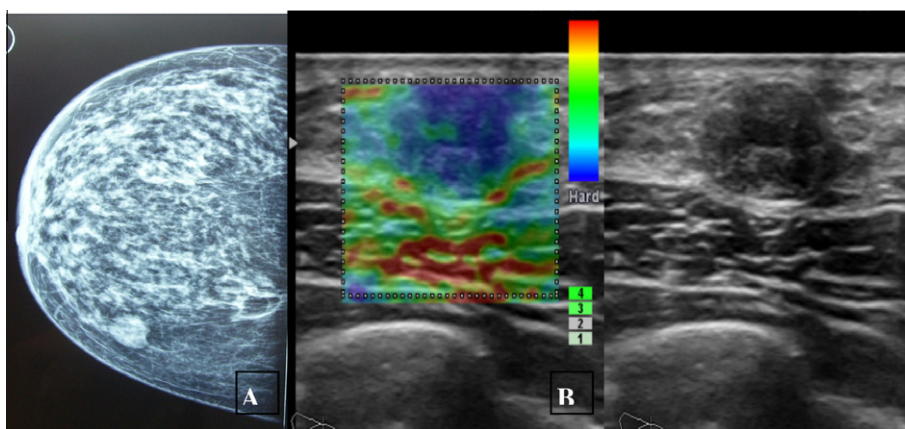
Fig. 4 A 54-year-old lady with a right breast palpable lump. Mammogram (with breast density of ACR 3) revealed a well defined nodule (A). US revealed it as a well defined hypoechoic solid lesion presenting a single angulation and was categorized as BIRADS 3. Elastography (B) revealed score 4 with a SR of 4.42 and consequently was categorized as BIRADS 4 a. Biopsy confirmed the elastographic classification as being mucinous carcinoma.
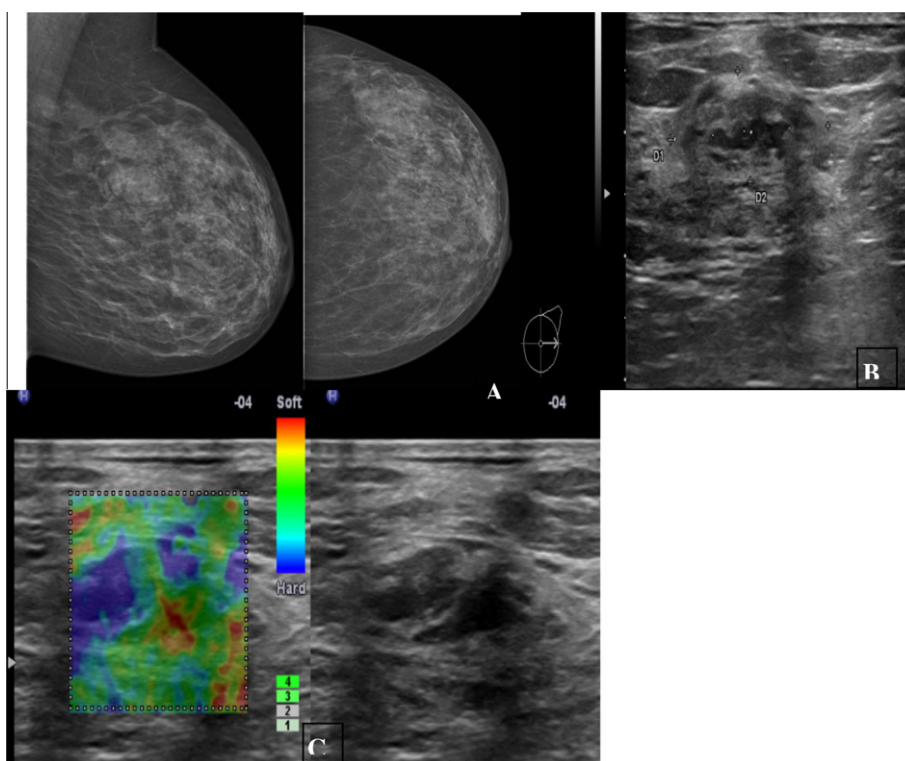

Fig. 5 A 40 year old woman complaining of bilateral mastalgia. Mammogram (with breast density of ACR 2) revealed a rather defined oval lesion with a lucent halo in the UOQ of the left breast (A). US (B) demonstrated an underlying focal lesion of heterogenous fibroglandular like echogenicity. Eastographic score 2 suggested its benign nature (C). Biopsy revealed it to be a hamartoma.

diagnostic tool that allows the exclusion of malignant breast tumors and identification of definitely benign lesions. This is why ultrasound has been referred to as the stethoscope of the future (16). Real-time elastography, a noninvasive method for revealing the physical properties of a tissue, has been developed as an alternative to breast biopsy (9). The elastographic information is immediately available and superimposed in color on the B-mode image. Sonoelastography is, therefore, not more time consuming than conventional breast US (17).

The ability of SE to evaluate the mechanical properties of different tissues is an useful diagnostic tool that provides further information about breast lesions in addition to the well-known morphologic parameters such as shape, orientation, margins, internal structure and the presence of calcifications. These additional findings may be very useful in distinguishing malignant from benign solid lesions; as well, the stiffness of a mass as perceived at palpation plays an important role in the clinical assessment (18). Changes in elastic properties between
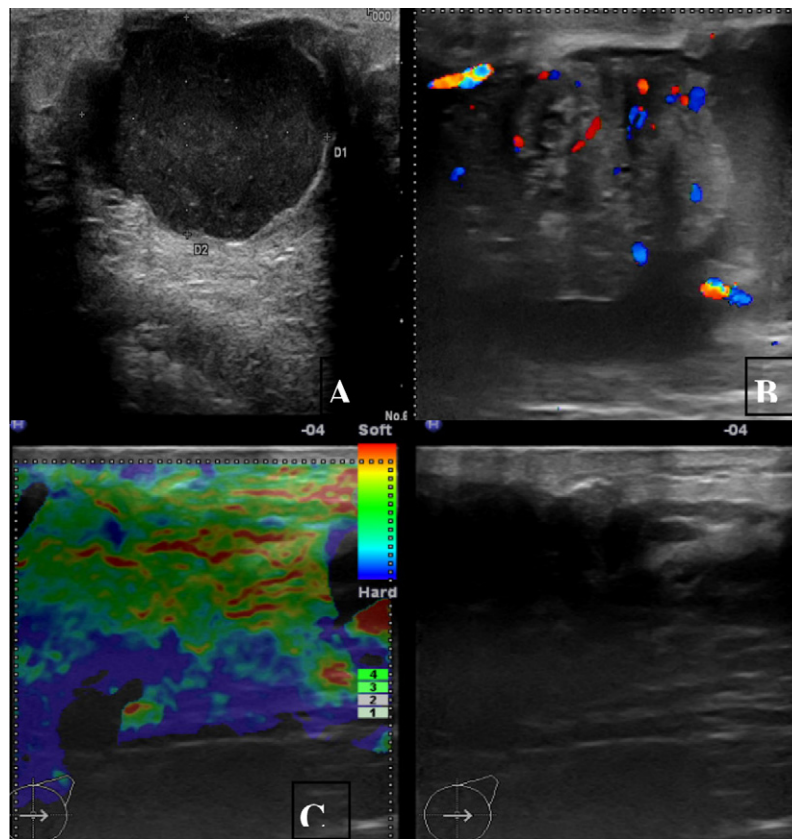
Fig. 6 A 29 year-old-lady doing US follow up (A) for a palpable left retroareolar intraductal heterogeneous hypoechoic solid lesion with high vascularity on color Doppler application (B) (classified as BIRADS 3). Elastography revealed score 3 (benign) (C). By Biopsy, it was proved to be an intraductal papilloma.
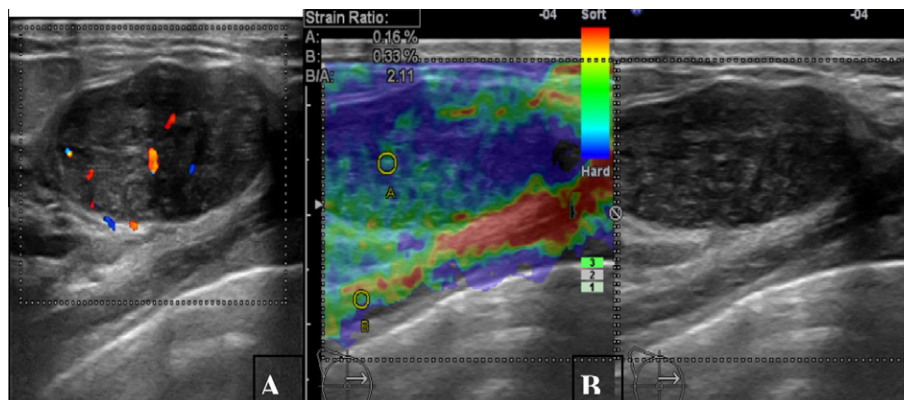

Fig. 7 US of a 26-year-old woman with a right breast palpable lump revealed a well defined lobulated hypoechoic solid mass with vascularity on color Doppler demonstration (A). Ultrasound elastography (B) revealed score: 2, and a strain ratio value of 2.11 (benign) between the mass and the surrounding tissue. By Biopsy, it was proved to be a fibroadenoma.

normal tissue, fibroadenoma and cancer have been reported in previous papers (19,20), assessing that neoplastic lumps are significantly harder than fibroadenomas. In addition, malignant lesions tend to be larger on US strain images than on corresponding B-mode US images, perhaps because of the desmoplastic reaction commonly associated with malignancy (8,13,21–25). The changes in contrast with deformation can only be appreciated in a sequence of images. The appearance

of masses on strain images and lesion size discrepancies between B-mode and strain images is a promising tool for distinguishing benign from malignant lesions.

In our work, elastographic images were assigned an elasticity score of 1 to 5 (1–3, benign; 4 and 5, malignant) according to the Multi-Center Team of Study – Locatelli et al. – (14). For SR measurement, we utilized Cohn's (15) results: the benign lesions produced a mean strain ratio of 1.83 while malignant

lesions produced a mean strain ratio of 8.38 using a cutoff point of 3.05. As in several studies, elastography showed less sensitivity but higher specificity than conventional sonography: we obtained B-mode sonography sensitivity of 85.1%, specificity of 93.9%, a positive predictive value of 92.5% and a negative predictive value of 87.8%, compared with a sensitivity of 80.1%, a specificity of 97.1%, a positive predictive value of 96.8% and a negative predictive value of 82.1% for elastography.

These results agreed with those of the other studies based on elasticity score as Navarro et al. (26) who stated that B-mode sonography had a sensitivity of 96.6%, a specificity of 76.9%, a positive predictive value of 79.2% and a negative predictive value of 96.2%, compared with a sensitivity of 69.5%, a specificity of 83.1%, a positive predictive value of 78.9%, and a negative predictive value of 75.0% for elastography. For Thomas et al. (17), sensitivity and specificity in the differentiation of benign and malignant lesions were 94% and 83% respectively for B-mode US while Elastography had a sensitivity of 82% and a specificity of 87%; while for Leong et al. (27) sensitivity and specificity were 88.5% and 42.9%, respectively, for conventional ultrasound, 100% and 73.8%, respectively, for elastography, and 88.5% and 78.6%, respectively, for combined imaging. Holst et al. (28) found in elastography a sensitivity of 77.6% and 79.6% and a specificity of 91.5% and 84.7% for two observers, respectively; and for B-mode ultrasound a sensitivity of 91.8% and a specificity of 78%.

In Cohn's (15) study for strain ratio evaluation, when the researchers used a cutoff point of 3.05, ultrasound elastography had 92.4% sensitivity, 91.1% specificity, and 91.4% accuracy. The sensitivity was higher than the five-point scoring system, the study authors said. Comparably Zhao et al. (29) stated that the strain ratios between benign lesion (2.26 ± 1.39) and malignancy (6.95 ± 4.08) were significantly different. The sensitivity, specificity and accuracy of 2-dimensional ultrasonography and strain ratio for breast cancer detection was 81.58%, 80.28%, 80.73% and 86.84%, 88.73%, 88.07% respectively. The rate of diagnostic sensitivity and accuracy was increased to 97.37% and 93.58% respectively by a combination of 2-dimensional ultrasonography and strain ratio measurement.

Our study emphasized Destounis' results that demonstrated the efficacy of elastography in identifying cancerous lesions being less effective at identifying benign lesions as well as Elizabeth Wende's who found that the technique agreed with B-mode ultrasound on 97% of cancers but elastography was only able to correctly point out 79% of benign lesions (30) compared to 87.8% and 82.1% respectively in our study.

For us, elastography was superior to B-mode US in diagnosing solid lesions in lipomatous involution (96.6% vs. 92.4% specificity) and less significantly in the dense glandular tissue (97.8% vs. 95.9% specificity); compared to other papers where elastography was superior to B-mode US in diagnosing Breast in lipomatous involution (80% vs. 69% specificity) (15) or elastography found the highest specificity of 100% in patients with dense breast tissue (28).

4.1. Limitations

Patient movement, respiratory motion, and slight changes in position are potential sources of error when performing ultra-

sound in humans: in elastography, errors in calculating elasticities would primarily affect "harder" tissues and make them appear "softer" and thus give rise to false negative findings. A reported limitation is in evaluating focal lesions located at a depth of more than 1 cm because of incomplete coloring. Further standardization of elastography is required with regard to the amount of compression applied, patient positioning, and subjective assessment of elastograms in the course of the examination (22).

According to univariate analysis, smaller lesion size ($P = .001$), shallower lesion depth ($P = .005$), less breast thickness where the lesion was located ($P < .0001$), and benign pathologic finding ($P = .004$) were significantly associated with higher image quality. There was no correlation of image quality with age ($P = .213$), BMI ($P = .191$), mammographic density ($P = .091$), or distance from the nipple ($P = .100$). Multivariable analysis showed that breast thickness at the location of target lesions was the most important factor influencing elasticity image quality ($P = .001$). There were significant differences in sensitivity between higher-quality and lower-quality images (87.0% vs 56.8%, respectively; $P = .015$) in the differentiation of benign from malignant masses (31).

5. Conclusions

In summary, real-time sonoelastography is an useful technique for the characterization of benign and malignant solid lesions as it increases the diagnostic specificity comparable to B-mode ultrasound, particularly in both ACR 1 and 2, thus reducing the false-positive rate.

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