Original Investigation

Diagnostic Value of ARFI (Acoustic Radiation Force Impulse) in Differentiating Benign From Malignant Breast Lesions

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Abbreviations

ARFI acoustic radiation force impulse
US ultrasonography
ROI region of interest
SWV shear wave velocity
LPR lesion-to-parenchyma ratio
IQR interquartile range
AUC area under the curve

Rationale and Objectives: The aim of this study was to correlate acoustic radiation force impulse (ARFI) imaging velocities with the pathology results and to evaluate the ability of ARFI in distinguishing benign from malignant breast lesions.

Materials and Methods: B-mode ultrasonography (US) and ARFI were performed in patients with previously diagnosed and selected breast lesions for biopsy. Shear wave velocity (SWV) was measured inside lesions and in the surrounding parenchyma (*m/s*). SWV measurements as well as lesion-to-parenchyma ratio (LPR) were compared between benign and malignant lesions, and receiver operating characteristic (ROC) curves were plotted. Two blinded readers independently classified the lesions as benign or malignant in two separate reading sessions, one using B-mode US alone and the other using a combined set of B-mode US and ARFI.

Results: Eighty-one patients with a total of 92 breast lesions were included (57 benign and 35 malignant nodules). SWV inside lesions were significantly higher for malignant neoplasms compared to benign (medians of 9.1 m/s vs 3.5 m/s; $P < 0.001$). LPR was also significantly higher for malignant lesions (3.0 vs 1.4; $P < 0.001$). Parenchyma SWV had no differences between groups ($P = 0.071$). ROC curves showed a significant discriminative power for lesion SWV (area under the curve [AUC] = 0.980; $P < 0.001$) and LPR (AUC = 0.954; $P < 0.001$). For lesion measures, a cutoff of 6.593 m/s was obtained, with sensitivity and specificity of 88.6% and 96.5%, respectively.

Conclusions: ARFI provides quantitative elasticity measurements, adding valuable complementary information to B-mode ultrasound, that can potentially help in breast lesion characterization and assisting the decision for biopsy recommendations.

Key Words: Ultrasonography; tissue elasticity imaging; ARFI imaging; breast; breast neoplasms.

INTRODUCTION

Ultrasonography (US) is a useful technique that has been increasingly used as an important diagnostic tool complement to mammography in differentiating benign from malignant breast tumors (1–3). Although US depicts more cancers than mammography alone, it has a considerable number of false-positives, which also leads to a higher number of benign mass biopsies (1).

In the last decades, US technology has experienced several advances, including real-time elastography, which evaluates tissue stiffness, detecting its displacement after slight manual compression (1,2,4–6). Information is converted into color-scale images and is superimposed to B-mode images. Knowing that malignant tumors tend to be stiffer and that benign masses are usually softer (2), real-time elastography is used as a complementary technique in addition to B-mode sonography, increasing its specificity (83.1% vs 76.9% for B-mode US alone) (7). However, this technique has some limitations. The first, and perhaps the most important, is the fact that it is operator dependent and has a higher interobserver variability, because

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it requires compression with the probe, preventing lateral or angulated movements, to obtain good quality images (2,7,8). Besides variability caused by technical limitations, there is also a certain degree of subjectivity in image interpretation (4,7). Another limitation is that real-time elastography only provides qualitative information, although ratios between the lesion and surrounding breast parenchyma can be calculated (2).

Acoustic radiation force impulse (ARFI) is a new sonographic technology that noninvasively assesses qualitative and quantitative tissue elasticity by measuring shear wave velocities (SWVs) of a selected region of interest (ROI) (3,8). A short-duration (0.03–0.4 millisecond) high-intensity acoustic "pushing pulse" is transmitted through the tissue, creating its displacement. The displacements of tissue induce shear waves that travel perpendicular to the initial "pushing pulse." As the shear wave travels through tissue, the generated displacements are detectable using ultrasound tracking beams and are correlated with elapsed time, and shear wave speed is calculated (m/s) (5,6). It does not require manual compression and provides not only qualitative but also quantitative information about hardness of a lesion.

The aim of this study was to evaluate the role of ARFI for the differential diagnosis between benignancy and malignancy of breast tumors.

MATERIALS AND METHODS

Patients and Lesions

From January 2013 to June 2013, 81 women who had been scheduled to undergo US-guided biopsy on the basis of suspicious conventional US findings were invited to participate in the study and were examined with B-mode US and ARFI. Informed consent was obtained from all patients. Only lesions that underwent subsequent biopsy confirmation were included in the study and evaluation was always performed before biopsy, to reduce potential artifacts.

B-Mode Ultrasound and ARFI Acquisition

B-mode US and ARFI were performed by one radiologist with knowledge of clinical and mammographic findings using an Acuson S3000 diagnostic ultrasound system (Siemens Medical Solutions, Mountain View, CA, USA) with ARFI imaging software and 9L4 high-frequency probe with a frequency of 9 MHz. Evaluation of color-coded tissue stiffness map and SWV measurements were performed using the application "*Virtual Touch tissue IQ.*"

For both B-mode US and ARFI examinations, patients were positioned in a dorsal decubitus position with both arms in maximal abduction (180 degrees). In some lesions located in the outer half, especially in large breasts, patients were positioned in a lateral decubitus (contralateral side of the lesion).

For ARFI acquisition, transducer was applied with light pressure together with a suitable amount of contact gel to avoid artifact areas.

An ROI box was created and adjusted to include the target lesion as well as the surrounding breast parenchyma. The *Virtual Touch tissue IQ* button was then pressed, keeping the transducer still, and a color-coded map was obtained according to the stiffness degree of tissues included on the ROI, with a scale from blue (lower SWV, softer) to red (higher SWV, stiffer). SWV (*m/s*) was obtained within the lesion and in the surrounding parenchyma (at least 1 cm away from the lesion) using a predetermined ROI with fixed dimensions of 2×2 cm. Measurements in the lesion were obtained preferentially in the stiffest areas as shown on the color map. To overcome problems regarding lesion heterogeneity, SWV was measured at least 3 times inside the lesion and 3 times in the surrounding parenchyma. All of the SWV values for an individual mass or the reference breast tissue were averaged to produce a mean SWV. SWV lesion-to-parenchyma ratio (LPR) was also calculated.

Because SWV is expressed as numeric values, only numeric results were taken into consideration in this study. All SWV value displayed as "X.XX" m/s were considered invalid measurements and excluded, and a new acquisition was performed.

Readers and Reading Procedures

Two radiologists who did not participate in the US acquisition participated as readers (reader A with 5 and reader B with 21 years of experience in breast US examination). Both readers were blinded to clinical, mammographic, and histologic findings, as well as the proportion of cases with benign and malignant histologic findings.

A two-step sequential reading was performed consisting of images of B-mode US alone and a combined set of B-mode US and ARFI. The readers independently classified the lesions at each reading session as benign or malignant.

In the first reading session, B-mode US images were shown, and readers evaluated the lesions on the basis of two orthogonal grayscale view. In the second session, the same images were shown for each lesion, as well as a color elastogram superimposed with the underlying B-mode image and the respective measurements of SWV (Figs 1–5). Reading sessions were separated by at least 1 month, with patients in different order and without the information of reader's scores from prior B-mode alone sessions to reduce recall bias (Fig 6).

Statistical Analysis

Quantitative values were represented as mean ± standard deviation or median and interquartile range (IQR). Sensitivity and specificity for B-mode US and B-mode US + ARFI for both readers were obtained with cross-tabulation of reader classification with histological diagnosis.

For inferential analysis, distribution of SWV values was assessed for normality using Kolmogorov-Smirnov test. Using histological diagnosis as groups, comparisons of SWV values inside the lesion, in the parenchyma and LPR, were performed using Student's *t* test for independent samples when there was a normal distribution or using Mann-Whitney *U* test otherwise.

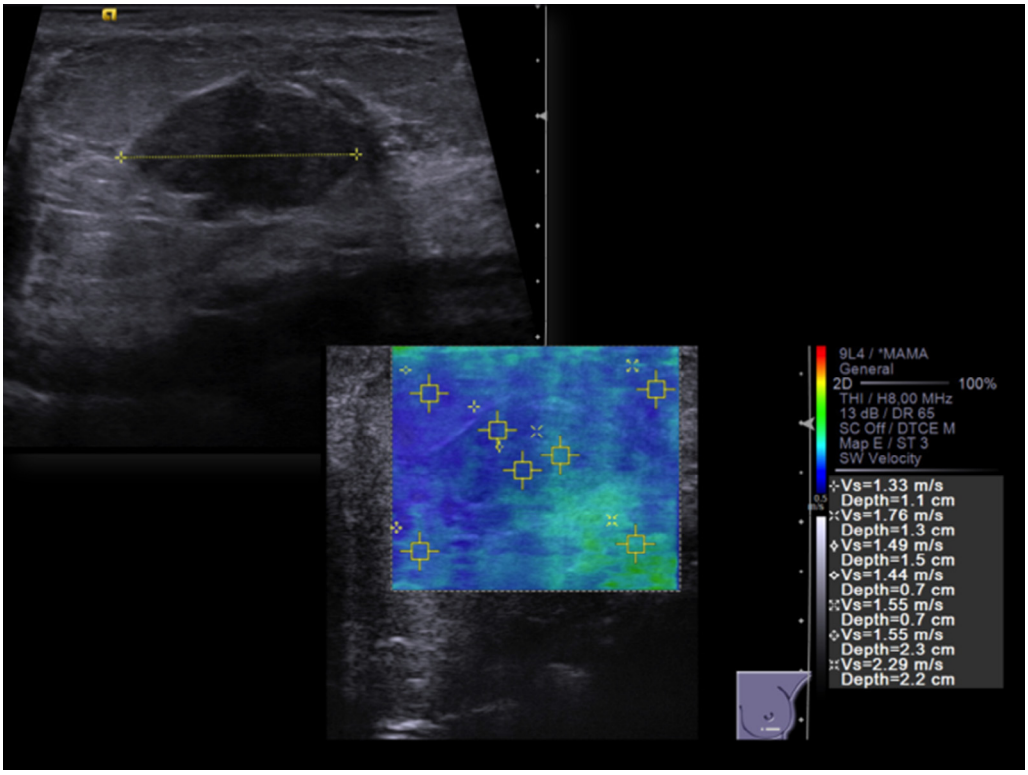

Figure 1. Example of a breast lesion in B-mode ultrasonography image (*left*), as well as a color elastogram superimposed with the underlying B-mode image and the respective measurements of shear wave velocity (*right*), which are low (<4.5 m/s). The pathological result was fibroadenoma.

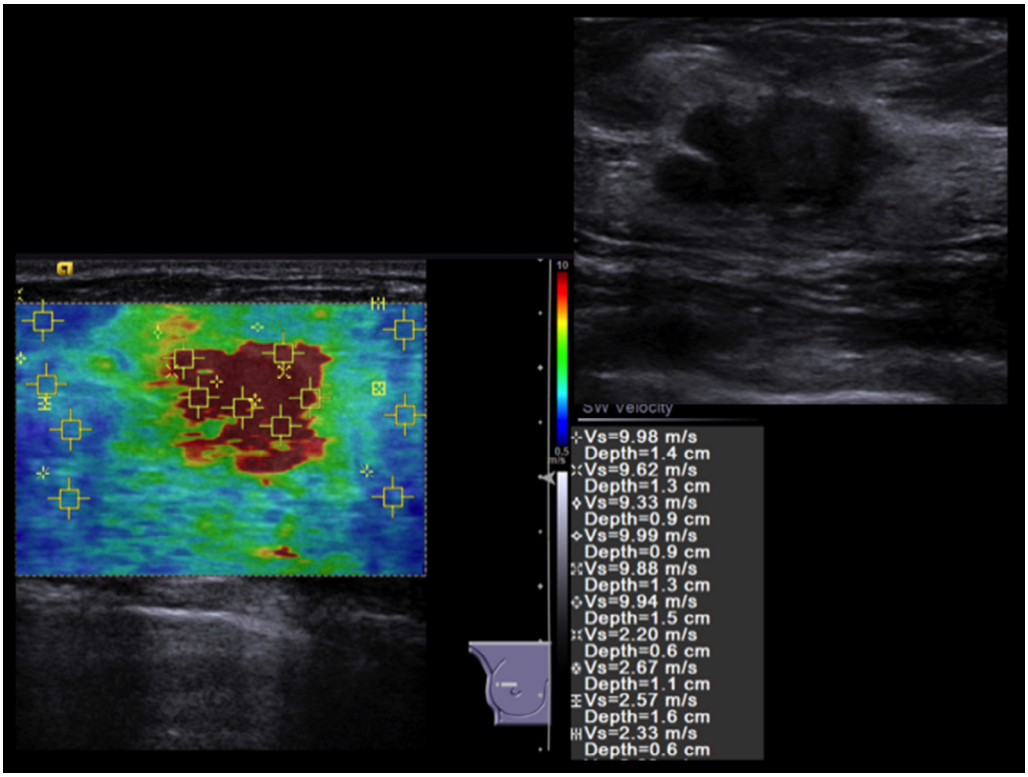

Figure 2. Example of a lobulated hypoechogenic lesion in B-mode ultrasonography image (*right*). The shear wave velocities are high (*left*), which were consistent with the diagnosis of a malignant lesion (invasive carcinoma of no special type).

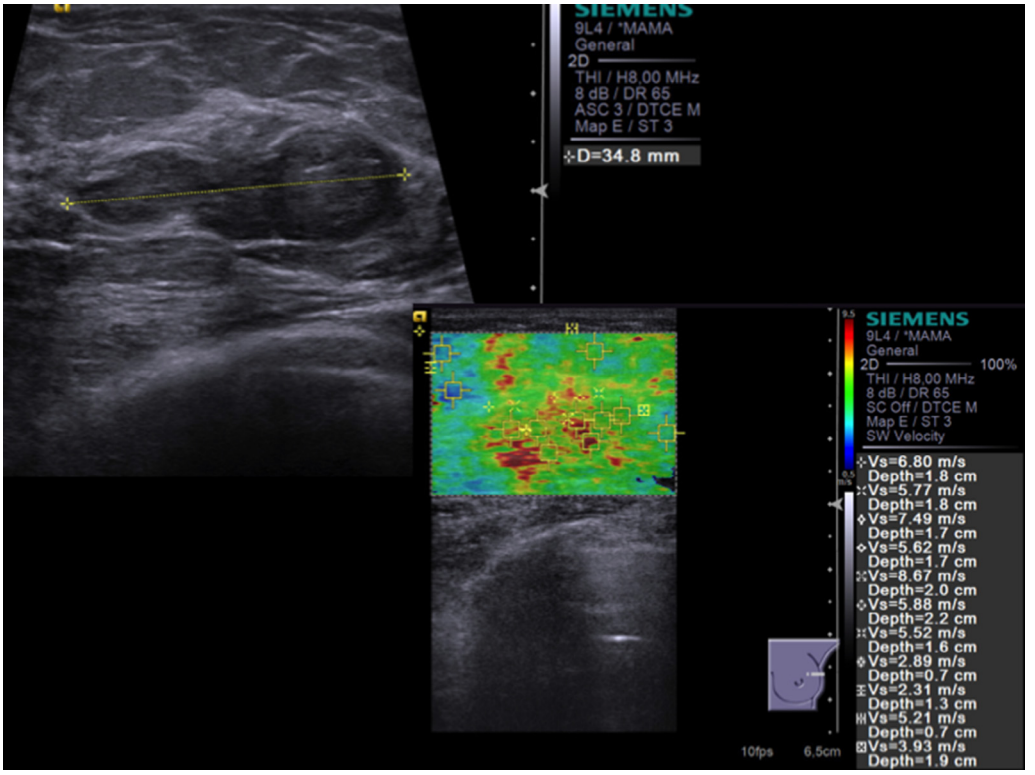

Figure 3. Example of a lobulated hypoechogenic lesion in B-mode ultrasonography image (*left*). The color elastogram and the respective measurements of shear wave velocity (*right*) revealed elevated velocities. The final diagnosis was fibroadenoma—with abundant collagen matrix.

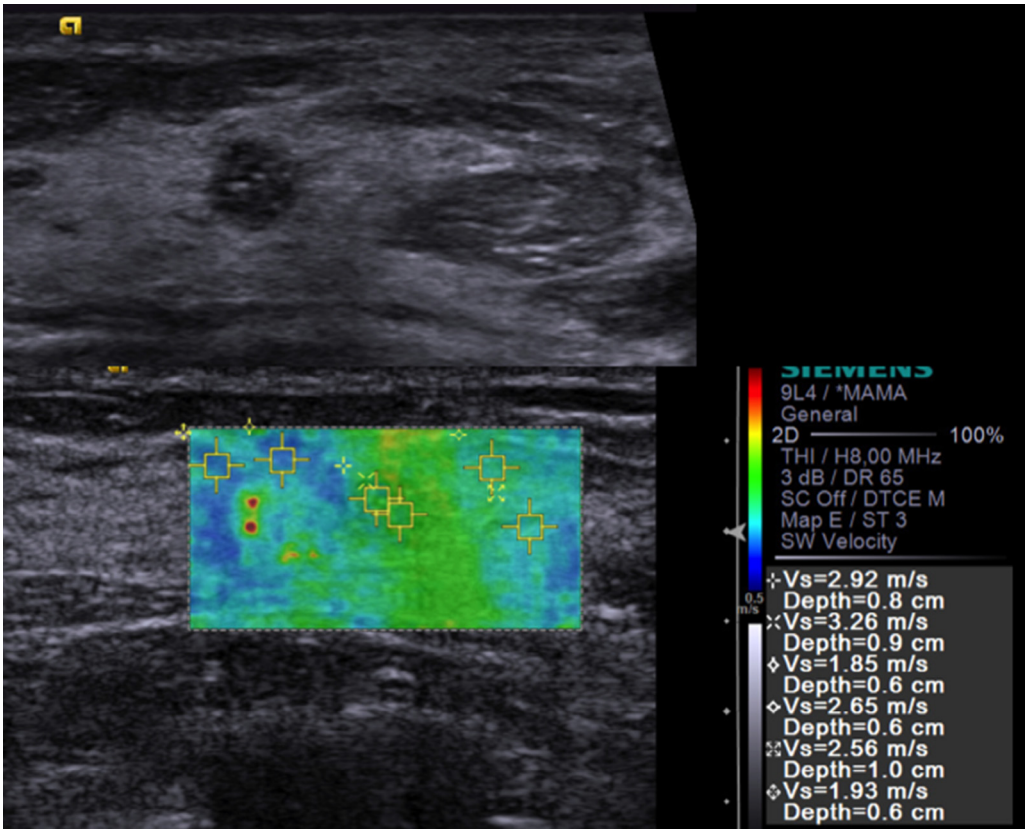

Figure 4. Example of a round hypoechogenic lesion (*superior image*) that presented low shear wave velocity (*inferior image*), which was consistent with the pathological result of a benign lesion (fibroadenoma).

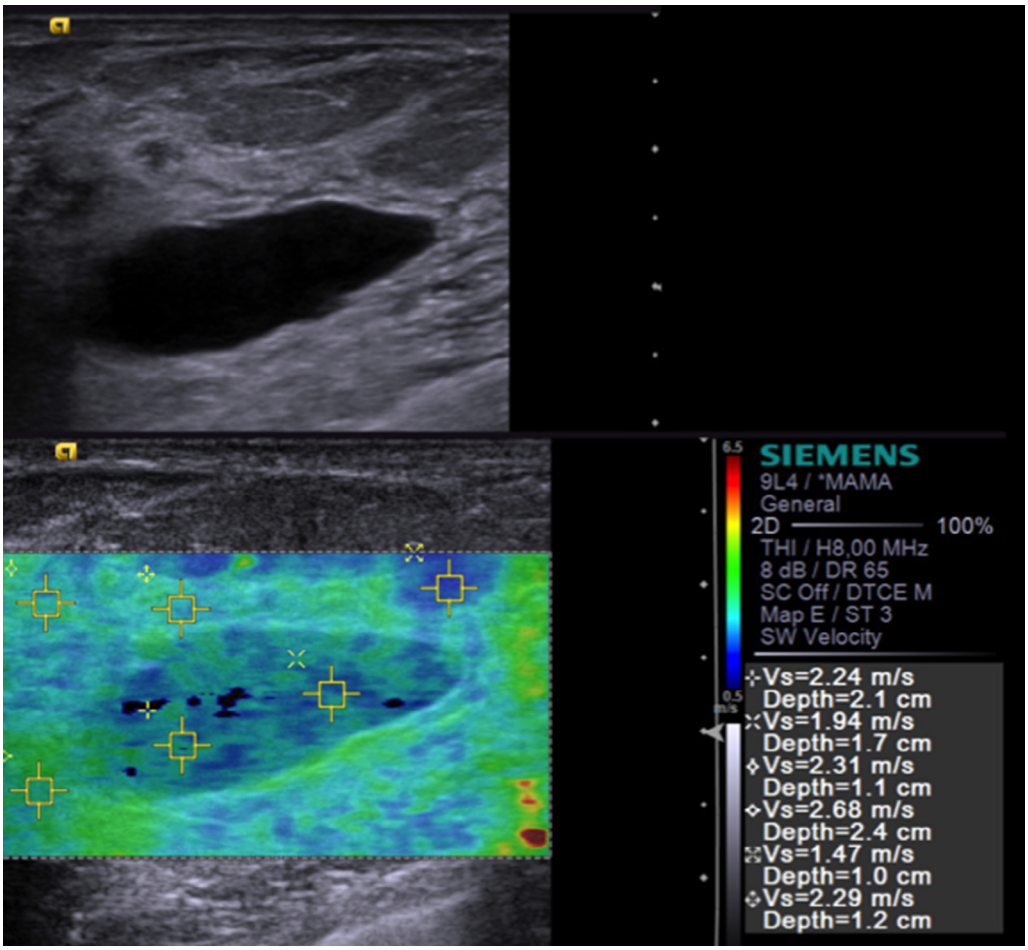

Figure 5. B-mode ultrasonography depicts a homogeneous, anechoic, oval lesion (simple cyst). The color elastogram shows a heterogeneous appearance, with "black areas."

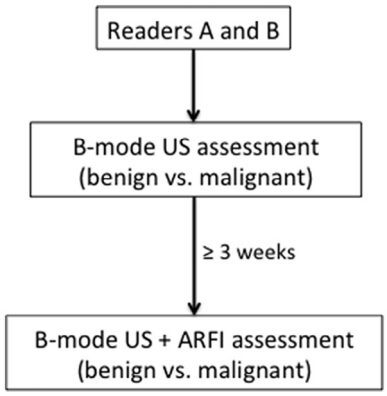

Figure 6. Scheme of the reading sessions performed by both independent readers. ARFI, acoustic radiation force impulse; US, ultrasonography.

For assessing accuracy of SWV values and LPR in distinguishing benign and malignant lesions, Receiver operating characteristic (ROC) curves were plotted and area under the curve (AUC) was determined. Youden Index was determined to find a cutoff value that maximizes discriminative power, and both sensitivity and specificity were determined for that value (9).

Agreement between both readers in rating the examinations was determined using Kappa parameter. Kappa values are represented as mean ± standard error.

A type I error of 0.05 was considered for all comparisons.

RESULTS

Eighty-one female patients were included, with a mean age of 50.0 ± 12.88 years and a total of 92 breast lesions. Of these, 52 (56.5%) were located on the left breast and 40 (43.5%) on the right breast. The majority was in the upper quadrants of the breast (66.3%), with a median size of 14 mm (IQR 10 mm).

The pathologic diagnosis revealed benignancy in 57 lesions (62.0%) and malignancy in 35 lesions (38.0%) (Table 1).

ARFI Quantification

ARFI measurements are displayed in Table 2. SWV differed significantly between benign and malignant lesions, with significantly higher SWV inside malignant lesions (8.7 ± 1.49 m/s) compared to benign lesions (3.8 ± 1.41 m/s, $P < 0.001$). Mean

velocity LPR was also significantly higher in malignant lesions (3.3 ± 1.20 vs 1.5 ± 0.52, $P < 0.001$).

ROC curves are represented in Figure 7. Measurements inside the lesion and LPR showed a significant discriminative power between malignant and benign lesions (AUC of 0.980 and 0.954, respectively) (Table 3), which was not observed in parenchyma measurements (AUC of 0.597). Using Youden's Index, cutoff values of 6.593 m/s and 2.181 were obtained for velocity inside the lesion and LPR, respectively, resulting in high sensitivity (88.6% and 88.6%) and specificity (96.5% and 93.0%) (Table 3).

TABLE 1. Histopathologic Diagnosis and Dimensions of Breast Lesions

		Malignant Lesions	
Tumor histology	Histologic grade	1	15
		2	13
		3	7
		Total	**35**
	Tumor type	Ductal	31
		Lobular	3
		Metaplastic	1
		Total	**35**
	Benign Lesions		
	Tumor type	Fibroadenoma	34
		Intraductal papilloma	4
		Complex cyst	7
		Hamartoma	4
		Tubular adenoma	1
		Radial scar	1
		Granuloma	2
		Other ANDI*	4
		Total	**57**
Lesion dimensions (mm)		≥ 5 and < 10	21
		≥ 10 and < 15	28
		≥ 15 and < 20	18
		≥ 20 and < 25	13
		≥ 25	11
		Total	**91**

* ANDI (aberrations of normal development and involution) including sclerosing adenosis and other fibrocystic changes of the breast.

Comparison between Readers

When comparing B-mode US with B-mode US + ARFI, we obtained higher specificity values for both readers adding ARFI (59.6% vs 49.1% for Reader A and 70.2% vs 40.4% for Reader B), without impairment of sensitivity (Tables 4 and 5).

Regarding variations between readers, we obtained significant Kappa values for agreement for both B-mode US and B-mode US + ARFI ($P < 0.001$). Kappa value was higher when using combined techniques (Kappa: 0.820 ± 0.060) than when using B-mode US alone (Kappa: 0.649 ± 0.088).

DISCUSSION

In this study we obtained higher SWV values inside malignant lesions and higher LPR, with no significant differences for the surrounding parenchyma. Using this technique, SWV values are also coded in a color map, which aids the reader in quickly assessing the lesion. In the case of malignant tumors, there is a higher contrast between the lesion and the adjacent parenchyma, which allows a faster categorization, even before quantitative measurements. We have deliberately chosen not to perform the parenchyma measurements in the lesion's most immediate adjacent areas, as it could be invaded in the case of malignancy, leading to higher SWV values. This could account for a lower difference in LPR between benign and malignant lesions, than when using exclusively SWV values inside the lesion, which implies that the latter could have higher accuracy for clinical use, as shown in our results.

In our study we perceived that some lesions are more heterogeneous concerning SWV values. We performed multiple measurements and used the mean value to account for variability. In fact, for more heterogeneous lesions, velocity values can be useful for biopsy guidance, preferably selecting regions with higher velocities.

Analyzing ROC curves, in-lesion SWV alone also had better accuracy than LPR. This could be an advantage of using ARFI instead of real-time elastography for breast lesion assessment. In fact, the latter can only provide ratios between lesion and surrounding breast parenchyma (2), which leads to a lower AUC compared to the one derived from absolute measurements.

TABLE 2. ARFI Measurements for Benign and Malignant Lesions

Measurement		Benign $n = 57$	Malignant $n = 35$	*P* Value
Inside lesion (m/s)	Mean ± SD	3.8 ± 1.41	8.7 ± 1.49	<0.001*
	Median (IQR)	3.5 (2.1)	9.1 (1.7)	
Parenchyma (m/s)	Mean ± SD	2.6 ± 0.65	2.8 ± 0.57	0.160†
	Median (IQR)	2.4 (0.95)	2.8 (0.84)	
LPR	Mean ± SD	1.5 ± 0.52	3.3 ± 1.20	<0.001*
	Median (IQR)	1.4 (0.59)	3.0 (1.37)	

ARFI, acoustic radiation force impulse; IQR, interquartile range; LPR, lesion-to-parenchyma ratio; SD, standard deviation.

* Mann-Whitney test.

† Student's *t* test for independent samples.

TABLE 3. AUC, Cutoff, Sensitivity, and Specificity for ARFI Measurements

Measurement	AUC (SE)	*P* Value	Cutoff	Sensitivity (%)	Specificity (%)
Inside lesion	0.980 (0.011)	<0.001	6.593 m/s	88.6	96.5
Parenchyma	0.597 (0.060)	0.118	2.527 m/s	71.4	54.4
LPR	0.954 (0.020)	<0.001	2.181	88.6	93.0

ARFI, acoustic radiation force impulse; AUC, area under the curve; LPR, lesion-to-parenchyma ratio; SE, standard error.

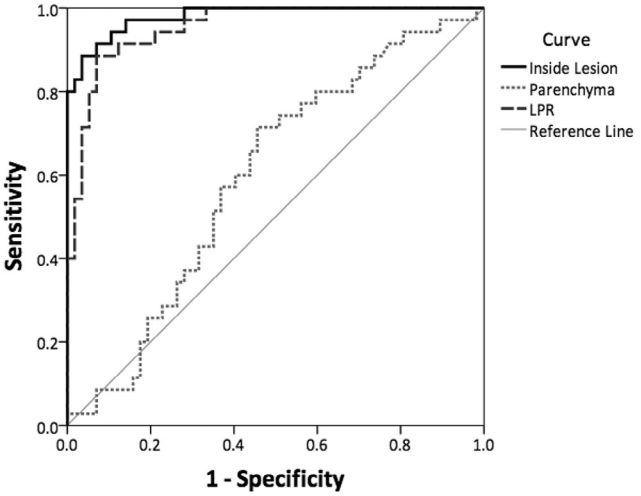

Figure 7. Receiver operating characteristic curves for acoustic radiation force impulse measurements inside the lesion and in parenchyma, as well as lesion-to-parenchyma ratio (LPR).

TABLE 4. BI-RADS Classification by Reader

	BI-RADS 3	BI-RADS 4	BI-RADS 5
Reader A (B-mode US)	28	55	9
Reader A (B-mode US + ARFI)	32	51	9
Reader B (B-mode US)	23	60	9
Reader B (B-mode US + ARFI)	40	43	9

ARFI, acoustic radiation force impulse; BI-RADS, Breast Imaging - Reporting and Data System; US, ultrasonography.

TABLE 5. Sensitivity and Specificity for Each Reader

		B-mode US (%)	B-mode US + ARFI (%)
Reader A	Sensitivity	100	100
	Specificity	49.1	59.6
Reader B	Sensitivity	100	100
	Specificity	40.4	70.2

ARFI, acoustic radiation force impulse; US, ultrasonography.

Considering the distinction of benignancy from malignancy, we have obtained a cutoff value of 6.593 m/s for SWV measured inside the lesion. Using this value, a sensitivity of 88.6% and a specificity of 96.5% were obtained. In clinical practice, for the decision of biopsying breast lesions, it might be preferable to maximize sensitivity, at the cost of specificity, to assure that all malignant lesions are correctly detected. With the results obtained in our study, a cutoff of 4.5 m/s can enhance sensitivity (100%), with a reasonable value of specificity (71.9%), which is consistent with previous studies (3,10,11). However, Barr and Zhang (12) and Yao et al. (13) reported higher specificity and lower sensitivity values for a similar cutoff (4.5 and 4.22 m/s). This could be partially explained by the fact that in the current series, some histologic subtypes of breast tumors, specifically those assigned as softer malignant lesions, such as medullary, mucinous, papillary, cystic, and some necrotic infiltrating ductal carcinoma variants, were not included.

The classification assigned by readers was independent of any cutoff values. We noticed that the addition of ARFI to B-mode US enhanced specificity without lowering sensitivity (100%) for both readers. The use of ARFI could therefore assist in reducing the number of unnecessary biopsies.

Regarding inter-reader variation, a different specificity was observed when using B-mode US + ARFI (59.6% and 70.2%). If we have used a pre-established cutoff value as guidance, perhaps this difference could be attenuated. In fact, considering the previously mentioned cutoff of 4.5 m/s, we would expect an enhancement in the specificity of reader 1. The use of cutoffs could, therefore, reduce inter-reader variability, always adapting the reading to the particular clinical situation.

The agreement between readers was also superior when combining the results from both techniques instead of B-mode US alone (0.820 vs 0.649), which has also been concluded in other studies (14). This supports that ARFI decreases subjectivity when assessing breast lesions. As before, if a cutoff was pre-established, these results could even be improved.

Our study had some limitations. First, readers classified the lesions as benign or malignant only based on a single orthogonal view. Some lesions are significantly heterogeneous and can seem to have different elasticity and morphology depending on the selected image plane. Possibly, suspicious features would be better depicted by image examination in more planes. In fact, Lee et al. reported a better diagnostic performance with two-orthogonal-view acquisition when compared to single-view shear wave elastography images (15). Therefore, lesions should be evaluated in more than one plan, so that stiffer areas are also included in the evaluation.

As already mentioned, the influence of different histologic types of malignant lesions in ARFI measurements was not assessed. This could be of importance to better understand how the individual histological subtypes affect specificity. Based on different types of tumors, it is possible that we can find different diagnostic accuracy values and this could explain some differences of our results with some previous studies. Although uncommon, as mentioned earlier, some malignant tumors are softer to the touch and consequently will show lower SWV when compared to other breast cancers (16,17,18). A cutoff taking these differences into account would be necessary to categorize lesions as benign or malignant, so that in the future this technique could be incorporated in clinical practice. Therefore, the way in which the histology of tumors will influence SWV might be significant, as it will probably affect values of sensitivity and specificity for a certain cutoff. This emphasizes the importance of adding all data available (B-mode ultrasound, mammography, and clinical information) to lower the number of false-positive and false-negative results, namely in those lesions with SWV values close to the established cutoff.

Another point to be considered is that SWV values obtained with different equipment may not be reproducible.(19) It could be important to assess if these differences exist, as it could lead to different cutoffs for distinguishing benign from malignant breast lesions.

CONCLUSION

Our investigation shows that ARFI is a promising technique in differentiating benign from malignant breast lesions. It provides quantitative elasticity measurements, adding valuable complementary information to B-mode ultrasound, improving its specificity and reducing the false-positives, potentially assisting the decision for biopsy recommendations. More studies on this subject are necessary so that optimization and validation of this method is accomplished, to recommend its routine use in clinical practice.

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REFERENCES

1. Cho N, Jang M, Lyou CY, et al. Distinguishing benign from malignant masses at breast US: combined US elastography and color Doppler US—influence on radiologist accuracy. Radiology 2012; 262:80–90. doi:10.1148/radiol.11110886; [Epub 2011 Nov 14].
2. Hooley RJ, Scoutt LM, Philpotts LE. Breast ultrasonography: state of the art. Radiology 2013; 268:642–659. doi:10.1148/radiol.13121606.
3. Berg WA, Cosgrove DO, Doré CJ, et al. Shear-wave elastography improves the specificity of breast US: the BE1 multinational study of 939 masses. Radiology 2012; 262:435–449. doi:10.1148/radiol.11110640.
4. Chang JM, Moon WK, Cho N, et al. Breast mass evaluation: factors influencing the quality of US elastography. Radiology 2011; 259:59–64. doi:10.1148/radiol.10101414; [Epub 2011 Feb 17].
5. Faruk T, Islam MK, Arefin S, et al. The journey of elastography: background, current status, and future possibilities in breast cancer diagnosis. Clin Breast Cancer 2015; 15:313–324. doi:10.1016/j.clbc.2015.01.002.
6. Shiina T, Nightingale KR, Palmeri ML, et al. WFUMB guidelines and recommendations for clinical use of ultrasound elastography: part 1: basic principles and terminology. Ultrasound Med Biol 2015; 41:1126–1147. doi:10.1016/j.ultrasmedbio.2015.03.009.
7. Navarro B, Úbeda B, Vallespí M, et al. Role of elastography in the assessment of breast lesions: preliminary results. J Ultrasound Med 2011; 30:313–321.
8. Balleyguier C, Canale S, Hassen WB, et al. Breast elasticity: principles, technique, results: an update and overview of commercially available software. Eur J Radiol 2013; 82:427–434. doi:10.1016/j.ejrad.2012.03.001.
9. Youden WJ. An index for rating diagnostic tests. Cancer 1950; 3:32–35.
10. Tang L, Xu HX, Bo XW, et al. A novel two-dimensional quantitative shear wave elastography for differentiating malignant from benign breast lesions. Int J Clin Exp Med 2015; 8:10920–10928.
11. Park J, Woo OH, Shin HS, et al. Diagnostic performance and color overlay pattern in shear wave elastography (SWE) for palpable breast mass. Eur J Radiol 2015; 84:1943–1948. doi:10.1016/j.ejrad.2015.06.020.
12. Barr RG, Zhang Z. Shear-wave elastography of the breast: value of a quality measure and comparison with strain elastography. Radiology 2015; 275:45–53. doi:10.1148/radiol.14132404.
13. Yao M, Wu J, Zou L, et al. Diagnostic value of virtual touch tissue quantification for breast lesions with different size. Biomed Res Int 2014; 2014:142504. doi:10.1155/2014/142504.
14. Ng WL, Rahmat K, Fadzli F, et al. Shear wave elastography increases diagnostic accuracy in characterization of breast lesions. Medicine (Baltimore) 2016; 95:e3146. doi:10.1097/MD.0000000000003146.
15. Lee SH, Cho N, Chang JM, et al. Two-view versus single-view shear-wave elastography: comparison of observer performance in differentiating benign from malignant breast masses. Radiology 2014; 270:344–353. doi:10.1148/radiol.13130561.
16. Athanasiou A, Tardivon A, Tanter M, et al. Breast lesions: quantitative elastography with supersonic shear imaging—preliminary results. Radiology 2010; 256:297–303. doi:10.1148/radiol.10090385.
17. Evans A, Sim YT, Thomson K, et al. Shear wave elastography of breast cancer: sensitivity according to histological type in a large cohort. Breast 2016; 26:115–118. doi:10.1016/j.breast.2016.01.009.
18. Kapetas P, Pinker-Domenig K, Woitek R, et al. Clinical application of acoustic radiation force impulse imaging with virtual touch IQ in breast ultrasound: diagnostic performance and reproducibility of a new technique. Acta Radiol 2016; [Epub ahead of print]; 0284185116641347[pii].
19. Giannotti E, Vinnicombe S, Thomson K, et al. Shear-wave elastography and greyscale assessment of palpable probably benign masses: is biopsy always required? Br J Radiol 2016; 89:20150865. doi:10.1259/bjr.20150865.