Maximum elasticity and elasticity standard deviation efficacy of shear wave elastography in female breast lesions

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Abstract

Aim: Shear-wave (SW) elastography is a new method of obtaining quantitative tissue elasticity data during breast ultrasound (US) examinations. The aim of this study was to correlate the maximum elasticity and standard deviation values of breast masses with histological findings, and to compare the validity of these procedures.

Methods: This is a cross-sectional study among 76 consecutive patients conducted in the "Evangelism" medical center from January 2012 to April 2013. Patients underwent standard breast US supplemented by quantitative SW elastography using the Aixplorer® ultrasound system. SW elastographic evaluation (maximum elasticity of stiffest portion of mass and surrounding tissue and standard deviation [SD]) was calculated for each lesion. Elastography measurements were correlated with histology results. Maximum elasticity and standard deviation cut-off values of <60 kilopascals (kPa) and ≤10, respectively, were used for benign/malignant differentiation.

Results: Mean age of participants was 51 years (range 25-65 years). In total, 79 lesions were noticed. Mean ultrasound mass diameter was 16.7 mm, while mean elastography mass diameter was 17.2 mm. Histologic results detected 36 benign lesions and 43 malignant ones. Maximum elasticity vs. SD sensitivity, specificity, positive predictive value, negative predictive value, misclassification rate and accuracy rate were respectively 95.3% vs. 83.8%; 86.1% vs. 88.9%; 89.1% vs. 90%; 93.9% vs 82.1%; 8.9% vs. 13.9% and 91.1% vs 86.1%.

Conclusion: SW elastography yields useful quantitative information on breast masses. The performance of maximum elasticity is comparable with that of standard deviation.

Keywords: breast masses, elastography, maximum elasticity, standard deviation, stiffness.

Introduction

Grayscale ultrasound has a long-established role in the assessment of palpated breast masses, screen detected abnormalities and the local staging of breast cancer (1). Ultrasound is highly accurate in the benign/malignant differentiation of breast masses (2,3) and is useful in predicting the invasive extent of breast cancers in many cases (4). Breast ultrasound (US) is widely used as a diagnostic tool in evaluating mammographically detected masses (5), palpable lumps (6,7), and nipple discharge (8) and in guiding biopsy (9,10). Standardized criteria have been proposed for breast ultrasound (11,12) that emphasize mass margins, shape, and orientation, together with effects on the surrounding tissue such as distortion or edema.

Most breast masses still undergo percutaneous breast biopsy, however, usually under ultrasound guidance (13). Assessment of anatomical structures by palpation in medical practice relies partly on perceived differences in tissue firmness. This property can be described by Young's Modulus, which is defined as: $E=\sigma/\varepsilon$, where σ is the applied stress and ε is the resultant deformation of the tissue (14). This can also be termed stiffness or elasticity. Elastography depicts strain, which allows qualitative estimation of the stiffness of a lesion, independent of morphologic features. Benign lesions tend to be soft, while malignant lesions tend to be firmer (15).

Exceptions do occur – for example – mucinous cancers can be soft while postoperative scarring can be stiff (14). Ultrasound static elastography provides a color map of tissue elasticity that is superimposed on the real-time grayscale ultrasound image (16). Invasive breast cancers have been shown to be stiffer than benign or normal tissues. A static elastography abnormality larger than the grayscale abnormality is highly suggestive of invasive malignancy (17). Areas of ductal carcinoma in situ (DCIS) have static elastography values that are intermediate between those seen in invasive cancer and in fibro adenomas (17). Shear wave elastography is a new method of obtaining elastography images based on the combination of a radiation force induced in a tissue by an ultrasonic beam and an ultrafast imaging sequence capable of catching in real time the propagation of the resulting shear waves (18,19). The local shear wave velocity is recovered, enabling the production of a two-dimensional map of shear elasticity. The technique is performed using a conventional linear array probe and so can be incorporated into standard diagnostic ultrasound examinations (20). The production of the radiation force by the probe rather than the operator (as applied in conventional ultrasound elastography) means shear wave elastography is more efficient than conventional elastography. Within a given region of interest, defined by an electronic cursor we can obtain the values of the maximum stiffness, minimum elasticity, mean stiffness and standard deviation (SD). Areas of stiffness are fixed like a map. This reproducible, quantitative information is not available with standard elastography (14). The former studies has shown good separation of mean elasticity, measured in kilopascals, between fatty tissue (3 kPa) and dense parenchyma (45 kPa); benign lesions (<80 kPa) and malignant lesions (>100kPa) (20). One of the criteria used for differentiation of benign/malignant masses by standard ultrasound is the heterogeneity. Equivalent elastography of this grayscale features is the standard deviation. It is possible that the addition of shear wave elastography may increase the ability of breast ultrasound to differentiate between benign and malignant masses. Likewise, instead of biopsy, many patients can be set in ultrasound follow up group (specially the lesions that are classified as "borderline" by ultrasound).

The present study aimed to compare the maximum elasticity and standard deviation values of a series of breast masses with histologic findings, and to investigate the accuracy of maximum elasticity and standard deviation of elastography comparing them with each-other in an attempt of distinguishing benign from malignant breast lesions.

Methods

This was a cross-sectional study involving 76 consecutive patients who underwent shear wave elastography and breast biopsy from January 2012 to April 2013.

The study group consisted of consecutive patients with breast lesions identified during routine breast scans using the Aixplorer® ultrasound system (SuperSonic Imagine), which was installed in one of two ultrasound rooms within radiology departments in Medical Orthodox Center "Evangelism". The probe of the equipment used for the grayscale and shear wave elastography was linear and had a frequency range of 7.5 to 15 MHz, with SW elastography capacity and standard sonography features assessments, and size recorded.

Patients included women with symptoms and women with non-palpated but with screen-detected abnormalities who were scanned by one breast radiologist. The physician had 11 years of breast ultrasound experience, with an average of 400 examinations per month.

In particular, it was important to avoid compressing the breast with the transducer while performing SW elastography imaging, because tissue becomes artificially stiffer when it is compressed. Participants were asked to hold on respiration as necessary to prevent motion artifacts.

Only women with lesions subjected to biopsy were included in our study (women from 25 up to 65 years old with clinically and sonography breast lesions).

Elastography images were obtained within the standard ultrasound. The combined standard ultrasound and elastography examination time was approximately 15-20 minutes. At least one elastography image was obtained from each breast lesion.

The probe needed to be very lightly applied with generous amounts of contact jelly, to avoid the artifact stiffness radiating from the skin surface. The probe was kept still for 15 seconds during acquisition of the elastography images, and this was often best done during a breath hold. The maximum areas of stiffness in malignant cases in biggest part was found in the peri-tumoural area rather than in the cancer itself, so it was important to make sure these peri-tumoral areas were adequately imaged. The elastography views selected were those most clearly displaying abnormal stiffness within the plane, but with the absence of movement or pressure artifact. The elasticity measurements were done during the examination by the radiologist. He recorded the maximum stiffness and SD within a region of interest placed in the stiffest areas on the color maps on all the elastography images. As the region of interest is moved around the image with a cursor, the elastography values are displayed instantaneously in a data box to the side of the image, allowing the region of interest to be placed in the area of greatest stiffness on the image. The fixed cut-off values for maximum elasticity <60 kPa and for the SD $\leq$10 kPa were selected for benign/malignant differentiation on shear wave elastography.

Benign/malignant differentiation of shear wave elastography using the defined cut-off values were compared with histology to provide their efficacy. This performance of maximum elasticity was then compared with that of elastography standard deviation.

For statistical analysis, SPSS (Statistical Package for Social Sciences, version 18), was used. A receiver operating characteristic (ROC) analysis was used to assess the cut-off value for sensitivity and specificity of maximum elasticity and elastography standard deviation. The null hypothesis was rejected at a level of $P \leq 0.05$.

Results

Among study participants, 73 patients had one breast mass, and 3 patients had 2 lesions. These patients underwent percutaneous or excisional biopsy. The mean age was 51.4±8.2 years (range 25-65 years). The median age was 52.5 years. Sixty-four lesions were palpated, while 15 lesions were detected by another screening technique. The mean mass diameter measured with elastography was 17.196 mm. Median mass diameter was 16 mm. In total, 36 lesions were benign and 43 were malign after histology (one DCIS, one LCIS, 41 were invasive cancers).

Mean value of maximum elasticity for benign and malign lesions was respectively 36.53 kPa and 166.33 kPa; median maximum elasticity value for benign and malignant masses was 33 kPa and 173 kPa, respectively; interquartile range for benign and malignant lesions was 26.2-41.7 kPa and 116-210 kPa, respectively. Minimum and maximum values were 7 kPa and 87 kPa, respectively, for benign masses and 50 kPa and 283 kPa, respectively, for malignant masses.

Maximum elasticity classified as benign 33 lesions, of which 31 resulted as benign after biopsy as well, and 2 of them were malignant. Maximum elasticity value of first lesion-micro-invasive carcinoma was 50 kpa; second lesion was lobular carcinoma in situ (LCIS) with maximum elasticity value of 54 kPa. These lesions were classified as benign even from elastography standard deviation with the same value of 5 (Table 1).

Maximum elasticity classified as malignant consisted of 46 lesions. Of these, 41 masses were true positive and 5 were false positive, compared to biopsy results. Four out of five were fibro-cystic lesions with respective maximum elasticity values of 61 kPa, 77 kpa, 80 kPa and 87 kPa. One out of five lesions was fibro-adenoma with maximum elasticity value 68 kpa. According to the elastography standard deviation two out of former five lesions were classified correctly as benign masses (1 fibro-cystic and fibroadenoma lesion; SD<10). The other three lesions (fibro-cystic) were misclassified by standard deviation too ($SD \leq 10$) (Table 1).

Table 1. Validity parameters of maximum elasticity in benign/malignant diferentation of breast masses compared to biopsy, according to the palpated status

Variable	Non palpated lesions			Palpated lesions		
	Biopsy		Total	Biopsy		Total
	Negative	Positive		Negative	Positive	
Maximum elasticity:	A			A		
Negative	10 (100.0) *	1 (20.0)	11 (73.3)	21 (80.8)	1 (2.6)	22 (34.4)
Positive	0 (00.0)	4 (80.0)	4 (26.7)	5 (19.2)	37 (97.4)	42 (65.6)
Total	10 (100.0)	5 (100.0)	15 (100.0)	26 (100.0)	38 (100.0)	64 (100.0)
Sensitivity (SE)	80% (4/5)			97.4% (37/38)		
Specifity (SP)	100.0% (10/10)			80.8% (21/26)		
Positive Predictive Value (PPV)	100.0% (4/4)			88.1% (37/42)		
Negative Predictive Value (NPV)	90.9% (10/11)			95.5% (21/22)		
Accuracy	93.3% (14/15)			90.6% (58/64)		
Misclassification rate	6.7% (1/15)			9.4% (6/64)		

A $P<0.001$ according to X^2 test.
* Number of lesions and percentage.

Elastography standard deviation classified as malignant consisted of 39 lesions. Of these, 32 were truly malignant and in seven cases the result was false positive. One was LCIS and six of these masses were breast invasive carcinoma.

Two out of seven lesions were misclassified even of maximum elasticity, while five out of seven lesions were classified correctly of maximal elasticity (Table 2).

Elastography standard deviation classified as malignant 40 lesions. Of these, 36 were correctly classified as malignant and 4 were misclassified. Three out of these 4 lesions were misclassified by maximal elasticity too, while one of them was correctly classified by maximal elasticity (Table 2).

Maximum elasticity vs. standard deviation parameters of test validity were as follows: sensitivity - 95.3% vs. 83.8%; specificity - 86.1%

vs. 88.9%; positive predictive value (PPV) - 89.1% vs. 90%; negative predictive value (NPV) - 93.9% vs. 82.1%; misclassification rate - 8.9% vs. 13.9%; accuracy rate - 91.1% vs. 86.1%, respectively.

When we compare the performance of maximum elasticity in two sub groups palpated and non-palpated lesions (Table 1), it can be noted that the specificity is better in non-palpated group, while sensitivity is better in palpated one (P<0.001). When we study the performance of elasticity standard deviation in the same sub groups (Table 2), than we conclude the same, i.e. a better sensitivity in palpated lesions division and better specificity in non-palpated lesions group. When the performance of the two parameters in non-palpated lesions group is compared it is noted that the efficacy of them has the same sensitivity of 80% and a specificity of 100%. When tests performances in palpated lesions group are compared it was noted that maximum elasticity has a better sensitivity, but worse specificity than elastography standard deviation.

When ROC curves were analyzed, it resulted that the maximum elasticity test was superior compared to elastography standard deviation: the area under the curve (AUC) for maximum elasticity test and elastography standard deviation test were 0.990 and 0.949, respectively (Figure 1).

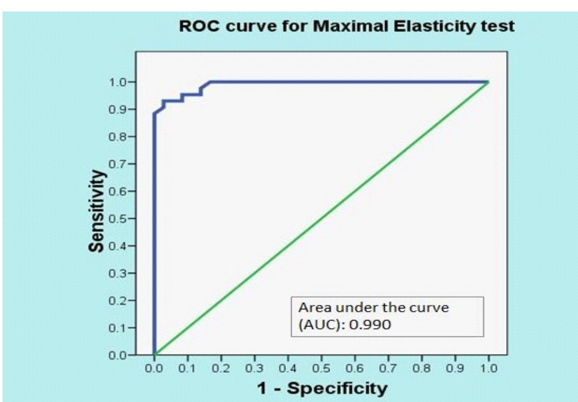
Table 2. Validity parameters of elastography standard deviation in benign/malignant diferentation of breast masses compared to biopsy, according to the palpated status

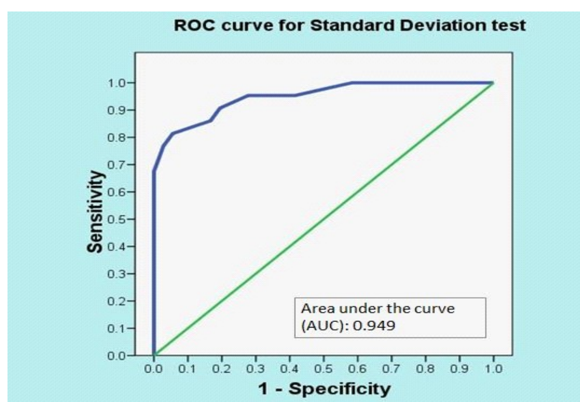
Variable	Non palpated lesions			Palpated lesions		
	Biopsy		Total	Biopsy		Total
	Negative	Positive		Negative	Positive	
Elastography Standard Deviation	A			A		
Negative	10 (100.0) *	1 (20.0)	11 (73.3)	22 (84.6)	6 (15.8)	28 (43.8)
Positive	0 (00.0)	4 (80.0)	4 (26.7)	4 (15.4)	32 (84.2)	36 (56.3)
Total	10 (100.0)	5 (100.0)	15 (100.0)	26 (100.0)	38 (100.0)	64 (100.0)
Sensitivity (SE)	80% (4/5)			84.2% (32/36)		
Specifity (SP)	100.0% (10/10)			84.6% (22/26)		
Positive Predictive Value (PPV)	100.0% (4/4)			88.9% (32/36)		
Negative Predictive Value (NPV)	90.9% (10/11)			78.6% (22/28)		
Accuracy	93.3% (14/15)			84.4% (54/64)		
Misclassification rate	6.7% (1/15)			15.6% (10/64)		

A P<0.001 according to X^2 test.

* Number of lesions and percentage

Figure 1. Left: ROC curve for maximum elasticity parameter; Right: ROC curve for elastography standard deviation parameter





Discussion

Shear wave elastography provides qualitative and quantitative data (21). Shear-wave elastography is useful in aiding benign/malignant differentiation of breast masses.

One of the useful shear-wave features is the maximal stiffness within a region of interest (ROI) placed on the stiffest area of a saved image. A maximum stiffness of over 60 kPa is suggestive of malignancy. The cut-off value of 60 kPa gives a good balance of high sensitivity and specificity.

SD is a measure of heterogeneity of the mass, so is useful in benign/malignant differentiation. Malignant lesions are more heterogeneous compared with benign lesions. Heterogeneity has been used to aid benign/malignant differentiation using grayscale ultrasound for many years (3).

On average, small cancers were not as stiff as larger cancers. About the peritumoral stiffness this might be surrounding DCIS, or desmoplastic reaction associated with many breast cancers (14). It might be invasive tumor infiltration too small to be seen by conventional ultrasound imaging (17,22).

In our study, the benign lesions that had high values of elasticity were pathologies of unknown malignancy (fibrocystic lesions).

This is a small scale study including a relatively small number of lesions, reduced number of radiologists and limited in only one medical center. It is necessary for future studies of this nature to include more medical centers and patients. In our study, we concluded that maximum elasticity has a better sensitivity, negative predictive value, misclassification rate and accuracy rate. Elastography standard deviation has a better specificity and positive predictive value. When we compared the performance under the ROC curve, we concluded that the area under the curve for maximum elasticity was larger than the area under the curve for elastography standard deviation, respectively (AUC): 0.990 and (AUC): 0.949 ($P<0.001$) (Figure 1).

The results of this study should encourage the practitioners to use the SW elastography examination after each standard ultrasound screening of breast lesions. Both parameters, maximum elasticity and standard deviation, are very useful in distinguishing benign/malignant masses.

Conflict of interest: None declared.

References

1. Zonderland HM, Coerkamp EG, Hermans J, Van De Vijver MJ, Van Voorthuisen AE. Diagnosis of breast cancer: contribution of US as an adjunct to mammography. Radiology 1999;213:413-22.
2. Lister D, Evans AJ, Burrell HC, Blamey RW, Wilson ARM, Pinder SE, Ellis IO, Elston CW, Kollias J. The accuracy of breast ultrasound in the evaluation of clinically benign discrete, palpated breast lumps. Clin Radiol 1998;53:490-2.
3. Stavros AT, Thickman D, Rapp CL, Dennis MA, Parker SH, Sisney GA. Solid breast nodules: use of sonography to distinguish between benign and malignant lesions. Radiology 1995;196:123-34.
4. Fasching PA, Heusinger K, Loehberg CR, Wenkel E, Lux MP, Schrauder M, Koscheck T, Bautz W, Schulz-Wendtland R, Beckmann MW, Bani MR. Influence of mammographic density on the diagnostic accuracy of tumor size assessment and association with breast cancer tumor characteristics. Eur J Radiol 2006;60:398-404.
5. Dennis MA, Parker SH, Klaus AJ, Stavros AT, Kaske TI, Clark SB. Breast biopsy avoidance: the value of normal mammograms and normal sonograms in the setting of palpable lump. Radiology 2001; 219:186-91.
6. Georgian-Smith D, Taylor KJ, Madjar H, et al. Sonography of palpable breast cancer. J Clin Ultrasound 2000;28:211-6
7. Hild F, Duda VF, Albert U, Schulz KD. Ductal orientated sonography improves the diagnosis of pathological nipple discharge of the female breast compared with galactography. Eur J Cancer Prev 1998;7:S57-62.
8. Parker SH, Burbank F, Jackman RJ, et al. Percutaneous large-core breast biopsy: a multi-institutional study. Radiology 1994;193:359-64.

9. Parker SH, Jobe WE, Dennis MA, et al. US guided automated large-core breast biopsy. Radiology 1993;187:507-11.

10. Mendelson EB, Baum JK, Berg WA, Merritt CRB, Rubin E. Breast Imaging and Data System, BI-RADS ultrasound. American College of Radiology; 2003.

11. Mendelson EB, Berg WA, Merritt CR. Toward a standardized breast ultrasound lexicon, BI-RADS: ultrasound. Semin Roentgenol 2001;36:217-25.

12. Varas X, Leborgne JH, Leborgne F, Mezzera J, Jaumandreu S, Leborgne F. Revisiting the mammographic follow-up of BI-RADS category 3 lesions. AJR Am J Roentgenol 2002;179:691-5.

13. Parker SH, Jobe WE, Dennis MA, Stavros AT, Johnson KK, Yakes WF, Truell JE, Price JG, Kortz AB, Clark DG. US-guided automated large-core breast biopsy. Radiology 1993;187:507-11.

14. Andrew Evans, Patsy Whelehan, Kim Thomson, Denis McLean, Katrin Brauer, Colin Purdie, Lee Jordan, Lee Baker, Alastair Thompson. Quantitative shear wave ultrasound elastography: initial experience in solid breast masses. Breast Cancer Res 2010;12:R104.

15. Landis JR, Koch GG. An application of hierarchical kappa-type statistics in the assessment of majority agreement among multiple observers. Biometrics 1977;33:363-74.

16. Fleury E, Fleury JSV, Piato S, Roveda D Jr. New elastographic classification of breast lesions during and after compression. Diagn Interv Radiol 2009;15:96-103.

17. Itoh A, Ueno E, Tohno E, Kamma H, Takahashi H, Shiina T, Yamakawa M, Matsumura T. Breast disease: clinical application of US elastography for diagnosis. Radiology 2006;239:341-50.

18. Bercoff J, Tanter M, Fink M. Supersonic shear imaging: a new technique for soft tissue elasticity mapping. IEEE Trans Ultrason Ferroelectr Freq Control 2004;51:396-409.

19. Fink M, Tanter M. Multiwave imaging and super resolution. Phys Today 2010;63:28-33.

20. Tanter M, Bercoff J, Athanasiou A, Deffieux T, Gennisson J-L, Montaldo G, Muller M, Tardivon A, Fink M. Quantitative assessment of breast lesion visco elasticity: initial clinical results using supersonic shear imaging. Ultrasound Med Biol 2008;34:1373-86.

21. Berg WA, Cosgrove DO, Doré CJ, Schäfer FKW, Svensson WE, Hooley RJ, et al. Shear-wave Elastography improves the specificity of breast US: the BE1 multinational study of 939 masses. Radiology 2012;262:435-49.

22. Burnside ES, Hall TJ, Sommer AM, Hesley GK, Sisney GA, Svensson WE, et al. Differentiating benign from malignant solid breast masses with US strain imaging. Radiology 2007;245:401-10.