Clinical benifits evaluation of shear wave elastography in ultrasound examination of breast lesions

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Purpose

Elastography is a recent ultrasound imaging modality that has been developed for 5 years. It assesses the stiffness (or elasticity) of tissue or relative tissue displacements to provide an image of tissue elasticity. This clinical information has been historically accessed by palpation, which has been an important step in making a clinical diagnosis. However, the information reached by clinical palpation depends on the operator, on the size of the lesion, its location, its depth and on the global structure of the breast as well.

1. Elastography techniques

All existing techniques rely on the 3 similar steps:

- An action, a constraint or an excitation is applied on tissue. This leads to a static or dynamic answer from the tissue, depending on its longitudinal elastic properties or its shear properties,

- An image of the constrained tissue is acquired,

- From a series of different images, a parameter is determined that is linked to tissue stiffness and depends on the type of excitation applied.

The various techniques are classified depending on action applied on tissue and include, in ultrasound imaging, 2 different types:

- Static elastography analyses the deformation of tissue. Information is coded on a color scale that codes tissue displacement. Images of tissue undergoing small amplitude compression-decompression cycles are acquired in real time, in color and are then graded using the 5-level Ueno classification.
However, this technique is not quantitative. It provides nonobjective values that depend on surrounding tissue and on the force applied to tissue (1-4). A semi-quantitative estimation has been further set-up to evaluate the ratio of deformation between the lesion and surrounding fatty tissue.

- Shear wave (ShearWave™) elastography (SWE™) uses focused ultrasound pulses to locally deform tissue, generating a shear wave that propagates transversely in tissue. Tissue elasticity is directly deducted from the speed at which the shear waves are propagating in tissue. This method is the only one that is able to provide a local quantitative measurement of tissue elasticity in real time; it is patented by SuperSonic Imagine (5).

2. Shear wave elastography

SWE™ is a new mode for ultrasound imaging that displays elasticity maps in kilopascals (kPa) in real time. The color-coded elasticity map has a millimeter spatial resolution and is displayed as an overlay over the B Mode image. In the default setting, blue colors indicate softer areas while red colors demonstrate stiffer areas. The image frame rate in SWE Mode has been optimized to fit to international regulations.

a. Generation of the shear waves

SWE™ uses focused ultrasound beams to create a radiation force in the focal region. This radiation force generates a shear wave whose propagation is captured by another ultrasound plane wave. The complete process is run automatically with a linear ultrasound probe, without any compression from the operator.

The radiation force could be interpreted as an acoustic wind. It pushes tissue in the direction of the force. An elastic medium such as the human body reacts to this deformation with a force that goes in the opposite direction, thus creating in tissue an oscillating movement that propagates away from the source transversely. However, shear waves being of low intensity, the initial perturbation in tissue is increased by moving the focal point of the radiation force deeper and deeper in tissue at a supersonic speed, i.e. faster than that propagation of the shear wave itself. This amplification process creates a "Mach Cone" (SonicTouch™, patented technology owned by SuperSonic Imagine), which generates shear waves at an amplitude that is high enough to be able to visualize their propagation, while limiting the acoustic energy delivered in tissue below the maximum output limits.

b. Capture of the propagation of the shear wave

The propagation of the shear wave must be followed and captured by the system. Shear waves typically propagate at speeds ranging from 1 to 10 m/s (which respectively correspond to elasticity values of 1 to 300 kPa). These waves cross a complete 2D ultrasound image (from 3 to 6 cm wide) in a few milliseconds, i.e. in less than 1/50 s (20 ms). Therefore, with conventional ultrasound imaging systems with limited imaging frame rates of 50 to 60 images per second, it is impossible to capture a shear wave that disappears from the field of view in the time required to build one single image. An acquisition frame rate of thousands of images per second is needed to capture a shear wave: 100 times more than what is feasible with conventional ultrasound imaging technology. Such very high acquisition frame rates can be reached thanks to the UltraFast™ imaging technology, also patented by SuperSonic Imagine, and allow the imaging system to follow the shear wave precisely while it is crossing the field of view. For a usual image of a breast at 4 cm in depth, the maximum acquisition frame rate possible is 20,000 images per second (20,000 Hz).

A velocity map is deducted from the recording of the shear wave propagation. In biological tissue, elasticity can be estimated as being proportional to the square of the shear wave speed, thus an elasticity map can be built from the velocity map (the formula used is E =

3#c² where # stands for tissue density in kg/m³, supposed to be constant at 1000 kg/m³, and c stand for the speed of propagation of the shear wave).

Therefore, SWE™ brings 3 essential innovations to elastography: it is quantitative, it has a very high spatial resolution, and it can provide elasticity maps in real time.

Methods and Materials

1. Clinical studies evaluating ShearWave™ Elastography.

a. BE1 multicenter international study

The international BE1 study aimed at evaluating the clinical benefit of SWE within the framework of ultrasound diagnosis of breast lesions. The primary goal was to assess the potential benefit of SWE to help in characterizing breast lesions and the secondary goal was to determine whether SWE improves the visualization and localization of the lesions.

This multicenter study enrolled 16 centers, of which 6 in the USA and 10 in Europe. In France, 4 sites joined the study: (1) La Timone Hospital, Marseille, (2) Institut Curie, Paris, (3) Jean Mermoz Private Hospital, Lyon, and (4) Antoine Lacassagne Center, Nice.

The study used prototype systems from October 2008 to October 2010 and recruited a total of 1,800 breast lesions. Inclusion criteria featured age over 21, lesion detected by clinical exam and/or mammography and/or MRI and/or ultrasound; all patients gave their informed consent to join the study. Exclusion criteria were: mammary implants, superficial lesions (<5mm from skin), patients who were breast feeding, running chemotherapy or radiotherapy treatment for cancer, history of breast surgery on the same breast, lesions previously biopsied.

Results were correlated to histology results from cytology and/or core biopsy and/or surgery for biopsied lesions and to final assessment for followed-up lesions. The ultrasound exam was performed for each lesion on the system usually used in the department and on the SuperSonic Imagine prototype. An independent expert reviewer (DR W. BERG, USA) performed a blind read of all lesions analyzed.

A model building phase was run on lesions classified BI-RADS 3 and 4 only, BI-RADS 2 and 5 lesions were supposed not be reclassified by SWE. The logistic regression performed on 791 BI-RADS 3 and 4 lesions resulted in the determination of several 2- or 3-variable models, each containing the BI-RADS score and 1 or 2 added SWE features, which included qualitative and quantitative variables, for which thresholds were

established. The global performance each model was assessed with the area under the ROC curve. Reclassification rules were derived for each model on BI-RADS 3 and 4a lesions, depending on suspicious an benign SWE features. Diagnostic performances for each rule were calculated: sensitivity, specificity, PPV, NPV and accuracy of the test.

The most discriminating SWE features were found to be homogeneity of the SWE map (SWE Homogeneity) and the mean SWE value of elasticity over the stiffest part of the lesion (E max) with a threshold at 100 kPa. The reproducibility of SWE measurements were very high (>0.90). Two models were determined that added SWE Homogeneity and E max to the BI-RADS score of the lesion.

Areas under the ROC curves were 0.947 (BI-RADS alone), 0.950 (BI-RADS + SWE Homogeneity), 0.954 (BI-RADS + E max) and 0,953 (BI-RADS + SWE Homogeneity + E max).

b. Analysis of the French sub-group

This analysis was achieved on French lesions, some of which were already included in the sample used above, and other supplementary cases not used above. The sample population refers to 321 patients (mean age 56.3). The breakdown of the 300 mammary lesions, of which 129 malignant, is reported in table 1.

Tableau 1. Population studied.

BI-RADS score	**Benign**	**Malignant**	**% malignant**	**Total**
2	11	0	0.0	11
3	95	6	5.9	101
4	63	44	41.1	107
5	2	79	97.5	81
Total	**171**	**129**	**43.0**	**300**

Lesions were reclassified according to the rules:

- Rule 1: upgrade BI-RADS 3 lesions with 2 suspicious SWE signs, namely not homogeneous SWE map + E max above 100 kPa.

- Rule 2: downgrade BI-RADS 4a lesions with 2 benign SWE signs, namely homogeneous SWE map + E max below 100 kPa.

- Rule 3: mix the 2 rules above: upgrade BI-RADS 3 lesions with 2 suspicious SWE signs and downgrade BI-RADS 4a lesions with 2 benign SWE signs.

Results

Results from the French subgroup

The performances of the BI-RADS ultrasound test alone are presented in table 2.

Table 2. Performances of the ultrasound BI-RADS diagnostic test.

Sensitivity	Specificity	PPV	NPV	Accuracy
95.3	62.0	65.4	94.6	76.3

Table 3 presents the performances of the new BI-RADS + SWE diagnostic test, according to the different rules used for lesions reclassification.

Table 3. Results of the reclassification rules used.

SWE features added and rule	**Sensitivity**	**Specificity**	**PPV**	**NPV**	**Accuracy**
None	95.3	62.0	65.4	94.6	76.3
SWE Homog + E max	97.7	53.8	61.5	96.8	72.7
Rule 1					
SWE Homog + E max	93.8	80.1	78.1	94.5	86.0
Rule 2					
SWE Homog + E max	96.1	71.9	72.1	96.1	82.3
Rule 3					

Images for this section:

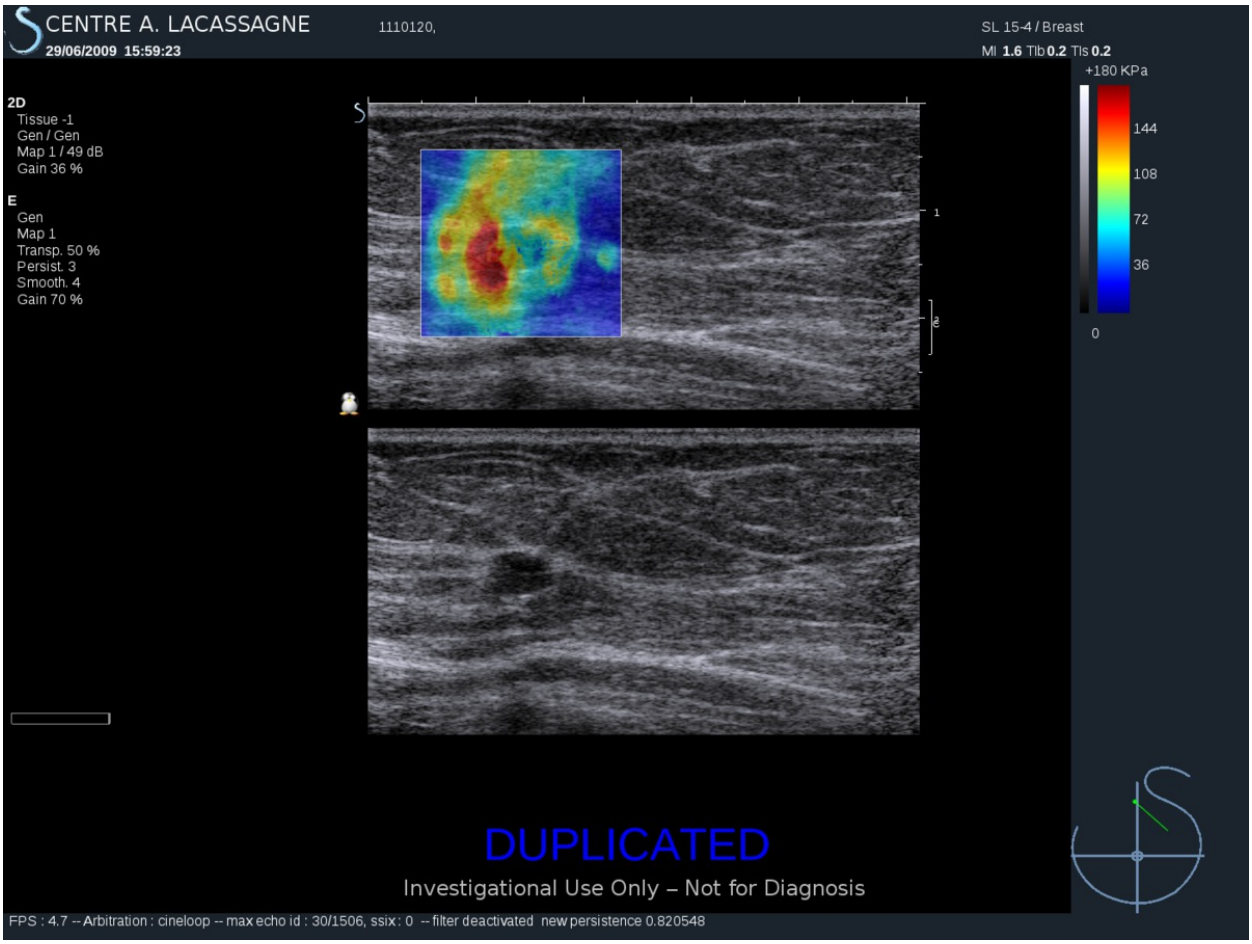

Fig. 1: FIG 1.BI-RADS 3 lesion.the SWE™ map shows an heterogeneous signal, with stiff areas in the lesion periphery, with high SWE™values. Maximum elasticity was …kPa. Rule 3 would reclassify this lesion in BI-RADS 4; histology: invasive ductal carcinoma.

Conclusion

Conclusion of the analysis of the French sub-group

Considering the expected benefit of adding SWE to breast ultrasound, i.e. increasing specificity while preserving ultrasound sensitivity and NPV, the best rule is #3, where BI-RADS 3 lesions, suspicious in SWE, were upgraded to 4a and at the same time, BI-RADS 4a lesions, non-suspicious in SWE, were downgraded to BI-RADS 3.

Indeed, rule 1 allows increasing sensitivity with a decrease in specificity, rule 2 provides the best increase in specificity (+18 point) and in test accuracy (+ 20 points) at the expense of the highest decrease in sensitivity.

Rule 3 provides the best compromise: specificity increases by 10 points, sensitivity even increases a little, PPV increases by over 6 points, NPV also increases by 1.5 points and accuracy is increased by 6 points.

ShearWave™ Elastography appears to be a promising technique because it provides an objective and independent way to assess tissue elasticity. When SWE is added to the BI-RADS classification of breast masses, it allows increasing all the performances of the ultrasound diagnostic test.

Images for this section:

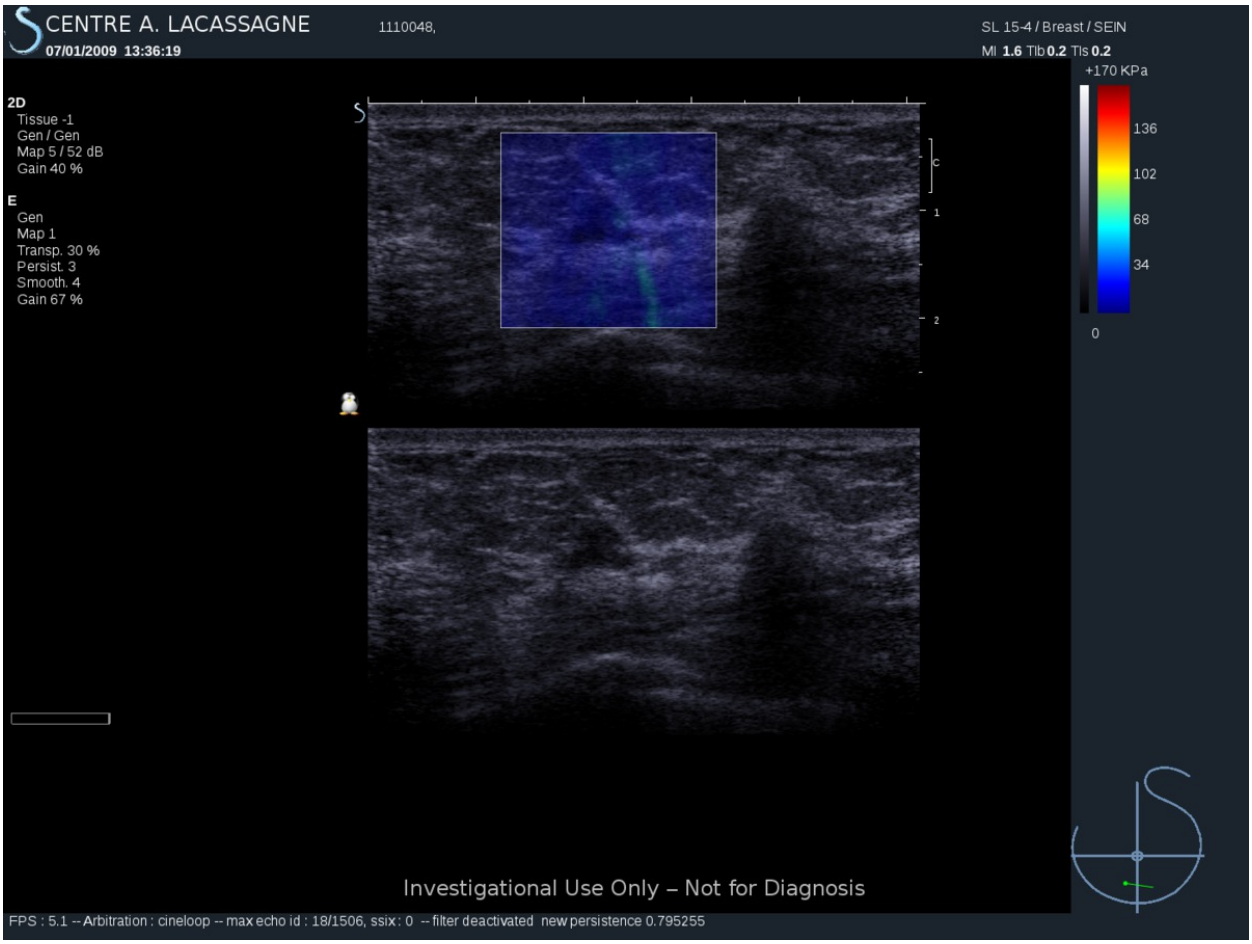

Fig. 1: FIG 2.This BI-RADS 4 lesion showed an homogeneous SWE™ map and low SWE™ values (below 30 kPa). This lesion would be downgraded as a BI-RADS 3 according to rule 3 ; histology was a nodular adenosis

References

1. References

1 Tardivon A, El Khoury C, Thibault F, Wyler A, Barreau B, Neuenschwander S. Elastography of the breast: a prospective study of 122 lesions. J Radiol. 2007 May;88(5 Pt 1):657-62.

2 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 May;239(2):341-50.

3 A.. Tardivon, A. Delignette, S. Lemery, B. Baratte, L. Levy, P. David, A. Le Mouel, C. Balu-Maestro, B. Scheffer. Ultrasound elastography: Results of a French multicentric prospective study about 345 breast lesions. Communication orale ECR Vienne 2-6 mars 2006. European Journal of Radioloy Abstract B-344.

4 Zhi H, Ou B, Luo BM, Feng X, Wen YL, Yang HY. Comparison of ultrasound elastography, mammography, and sonography in the diagnosis of solid breast lesions. J Ultrasound Med. 2007 Jun;26(6):807-15.

5 Tanter M, Bercoff J, Athanasiou A, Deffieux T, Gennisson JL, Montaldo G, Muller M, Tardivon A, Fink M. Quantitative assessment of breast lesion viscoelasticity: initial clinical results using supersonic shear imaging. Ultrasound Med Biol. 2008 Sep;34(9):1373-86.

6 Athanasiou A, Tardivon A, Tanter M, Sigal-Zafrani B, Bercoff J, Deffieux T, Gennisson JL, Fink M, Neuenschwander S. Breast lesions: quantitative elastography with supersonic shear imaging--preliminary results. Radiology. 2010 Jul;256(1):297-303.

7 BE1 Study Collaborative Group.D.Cosgrove and coll. Preliminary assessment of ShearWave™ Elastography features in predicting breast lesion malignancy. ECR Vienne 2010.

8 C Balu-Maestro C Chapellier ,V Juhan,A Athanasiou,C Tourasse, A Tardivon. Evaluation du bénéfice clinique de l'élastographie SHEARWAVE dans l'examen ultrasonore des lésions mammaires. Résultats des sites français. Jfr Paris 2010 Journal de Radiologie oct,10,p 1318.

9 D O Cosgrove, WA Berg,C Dore ,C Balu-Maestro,C Tourasse,V Juhan,A Tardivon, H Majar,E Mendelson,M Locatelli. Amélioration de la spécificité de l'examen échographique des lésions mammaires grâce à l'élastographie SHEARWAVE : résultats pour 1000 lésions dans le cadre de l'étude multicentrique internationale. M Locatelli JFR Paris oct 2010. Journal de Radiologie oct ,10 p 1318.

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