Preliminary assessment of ShearWave(TM) elastography features in predicting breast lesion malignancy

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Purpose

To analyse a preliminary series of cases from an ongoing prospective multi-centre international study to evaluate the impact of adding ShearWave™ Elastography (SWE) features to the BI-RADS® classification of breast masses.
Methods and Materials

ShearWave™ Elastography imaging technique

Shear wave elastography is a novel technique for obtaining elastograms of soft tissue by tracking the transverse shear waves that spread laterally away from a mechanical disturbance of the tissue. They have special properties that differ from both the longitudinal waves of conventional ultrasound imaging (which relies on the bulk modulus of elasticity) and from conventional compression elastography. They travel at a few metres per second, depending on the visco-elastic properties of the tissue, and are rapidly attenuated, so that for practically achievable disturbances they have dissipated after travelling for a few centimetres (Fig 1 and Fig 2).

A particularly important feature is that their velocity is related to the Young's modulus of elasticity so that a direct conversion to this fundamental figure is easily made. Though they travel relatively slowly through tissue, they traverse the typical 5 cm window of a small parts transducer in a few milliseconds and so are difficult to image using conventional scanning systems. In the Supersonic Imagine SWE system their progress is tracked using an ultrafast imaging system which insonates the entire field in a single plane pulse and then uses beam-forming to process the echoes on receive. This method can achieve frame rates of several thousands per second, which is required to image the passage of the shear wave and to calculate its velocity. The SWE information is presented as a colour overlay on the B-mode information at frame rates of around 2 per second and the images are stable once they have settled around 2 seconds after turning the SWE on (Fig 3).

The shear wave is generated within the tissue using acoustic radiation force. In simple systems, the acoustic pressures required result in overheating of the transducer. In the Supersonic Imagine system a series of push pulses is sent faster than the velocity of the shear wave; this augments the effect by generating a supersonic front without transducer heating problems (Fig 4). The transmit power is well within the output limitations set by regulatory bodies (the MI is less than 1.5) and the resulting tissue excursion is great enough to be visualized while causing no risk of tissue damage.

Study protocol

A multinational clinical study, the BE1 (Breast Elastography 1) trial, aiming to recruit 2,300 patients with breast masses is at the half way mark. It started in mid-2008 and patients' enrolment is closed by the time of writing. Prototype systems of the Aixplorer® ultrasound
system were placed at 16 clinical sites to capture both grayscale ultrasound and SWE images from a targeted two thousand three hundred lesions.

The study protocol was performed by licensed physicians or sonographers adequately trained in performing breast ultrasound examinations and interventional procedures. The protocol followed a methodology which fitted with the usual clinical workflow of breast ultrasound examination. Lesions that had been detected by palpation, mammography and/or ultrasound and/or MRI and for which an ultrasound examination (diagnostic or ultrasound guided procedure) was prescribed to characterize the lesion were included. Patients who met the inclusion criteria received both a conventional grayscale ultrasound exam and a SWE ultrasound exam. Images and data pertaining to the physical examination, mammograms, ultrasound and MRI studies were collected; when a biopsy and/or surgical excision were required, the histology results were made available to the study.

The main goal of the study was to assess the potential value of SWE for the characterization of breast lesions. More specifically, the protocol intended to assess if SWE information could potentially change the BI-RADS® classification with a benefit in specificity without degrading the sensitivity. Also, it would analyze the potential benefits of SWE images to differentiate cystic from solid lesions and benign from malignant lesions when FNA/biopsy results were available. Furthermore, we aimed at determining if quantitative SWE stiffness information as well as other SWE image features were reproducible.

A subset of 192 female breast lesions was analysed; 110 were benign and 82 were malignant. The reproducibility of SWE size and elasticity measurements was assessed using three still frames taken from the real-time sequence to measure intra observer reproducibility (IOR).

Logistic regression analysis was performed by adding features from the SWE data to predict the pathology findings, which were used as the gold standard. The reference model considered BIRADS®#4 as a positive test for malignancy. One or two SWE features were added to BIRADS®#4 cases sequentially to give models with two, three and more variables. These features were selected from the complete set of 8 features scored in the trial. They included three subjective features (Similarity between B Mode and SWE Mode shape of the lesions, SWE Mode shape of the lesions, Elasticity signal homogeneity) and five quantitative features (elasticity ratio between lesion over fat, Minimum SWE value of the lesion (kPa), Maximum SWE value of the lesion (kPa), Mean SWE value of the lesion (kPa), Ratio of the lesion area in SWE Mode over B Mode).
The impact of the adding the SWE features was assessed using the area under the receiver operator characteristics (ROC) curve, and the sensitivity, specificity, positive predictive value and negative predicted value for a given cut-off value of predicted probability of malignancy.
Fig. 0: 3 successive screenshots after 2, 5 and 10 milliseconds respectively a plane shear wave front was induced by SonicTouch(tm) technology in a medium containing a harder inclusion (red circle). The plane front gets deformed when the shear wave reaches the harder inclusion, where it travels faster.

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**Fig. 2:** Accelerated movie of the same plane shear wave front as in Figure 1 in the same medium containing a harder inclusion. The plane front gets deformed when the shear wave reaches the harder inclusion, where it travels faster.

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**Fig. 1:** The lack of propagation of shear waves in a true fluid results in a black patch corresponding to the fluid part of this cyst. Note the stability of the real-time image, with no flickering or dropped frames. These features make the technique easier to learn.

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**Fig. 0:** SonicTouch(tm) technology: The shear wave plane front is induced by the combination of successive shear waves that are generated at increased depths, faster than the speed of the shear waves themselves. The focal zone of the shear waves is moving deeper and deeper at a supersonic speed. Shear waves get amplified in a Mach cone, which increases the propagation distance of shear waves, while minimizing acoustic power.

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Results

Out of the 224 cases submitted for the statistical analysis, the 2\textsuperscript{nd} lesions in 2 patients were discarded. Therefore, the analysis of reproducibility was achieved on 222 cases.

The reproducibility of SWE size measurements and the maximum and mean elasticity measurements were very high (IOR> 0.93, 0.84 and 0.88 respectively, maximum $= 1$).

Thirty more cases were discarded from the logistic regression analysis due to missing data. This 192-lesion sample showed 12 BI-RADS\textsuperscript{®} 2 lesions (all benign), 62 BI-RADS\textsuperscript{®} 3 lesions of which 56 were benign and 6 were malignant, 71 BI-RADS\textsuperscript{®} 4 lesions of which 42 were benign and 29 were malignant, and 47 BI-RADS\textsuperscript{®} 5 lesions (all malignant).

This sample had 82 malignant lesions, leading to a prevalence of breast cancer in this sample population of 43%.

Using the BIRADS\textsuperscript{®}#4 test alone, we found a sensitivity of 92.7\%, a specificity of 61.8\%, a positive predictive value of 64.4\% and a negative predictive value of 91.9\%. When applied to this classification, the logistic regression model lead to a ROC curve with an area under the curve of 0.773 (Fig 1).

When added to the BIRADS\textsuperscript{®}#4 scores, the maximum and mean elasticity increased the ROC area from 0.773 to 0.925 and 0.917 respectively (Fig 2 and Fig 3).

Adding further features did not improve the performance of the system. The best three-variable model (BIRADS\textsuperscript{®}#4 + elasticity shape + maximum elasticity) increased the area under the ROC curve to 0.934 (Fig 4). In this model, sensitivity decreased from 92.7\% to 87.8\%, but specificity increased from 61.8\% to 87.3\%. The rate of correctly classified lesions increased from 75 to 87.5\%. 


**Fig. 0**: Receiver Operating Characteristic (ROC) curve of the diagnostic test using the binarized BI-RADS(r) score variable alone. Lesions of BI-RADS(r) scores of 2 or 3 were classified as benign, while lesions of BI-RADS(r) scores of 4 or 5 were classified as malignant. The area under the ROC curve was 0.773, demonstrating an acceptable discriminating power of the model.

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**Fig. 0:** ROC curve of the diagnostic test using the binarized BI-RADS(r) score variable with the added Maximum elasticity value within the lesion. The area under the ROC curve was 0.925, thus showing a significant increase in diagnostic strength of the 2 variable model, as compared to BI-RADS(r) alone.

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Fig. 0: ROC curve of the diagnostic test using the binarized BI-RADS(r) score variable with the added Mean elasticity value within the lesion. The area under the ROC curve was 0.917, also demonstrating a high increase in the diagnostic performance of this other 2-variable model as compared to the BI-RADS(r) model alone.

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Fig. 0: ROC curve of the best predicting 3-variable model including the BI-RADS(r) binarized classification, the shape of the lesion as seen with ShearWave(tm) Elastography, and the Maximum elasticity value within the lesion. The area under the curve was 0.934, assessing a far better diagnostic strength as compared to the binarized BI-RADS(r) model alone (ROC area=0.773).

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Conclusion

This novel SWE system using acoustic radiation force to produce shear waves that are tracked using ultrafast ultrasound imaging proved successful in this study of breast masses. The good reproducibility of the data obtained is consistent with the real-time elastography images and stable movies produced, a feature which makes the system easy to use.

The added features that led to the highest diagnostic performance (mean and maximum elasticity values in kPa, homogeneity and shape of the SWE image) depend directly on the special features of SWE: local quantification and millimetre resolution.

The design of the study in which SWE features are used as additional diagnostic criteria mirrors the real life situation better than those attempting to use elastography as an alternative to B-mode data.

The results of the completed BE1 trial are eagerly awaited.
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