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Editorial

Virtual Special Issue: Breast shear-wave elastography: bringing colour to breast ultrasound

The routine use of shear-wave elastography (SWE) during breast ultrasound in Europe has still not occurred, as adoption has been slow particularly in the UK. At first, this may seem surprising as SWE can be used to confirm benignity of fibroadenomas. In combination with grey-scale ultrasound, SWE can reduce the number of fibroadenoma biopsies performed in symptomatic clinics. One cause of the slow adoption was that, until recently, the best SWE system was only available from a small manufacturer whose machine, in the past, had a suboptimal grey-scale imaging; however, ultrasound machines that combine excellent grey-scale and SWE imaging are now available from a number of vendors.

There is also a misconception that SWE is both difficult to perform and, because a number of numerical values are obtained, complicated to analyse. Neither is true. Obtaining good-quality images is simple as long as no pressure is placed through the probe and the probe is held still for a few seconds to allow the image to build. The analysis of the numerical data is easy, a region of interest (ROI) in drawn, usually over the region of maximum stiffness. Software then calculates the maximum (E_{max}) and mean (E_{mean}) elastography values. It is recommended that four measurements are taken, which are then averaged, and the result is compared with an agreed cut-off value. Viewing the colour map alone also gives very good results, especially as the ring sign (a halo of stiffness around a lesion) is highly suggestive of malignancy even if the quantitative threshold is not reached. Obtaining the images and the quantitative results takes on average 4 minutes. The great advantage of SWE over of other techniques is that it has comparable sensitivity for lobular cancer as for ductal cancers of no specific type.

SWE has a number of other roles in breast imaging besides benign and malignant differentiation as highlighted in some of the papers discussed below. It is very useful in monitoring cancers being treated with neoadjuvant chemotherapy. This could be particularly useful in units that find it difficult to find MRI slots for these patients. It can be used to identify invasive foci in women with large areas of ductal carcinoma in situ (DCIS). Furthermore, SWE can confirm a lesion is a cyst due to absence of SWE signal in fluid. This is useful when confronted with a lesion that may be a cyst with debris or a hypoechoic solid lesion.

We hope the discussion of the papers below will encourage you to adopt SWE examination into your routine breast ultrasound practice. Once you do, we are confident you will never want to perform breast ultrasound without it. View full issue at (https://www.clinicalradiologyonline.net/content/breastelastography).

In the paper by Choi *et al.* from Korea,[1] the diagnostic performance of two- (2D) and three-dimensional (3D) SWE are compared. The bottom line in this study is that 2D SWE has a similar diagnostic performance as measured by receiver operator curves (ROC) as 3D in the axial or sagittal plane. As 2D is faster and easier than 3D and does not require a dedicated 3D probe, it is good to be reassured that less is as good as more in this regard. The study has a few weaknesses: the ROI size was 3 mm, which is suboptimal when measuring maximum (E_{max}) and mean (E_{mean}) elastography values where a small (1 mm) ROI size has been shown to be optimal. A large ROI size is only helpful when using standard deviation (E_{SD}) of elastography values as a parameter. E_{SD} is essentially a measure of inhomogeneity of the SWE signal. Thus, it is not surprising that a large ROI allows better assessment of this parameter; however, E_{SD} was not assessed in this study. There appears to have been a combination of using data from the original reports and retrospective review. One assumes the retrospective reviewers were blinded to the histological outcomes but this is not clearly stated. Obviously, if this was not the case, the results would be invalid. The cut-off values used in this study were those derived using Youden's index from the ROC curves. Youden's index is a statistic that can be used to assess the effectiveness of a dichotomous test. Equal weighting is given to sensitivity and

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specificity when generating cut-off points. This is not appropriate in breast imaging where the need for high sensitivity far outweighs the requirement for high specificity. Missing a cancer is catastrophic whereas undertaking a biopsy of a fibroadenoma is not. The clinically useful cut-off should therefore be much lower than that suggested by Youden's index so the sensitivity is reassuringly high.

The paper by Shi *et al.*[2] on correlations between stiffness detected by SWE and collagen structure and alignment is important because it explains why cancers are stiff and why some cancers are stiffer than others. This paper confirms that stiffness increases as collagen becomes more abnormally aligned and cross-linked in the tumour associated stroma. As such, structural changes are key to tumour progression, invasion, and metastasis, SWE can provide a non-invasive method of quantifying the aggressiveness of breast cancers. This explains why stiffness at SWE is an independent predictor of nodal metastasis, chemo-resistance, and breast cancer death after correcting for standard pathological variables. Shear-wave stiffness information is available preoperatively, and could therefore, be used to guide discussion about the appropriateness of neoadjuvant therapy.

The methodology of the SWE examinations in this study is not perfect, the SWE images were all taken in one plane, and we know that stiffness of cancers is often anisotropic. A large ROI was used to include the whole lesion. This will not have affected the E_{max} measurements, but will have led to sub-optimal measurement of E_{mean} measurements.

The paper by Evans *et al.*[3] considers SWE for identification of complete pathological response (pCR) for breast cancer following neoadjuvant chemotherapy (NACT). In this prospective study of 80 patients, grey-scale ultrasound, SWE, and MRI were performed pre- and post-NACT. Four SWE images in two orthogonal planes were produced for each study. A ROI of 2 mm was used and E_{mean}, E_{max} and E_{SD} values calculated. pCR was seen in 21 (26%) of patients. Temporal changes between initial and end of treatment imaging were correlated with pCR and the different imaging techniques compared. This study confirmed that residual tumour was stiffer on shear-wave than scar tissue. It also demonstrated that the combination of the change in tumour size and change in E_{mean} yielded a similar AUC to MRI for predicting pCR. Results were similar for both the triple-negative cancers and HER-positive subgroups. This work is important as it demonstrates that the additional functional data provided by SWE combined with the anatomical assessment may offer an alternative to MRI for monitoring NACT patients. This is particularly important, as in the future it may be possible to treat patients with a pCR without recourse to surgery, if pCR can be reliably identified on imaging. Instead, the tumour bed could be sampled with core or vacuum-assisted biopsies to confirm pCR.

Unfortunately, the numbers in the luminal group were insufficient for separate subgroup analysis. In this study, mid-treatment imaging was not considered. This would be an interesting topic for further research, as it may allow early treatment modification.

Zhao *et al.*[4] consider elastography for the identification of metastatic nodes. Their research suggests that the addition of elastography to morphological features on grey-scale ultrasound significantly increases the diagnostic accuracy of ultrasound. The increased accuracy of axillary assessment has the potential for both reducing the number of negative biopsies and re-operation rates caused by previously undiagnosed metastatic nodes found at sentinel node biopsy; however, their methodology has several significant weaknesses. Critically, only seven of the 78 lymph nodes imaged were biopsied using an ultrasound-guided core technique, the remaining 91% (71 cases) were surgically excised following skin marking. In these instances, it is impossible to be certain that the excised node was truly the node that had been imaged. Furthermore, elastography was measured using a four-point subjective scale according to the proportion and distribution of high elasticity as assessed by colour. No qualitative measures such as E_{max}, E_{mean}, or E_{SD} were reported.

In the paper by Xiao et al.[5] they confirm that the SWE features of the peripheral tissue of breast lesion differ significantly between benign and malignant lesions. This is a useful finding, and highlights the importance of ensuring the entire breast lesion is included in the shear-wave image; however, their preferred measure was E_{rat}, a ratio of peripheral elasticity to that of normal fatty tissue. This requires a computer-aided (CAD) tool and additional software. It is therefore difficult to envisage how this would be practicable in a busy breast clinic. They suggest that this technology may allow downgrading of some BIRADS 4 lesions to BIRADS 3, thus avoiding biopsy; however, as in Choi's paper, Youden's index, which gives equal weighting to sensitivity and specificity, has been used. This is not appropriate in this setting where the need for high sensitivity far outweighs the requirement for high specificity. In other words, it is far more important to ensure that malignant lesions are not missed than it is to avoid benign biopsies.

In summary, the combination of these papers (https://www.clinicalradiologyonline.net/content/breastelastography) demonstrates that SWE stiffness is related to collagen structure and alignment, and as such is an indicator of the aggressiveness of tumours. The peripheral rim of the tumour should be fully imaged as this is often more indicative of the true stiffness of a lesion. The addition of SWE significantly increases the accuracy of detecting pCR preoperatively, as residual tumour is stiffer than scar tissue, and may be useful for identifying metastatic nodes. Finally, reassuringly, 2D SWE is as good as 3D SWE, making the technology cheaper and more accessible.

References

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