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Breast Shear Wave Elastography in Clinical Practice

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***Abstract*— Shearwave elastography (SWE) is used in the breast mainly to aid benign/malignant differentiation. Its accuracy is similar that of grayscale US but when the two are combined a very high NPV can be obtained. This means that many benign masses which previously required a biopsy to prove benignity can be diagnosed as benign without a biopsy. The stiffness of cancers also has associations with poor prognostic features such as size, histological grade and lymph node involvement. SWE has also been shown to be useful in predicting and monitoring response to neo-adjuvant chemotherapy. It has recently been shown that stiffness of breast cancer is independently associated with breast cancer mortality.**

Keywords—breast cancer, shearwave elastography

I. Introduction

Shear Wave Elastography (SWE) is useful in the breast because benign lesions tend to be soft and malignant lesions are mainly stiff. The stiffness or softness of breast lesions is determined by the characteristics of the collagen within and around these lesions. Fibroadenomas have a large collagen component but the collagen is well ordered and has few cross links making them soft at SWE. Breast cancer contain cancer associated fibroblasts (CAF's). These CAF's produce abnormal collagen which is thicker, disorganised in orientation and has increased cross links making the cancer and the surrounding tissues stiff (1). In a study where the size of surrounding stiffness and the size of the US abnormality were compared with the histological size of the tumour, the US estimates were often under estimates while the SWE size were over estimates. The most accurate prediction was found when 50% of the SWE stiffness was added to the US size (2). This data suggests that the stiffness surrounding the greyscale abnormality is a combination of tumour and stiff stroma immediately adjacent to the cancer but stiff stroma alone more peripherally. CAF's also secrete metalloproteinases which dissolve collagen as well as forming collagen so this increased collagen turnover allows invasion and the creation of blood vessels which in turn promote tumour growth and metastasis.

II. Technique

During acquisition it is important that the probe is held still as the stiffness colour map builds up in real time and that no pressure is applied. Images should be obtained in orthogonal planes as breast lesions often display quite marked anisotropy. Malignant lesions usually display greater anisotropy than benign lesions (3).

The use of four images rather than two has been shown to improve reproducibility. The intra-class correlation coefficient for 4 image SWE images taken by different examiners is 0.85(4).

Once the colour map image has been obtained quantitative data can be obtained using a region of interest (ROI). This is ussually 1 or 2 mm in diameter. This diameter gives optimal benign/malignant differentiation when using of maximum elasticity (Emax) and mean elasticity (Emean) (5).

The display also gives the standard deviation (SD) whIch is a measure of stiffness heterogeneity. SD is a less useful parameter than Emean and Emax when using a small ROI but if a large ROI is used (>2mm) then the performance of SD is similar to that of Emax and Emean. Acquiring SWE images takes about 2 minutes and extraction of the quantitative data takes a similar time. Algorithms are being developed which will allow quantitative information to be extracted from images stored on PACS.

The pattern of stiffness around breast lesions can be useful. The "ring sign" when a halo of stiffness is seen around small, indolent cancers is particularly useful as such lesions may not be stiff enough to reach the thresholds used for Emax and Emean evaluation(6). 3D SWE probes allow the volume of stiffness in and surrounding the lesion to be measured. Volume estimates requires freehand ROI's to be drawn on a number of slices taking about 4 minutes per lesion. 3D SWE has a similar diagnostic performance as 2D SWE. 3D SWE might be useful in assessing response of cancers to neoadjuvant systemic therapy

I. Normal and benign findings

Normal breast tissue is soft on SWE with Emean values of around 10-30kPa. Only minor differences are seen in the stiffness of fatty and dense breast issue. This small difference in stiffness between because dense and fatty tissue is because although dense tissue has a high collagen content, it is made up of well ordered, thin collagen fibres with little cross linking.

Most benign masses are soft on SWE making SWE a useful technique in differentiating benign from malignant breast masses. Larger fibroadenomas can be stiff, possibly due to pressure on the capsule from enlarging lesions (7). The "black

hole" seen within cystic lesions can be useful in differentiating cysts with echogenic contents from solid lesions.

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A. Malignant findings

95% of invasive cancers are stiffer than commonly used cut off values used for SWE. Around 98% of symptomatic invasive cancers are stiff compared to 75% of screen detected cancers. This why SWE is most useful in patients with symptoms.

Stiffness at SWE has been shown to be associated with many pathological variables. The strongest association is with invasive size. Around a quarter of sub centimetre cancers are soft. Some have advocated using lower cut-off values for Emean and Emax when assessing small lesions (8). High grade cancers are stiffer than low grade cancers even when correcting for size (9).

The characteristics features on grey scale US of low grade cancers and the stiffness of high grade cancers on SWE means the two techniques are complimentary in benign/malignant differentiation. The high grade cancers missed by greyscale US are detected on SWE while the low grade cancers missed on SWE are diagnosed on grey scale US.

Nodal metastases from breast cancer are not much stiffer than normal nodal tissue probably due to the limited stromal reaction to tumour cells in lymph nodes. This makes SWE of axillary nodes in breast cancer patients less accurate then determining the nature of a primary breast lesion (10). The stiffness of the primary tumour on SWE is a powerful predictor of nodal metastases even when corrected for tumour size tumour grade and vascular invasion status. The nodal metastasis rate in tumours which have a mean stiffness less than 50kPa is only 5% while tumours with a mean stiffness of over 200 kPa the nodal metastasis rate is around 40%. The reason stiff tumours have a high rate of nodal metastasis is because the activated stroma seen in stiff tumours promotes neo-angiogenesis and stromal invasion which are required for nodal metastasis to occur (11).

B. Neoadjuvant chemotherapy

A number of studies have shown that tumours which are stiff on SWE are more resistant to NACT than breast cancers which are soft. Tumour stromal interactions are important in defining the response of breast cancer to NACT. A number of studies have shown that stromal gene signatures are as important in predicting resistance to NACT as epithelial gene signatures. A number of studies have shown that changes in stiffness from baseline at interim and at the end of treatment are helpful in predicting response to NACT at the end of treatment(12). This is because areas of fibrosis in women whose tumours have had a complete response are softer than masses containing residual tumour. SWE is particularly helpful at interim scanning where it outperforms both grey scale US and standard MRI assessment in the predicting final pathological response. SWE also has the advantage over MRI in terms of cost, time and convenience and availability

C. Prognosis of breast cancer

Increased stiffness of breast cancer is associated with many known poor prognostic factors such as large invasive size, nodal involvement, high histological grade and lympho-vascular invasion. In addition stiffness at SWE is associated with resistance to chemotherapy.

These prognostic factors are only fully available following resection of the cancer, however, stiffness at SWE is available pre-operatively. It has recently been shown that stiffness at SWE is a strong prognostic factor and that it is independent of other pre-operative prognostic indicators such as ultrasound size, core biopsy grade, pre-operative nodal status, ER status and presentation (screening or symptomatic.)(13). It is possible that stiffness at SWE could be part of a pre-operative prognostic index which could be used when considering the appropriateness of neoadjuvant systemic therapy.

[a] Sample of a Table footnote. (*Table footnote*)

Fig. 1. Example of a figure caption. (*figure caption*)

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