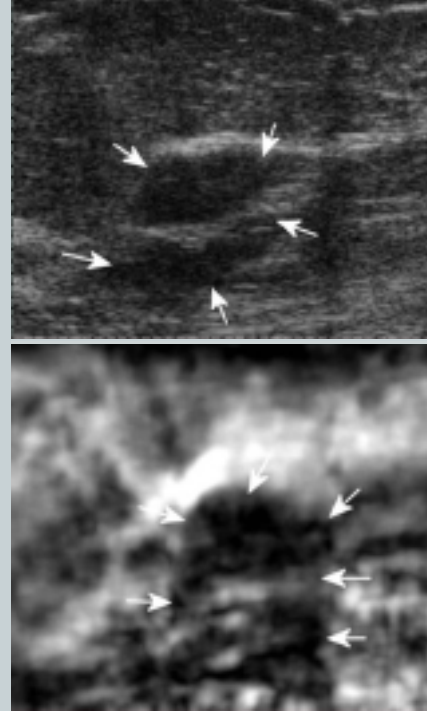


Whitepaper



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Order No. A91ES-0301-C1-7600
Printed in Germany
WS 1007 2.0

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The Use of Elasticity Imaging in Breast Ultrasound

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Introduction

Quoted rates of benign:malignant ratio for fine needle aspiration biopsy, core biopsy and excisional biopsy of breast abnormalities range from under 4:1 for mammographic screening abnormalities [1] to over 7:1 for symptomatic breast problems[2]. These biopsy rates reflect the use of ultrasound for abnormal clinical findings and as an adjunct to mammography for abnormal mammograms. When ultrasound is used to screen the clinically and mammographically dense but normal breast the benign:malignant ratio is almost 10:1 [3]. It rises still further to almost 20:1 if complex cysts which need aspirating and follow up of presumed benign lesions (instead of biopsy) are included [4]. In the USA more than two billion dollars per annum is spent on biopsies and follow up ultrasound with the majority being spent on benign lesions [5].

Recent publications report reoperation rates of 15% to 50% following breast conserving local excision [6,7,8] at an additional cost of approximately £25,000,000 per annum in the UK [9, 10]. MR has been recommended as the imaging method of choice to assess extent of tumour within the breast [11] but its greater cost than ultrasound means that development of more accurate methods of ultrasound measurement of tumour extent could also provide significant cost savings by reducing reoperation rates. Ultrasound has an additional advantage compared with MR because it can be done in the same position as that used for surgery.

Innovations in Ultrasound:
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Imaging

Elasticity Imaging.

The Basics

Malignant tumours feel harder than benign ones and this physical property relates to their coefficient of elasticity. Hippocrates described the hardness of breast cancers almost two and a half millennia ago and palpation was the only diagnostic method available for the detection of breast tumours before the advent of diagnostic imaging.

Deformability, which is also related to the elastic properties of tissues, is part of the algorithm to determine the likelihood of malignancy in routine breast ultrasound but it has only moderate sensitivity in many lesions, except for semi normal conditions such as gynaecomastia (benign lesions are more easily deformed than malignant lesions).

Direct comparison of tissue images before and after application of a force is too crude a measure of elasticity except at extremes of differences in elasticity. Analysis of the raw ultrasound image data, which contains very much more information than can be displayed for visual perception, can detect very much smaller differences in elasticity. Measurement of tissue deformation (strain), with applied force (stress), by analysis of the returning ultrasound echoes, was

described over 20 years ago [12, 13]. Ultrasound tissue elasticity has been an area of increasing research for the last two decades [14, 15, 16] and has been applied to many different clinical situations including breast, prostate, skin [17], intra-operative brain imaging [18], cardiac [19, 20] and vascular imaging [21, 22, 23].

The physics of elasticity, described by Hooke's law, Young's modulus and Poisson's ratio, is based in mechanics and relates to the distortions which occur when matter is subjected to an external force or stress. Understanding these principles forms the basis of tissue elasticity imaging but the changes which occur when soft tissues are deformed are of much greater complexity than occurs in a simple isotropic body such as a piece of steel. Soft tissues are a solid matrix with over 70% fluid content resulting in many other factors which affect the co-efficient of elasticity within the tissues including boundary effects, poroelasticity and viscoelasticity.

Interpretation of elasticity imaging requires a good understanding of:

- the histology and pathophysiology of the tissues being imaged;
- the basis of elasticity physics in an inhomogeneous matrix;

- the factors which affect uniformity or non-uniformity of the stress and shear forces within the tissues when they are deformed;
- the relative differences in coefficients of elasticity of the tissues within the image and in the tissues adjacent to the plane of the image.

When tumours grow in or infiltrate through tissues, they change the stiffness or hardness characteristics of those tissues. Where there is relative homogeneity of tissues, this change is well demonstrated on elasticity imaging. It becomes more complex where there is inhomogeneity of the tissues with different inherent stiffness or elasticity, such as the difference of stiffness between fat and breast glandular tissue. Provided uniform force fields (stress) are applied through a region of breast being imaged, good comparative distortion (strain) data can be obtained giving good comparative strain or elasticity images.

Despite the complexity of elasticity physics in soft tissues, excellent results have been obtained with real time free hand elasticity imaging in the breast. Early results using real time elasticity imaging have been remarkably good at distinguishing benign from malignant tissue based on the higher coefficients of elasticity of malignant tumours compared with benign

pathology and normal tissues. Though there is overlap of the coefficients of elasticity a significant number of benign lesions never reach the range of coefficients of elasticity of malignant tumours. Elasticity imaging has the potential to focus biopsies for more consistent diagnosis of cancer, determine tumour extent and measure response to non surgical therapy as well as to exclude malignancy with a possible safe reduction of benign biopsy rates. Elasticity imaging, when used as an adjunct to conventional B-mode and colour Doppler imaging, should improve diagnostic accuracy.

The very high sensitivity to changes in stiffness allows elasticity imaging to show changes on breast ultrasound which are not visible on the conventional ultrasound imaging. Pathology which has the same echo pattern as the tissues that surround it can be identified because it is very slightly stiffer even though it still cannot be felt with the examining hand. The phantom, (figure 1) with a stiff inclusion body, is isoechoic on conventional B-mode but is very obvious on strain imaging. The difference is very dramatic with a homogeneous gel containing a stiffer homogeneous inclusion. With the greater inhomogeneity of breast tissues similar anatomical appearances on conventional B-mode ultrasound can have very different strain imaging appearances.

Elasticity imaging displays mechanical strain
• Images of relative motion

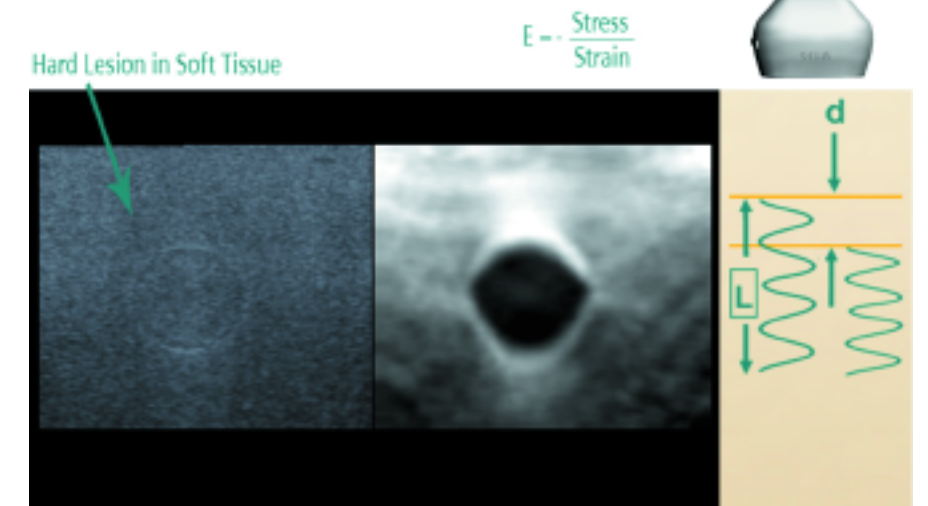


Figure 1

Strain = d/L (deformation divided by Length / depth)

Figure 2

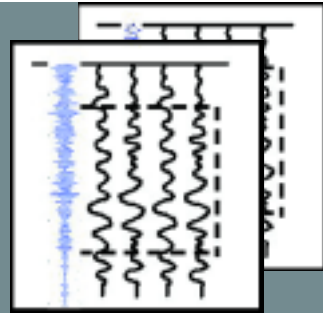


Figure 3

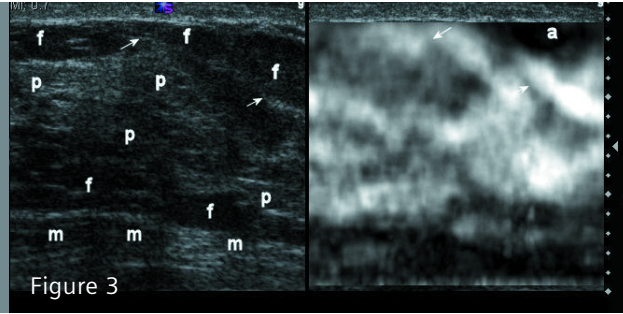


Figure 4

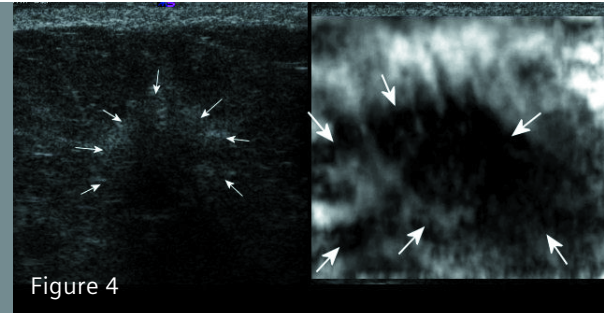


Figure 5

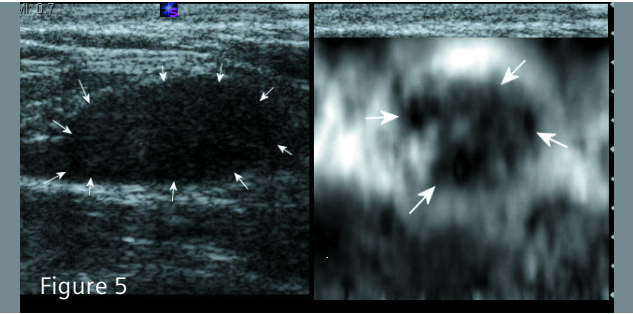


Figure 6

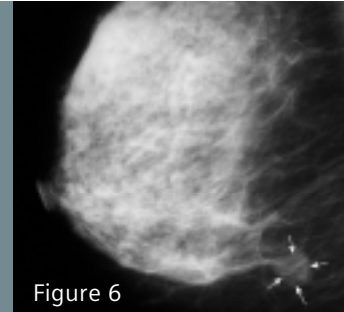


Figure 7

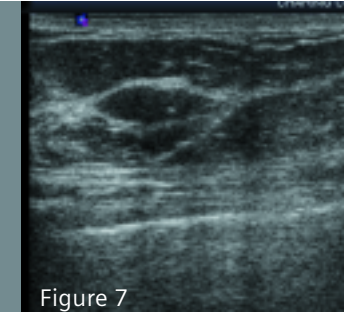
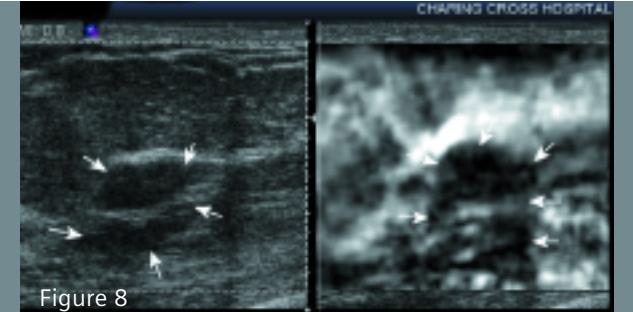


Figure 8



Elasticity Imaging.

The Method

A wide variety of approaches can be used to determine the elasticity of different tissues based on comparing whole frame raw ultrasound data (RF data) while changing the external force applied to tissues. Changes in this RF data can be recognized if there are distortions in some areas but not in others. Stiff tissues distort less than soft tissues, for a given force, and the variation in the amounts of distortion can be detected in the RF data changes providing information on the elastic properties of the tissues under the investigation.

Free hand or compression elastography is used in eSie Touch™ Elasticity Imaging Technology on the Siemens ACUSON Antares™ ultrasound system, premium edition. The tissue under investigation is compressed with the transducer while the scan line RF data is analysed and compared with previous image frames. The same region of interest is kept within the frame from image to image, whilst slowly deforming the tissues with the probe. Small amounts of displacement of between 0.5 and 1% are necessary between frames to allow estimation of stiffness [24, 25].

During very small amounts of movement to distort the tissue, comparative sampling of all the RF data lines in one image with those in the next image builds up a map of movement from frame to frame (figure 2). The amount of movement is related to the stiffness of the tissues. Where there are differences in stiffness the amount of movement varies. These minute differences in movement enable a strain map of comparative elasticity to be constructed so that the difference in

stiffness between fat, Cooper's ligaments and normal parenchyma can be appreciated (figure 3).

The Strain imaging data is acquired in real time with a frame rate of 20 frames per second. Because there are nearly always some small changes in the tissues present from frame to frame there are some changes in strain pattern from frame to frame. When there is good uniform distortion with no significant movement away from the section of tissue being deformed these changes can be quite small, but breathing movements and cardiac pulsation usually result in less than continuous uniformity of strain maps from frame to frame. The real time nature of the acquisition means that when the image is frozen the retrospective cine loop facility allows careful inspection of individual frames to ensure accurate data and good images are obtained for recording and measuring areas of abnormal stiffness.

Because the stiffness (coefficient of elasticity) of tissues can vary with different amounts of pressure, strain images should be obtained with minimal pressure (pre-compression imaging) so that comparative elasticity imaging can provide consistent results from case to case.

Ensuring lightness of touch can be difficult on occasions and one possible method of ensuring minimal pressure is to ensure there is a visible layer of gel between probe surface and skin. The pressure should be small enough so that the gel is not displaced. Pre-compression is the equivalent of the point at which the probe just begins to make contact with the skin surface to allow imaging before the skin surface is depressed below the level of the adjacent skin. B-mode imaging with this

little pressure may result in a "poor" B-mode image due to increased interface shadowing and a need for higher gain levels than that used with normal firm pressure B-mode imaging. This resultant "apparent low echogenicity" does not result in any loss of elasticity imaging because it still contains echo information used by the elasticity software algorithms. The information becomes visible if gain or TGC are increased, but because strain imaging uses the pre-amplified data it is not critical for it to be visible on B-mode to get a good strain image.

Results

Recent work has confirmed that cancers tend to appear larger in a strain (elasticity) image than in the typical ultrasound greyscale image (figure 4) whilst benign lesions tend to appear smaller in the strain image than in the greyscale image (figure 5) [26, 27]. The extent of the strain image of cancers may be more accurate in demonstrating tumour size than the greyscale image [28]. Even ductal carcinoma in situ and mucinous cancers cause increased stiffness compared with the surrounding normal tissues. Mucinous cancers and cancers with internal tumour necrosis may exhibit a more heterogeneous strain pattern than more solid tumours.

Elasticity imaging adds useful diagnostic information which can help clinical management. Particular areas where it is showing promise are in the accurate, unequivocal identification of lesions such as fat islands

which can be a source of confusion, particularly for the less experienced breast sonographer. The absence of any stiffness confirms the benign nature of the ultrasound abnormality.

Impalpable masses like fibroadenomas picked up on screening mammograms are another area in which Strain imaging can help with patient management. They are often very visible on mammogram because they are surrounded by fat (figure 6). The patient shown in figure 6 did not have any palpable mass in the right breast. Ultrasound of the inferior part of the breast revealed an area, isoechoic with fat, which was the right size to be the lesion and in the right position at the edge of the breast disk (Figure 7). Elasticity imaging (figure 8) shows that this fat lobule-like lesion is stiffer (darker) than the surrounding fat. Ultrasound guided 14G needle core biopsy confirmed that this was a fibroadenoma.

Conclusion

Elasticity or Strain imaging is a very different method, technique and image to learn, but increasing skill in interpretation appears to be providing greater accuracy in diagnosis. Like colour Doppler, used as a stand alone method of differentiating benign from malignant, it is reasonably sensitive and specific, but taken with other observations within breast ultrasound imaging, it can help to improve diagnostic accuracy. Initial work suggests that elasticity imaging may add to the accuracy of ultrasound determined tumour extent as it can demonstrate areas of tumour related stiffness in adjacent tissue to the grey scale abnormality. A number of recent studies suggest that it may have the potential to safely reduce biopsy rates of benign lesions.

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Legends.

Figure 1

The inclusion body is isoechoic with the adjacent gel within in an ultrasound test tool when seen on B-mode. On the elasticity image (EI) the difference in elasticity coefficient is displayed as darker for increased stiffness and lighter for decreased stiffness (coefficient of elasticity). The variations in the remainder of the image reflect the changes in strain which occur with a uniform stress applied across a body which is not homogenous. The presence of an inclusion of different stiffness introduces inhomogeneity in the strain field.

Figure 2

Diagram of RF data changes from frame to frame with a minimal increase in pressure between frames.

Figure 3

B-mode (left) and strain (right) images taken from a case of gynaecomastia. Tissues are labelled f = fat, p = parenchyma, m = pectoral muscle on the chest wall. Arrows show the position of Cooper's ligaments and the lines of increased stiffness caused by them in the strain image. Areas of greater stiffness are darker whilst lesser stiffness is lighter. One possible explanation for the dark area on the strain image labelled "a" is an artefact caused by a lack of uniformity of stress by the probe surface across the whole image. The fat in this area is not being deformed as much as the tissue in the rest of the region. A small triangle of gel on the skin surface labelled "g" shows that there is less pressure at this point because it is not being compressed as much as the remainder of the skin surface. Another explanation is the inhomogeneity of the tissues resulting in variation of the stress field which in turn causes differences in the degrees of strain.

Figure 4

Grade II invasive ductal carcinoma (small arrows) which measured about 1.5 cm on B-mode. The pathology specimen had a maximum diameter of 1.5cm plus a further 0.9 cm of ductal carcinoma in situ giving a total tumour diameter of 2.4cm. The strain image shows a larger area of increased stiffness (large arrows) than the B-Mode image. The increased stiffness is caused by a combination of sclerotic reaction around the tumour and also by the DCIS.

Figure 5

Fibroadenoma (small arrows) which has a much larger B-mode size than the corresponding elastogram area of increased stiffness (large arrows). Note how the inhomogeneity of tissue elasticity and boundary effects give lower strain values in the tissue, on the muscle surface, directly deep to the area of increased strain within the fibroadenoma with increased strain in the tissue to each side of it.

Figure 6

Mammogram. The medio-lateral oblique view shows a lesion in the inferior part of the right breast. A rounded density (arrowed) is surrounded by fat but the lack of a sharply defined margin means that biopsy is indicated.

Figure 7

On the corresponding B-Mode ultrasound, the lesion has not been marked to "prove" its similarity to the surrounding fat.

Figure 8

Corresponding Strain image of the lesion showing the biopsy-proven fibroadenoma isoechoic with surrounding fat. Arrows outline the B-mode lesion and the area of increased stiffness associated with it. Fibroadenomas, especially when surrounded by fat, may have a strain footprint which is as large as the B-mode abnormality.

