Clinical Applications of Advanced High Frequency Ultrasound Techniques

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Introduction

High frequency ultrasound techniques continue to improve with better resolution and exquisite B-mode imaging, particularly with improved compounding techniques as seen with the ApliPure+ product. Particular focus however has been paid to improving techniques for breast imaging and one novel idea is to be able to highlight microcalcifications within tissues.

MicroPure

MicroPure highlights these microcalcific foci as a "twinkling" focus on a darkened blue background, although the latter can be altered to personal taste. This is the first time that an ultrasound device has been developed to help the operator confidently visualise microcalcifications, which previously would have been deemed too difficult with just conventional ultrasound. This could be particularly helpful with biopsy where traditional methods would necessitate stereotactic sampling. The latter would require 10–20 core biopsies whereas, with the help of ultrasound guidance, this could be reduced, although its efficacy remains to be proven.

Figures 1a-1c illustrate how the microcalcific foci in the 12 o'clock position of the right breast seen mammographically were difficult to identify on the B-mode image but the MicroPure software highlights the foci.

Elastography

Elastography is another technique which has been shown to have success in distinguishing benign from malignant breast lesions[1,2]. It is a method of quantifying ultrasonically "manual palpation" where

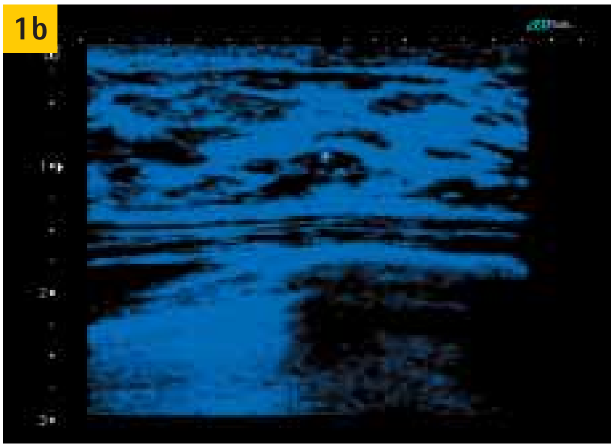


Fig. 1a: The microcalcific foci within these glandular breasts are difficult to visualise (arrow).
Fig. 1b: The microcalcification "twinkles" with MicroPure. Note the darkened blue background that makes the foci stand out. A second focus is also more easily appreciable.
Fig. 1c: Mammogram (craniocaudal view) demonstrating the microcalcification in the 12 o'clock position.

Fig. 2a: Preprocessing image with the strain colour map on the right and B-mode image on the left. This is to ensure that compression and decompression cycles have been correctly obtained prior to postprocessing in figures 2b–2d.

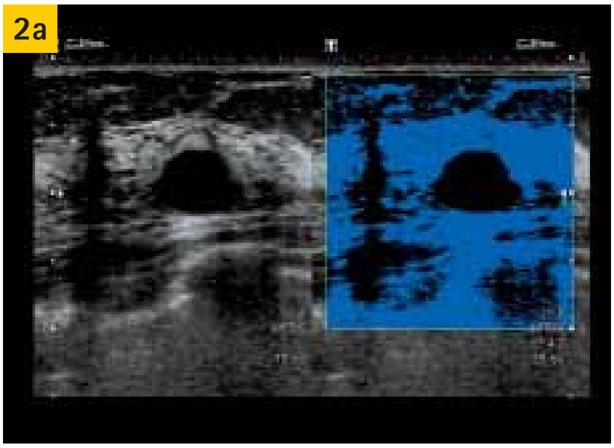
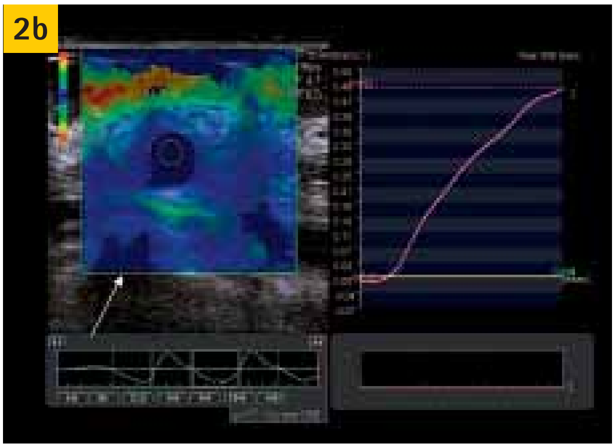


Fig. 2b: The strain image is shown as a colour map (arrow) but it is also possible to choose the compression or decompression phase of the clip stored based on the graph below the image. The large graph shows the strain over time on the region of interest drawn. Note the stiffness of this cyst which produces a similar strain graph to a cancer and can sometimes be a pitfall but the B-mode image should be diagnostic.



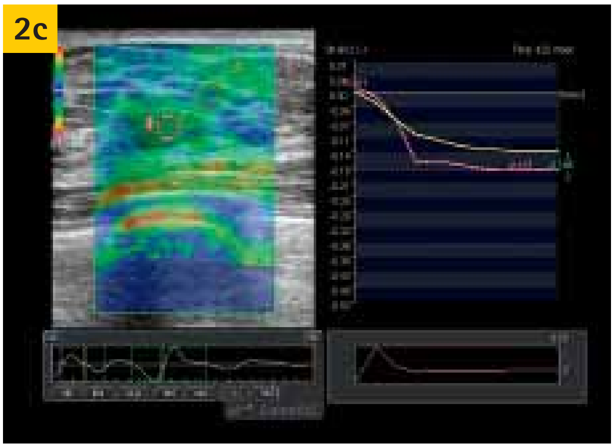


Fig. 2c: Strain graph of a fibroadenoma showing that it has a strain pattern similar to the adjacent fatty breast tissue. Note that the graph is below baseline as it is in the compression phase while it will be above baseline if in a decompression phase.

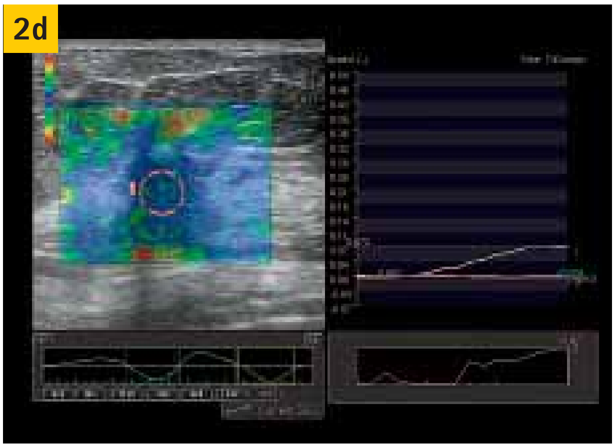


Fig. 2d: Elastography showing marked stiffness in a cancer with a high fat to lesion ratio of 17. Note the lesion has a stiffness curve (pink line) which approximates to the baseline and is significantly different to that of the adjacent normal breast tissue (yellow line).

the stiffer a lesion is, the more likely it is malignant. Much of the published work have concentrated on providing colour maps of the area of stiffness of the lesion and surrounding tissues. Toshiba has added this capability to the Aplio but provides an extra dimension by allowing time elasticity graphs to be plotted over a region of interest in the compression or relaxation cycles. By quantifying the elasticity, it removes the subjectivity of colour maps and some recent pilot studies (as yet unpublished) have suggested that the ratio of the adjacent normal fatty breast tissue to the lesion can be an indicator of malignancy when the ratio is at least 10. There are however exceptions to the rule, particularly if a malignant lesion is necrotic or in cysts which can also show stiffness. Figures 2a-2d demonstrate examples of benign and malignant lesions.

Volume imaging

Another area of ultrasound development has been the ability to generate three-dimensional volumetric images with high-frequency probes. Particularly successful in obstetrics, this has yet to find its clinical application in general imaging, but it has become apparent that the coronal plane reformatted images of breast cancers provides an appreciation of the retraction of the lesion and perhaps gives a better estimation of the true size and extent of the mass. Further trials are required to assess whether this truly does provide a better representation of tumour size. Figures 3a and 3b show the extent of a carcinoma with the "finger-like" projections closely resembling those seen on the MRI images. 3D elastography techniques have also been suggested to be helpful in assessing breast mass lesions[3].

Fig. 3a: 3D coronal view depicting a cancer as well as the finger-like projections radiating from this lesion and its true extent.

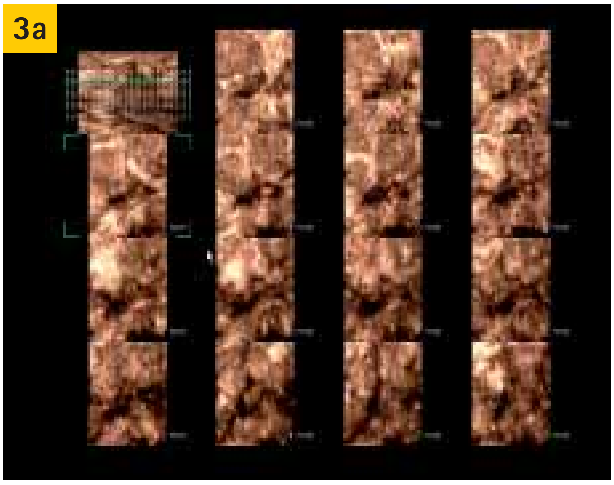
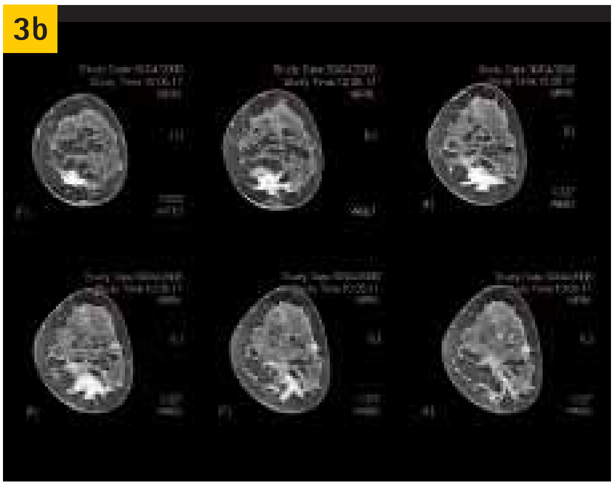


Fig. 3b: Corresponding MRI showing the extent of the carcinoma. The ultrasound images mimic this although on a small field of view magnification.



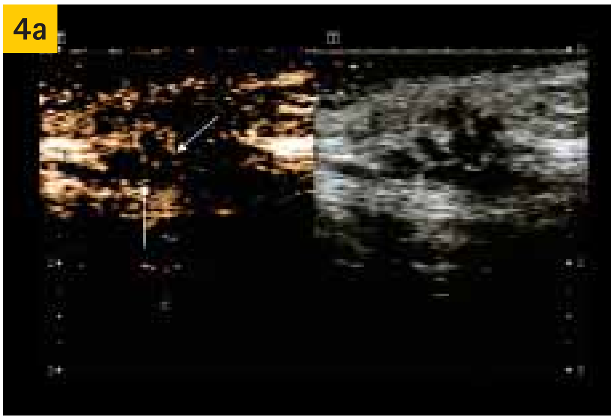


Fig. 4a: Twin view contrast image showing low mechanical index contrast specific mode on the left with the grey-scale image on the right. The gold colour depicts the microbubbles and note the tracks of angiogenic vessels (arrows).

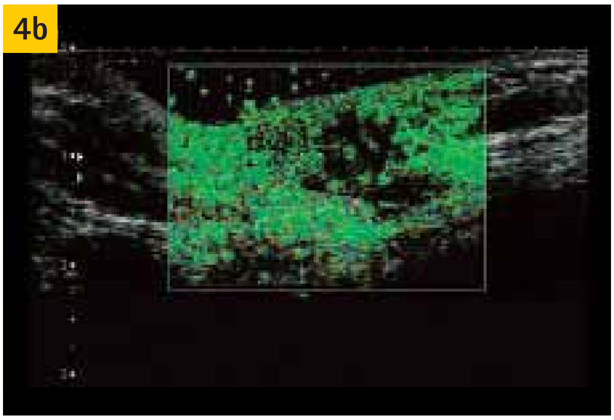


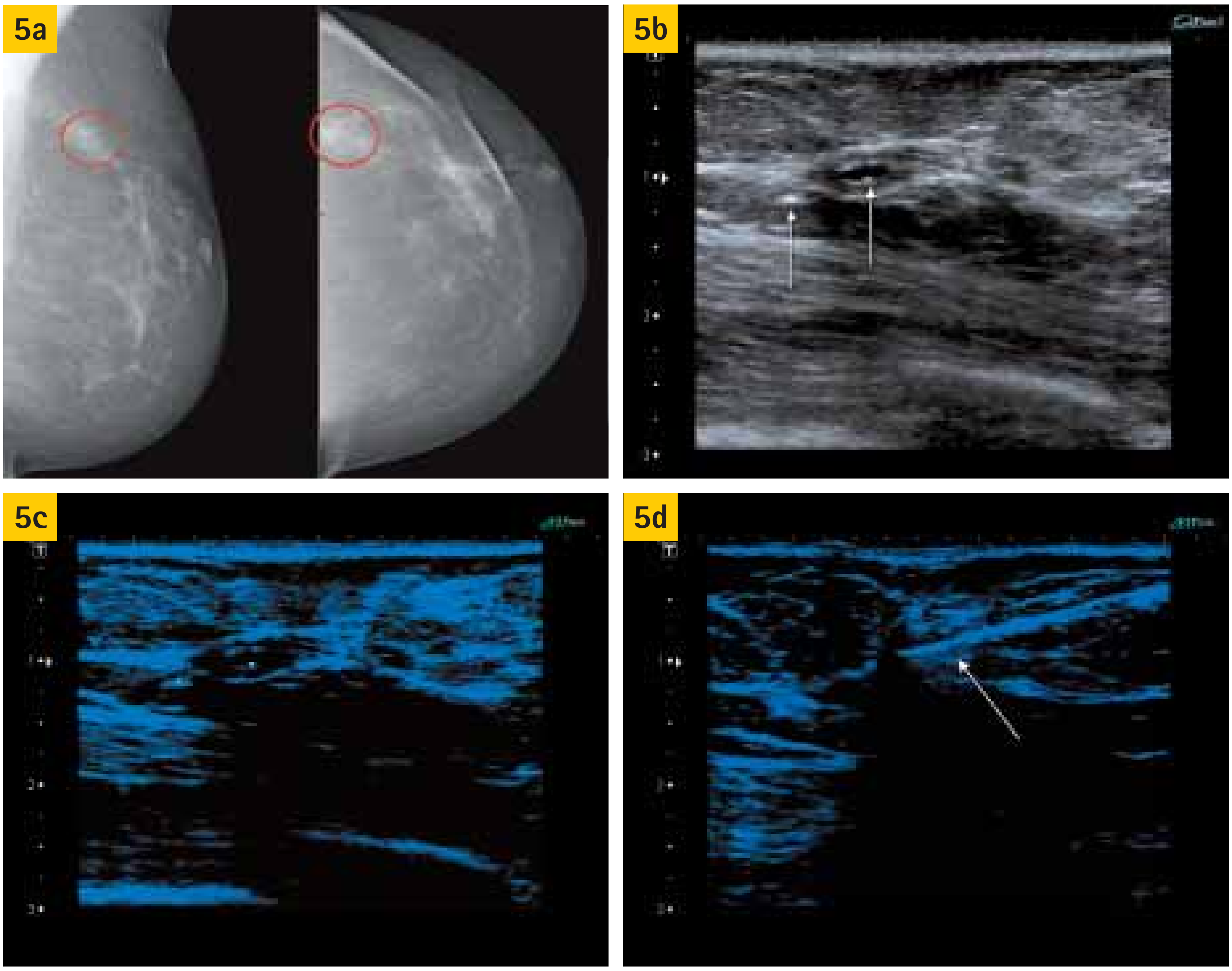
Fig. 4b: The same information can also be displayed with Vascular Recognition Imaging (VRI) where the stationary microbubbles are depicted in green overlayed on the grey-scale image.

Contrast enhanced ultrasound

Ultrasound contrast agents have established their use in abdominal studies, particularly for characterising focal liver lesions but have yet to find their niche with superficial lesions and high frequency scanning, particularly for breast lesions. Figures 4a and 4b show how the enhancement pattern and angiogenic vessels of a malignant tumour can be depicted with microbubble enhancement. It remains controversial as to how much this adds for distinguishing benign from malignant lesions[4,5]. Since breast biopsies are easily performed with few complications or significant morbidity, the role of contrast enhancement may not be major; however, it may find a role in assessing response to treatment. The following two cases illustrate the potential clinical applications of the techniques discussed so far.

Case I

Case 1 is of a 45 year old woman who has had a previous wide local excision of a breast carcinoma. Dystrophic microcalcification was visualised on a follow up mammogram (Fig. 5a). An ultrasound revealed scar tissue but no mass. The microcalcification was made easier to identify with MicroPure (Fig. 5a and 5b). The dystrophic nature of the microcalcification warranted sampling and this was attempted ultrasonically with the help of MicroPure (Fig. 5d). Six core biopsies of the microcalcific foci were performed and calcium was seen on the mammogram of the second set of 3 cores (Fig. 5e). Histology confirmed the presence of calcium together with an area of fat necrosis and scar tissue. This example highlights the potential use of MicroPure which obviated the need for stereotactic core biopsies, saving time and also the number of biopsies needed for the patient.



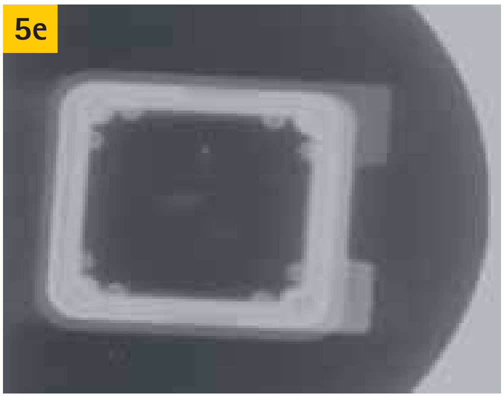


Fig. 5a: Mammographic views of the left breast where there had been a wide local excision in the left upper outer quadrant and there was now some dystrophic microcalcification (red circle).
Fig. 5b & 5c: Ultrasound of this area showed some cystic change and probable microcalcification (arrows) which was confirmed on MicroPure. No mass was evident.
Fig. 5d: The microcalcification was biopsied with the help of MicroPure. Six core biopsies were obtained and the needle (arrow) is shown prior to biopsy.
Fig. 5e: The second set of three core biopsies confirming the presence of microcalcification. The patient therefore did not require a stereotactic core biopsy. Histology confirmed scar tissue and fat necrosis with no malignancy evident.

Case 2

In case 2, this patient had a palpable 1 cm lobulated mass in the left upper outer quadrant. It was mildly vascular (Fig. 6a) and scanning with MicroPure revealed a couple of probable microcalcific foci (Fig. 6b) which were not clearly visualised on the B-mode image. This was subsequently confirmed on the mammogram requested after the ultrasound examination (Fig. 6c).

Elastography revealed a stiff lesion with a fat:lesion ratio of 10.4. Note however a "finger-like" projection area of stiffness (Fig. 6d) which is also seen in the coronal plane on the three-dimensional image (Fig. 6e) suggesting that there is probably more extensive involvement than initially thought based on the grey-scale image.

Conclusion

These cases illustrate the immense potential of the latest developments in breast ultrasonography, in particular MicroPure and elastography time/ stiffness curves which provides quantification and do not rely solely on subjective visualisation.

Together with the 4D and small parts contrast capabilities, the new version 3 Aplio XG provides the radiologist with a great armamentarium for evaluating complex breast lesions. It is not envisaged that MicroPure would replace mammography in screening for microcalcifications but what would be of particular value is the ability to biopsy microcalcifications under ultrasound guidance, therefore obviating the need for stereotactic biopsies. The ability to depict the true extent of malignant breast tumours

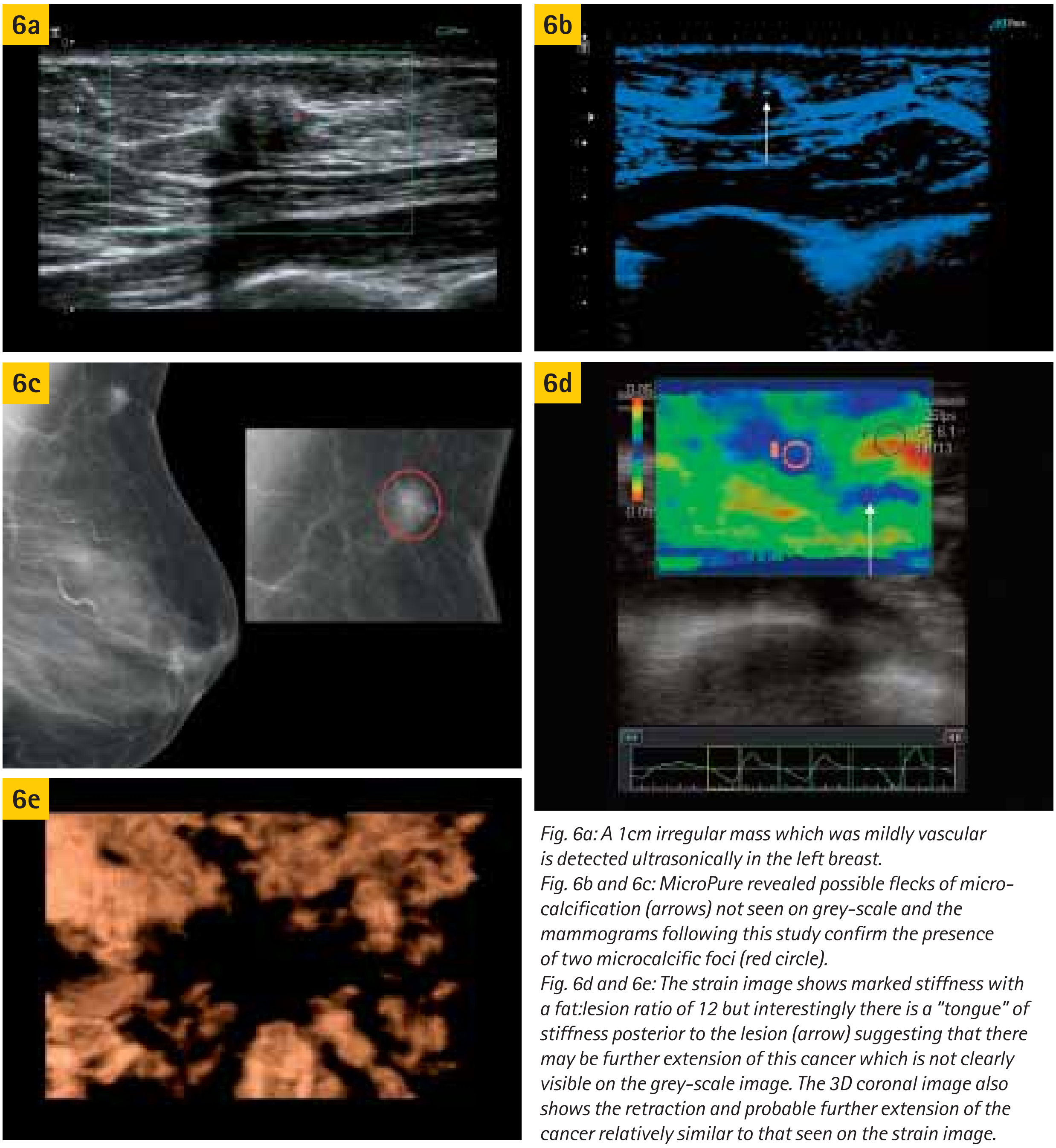


Fig. 6a: A 1cm irregular mass which was mildly vascular is detected ultrasonically in the left breast.
Fig. 6b and 6c: MicroPure revealed possible flecks of microcalcification (arrows) not seen on grey-scale and the mammograms following this study confirm the presence of two microcalcific foci (red circle).
Fig. 6d and 6e: The strain image shows marked stiffness with a fat:lesion ratio of 12 but interestingly there is a "tongue" of stiffness posterior to the lesion (arrow) suggesting that there may be further extension of this cancer which is not clearly visible on the grey-scale image. The 3D coronal image also shows the retraction and probable further extension of the cancer relatively similar to that seen on the strain image.

more accurately with elastography, 4D imaging and the use of microbubbles would not only help surgical management but has potential in assessing response to chemotherapeutic treatment, thereby aiding the oncologist.

The potential of these techniques to detect problematic breast tumours such as lobular or multifocal breast carcinomas and also in screening should be fully investigated. Ultimately, these latest developments require multicentre studies to evaluate their true value and potential.

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