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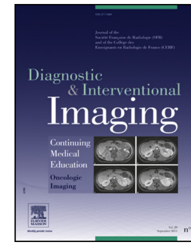

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Breast elastography: The technical process and its applications

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KEYWORDS
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Abstract Breast elastography is being increasingly used to better characterize breast lesions. Published studies have shown that it improved specificity of B mode ultrasound. Two elastography modes are available: free-hand elastography and shear wave elastography. Free-hand elastography is obtained by a mechanic wave induced by the ultrasound probe, deforming the target, either by small movements induced by breathe. An elastogram is obtained and displayed either as a colour map or a size ratio or elasticity ratio measurement. The second mode is shear wave elastography; two methods are available: Shear Wave Elastography (SWE) and ARFI mode (Acoustic Radiation Force Impulse). Shear wave elastography is less operator-dependent than free-hand elastography mode and provides a quantitative approach. A value of over 80 kPa (SWE) or velocity results of over 2 m/s (ARFI) are considered as suspicious. False negatives may occur in soft breast cancers (mucinous carcinoma, carcinoma with an inflammatory stroma, etc.) and false positives may be seen with poorly deformable benign lesions such as old fibrous adenomas. In practical use, elastography is a useful complementary tool for undetermined breast lesions categorized as BI-RADS 4a or BI-RADS 3, or for cystic lesions but cannot avoid fine needle aspiration or core biopsy if ultrasound features are clearly suspicious.

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Breast elastography: principles

Technique

Technique of breast elastography varies if images are being acquired by free-hand mode or shear wave elastography mode.

Elastography is used to characterize a lesion that has already been detected in B mode. It is a characterization tool, not a detection tool. The pressure applied on the probe must always be as low as possible. This requires a learning curve. With the first ultrasound machines equipped with elastography modules, small regular pressure movements on the probe were mandatory in order to obtain an elastogram [1] whereas actually, with new machines, sensitivity of software to the movement is so high that breath alone is sufficient to create an image [2]. Thus, technical procedure is easier to perform and less operator-dependent. B mode image must be located in the centre of the screen before activating the elastography mode and it is recommended to surround the lesion with adjacent tissue in order to obtain a high quality image. The image generated is an elastogram which may be displayed differently according to the manufacturer, either as a colour image [3] or as a black and white elastogram [4] with differences in size and contours in comparison with B mode image, or with an elasticity measurement in speed level (ARFI, Siemens®) or in elasticity in kPa (Aixplorer, SuperSonic Imagine®) [5]. In free-hand elastography techniques, relative strain values can be obtained in comparison with surrounding tissues, with a colour map or elasticity ratios. In most ultrasound machines, elastography mode is easily activated on the keyboard. Elastography is usually performed with the same superficial ultrasound probe that is used for B mode: with some companies, breast elastography cannot be used with very high frequencies, and superficial probes with lower frequencies are then required.

Black and white or colour images are recorded and compared to the images acquired in B mode. It can also be useful to record video cineloops that facilitate the review. Images are transferred in DICOM format and can be archived in a PACS system. After a short training, breast elastography is a very fast examination, adding only 2 to 5 minutes to a normal breast ultrasound.

Advantages and limitations of the two elastography techniques

Free-hand technique

After a short learning time, the technique is fast and easy to use. The cost of equipment is usually slightly reduced in comparison with shear wave technique (SWE). Its main disadvantage is that it is relatively operator-dependent, particularly in terms of the pressure applied to the probe and large variations can be obtained in images and values [6]. Some manufacturers provide quality scales which makes more reliable to establish whether or not the acquisition has been correctly obtained.

Shear wave elastography

This more recent mode is available in last generation of ultrasound machines, with also high quality of B mode ultrasound. Shear wave elastography (SWE) technique is classically less operator-dependent, although some degree of variability may occur if too much pressure is applied on the probe (elasticity values of kPa or shear wave measurement velocities can be artificially increased). The equipment is usually more expensive, and two different ultrasound probes are required, a very high frequency probe to obtain high resolution superficial ultrasound images and a lower frequency ultrasound probe used to obtain shear wave measurement.

Interpretation basis

Interpretation varies according to the manufacturer. Elastogram may be either a colour map, a black and white image where contours and differences in size between B mode/ultrasound can be measured, time curve in elasticity, or an image on which the regions of interest (ROI) can be set in order to calculate relative differences in elasticity with the surrounding tissue, etc. Occasionally, according to the manufacturer, colour code of elastogram may change. This may increase interpretation difficulties in case of several different ultrasound machines with elastography software are used in the radiology centre. Thus, it is clear that the operator must be informed in elastography technique of its own machines in order to improve his/her elastography technique. Elastography is now increasingly used to improve the differential diagnosis of breast lesions and will be incorporated into the new BI-RADS breast lesion ultrasound classification that will be published in 2013. However, only qualitative elastography parameters (colour map, black and white, morphology) will be incorporated in this new version.

Specific situations according to the manufacturer

Hitachi® models produce a colour elastogram. Itoh et al. [3] have proposed an elasticity score (Fig. 1), which has been validated in large series of biopsied breast lesions and compared to the BI-RADS classification of ACR for breast lesions. In order to categorize these images, Itoh et al. assessed the lesion colour scale both in the hypoechoic lesion and in the adjacent tissue. A 5-point elasticity score was joined for each image. A score 1 represents an entirely green lesion with the same elasticity throughout the lesion, a score 2 represents a lesion of which the greater part can be deformed although it may also contain non-deformable areas (green and blue mosaic), a score 3 corresponds to high elasticity level in the periphery of the lesion (green) whereas the centre of the lesion is blue, a score 4 indicates no deformability throughout the lesion (entire lesion is blue although the adjacent tissue is not affected) and a score 5 indicates no deformation throughout the hypoechoic lesion or the adjacent tissue (lesion and adjacent tissue are blue). The risk of malignancy increases from 1 (benign lesion) to 5 (malignant lesion) (Fig. 2).

The appearance of images is different with Toshiba® elasticity software. Two ROI are set in the centre of the lesion and in the adjacent tissue. Elasticity values are seen on compression-decompression time-curves. Increased

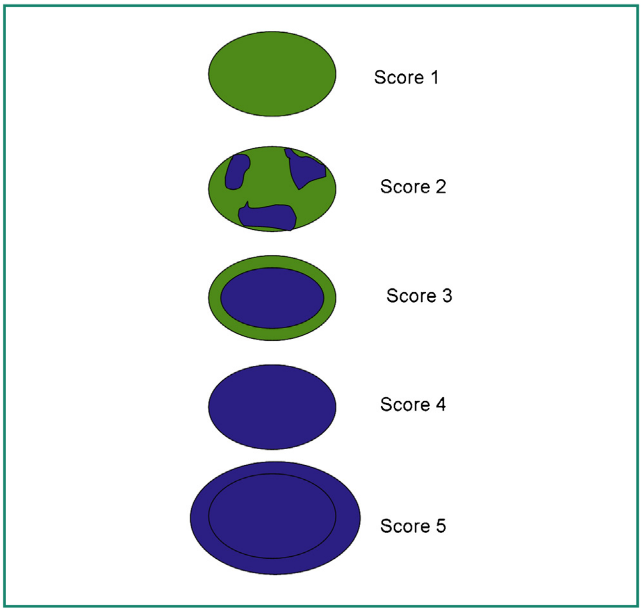

Figure 1. Tsukuba University score (Hitachi®). Score 1: lesion entirely green (same elasticity throughout the lesion). Score 2: blue and green mosaic (most of the lesion is deformable although there are areas which are not deformable). Score 3: deformability in the periphery of the lesion although the centre is blue. Score 4: blue lesion, surrounding tissue not affected (no deformability throughout the entire lesion only). Score 5: the lesion and adjacent tissues are blue (no deformation throughout the entire lesion or in adjacent tissue). The risk of malignancy increases from 1 to 5.
From Itoh et al., 2006 [3].

ratios between two time-curves reflect low deformability of the lesion and a increased risk of malignancy (Fig. 3). The best cut-offs are: N < 3.25% deformation = 91%, malignancy = specific and N > 6% = 90% sensitive for a benign lesion [7]. Deformability value is displayed on the image. The maximum deformation percentage of the adjacent breast in the same phase is also displayed. This is a semi-quantitative method which is still operator-dependent but easy to use in routine practice with a rapid learning curve. On the other

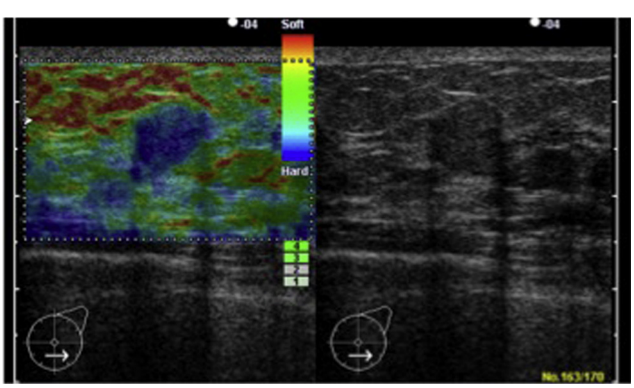

Figure 2. 45-years-old, infiltrative ductal carcinoma. Free-hand elastography and B mode ultrasound (Hitachi®). The elastogram is homogeneously blue, indicating a poorly deformable lesion. However adjacent tissue is not blue and the Ueno score is 4, indicating a suspicious lesion requiring a biopsy, with irregular margins.
Acknowledgement: Dr Anne Tardivon, Curie Institute, Paris.

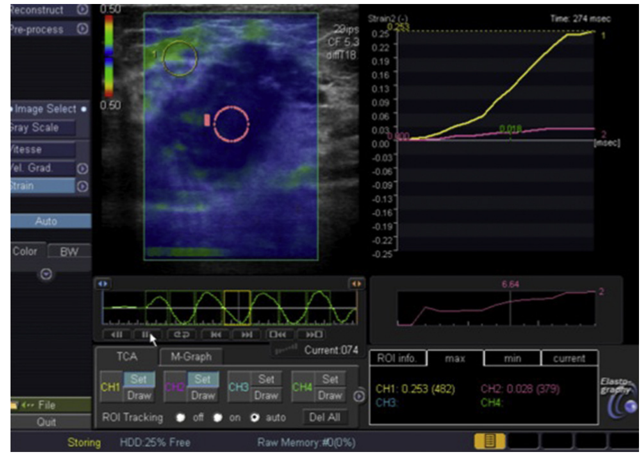

Figure 3. Grade 2 infiltrative ductal carcinoma, free-hand elastography (Toshiba®). The maximum percentage deformation of the lesion in decompression phase (DMD score) is 2.8% in the lesion and 25% in the adjacent tissue, which supports a malignant lesion.
Acknowledgement: Dr Luc Rottenberg, Hartmann Clinic, Neuilly-sur-Seine.

hand, a benign lesion has similar strain features over time compared to the adjacent tissue [8].

With Philips®, elastograms are displayed either in black and white or in colour mode. In black and white mode, a malignant lesion is usually very dark with irregular contours and a larger size in comparison with B mode (Fig. 4a). In colour mode, malignant lesions are blue, whereas benign lesions are red (Fig. 4b). Cystic lesions have typically a triple layout colour appearance (like on Hitachi® machines (red, green, blue)) (Fig. 5) [9]. Elasticity can also be calculated with an ROI positioned in the lesion and another one positioned in the adjacent tissue. Relative elasticity curves can be obtained for each tissue to compare strain values.

Siemens® has a free-hand elastography mode similar to Philips®. Malignant lesions are usually larger in size than benign ones (usually more than 1.5 times larger); margins are irregular with a hypoechoic centre, whereas benign lesions are more likely seen with a hyperechoic centre. Cysts have a typical ''bull's eye'' appearance (small size, white centre, peripheral black circle) (Fig. 6) [10]. In colour mode, malignant lesions are usually red whereas benign lesions are blue. However, new colour modes are available and the colour scale can be inversed. Strain level can also be quantified with an ROI positioned in the lesion and the other in the adjacent normal tissue at the same depth: the risk of malignancy increases with increasing ratio.

In shear wave elastography mode (ARFI), three modes are available: a colour map can be obtained, or velocity measurements may be recorded in m/s or as a colour velocity map. According to data published in the literature and from our own personal experience, velocities of over 2 m/s in the lesion are more often seen on malignant lesions (Fig. 7).

With shear wave elastography technique, a relevant elasticity value cannot be measured in a pure cyst as shear waves are not induced when the ultrasound beam encounters a cyst. A such kind artifact induces a signal defect in a pure cyst, which can help for the diagnosis (Fig. 8).

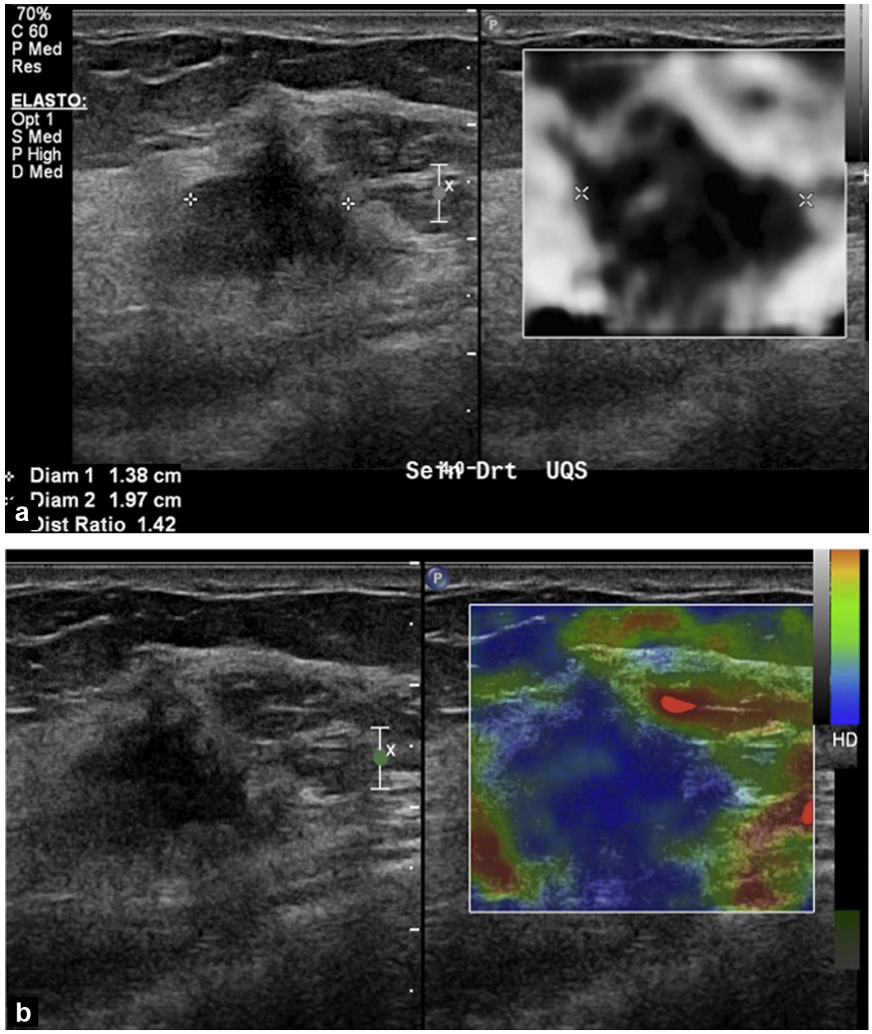

Figure 4. Infiltrative ductal carcinoma, free-hand elastography, black and white mode, (a), colour mode (b) (Philips ®). The size of the lesion on the black and white elastogram is larger than on B mode ultrasound: the lesion is very dark with irregular contours, which suggests a poorly deformable lesion as seen on malignant lesions. In colour mode, the lesion and adjacent tissues are blue, indicating a poorly deformable lesion. Biopsy confirmed a grade 2 infiltrative ductal carcinoma.

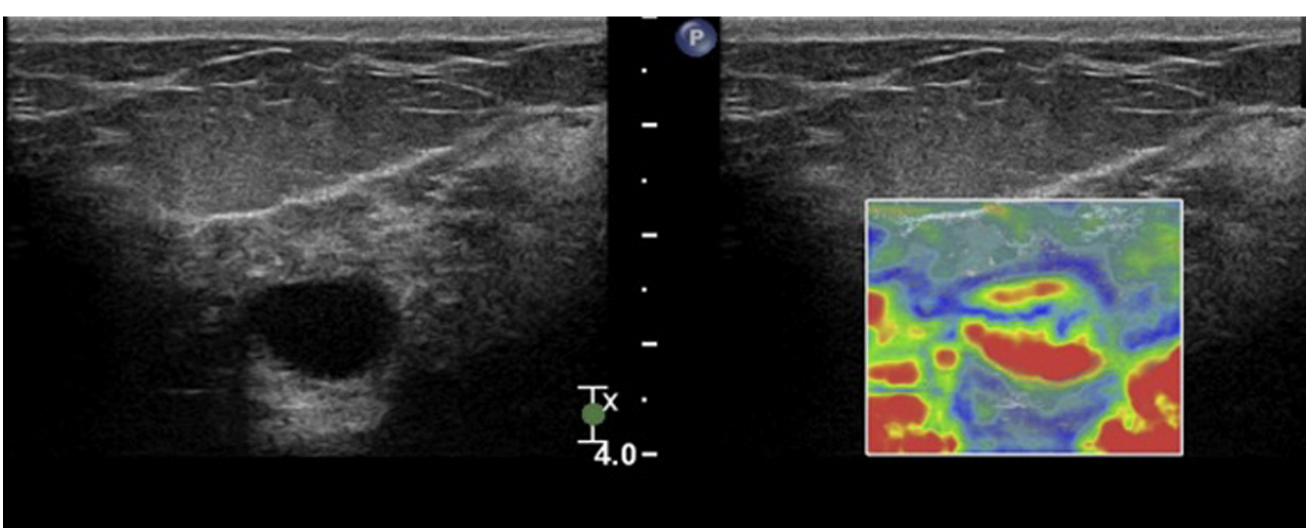

Figure 5. Cyst. Free-hand elastography, colour mode (Philips®). This typical cyst shows a triple layout couloured lesion, which is a typical feature of a cystic lesion. It is therefore be used to differentiate cystic lesions from solid fine echoic lesions as seen on atypical cyst.

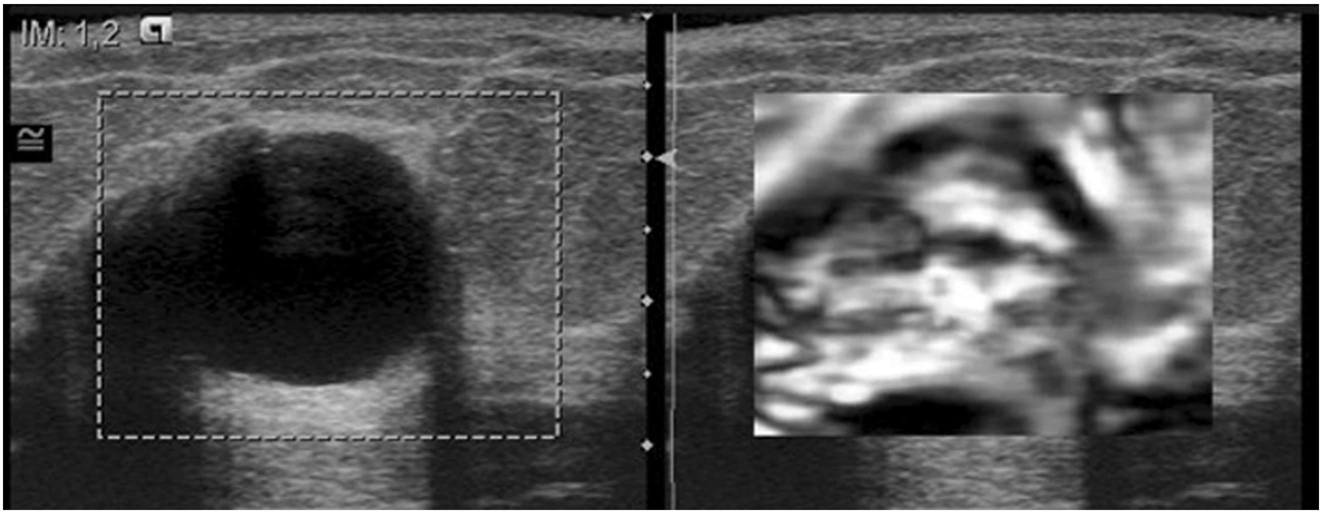

Figure 6. Cyst. Free-hand elastography, black and white mode (Siemens®). The typical appearance of a pure cyst with this mode is described in the literature as a ''bull's eye'' appearance. It corresponds to a very white characteristically shiny centre surrounded by a thin external black line. This feature is typical of a cystic lesion and can also help to differentiate an echoic cyst from a solid lesion.

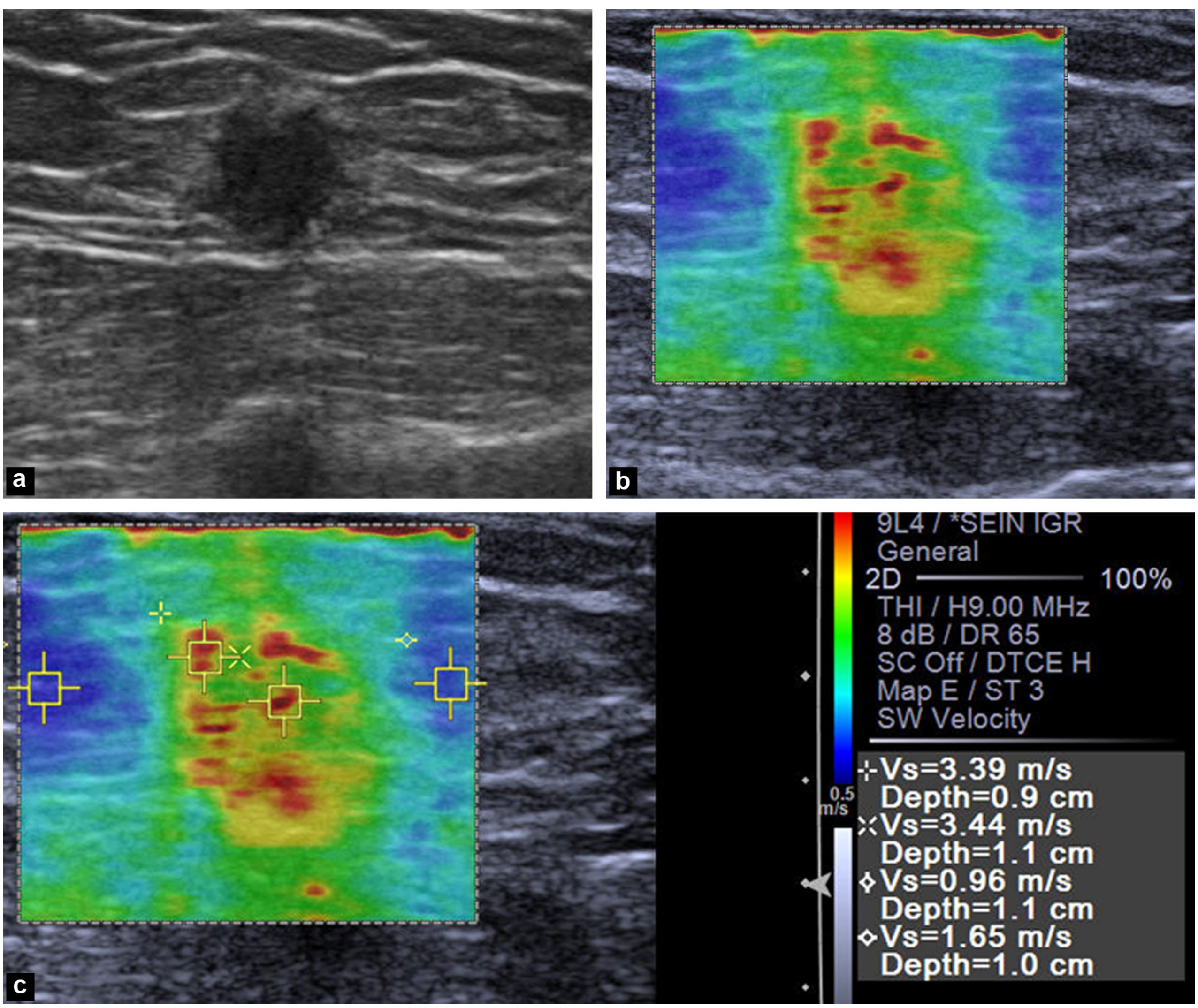

Figure 7. Grade 2 infiltrative ductal carcinoma. Acoustic Radiation Force Impulse (ARFI) mode (Siemens®). This 6 mm lesion is microlobulated with suspicious features (a). It is poorly deformable in colour ARFI mode with red and orange areas in and around the lesion (b). Velocities measured in the lesions are very high (> 3 m/s), which suggests a malignant lesion (c).

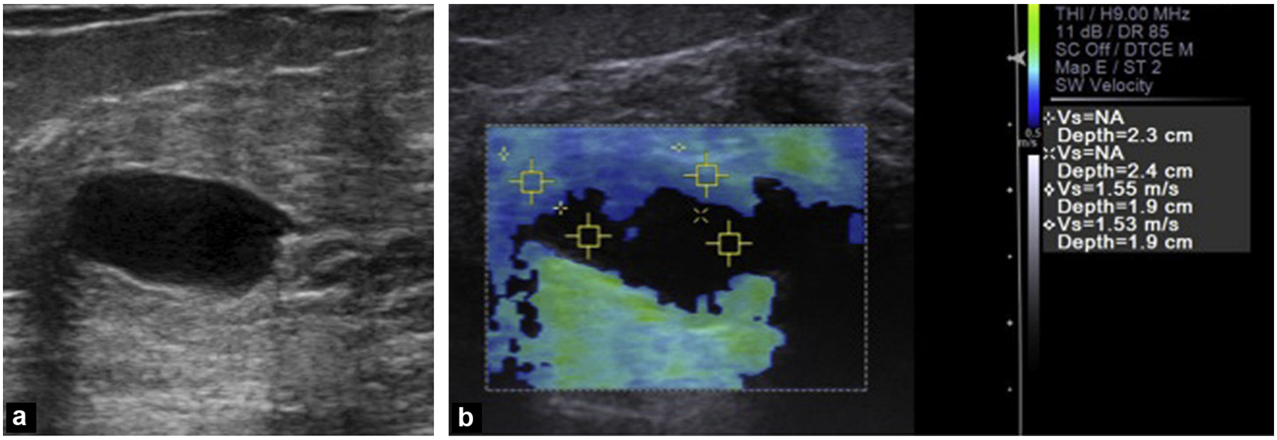

Figure 8. Cyst. Acoustic Radiation Force Impulse mode (Siemens®). The shear waves are not generated when the ultrasound beam encounters a pure cyst (a) as in this example. With this technique, the defect appears as an area of blank signal (b) although this elastographic feature provides the diagnosis. Speed measurement or kPa measurements cannot be done in the blank signal areas of the cyst.

On Supersonic Imagine® ultrasound machines, elasticity is measured in kPa and images are displayed on a real time colour map with an adjustable elasticity scale shown in kPa configured by default for the breast at 180 kPa (Fig. 9). Once the acquisition has been performed (on a freeze image), the operator can measure elasticity and elasticity ratios on a region of interest. Several studies have shown variable elasticity threshold for benign or malignant lesions [11,12]. A recent study on a large cohort of patients has established that values under 80 kPa associated with an oval shape breast lesion were accurate parameters to assess a benign lesion [13]. Using this cut-off, specificity was improved in comparison with B mode (77.4% versus 69.4%) without loss of sensitivity [13]. Malignant lesions usually have values over 120 kPa (Fig. 9b).

This review is not exhaustive and other manufacturers can offer other modes which are not described here.

False positives and false negatives

False positives

Free-hand or shear wave elastography measures elasticity and strain of a lesion. Breast cancers are usually poorly deformable in comparison with benign lesions. Nevertheless, some benign lesions can be poorly deformable: such as fibrous fibroadenoma or scars. Thus elastography is not an accurate tool to evaluate treated breasts. The presence of implants can also change strain of breast tissue around the implant; lesion characterization may be impossible [14].

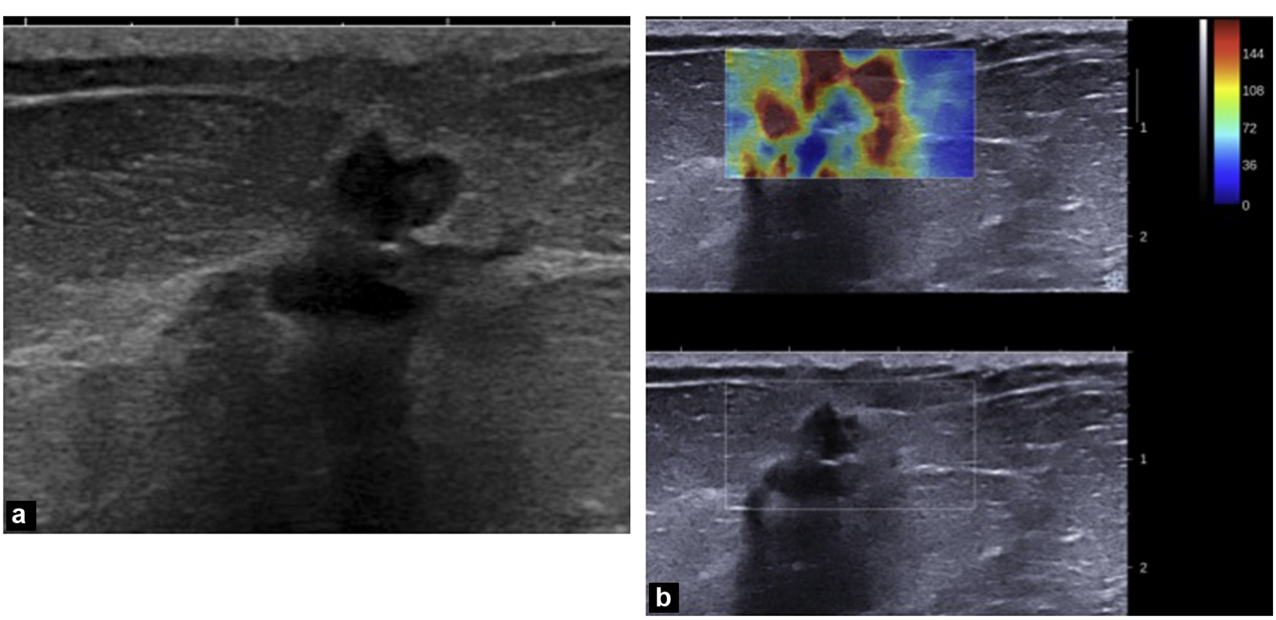

Figure 9. Grade 3 infiltrative ductal carcinoma. Shear wave elastography (SWE) (SuperSonic Imagine®). The lesion appears morphologically malignant with spiculated contours and posterior attenuation in B mode (a). In SWE mode, periphery of the lesion is red. This is very common in poorly deformable malignant lesions with measured values of 140 kPa (b). Biopsy confirmed an infiltrative ductal carcinoma.

Some authors, however, have tried to assess the presence of a capsule with this feature [15].

False negatives

Some breast cancers (such as mucinous cancers, cancer with an inflammatory stroma or lesions less than 5 mm in size) appear highly deformable with pseudo-benign features on elastography. However morphology of these lesions is usually highly suspicious on B mode; that may explain why both modes are then complementary.

Deep lesions (> 4—5 cm) are also not always easily analysed with elastography, particularly with free-hand mode [16].

Inconsistent results can also be obtained if the density of the breast tissue is high, and lead to false negative results [17].

Literature review

Characterisation of benign/malignant solid lesions

The main interest of breast elastography is to improve the characterisation of benign and malignant breast lesions [10,18]. Many studies have shown that the use of elastography parameters in adjunct to ultrasound parameters can improve BI-RADS score [19—21]. These results have been obtained either with free-hand or shear wave modes. While elastography may be useful to characterize a cystic content without fine needle aspiration, it is mandatory to avoid a false interpretation when a malignant lesion presents as highly deformable. On the other hand, it appears to be useful for malignant lesions presenting as benign lesions on B mode, which appear poorly deformable on elastography (Fig. 10). The best application seems to be applied to solid BI-RADS 3 or 4a lesions. Elastography can also increase the ultrasonographer's confidence in his/her diagnosis before a biopsy.

Free-hand elastography

A series of 370 patients with lesions under 2 cm (39% cancers) was studied using a free-hand elastography technique [22]. BI-RADS score was improved with sensitivity and specificity increasing from 90.3% and 68.3% to 83.9% and 87.8% respectively when elastography was added. In another study of 193 lesions using a cut-off of 3:4 (Itoh classification), Schaefer et al. [23] showed that sensitivity was 96.9% with a specificity of 76% and recommended that static elastography

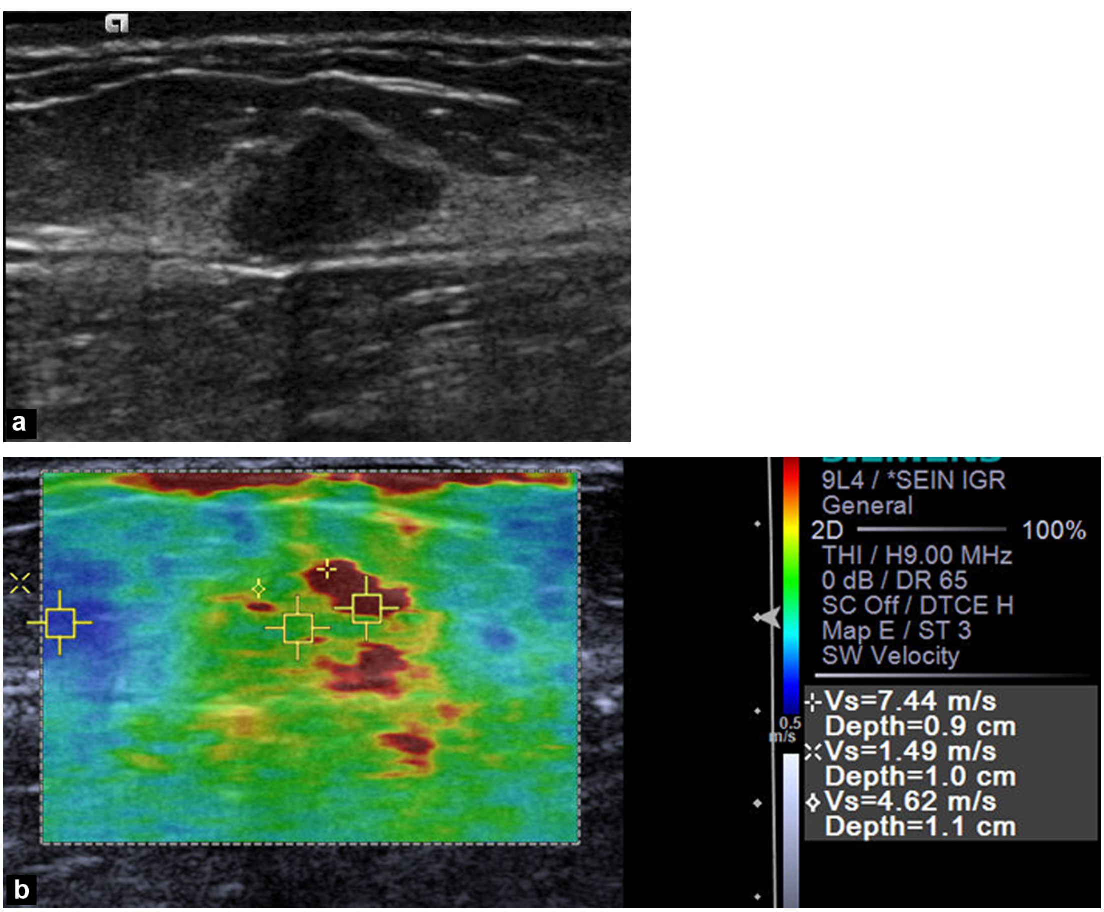

Figure 10. Grade 2 infiltrative, ductal carcinoma. Acoustic Radiation Force Impulse mode (Siemens®). In B mode, this lesion appears non-suspicious with an oval shape, no posterior attenuation and regular margins excepted few microlobulations (a). It was categorized as BI-RADS 4a, as it was found in a 40-year-old woman. On the other hand, elastography is more suspicious with very high speed superior than 7 m/s (b). Histology confirmed a grade 2 infiltrative ductal carcinoma.

should be used in addition to B mode ultrasound, as only two cancers in their study had a score of 1 (benign). Fischer et al., in another study of 200 histologically proven lesions (116 cancers), demonstrated that elasticity ratio was more sensitive and specific than B mode or even mammography with values of 95% and 74% respectively with a cut-off of 2.27 [24].

Another important point to differentiate benign/malignant lesions is that cancers appear larger in elastography than on B mode ultrasound [3,25,26]. This may be due to the fact that local extension of the cancer is not always seen on B mode ultrasound but can be imaged by elastography. It is useful in free-hand elastography to measure the quantitative ratio between the lesion on B mode and on elastography. Barr et al. showed, in a multicentric study including 222 atypical malignant lesions and 413 benign lesions, that a size ratio greater than 1 was found in 219 of 222 malignant lesions and that a size ratio less than 1 was found in 361 of 413 benign lesions, allowing a sensitivity of 98.6% and a specificity of 87.4% [4]. Elastography size appears also better correlated with histological size [4].

Two recent meta-analyses have been reported on free-hand breast elastography. In the analysis of Gong et al. [27], the authors examined 23 of 212 manuscripts published in English language journals. The 5-point scale published by Itoh et al. [3] was used in most studies. Mean sensitivity and specificity values to diagnose breast cancers were 0.83 (95% CI, 0.814—0.853) and 0.84 (95% CI, 0.829—0.854) with an area under the ROC curve of 0.93 [27]. The second meta-analysis by Sadigh et al. [21] examined 12 of 3000 articles. The elasticity and size ratios were both examined. The cut-off for the elasticity ratio ranged from 4.5 to 0.5 in the different studies and mean sensitivity was 88% (95% (CrI), 84—91%), with a specificity of 83% (CrI 78—88%) for elasticity ratios and 98% (CrI 93—99%) and 72% (CrI 31—96%) for the size ratio.

Elastography appearances of cysts in these studies were variable according the techniques used although free-hand elastography appeared to be accurate to confirm that an echoic lesion had a liquid content [28—30].

Shear wave elastography

Like free-hand elastography, characterization of benign/malignant lesions is improved for solid breast lesions with shear wave elastography (SWE). Several studies [11,31] have evaluated the input of SWE elastography to characterize breast lesions [13] and have shown its ability to reclassify masses which were initially classified as BI-RADS 3 and 4a. In this multicentric study, SWE elastography improved specificity of conventional ultrasound from 61.1% to 78.5% in 650 lesions without significantly reducing specificity. These values were obtained with a maximum shear wave velocity cut-off of 5 m/s (80 kPa) to improve specificity [13]. The same study also evaluated reproducibility, which was extremely high: intra-observer correlation by SWE elasticity for maximum and mean elasticity values was excellent (ICC = 0.84 and 0.87). Correlations were slightly inferior for inter-observer correlation [32]. In these different studies, strain values of malignant lesions were high (between 146 and 153 kPa) [13,31,33]. These different studies concluded that SWE elastography is highly reproducible to assess BI-RADS 3 lesions with benign features, with elasticity values less than or equal to 20 kPa. On the other hand, it appears that the combination of the BI-RADS classification and elastography score offers greater sensitivity to diagnose malignancy [34]. Anyway, elastography score must not be used alone independently of the BI-RADS score. Similar results were found with the other mode of SWE elastography, Acoustic Radiation Force Impulse (ARFI) mode. A 3.6 m/s cut-off was found to differentiate benign from malignant lesions in a series of 161 masses including 43 cancers, with a sensitivity of 91% and a specificity of 80.6% [35]. In practice, the discrimination cut-off between benign and malignant can vary from 2.20 m/s to 4.5 m/s depending on the studies where this technique was evaluated [35—37]. We have found that a velocity score of 2.20 m/s reaches a sensitivity of 94% with a specificity of 84% in a personal study of 112 lesions including 62 cancers.

In both shear wave elastography techniques, SWE and ARFI, elasticity sometimes cannot be calculated when deformation of a tissue is too low. This may occur in large, very rigid infiltrative cancers [36]. In this case, ultrasound beam cannot penetrate high attenuating areas such as the deepest part of scirrhous cancers. Colours are not seen on SWE mode (Fig. 11) or XXX value is displayed instead a register speed in m/s on ARFI mode. These features must not be misunderstood with low values seen on benign lesions. The systems cannot measure elasticity values in lesions where the tissue does not vibrate enough or because the amplitude of the shear wave is too low and thus lost in the background noise [38].

Similarly, non-viscous cysts do not generate shear waves and can appear as black areas in the hypoechoic area on B mode ultrasound. When the cyst has a minimum level of viscosity, however, shear waves can be recorded with low values.

Role of elastography to assess microcalcifications clusters

Some publications reported that the different breast tissues have variable elasticity characteristics depending on their values of fat, gland and connective tissue and that it is possible to differentiate the intraductal or infiltrative malignant component of a malignant lesion [39]. Cho et al. in a recent study assessed elasticity of microcalcifications clusters associated with hypoechoic lesions [40]. Benign lesions associated with microcalcifications were significantly more deformable than malignant lesions associated with microcalcifications. The technique used was however more sensitive than specific (97% versus 62%) and cannot therefore replace mammography or biopsy.

Elastography of lymph nodes

Few studies have evaluated elasticity imaging to characterize axillary lymph nodes [41—44]. Metastatic axillary nodes appear to be more vascularized and less deformable than benign inflammatory lymph nodes [45]. Choi et al. [44] evaluated the input of elastography to differentiate benign from

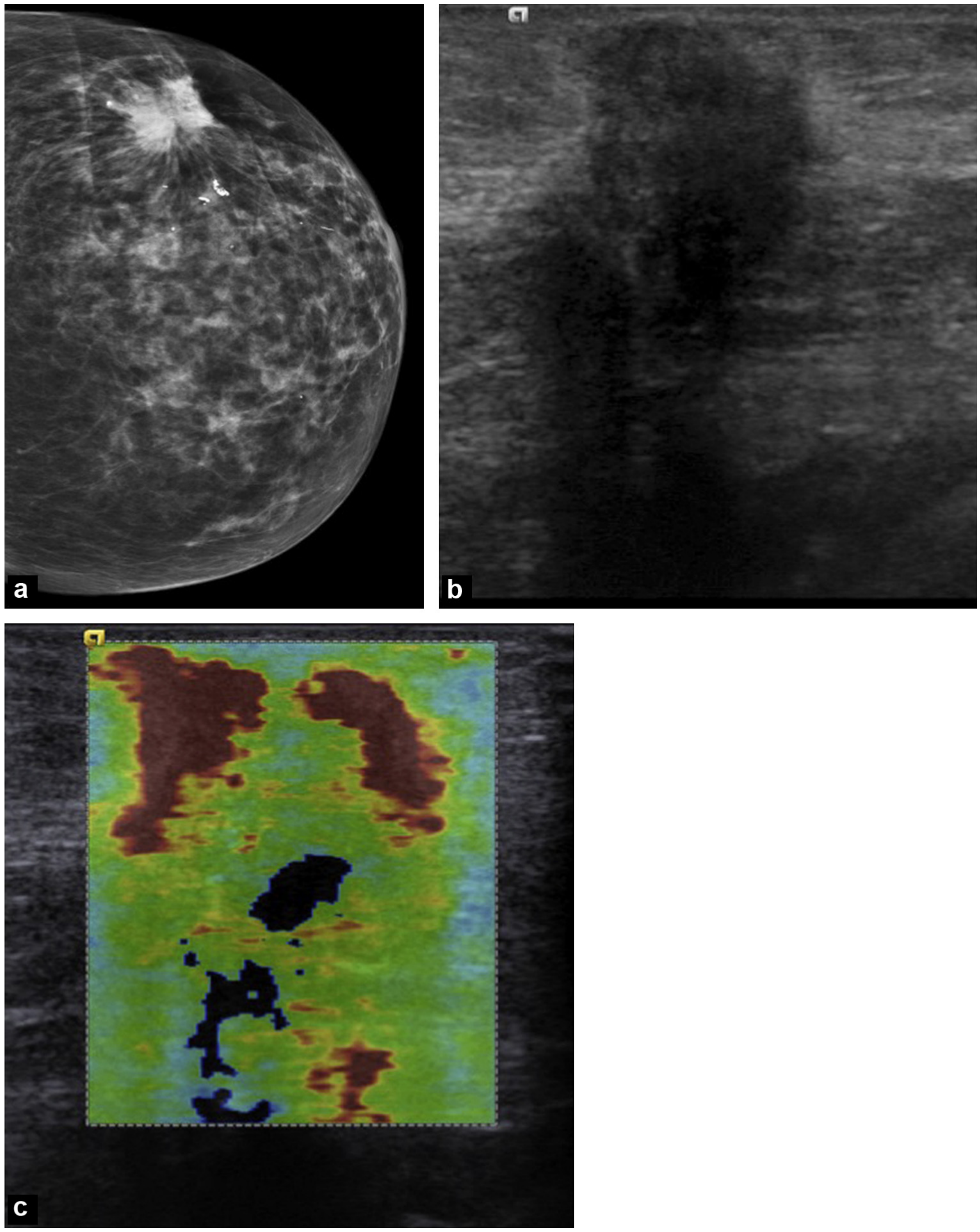

Figure 11. Grade 3 infiltrative ductal carcinoma. Acoustic Radiation Force Impulse mode (Siemens®). In this spiculated malignant lesion (a), attenuation is very high (b), which is commonly seen in very rigid scirrhous lesions. In this type of lesion, shear waves are not generated, leading to signal defects in the centre of the lesion (c).

malignant lymph nodes in a series of 64 lymph nodes (33 reactive, 31 malignant) and showed that elasticity score for malignant lymph nodes (average 3.1) was higher than for benign lymph nodes (average 2.2; $P < 0.0001$). With an elasticity score of 2—3, sensitivity reaches 80.7% as specificity was 66.7%. Same results were found by Tourasse et al. [42] in a population of 65 patients undergoing surgery for breast cancer, in whom 103 lymph nodes were examined by SWE elastography, as 81 lymph nodes were correlated histologically (70 normal, 11 malignant). Elasticity values were significantly different between normal and metastatic lymph nodes ($P < 0.05$). These studies, however, should be interpreted carefully as only a small number of lymph nodes were malignant; moreover, no study has proved that elastography can confirm accurately a micrometastatic invasion.

Conclusion

Free-hand or shear wave elastography is a complementary technique to B mode ultrasound in the ultrasound assessment of breast lesions. If biopsy is still recommended, if ultrasound features are suspicious, elasticity imaging may be useful to increase the diagnostic confidence in an indeterminated BI-RADS 3 or 4a lesion. Elastography also appears to be particularly useful to assess the cystic content of a breast lesion with a pseudo-solid feature.

Disclosure of interest

Corinne Balleyguier has been an invited speaker in symposia organized by Siemens®.

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