Breast elastography: A literature review

A. Goddi ^{a,*}, M. Bonardi ^b, S. Alessi ^c

^a SME – Diagnostic Imaging Medical Center, Varese, Italy

^b Institute of Radiology, San Matteo Hospital IRCCS, University of Pavia, Italy

^c European Institute of Oncology, Department of Radiology, Milan, Italy

KEYWORDS

Sonoelastography;
Breast elastography;
Breast lesions.

Abstract Breast elastography is a new sonographic imaging technique which provides information on breast lesions in addition to conventional ultrasonography (US) and mammography. Elastography provides a noninvasive evaluation of the stiffness of a lesion. Today, two technical solutions are available for clinical use: strain elastography and shear wave elastography. Initial evaluations of these techniques in clinical trials suggest that they may substantially improve the possibility of differentiating benign from malignant breast lesions thereby limiting recourse to biopsy and considerably reducing the number of benign breast biopsy diagnoses. This article reviews the basics of this technique, how to perform the examination, image interpretation and the results of major clinical studies. Although elastography is easy to perform, training and technical knowledge are required in order to obtain images permitting a correct interpretation. This paper will highlight the technique and point out common pitfalls.

Sommario L'elastosonografia mammaria è una nuova tecnica di imaging a ultrasuoni che fornisce informazioni aggiuntive sulle lesioni della mammella rispetto all'ecografia e alla mammografia. Consente una valutazione non invasiva della rigidità tessutale di una lesione. Sono attualmente disponibili due soluzioni tecniche per uso clinico: l'elastografia con strain e l'elastografia shear wave. I primi studi clinici di valutazione di queste tecniche suggeriscono che esse possano migliorare la caratterizzazione delle lesioni mammarie differenziando quelle benigne dalle maligne e riducendo in modo sostanziale il numero di biopsie per lesioni benigne. Questo articolo rivisita le basi tecniche, i criteri interpretativi delle immagini, i principali studi clinici e le possibili cause di errore. Per quanto l'elastosonografia sia di facile esecuzione, richiede tuttavia un training e delle conoscenze tecniche adeguate per ottenere immagini correttamente interpretabili.

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* Corresponding author. SME – Diagnostic Imaging Medical Center, Via L. Pirandello 31, 21100 Varese, Italy.
E-mail address: goddi.alfredo@libero.it (A. Goddi).

Introduction

Mammography and ultrasonography (US) are the diagnostic methods which have shown the highest sensitivity in the detection of breast cancer. However, both methods present some limitations. Mammography performed in dense breasts may often yield false-negative results [1]. US is sensitive in the detection of lesions, but specificity is poor as most solid lesions are benign. In order to obtain an acceptable specificity, various characteristics of the lesions must be evaluated according to the BI-RADS criteria defined by the American College of Radiology (ACR) [2]. Unfortunately, the BI-RADS criteria generate a significant number of false positive results [3]. This limitation leads to an increase in biopsies with a cancer "detection rate" of only 10%–30% [4,5]. Many biopsies are performed in benign lesions causing discomfort to the patients and increased costs.

To overcome these limitations and obtain a more accurate characterization of breast lesions, US elastography was introduced. This technique combines US technology with the basic physical principles of elastography. US elastography is noninvasive and assesses tissue deformability by providing information on the elasticity [6,7]. It is based on the premise that there are significant differences in the mechanical properties of tissues that can be detected by applying an external mechanical force [8,9].

Elastography has proven to be highly specific in the evaluation of lesions situated in various organs: breast, prostate, thyroid, lymph nodes and testes [10–19]. However, this technique is still new, and considering that there are several technological solutions, its role in clinical practice is still to be defined. The aim of this literature review was to clarify the current role of breast elastography.

Elastographic techniques

Elasticity is the property of a body or substance that enables it to be deformed when it is subject to an external force and resume its original shape or size when the force is removed. Different tissues are expected to respond differently according to the specific elastic modulus [22]. Tissue deformation is inversely proportional to the stiffness of the material, and response time (i.e. return to the natural condition) varies as a function of the histotype [23]. In general, adipose tissue is more easily deformed, and fibrous tissue returns to the initial condition more slowly than adipose or muscle tissue [24].

Various tissue compression methods have been proposed in elastography (strain imaging by compression [7], acoustic radiation force impulse (ARFI) [20] and real-time shear velocity (RSV) [21]) which are derived from two technical solutions known as strain elastography and shear wave elastography.

In "strain imaging" by compression the movement of the tissue occurs in the direction of US beam propagation. The most common way to deform the tissue is to apply a slight manual longitudinal compression/decompression using a conventional transducer, or alternatively deformation can be produced by respiratory movements.

The absolute value of the deformation along the longitudinal axis is proportional to the intensity of the compression exerted. However, the force exerted by manual compression is unknown to the equipment and the degree of deformation is calculated exclusively by measuring variations in radiofrequency of the US beam along the axis of the transducer before and after compression. The profile of tissue deformation is converted to an elastic modulus from which an image called elastogram is derived [7]. The impossibility of defining the intensity of the force exerted allows calculation only of the deformability ratio of the various tissues and not the absolute elasticity. For this reason elastography by compression provides only qualitative and not quantitative information.

An alternative solution to the external compression is an acoustic force created by a focused US impulse. This solution is the basis of ARFI and RSV [20,21].

ARFI can be used in two different ways. One is qualitative, as used in strain imaging which employs a short acoustic impulse of high intensity to deform the tissue elements and create a static map (elastogram) of the relative stiffness of the tissues. Another is quantitative, as used in shear wave elastography, which employs a primary acoustic impulse focused on a region of interest where it generates pressure waves in transverse propagation able to deform the tissues. The primary impulse is followed by a few interrogating impulses distributed in the surrounding tissues and designed to calculate the propagation velocity of pressure waves. Propagation velocity and attenuation of the waves are related to the stiffness and visco-elasticity of the tissue. The waves travel faster in stiff tissues than in non-stiff tissues [25]. ARFI quantification provides pressure wave velocity but not spatial distribution. Both the qualitative and quantitative variant of the ARFI method reduce interobserver variability but provide only static information and not dynamic information like elastography by compression.

Unlike ARFI, RSV provides a real-time evaluation of the wave propagation including lateral deformation of the tissues. This is possible because of an original technical solution that generates pressure waves using a conventional transducer and captures the motion by a sequence of thousands of images per second to create a specially designed beamformer [26,27]. Once local propagation velocity of the pressure waves is measured RSV creates a two-dimensional map representing the distribution. The exact values of tissue stiffness expressed in kiloPascals (kPa) can be measured in areas of lesser deformability [28]. ARFI "shear wave" and RSV are quantitative imaging techniques that provide quantitative measures of tissue stiffness with a reduced interobserver variability.

Elastographic imaging

The method which is currently the most widely used in clinical settings is real-time elastography (RTE) which generates "strain imaging" by compression. RTE can be performed using conventional US equipment with dedicated software, and this method assesses the relative elasticity of the tissues in a specific area of interest (the RTE-box)

creating an elastogram that is superimposed to the US image and updated in real-time at a frequency of 10–15 Hz [10,22].

Real-time display allows a quick assessment of the strain distribution. The spatial resolution of RTE, which is currently about 1 mm, depends on a number of factors, such as US beam frequency, pulse length and particularly the length of the correlation window [18]. The elastogram, which reflects the relative elasticity of the tissues, is created as a color coded map (the areas of great stiffness are coded in blue, those which are more deformable in red, and green indicates intermediate levels of elasticity). Lighter shades of the base color reflect the different degrees of tissue deformability and correlate with the dynamic range of the analytical system [29]. Some types of US equipment display a gray-scale map in which the stiff tissues are encoded in a darker shade, while tissues of higher deformability are encoded in a lighter shade. Regardless of the type of map, the representation of the relative elasticity may vary according to the tissues present in the area which is being studied, the size of the RTE-box and the intensity of the exerted pressure.

ARFI “strain imaging” provides a qualitative map in gray-scale showing the relative stiffness of the tissues in a region of interest defined by the operator (the ARFI-box) that is evidenced and compared to the corresponding US image. Also in this case the lighter areas represent more deformable tissues than the dark areas [23]. For safety reasons the ARFI method can only create static images and not dynamic sequences like RTE. ARFI “shear wave” imaging provides a numerical value of the pressure wave velocity in the region selected by the operator on the reference US image. It should be emphasized that this value indicates the tissue stiffness only in the region of interest [25].

RSV evaluates pressure wave propagation and provides a two-dimensional map of the visco-elastic properties of a region of interest. The maps show the distribution of tissue stiffness in color code (areas of great stiffness are red, areas of low stiffness are blue, while green indicates an intermediate level of elasticity). The technical equipment currently displays 3–4 elastographic images per second concurrently with the US image. When abnormal stiffness is identified in a specific area of interest, values of maximum and average stiffness and standard deviation can be measured [28]. RSV allows both qualitative and quantitative assessments.

The basic principles of elastography and related reports

Elastography is based on the assumption that cell density is increased in most solid tumors and that this condition changes the tissue elasticity. Krouskop et al. reported different coefficients of elasticity in normal and neoplastic breast and prostate tissues [30].

In the investigation of breast lesions, elastography assesses the deformation of all tissues (adipose, fibrogland and cystic or solid lesions). RTE shows that benign nodules are deformable, whereas malignant lesions tend to be stiff. The stiffness of malignant lesions may be influenced by an intra and extranodular desmoplastic reaction, by neoplastic

infiltration of the interstitial tissue (e.g. scirrhous carcinoma) or infiltration of the intraductal component (e.g. ductal carcinoma in situ) [10]. There are of course exceptions, e.g. tumors of low malignant consistency such as medullary, mucinous and papillary carcinoma and some infiltrating ductal carcinomas, which are less common [31].

Non-viscous fluids are incompressible, and simple cysts should therefore not display signals of deformability at RTE; however, artifacts may produce a typical “tri-stratified” or “target” pattern according to the type of algorithm used by the equipment [14,32]. In some cysts an acoustic “streaming” effect is obtained in response to ARFI [33].

With regard to shear wave elastography of the breast, different pressure wave propagation velocities have been observed in various tissues. This allows a good differentiation of medium elasticity measured in adipose tissue (3 kPa), dense parenchyma (45 kPa), benign lesions (<80 kPa) and malignant lesions (>100 kPa) [34]. In general, the stiffer the tissue, the greater is the velocity with which a pressure wave travels through it. Simple cysts yield a velocity value of 0 as the shear waves do not propagate in non-viscous fluids [35].

Elastographic criteria

In RTE evaluation of breast lesions the two most important characteristics are size and stiffness. Stiff nodules appear larger at elastography than at US resulting in a dimensional difference [36]. This phenomenon has been attributed to a desmoplastic reaction occurring in many breast tumors [37]. The dimensional difference can be expressed as the ratio between the diameter of the lesion on the elastogram as compared to the US image; a ratio of ≥ 1 is suggestive of malignancy [38,39].

As regards the stiffness criteria, various scoring systems have been proposed which compare the presence, distribution and extent of areas of abnormal elasticity. The elastographic score can help the physician choose the most appropriate management of lesions which appear uncertain or benign at US examination [10,11].

The scoring system suggested by Itoh et al. [10] assigns a score from 1 to 5: score 1 indicates deformability of the entire lesion; score 2, deformability of most of the lesion with some small stiff areas; score 3, deformability of the peripheral portion of the lesion with stiff tissue in the center; score 4, the entire lesion is stiff; score 5, the entire lesion and surrounding tissue are stiff. If a lesion is classified between 1 and 3 it is considered benign; if classified 4 or 5 it is considered to be malignant.

A multicenter Italian study proposed a different classification system which takes both solid and cystic lesions into account [14]. Also this system has 5 levels: score 1 indicates a tri-stratified pattern (blue, green and red) typical of cysts; score 2, a mainly elastic lesion; score 3, a mainly elastic lesion, but with some stiff areas; score 4, most of the lesion is not deformable; score 5, a non-deformable lesion surrounded by stiff tissue expressed by a blue margin around the lesion.

Both score systems were insensitive to the volume of the breast as well as the depth and the diameter of the lesions. They are considered accurate and reproducible, but they

should always be integrated with US examination or mammography.

In an attempt to reduce interoperator variability in the differentiation between malignant and benign lesions, some authors have proposed the use of a so-called “strain ratio” or “strain index” [40–44]. Calculation of the strain ratio value is based on determining the average strain measured in a lesion and comparing it to the average strain of a similar area of fatty tissue in the adjacent breast tissue. The strain ratio reflects the relative stiffness of the lesion. In some studies, the average strain index related to malignant lesions was found higher than the strain index related to benign lesions. However, the reported data are not comparable due to the use of different cut-off levels. The semiquantitative method is penalized by a lack of standardization and represents only an indirect measure [35].

Interpretation of images obtained at ARFI “strain imaging” uses criteria similar to those of RTE, evaluating size and stiffness of the lesions. Malignant tumors show a larger diameter at elastography as compared to US and they are encoded in darker shades of gray [36]. Elastography furthermore provides a better visualization of the nodular margins than the US images. It should be kept in mind that fibroadenomas may be less recognizable in the ARFI images as compared to the corresponding US images; in many cases fibroadenomas cannot be distinguished from the surrounding tissue, but in some cases they may appear stiffer or less stiff than the adjacent tissue [33].

A stiffness criteria based on a three-tier system has recently been proposed. This system evaluates if a lesion detected at US is or is not confirmed by the ARFI technique. If the lesion is confirmed it can be classified as Pattern 1 or 3 depending on the shade of gray, light or dark. Lesions which are not confirmed are classified as Pattern 2. Lesions classified as Patterns 1 and 2 are considered benign, whereas lesions classified as Pattern 3 are considered suspicious [45]. At present these criteria have not been tested on large patient populations.

The classification criterion used in ARFI quantification is based on shear wave velocity. Mean shear wave velocity ranges from the “marginal” value of 4.49 to 8.22 ± 1.27 m/s in malignant lesions and from 2.25 ± 0.59 m/s to 3.25 ± 2.03 m/s in benign lesions [46–48]. The individual values differ in the various studies, but the differences are probably related to the number of cases examined, the size of the lesions and their histological type. To ensure adequate sensitivity and specificity a cut-off of 3.065 m/s has been proposed [48].

The proposed RSV criteria are based on visual classification of elastography images and on the measurement of Young’s modulus expressed in kPa. Visual assessment uses a system of four levels: Pattern 1: a homogeneously blue signal indicates no anomaly; Pattern 2: vertical stripe pattern artifacts; Pattern 3: a localized colored area at the margin of the lesion; Pattern 4: heterogeneously colored areas inside the lesion. Patterns 1 and 2 are considered as benign whereas Patterns 3 and 4 are considered as malignant [49]. Quantitative evaluation is based on a calculation of the mean value of Young’s modulus in the areas of greater stiffness. The values that have emerged in clinical trials ($42\text{--}45.3 \pm 41.1$ kPa in benign lesions and

146.6 ± 40.05 kPa in malignant lesions) differ significantly between benign and malignant lesions [3,49]. Some authors have proposed the use of a mean elasticity cut-off of 50 kPa to differentiate benign from malignant lesions [28].

It should be pointed out that various types of tumors with increased tissue stiffness are not correctly encoded in the elastography map and do not allow measurement of Young’s modulus [3,35]. However, most of these tumors present a surrounding margin with elevated shear wave values [35]. Simple cysts are easy to classify because shear waves do not propagate in non-viscous fluids (elasticity index = 0) [3,35].

Clinical studies

This literature review includes studies which have contributed positively to the clinical validation of the method.

Real-time elastography (RTE)

Itoh et al. [10] published one of the first clinical trials aimed at evaluating the diagnostic possibilities of RTE by examining 111 nodules (59 benign, 52 malignant; confirmed by cytology/histology) dimension <30 mm in diameter. US images were classified according to the BI-RADS criteria and elastography images according to a 5 level score system proposed by the authors. Mean score of elasticity was significantly higher in malignant lesions (score 4.2 ± 0.9) than in benign lesions (score 2.1 ± 1). Using a cut-off value between 3 and 4, elastography achieved a sensitivity, specificity and accuracy of 86.5%, 89.8% and 88.3%, respectively. Using a BI-RADS cut-off value between 4 and 5, US reached 71.2%, 96.6% and 84.7%, respectively.

Giuseppetti et al. [50] evaluated the potential usefulness of RTE in the study of 91 nodules (27 benign, 64 malignant; confirmed by cytology/histology) based on the Ueno score system [51] which is identical to Itoh’s system [10] as it was designed by the same workgroup. The study demonstrated RTE sensitivity and specificity of 79% and 89%, respectively. The authors emphasized that histotype and size of the lesions have an influence on the degree of elasticity.

Rizzatto et al. [14] presented a multicenter study of 874 breast lesions submitted to RTE examination (614 benign, 260 malignant; confirmed by cytology/histology) which classified the lesions according to a 5 level score system which was different from the one designed by Itoh et al. [10]. They found a high specificity in benign lesions with a negative predictive value of 98% related to the entire group of lesions and 100% in lesions ≤ 5 mm. The authors also established guidelines for an appropriate use of RTE and image interpretation.

Zhi et al. [15] compared RTE, US and mammography in differentiating benign from malignant breast lesions in dense breasts. They studied 296 lesions (209 benign, 87 malignant) using the score system designed by Itoh et al. [10]. Elastography reached the highest specificity (95.7%) and the lowest false positive rate (4.3%) compared to the other two methods. Diagnostic accuracy and positive predictive value were higher than those of US: 88.2% vs.

72.6% and 87.1% vs. 52.5%, respectively, while sensitivity, negative predictive value and false-negative rate were similar to those of the other two methods. Most false-negative RTE results involved invasive ductal carcinomas in the initial stage and invasive carcinomas with a large central area of necrosis. A combination of RTE and US improved sensitivity (89.7%), accuracy (93.9%), false negatives rate (9.2%), specificity (95.7%) and positive predictive value (89.7%).

Barr et al. [39] presented the results of a multicenter study designed to evaluate sensitivity and specificity of RTE by compression in the characterization and differentiation of breast lesions. A total of 635 lesions were examined (413 benign, 222 malignant; confirmed by cytology) using the size criteria elasticity imaging/B-mode ratio resulting in an overall sensitivity of 98.6% and overall specificity of 87.4%. Sensitivity and specificity obtained by the various centers participating in the study ranged between 96.7% and 100% and between 66.7% and 95.4%, respectively. In view of the high sensitivity in the characterization of lesions, the variability between the different centers revealed an interoperator variability linked to individual differences in the examination technique. This fact suggested that a better standardization was required. Chung et al. [52] raised this issue starting from the observation that RTE is operator-dependent and that the variability between experienced and inexperienced operators might limit reliability and diffusion of the method. To this end, they evaluated the diagnostic potential of computer-assisted quantification by comparing the strain values of the nodules to the visual grading scores according to Itoh et al. [10]. They examined 120 lesions (70 benign, 50 malignant; confirmed by biopsy) documenting the comparability of semiquantitative and qualitative assessment in the differentiation of non-palpable breast masses.

Kumm et al. [53] combined elastographic score and strain ratio in the characterization of breast lesions at low risk in order to reduce the need for biopsies. They studied 310 lesions (223 benign, 87 malignant; confirmed by biopsy) obtaining a sensitivity of 76% and 79%, specificity of 81% and 76%, respectively. Negative predictive value was 90% related to both criteria. These values were lower than those obtained in other studies previously published and demonstrated the poor reliability of strain ratio.

Yerli et al. [54] presented a study of 78 lesions (62 benign, 16 malignant; confirmed by histological analysis) submitted to US examination and RTE to evaluate if the combination of elastographic score and strain index was useful in differentiating benign from malignant lesions. Sensitivity and specificity were 80% and 95%, respectively, related to the elastographic score, 87.5% and 72.6%, respectively, related to US and 80% and 93%, respectively, related to strain index using a cut-off value of 3.52. The authors concluded that semiquantitative evaluation using the strain index does not improve elastographic score accuracy.

Acoustic radiation force impulse (ARFI)

Tozaki et al. [45] studied 40 lesions (18 benign and 22 malignant; confirmed by histological analysis) to investigate the usefulness of qualitative elastography using ARFI in the

differential diagnosis of solid breast lesions. Classification was based on a 3-level visual pattern: all lesions classified as Patterns 1 and 2 were benign and 73% of the lesions classified as Pattern 3 were malignant. Negative predictive value was 100% and this led the authors to conclude that the method is promising in the diagnosis of benign disorders, particularly in complicated cysts without a cystic component on B-mode images.

Tozaki et al. [46] conducted another study in 50 patients to analyze shear wave velocity in normal and pathological breasts using ARFI quantification. Mean velocity in subcutaneous adipose tissue and breast parenchyma was 2.66 m/s and 3.03 m/s, respectively. Mean velocity in 76.5% of malignant lesions was significantly higher than in benign lesions (4.49 m/s vs. 2.68 m/s). In 23.5% of malignant lesions it was not possible to measure shear wave velocity. The authors emphasized that ARFI quantification may be useful in the diagnosis of benign lesions, but further studies are required to identify the most appropriate measurement method.

Meng et al. [47] evaluated the use of ARFI elastography in 92 breast lesions (65 malignant and 27 benign; mean dimension 25.7 mm) in order to compare area ratio (strain imaging) and shear wave velocity with histologic findings. Mean area ratio and mean shear wave velocity in benign lesions differed substantially from the values obtained in malignant lesions (1.08 ± 0.21 m/s vs. 1.99 ± 0.63 m/s and 3.25 ± 2.03 m/s vs. 8.22 ± 1.27 m/s, respectively). The authors concluded that ARFI combined with US may improve the characterization of breast lesions.

Bai et al. [48] investigated shear wave elastography and ARFI imaging for differentiating benign from malignant breast lesions. They examined 143 lesions (102 benign and 41 malignant; confirmed by histology) and found a significant difference between benign (2.25 ± 0.59 m/s) and malignant (5.96 ± 2.96 m/s) lesions. Sensitivity and specificity were 75.6% and 95.1%, respectively. In 63.4% of malignant lesions, shear wave velocity measurement was not possible.

Real-time shear velocity (RSV)

Tozaki et al. [49] studied 100 solid masses submitted to histological analysis to assess the usefulness of classifying visual elastographic images and measuring Young's modulus in the differentiation of benign from malignant lesions. The images were classified on the basis of 4 visual patterns: Patterns 1 and 2 were interpreted as benign and Patterns 3 and 4 as malignant. Sensitivity and specificity were 91.3% and 80.6%, respectively. Young's modulus mean values were 42 kPa and 146 kPa, respectively. The authors concluded that the combination of the two methods may improve characterization of solid breast lesions.

Athanasiou et al. [3] performed RSV and compared the quantitative values of tissue stiffness with histologic findings in 48 breast lesions (28 benign, 20 malignant; confirmed by cytology or histology) mean dimension 14.7 mm. The lesions were occult on mammography but identified by US. Mean elasticity was 146.6 ± 40.05 kPa in malignant lesions and 45.3 ± 41.1 kPa in benign lesions. Complicated cysts were differentiated from solid lesions by

the elasticity value of 0 kPa. RSV specificity was higher than that of US (0.96 vs. 0.63, respectively), while both methods presented a high sensitivity (0.95 vs. 0.96, respectively). Quantitative evaluation provided additional information which facilitated the characterization of breast lesions. The authors emphasized some limitations of the study, i.e. all malignant lesions were infiltrating carcinomas and the elasticity of carcinomas in situ was therefore not assessed.

Evans et al. [28] compared US and RSV in 53 solid breast lesions (23 benign, 30 malignant; confirmed by histology). In order to differentiate benign from malignant lesions they established a mean elasticity cut-off of 50 kPa. Comparison between RSV and US (using BI-RADS classification) showed sensitivity: 97% vs. 87%, specificity: 83% vs. 78%, positive predictive value: 88% vs. 84%, negative predictive value: 95% vs. 82% and accuracy: 91% vs. 83%, respectively. RSV yielded a higher diagnostic accuracy than US.

Conclusions

Breast elastography has recently been subject to substantial attention as it has proven to reach an adequate specificity and a high negative predictive value in combination with US. The usefulness of breast elastography has been confirmed particularly in small nodules, complex cysts or cysts with a corpuscular content. Elastography may reduce the need for biopsy in lesions classified as BI-RADS 3 on US image and postpone follow-up. Elastography has a significant role in the management of nodules <5 mm which are visible on the US image, but not on mammography, in which reduced deformability may lead to biopsy rather than monitoring as required by the current guidelines.

Strain imaging elastography is useful in the assessment of elastic tissue properties thanks to the short examination time required, real-time display, immediate interpretation and limited cost, and the criteria adopted in the image interpretation have proven to be adequate in clinical practice. However, the method has certain limitations, as it is an exclusively qualitative method which may be influenced by histotype and lesion size, it is an operator-dependent technique which requires special training, and the use of semi-quantitative indices does not improve the performance of the method and does not reduce interoperator variability.

The limitations of real-time elastography can be compensated by shear wave elastography, which is a quantitative method providing a more accurate assessment of the spatial distribution of tissue stiffness. However, also shear wave elastography has limitations such as the difficulty in measuring shear wave velocity in very stiff breast lesions. In this type of tumors real-time elastography has demonstrated a high sensitivity which can compensate for the limitations of shear wave elastography.

Considering that these two technical solutions can complete each other they should be combined to overcome the limitations of both.

Conflict of interests

The authors have no conflict of interests to disclose.

Appendix A. Supplementary material

Supplementary material related to this article can be found online at <http://dx.doi.org/10.1016/j.jus.2012.06.009>.

References

- [1] Saarenmaa I, Salminen T, Geiger U, Heikkinen P, Hyvärinen S, Isola J, et al. The effect of age and density of the breast on the sensitivity of breast cancer diagnostic by mammography and ultrasonography. *Breast Cancer Res Treat* 2001;67: 117–23.
- [2] Breast imaging reporting and data system (BI-RADS). <http://www.acr.org>.
- [3] Athanasiou A, Tardivon A, Tanter M, Sigal-Zafrani B, Bercoff J, Deffieux T, et al. Breast lesions: quantitative elastography with supersonic shear imaging – preliminary results. *Radiology* 2010;256:297–303.
- [4] Duncan 3rd JL, Cederbom GJ, Champaign JL, Smetherman DH, King TA, Farr GH, et al. Benign diagnosis by image-guided core-needle breast biopsy. *Am Surg* 2000 Jan;66(1):5–9. discussion 9–10.
- [5] Chiou SY, Chou YH, Chiou HJ, Wang HK, Tiu CM, Tseng LM, et al. Sonographic features of nonpalpable breast cancer: a study based on ultrasound-guided wire-localized surgical biopsies. *Ultrasound Med Biol* 2006;32: 1299–306.
- [6] Krouskop TA, Dougherty DR, Vinson FS. A pulsed Doppler ultrasonic system for making noninvasive measurements of the mechanical properties of soft tissue. *J Rehabil Res Dev* 1987;24(2):1–8.
- [7] Ophir J, Céspedes I, Ponnekanti H, Yazdi Y, Li X. Elastography: a quantitative method for imaging the elasticity of biological tissues. *Ultrason Imaging* 1991;13:111–34.
- [8] Chen EJ, Novakofski J, Jenkins WK, O'Brien WD. Young's modulus measurements of soft tissues with application to elasticity imaging. *IEEE Trans Ultrason Ferroelectr Freq Control* 1996;43:191–4.
- [9] Frey H. Realtime elastography. A new ultrasound procedure for the reconstruction of tissue elasticity. *Radiologe* 2003;43: 850–5.
- [10] Itoh A, Ueno E, Tohno E, Kamma H, Takahashi H, Shiina T, et al. Breast disease: clinical application of US elastography for diagnosis. *Radiology* 2006;239:341–50.
- [11] Pallwein L, Mitterberger MJ, Struve P, Horninger W, Aigner F, Bartsch G, et al. Comparison of sonoelastography guided biopsy with systematic biopsy: impact on prostate cancer detection. *Eur Radiol* 2007;17:2278–85.
- [12] Miyagawa T, Tsutsumi M, Matsumura T, Kawazoe N, Ishikawa S, Shimokama T, et al. Real-time elastography for the diagnosis of prostate cancer: evaluation of elastographic moving images. *Jpn J Clin Oncol* 2009;39:394–8.
- [13] König K, Scheipers U, Pesavento A, Lorenz A, Ermer H, Senge T. Initial experiences with real-time elastography guided biopsies of the prostate. *J Urol* 2005;174:115–7.
- [14] Rizzatto G, Aiani L, Baldassarre S, Bulzacki A, Della Sala S, Locatelli M, et al. Characterization of breast lesions with real-time sonoelastography: results from the Italian multicenter clinical trial. Abstract-RSNA; 2006. Chicago, USA.
- [15] Zhi H, Ou B, Luo BM, Feng X, Wen YL, Yang HY. Comparison of ultrasound elastography, mammography, and sonography in the diagnosis of solid breast lesions. *J Ultrasound Med* 2007; 26:807–15.
- [16] Lyschchik A, Higashi T, Asato R, Tanaka S, Ito J, Mai JJ, et al. Thyroid gland tumor diagnosis at US elastography. *Radiology* 2005;237:202–11.

- [17] Lyshchik A, Higashi T, Asato R, Tanaka S, Ito J, Hiraoka M, et al. Cervical lymph node metastases: diagnosis at sonoelastography – initial experience. *Radiology* 2007;243:258–67.
- [18] Goddi A, Sacchi A, Magistretti G, Almolla J, Salvatore M. Real-time tissue elastography for testicular lesion assessment. *Eur Radiol* 2012;22(4):721–30.
- [19] Aigner F, De Zordo T, Pallwein-Prettner L, Junker D, Schäfer G, Pichler R, et al. Real-time sonoelastography for the evaluation of testicular lesions. *Radiology* 2012;263:584–9.
- [20] Nightingale K, Bentley R, Trahey G. Observations of tissue response to acoustic radiation force: opportunities for imaging. *Ultrason Imaging* 2002;24:129–38.
- [21] Hoyt K, Parker KJ, Rubens DJ. Real-time shear velocity imaging using sonoelastographic techniques. *Ultrasound Med Biol* 2007;33:1086–97.
- [22] Shiina T, Nitta N, Ueno E, Bamber JC. Real time tissue elasticity imaging using the combined autocorrelation method. *J Med Ultrason* 2002;29:119–28.
- [23] Nightingale K, Soo MS, Nightingale R, Bentley R, Trahey G. In vivo demonstration of acoustic radiation force impulse (ARFI) imaging in the thyroid, abdomen, and breast. *Ultrasonics symposium. IEEE* 2001;2:1633–8.
- [24] Nightingale K, Soo MS, Nightingale R, Bentley R, Stutz D, Palmeri M, et al. Acoustic radiation force impulse imaging: remote palpation of the mechanical properties of tissue. *Ultrasonics symposium. IEEE* 2002;2:1821–30.
- [25] Nightingale K, Stutz D, Bentley R, Trahey G. Acoustic radiation force impulse imaging: ex vivo and in vivo demonstration of transient shear wave propagation. *Biomed Imag* 2002;525–8. Conference Publications.
- [26] Bercoff J, Tanter M, Fink M. Supersonic shear imaging: a new technique for soft tissue elasticity mapping. *IEEE Trans Ultrason Ferroelectr Freq Control* 2004;51:396–409.
- [27] Fink M, Tanter M. Multiwave imaging and super resolution. *Phys Today* 2010;63:28–33.
- [28] Evans A, Whelehan P, Thomson K, McLean D, Brauer K, Purdie C, et al. Quantitative shear wave ultrasound elastography: initial experience in solid breast masses. *Breast Cancer Res* 2010;12(6):R104.
- [29] Goddi A, Sacchi A, Magistretti G, Almolla J. Transrectal real-time elastography of the prostate: normal patterns. *J Ultrasound* 2011;14:220–32.
- [30] Krouskop TA, Wheeler TM, Kallel F, Garra BS, Hall T. Elastic moduli of breast and prostate tissues under compression. *Ultrason Imaging* 1998;20:260–74.
- [31] Tavassoli FA, Devilee P. Pathology and genetics: tumours of the breast and female genital organs. Lyon, France: IARC; 2003.
- [32] Barr RG, Lackey AE. The utility of the “bull’s-eye” artifact on breast elasticity imaging in reducing breast lesion biopsy rate. *Ultrasound Q* 2011;27:151–5.
- [33] Sharma AC, Soo MS, Trahey GE, Nightingale KR. Acoustic radiation force impulse imaging of in vivo breast masses. *Ultrasonics symposium. IEEE* 2004;1:728–31.
- [34] Tanter M, Bercoff J, Athanasiou A, Deffieux T, Gennisson JL, Montaldo G, et al. Quantitative assessment of breast lesion viscoelasticity: initial clinical results using supersonic shear imaging. *Ultrasound Med Biol* 2008;34:1373–86.
- [35] Barr RG. Shear wave imaging of the breast: still on the learning curve. *J Ultrasound Med* 2012;31:347–50.
- [36] Ginat DT, Destounis SV, Barr RG, Castaneda B, Strang JG, Rubens DJ. US elastography of breast and prostate lesions. *Radiographics* 2009;29:2007–16.
- [37] Insana MF, Pellot-Barakat C, Sridhar M, Lindfors KK. Viscoelastic imaging of breast tumor microenvironment with ultrasound. *J Mammary Gland Biol Neoplasia* 2004;9(4):393–404.
- [38] Barr RG. Initial results of breast real-time elasticity imaging to characterize lesions [abstr]. In: Radiological society of North America scientific assembly and annual meeting program. Oak Brook, IL: RSNA; 2006. p. 644.
- [39] Barr RG, Destounis S, Lackey 2nd LB, Svensson WE, Balleyguier C, Smith C. Evaluation of breast lesions using sonographic elasticity imaging: a multicenter trial. *J Ultrasound Med* 2012;31:281–7.
- [40] Ueno E. Fat-lesion ratio in breast elastography. In: 12th world congress of the world federation for ultrasound in medicine and biology; September 2009, Sydney, Australia.
- [41] Cho N, Moon WK, Kim HY, Chang JM, Park SH, Lyoo CY. Sonoelastographic strain index for differentiation of benign and malignant nonpalpable breast masses. *J Ultrasound Med* 2010;29:1–7.
- [42] Thomas A, Degenhardt F, Farrokh A, Wojcinski S, Slowinski T, Fischer T. Significant differentiation of focal breast lesions: calculation of strain ratio in breast sonoelastography. *Acad Radiol* 2010;17(5):558–63.
- [43] Zhi H, Luo B-M, Xiao X-Y, Yang H-Y, Ou B, Wen Y-Y. Strain ratio measurement method: a more objective breast lesion diagnosis method with UE. Vienna, Austria: ECR; 2010.
- [44] Todd R, Kumm, Alec Chau, Margaret Szabunio. Diagnostic performance of freehand elastography with strain ratio measurement in the characterization of breast lesions referred for ultrasound guided biopsy: initial clinical results at a single cancer referral center. In: Eighth international conference on the ultrasonic measurement and imaging of tissue elasticity; 2009, Vlissingen, The Netherlands.
- [45] Tozaki M, Isobe S, Yamaguchi M, Ogawa Y, Homma K, Saito M, et al. Ultrasonographic elastography of the breast using acoustic radiation force impulse technology: preliminary study. *Jpn J Radiol* 2011;29(6):452–6.
- [46] Tozaki M, Isobe S, Fukuma E. Preliminary study of ultrasonographic tissue quantification of the breast using the acoustic radiation force impulse (ARFI) technology. *Eur J Radiol* 2011;80(2):e182–7.
- [47] Meng W, Zhang G, Wu C, Wu G, Song Y, Lu. Preliminary results of acoustic radiation force impulse (ARFI) ultrasound imaging of breast lesions. *Ultrasound Med Biol* 2011;37(9):1436–43.
- [48] Bai M, Du L, Gu J, Li F, Jia X. Virtual touch tissue quantification using acoustic radiation force impulse technology: initial clinical experience with solid breast masses. *J Ultrasound Med* 2012;31:289–94.
- [49] Tozaki M, Fukuma E. Pattern classification of shear wave™ elastography images for differential diagnosis between benign and malignant solid breast masses. *Acta Radiol* December 2011;52:1069–75.
- [50] Giuseppetti GM, Martegani A, Di Cioccio B, Baldassarre S. Elastasonography in the diagnosis of the nodular breast lesions: preliminary report. *Radiol Med* 2005;110(1–2):69–76.
- [51] Ueno E, Iboraki P. Clinical application of US elastography in the diagnosis of breast disease. ECR 5–9 March, Vienna, Austria; 2004.
- [52] Chung SY, Moon WK, Choi JW, Cho N, Jang M, Kim KG. Differentiation of benign from malignant nonpalpable breast masses: a comparison of computer-assisted quantification and visual assessment of lesion stiffness with the use of sonographic elastography. *Acta Radiol* 2010;51(1):9–14.
- [53] Kumm TR, Szabunio MM. Elastography for the characterization of breast lesions: initial clinical experience. *Cancer Control* 2010;17(3):156–61.
- [54] Yerli H, Yilmaz T, Kaskati T, Gulay H. Qualitative and semi-quantitative evaluations of solid breast lesions by sonoelastography. *J Ultrasound Med* 2011;30:179–86.