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WFUMB GUIDELINES AND RECOMMENDATIONS FOR CLINICAL USE OF ULTRASOUND ELASTOGRAPHY: PART 2: BREAST

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Abstract—The breast section of these Guidelines and Recommendations for Elastography produced under the auspices of the World Federation of Ultrasound in Medicine and Biology (WFUMB) assesses the clinically used applications of all forms of elastography used in breast imaging. The literature on various breast elastography techniques is reviewed, and recommendations are made on evidence-based results. Practical advice is given on how to perform and interpret breast elastography for optimal results, with emphasis placed on avoiding pitfalls. Artifacts are reviewed, and the clinical utility of some artifacts is discussed. Both strain and shear wave techniques have been shown to be highly accurate in characterizing breast lesions as benign or malignant. The relationship between the various techniques is discussed, and recommended interpretation based on a BI-RADS-like malignancy probability scale is provided. This document is intended to be used as a reference and to guide clinical users in a practical way. (E-mail: rgbarr@zoominternet.net) **© 2015 Published by Elsevier Inc. on behalf of World Federation for Ultrasound in Medicine & Biology.**

Key Words: **Breast, Breast Cancer, strain, Shear wave, elastography, guidelines, artifacts.**

INTRODUCTION

Elastography is the most noteworthy of the new technologies in recent diagnostic ultrasound systems. Cancer tissue is stiffer than normal breast tissue, and it is believed that the stiffening process begins in the early stage of cancer. The idea of using this stiffness information for diagnosis evolved into a new diagnostic imaging method for detecting tissue elasticity (stiffness) and evaluating it noninvasively and objectively using ultrasound.

Initially introduced in 2003, elastography technology has since improved together with advances in diagnostic ultrasound systems; some form of elastography is available on most commercially available ultrasound

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systems today. Current elastography systems can not only differentiate between benign and malignant tissue but also evaluate histological information by depicting the distribution of tissue stiffness, which may have the potential to evaluate the therapeutic effect of treatment with anticancer agents. Elastography allows for diagnosis and evaluation not only of masses but also of non-mass lesions.

More recently, systems equipped with various methods that apply strain have become available. They include systems with strain elastography (SE), which requires manual compression vibration, and systems equipped shear wave elastography (SWE) technology that supply vibration energy by means of ultrasound. These methods share the concept of bringing qualitative diagnostic capability, i.e., imaging and numerical expression of the stiffness of a target, into the field of ultrasonography, which is primarily concerned with morphological diagnosis. However, these methods differ in terms of their theory, the direction of their development, and their accuracy. Moreover, there are various methods and terms related to diagnostic assessment, such as elasticity scores (Tsukuba score, strain pattern), E/B ratio (width ratio, length ratio), strain ratio (fat-lesion ratio (LFR)), and shear wave measurements (kPa, and m/s), which often lead to confusion when initially using elastography.

Guidelines have been proposed by EFSUMB (Cosgrove, Piscaglia et al. 2013) and JSUM (Nakashima et al 2013).

The WFUMB Guidelines and Clinical Practice Recommendations for Elastography of Breast advocate an elastography classification table (Table 1) to help organize and understand the wide variety of elastographic methods. This report describes this classification and presents and explains the evidence for elastography, its clinical utility, the characteristics of each method, clinical images, etc.

CLASSIFICATION OF ELASTOGRAPHY

Classification by technical method

The WFUMB Expert Members for Elastography Consensus Guideline advocated the following classification (Table 1).

In this table, the applied stress is classified (columns) into Manual Force (achieved by vibration caused by manual compression or involuntary movement of arm muscles, etc., or vibration caused by the patient's muscular contraction or breathing, etc.) and Acoustic Force (achieved by ultrasound irradiation force from a probe), while imaging information is classified (rows) into strain imaging, which is calculated based on (relative) displacement, and shear wave imaging, which is calculated based on the propagation speed of shear waves. In actual clinical practice, shear wave imaging using manual compression for applying vibration/compression is not used for breast imaging, so elastographic techniques can be classified into the following three groups.

- Strain Imaging: Esaote, GE, Hitachi-Aloka, Medison Samsung, Philips, Siemens, Toshiba, Ultrasonix, Zonare
- ARFI displacement: Siemens
- SWS Measurement and Imaging: Siemens, SuperSonic Imagine

Classification by interpretation

Three main diagnostic methods are used to classify lesions based on reported evidence and similar findings from clinical investigations and based on the manufacturer's recommended method in the absence of such reports. Each has its advantages and disadvantages, and not all are supported by good evidence. A detailed explanation of each unit will be given in the latter half of this report.

- Pattern diagnosis is based on color or grayscale elastography images, and a diagnosis is made based on the assessed score.

Terminology: Tsukuba score (Elasticity Score, Strain Pattern)

- Grayscale images from elastography are compared with B-mode images, and a diagnosis is made based on the size ratio of the target lesion.

Terminology: EI/B ratio, width ratio, length ratio

- Diagnosis is made by assigning a relative numerical value to the stiffness (tissue elasticity)

Terminology: Strain ratio (fat-lesion ratio (FLR)), kPa (unit of stiffness), m/s

a. Strain ratio (fat-lesion ratio (FLR)) Semi-quantitative method for numerically evaluating how many times stiffer a target mass is compared to subcutaneous fat by SE.
b. kPa (unit of stiffness), m/s (unit of SWS): quantitative values calculated for the SWS determined by stiffness in Shear Wave Elastography system.

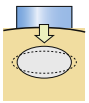
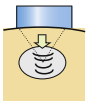
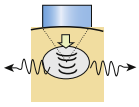
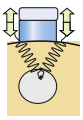
PROCEDURES (TIPS AND TRICKS)

How to obtain a good elastography

Be mindful of the following 3 points when generating images.

Obtain a good B-mode image to get a good elastography image!. Elastography images are often generated based on raw data from B-mode images, and many methods require good B-mode images to succeed. The examiner should switch to elastography after first ascertaining that the B-mode images are optimal.

Table 1. Information on the classification of ultrasound elastography. Different methods for the applied stress and imaging information are organized into columns and rows, respectively.

Measured physical quantity / Methods / Excitation methods	Strain or Displacement		Shear wave speed 
	Strain imaging		**Shear wave imaging**
(A) Manual compression - Palpation, - Cardiovascular pulsation - Respiration	**Strain elastography**		N/A
	ElaXto™ Real-time tissue elastography™ Elastography ElastoScan™ eSieTouch™ Elasticity Imaging 	Esaote Hitachi Aloka GE, Philips,Toshiba Ultrasonix, Mindray Samsung Siemens	
(B) Acoustic radiation force impulse excitation	***ARFI Imaging**		****Point shear wave speed measurement** (Average shear wave speed in a region of interest)
	VirtualTouch™ Imaging (VTI /ARFI) 	Siemens	Virtual Touch™ Quantification (VTQ/ARFI) ElastPQ™ 
			Siemens Philips
			Shear wave speed imaging
			ShearWave™ Elastography: (SWE™) Virtual Touch™ Image Quantification (VTIQ/ARFI)
			SuperSonic-Imagine Siemens
(C) Controlled external vibration			***Transient elastography (Point shear wave speed measurement)
			FibroScan™ 
			Echosens

Methods / Excitation method	Strain imaging	Shear wave imaging
(A) Manual compression Palpation, Cardiovascular pulsation Respiratory	**Strain elastography**	
	Strain or normalized strain Geometric measures Strain ratio E/B size ratio	
(B) Acoustic radiation force impulse excitation	**ARFI Imaging**	**Point shear wave speed measurement**
	Displacement or normalized displacement Geometric measures Displacement ratio E/B size ratio	Shear wave speed (m/s) Young's modulus (kPa)
		Shear wave speed imaging
		Shear wave speed (m/s) Young's modulus (kPa)
(C) Mechanical external vibration		**Transient Elastography**
		Young's modulus (kPa)

Keep the angle of the probe perpendicular to the skin.. Both manual compression and acoustic radiation force are meaningless if the probe moves across the target and this will occur with even slight changes in the probe angle, so it is of paramount importance to ensure that the probe remains perpendicular to the skin. Therefore, it is important to ensure that you find a position that allows for stable vibration, compression, and minimal patient motion (see WFUMB website for examples).

For Strain Imaging, know the best maneuver for each system and target.. There are three main types of compression or vibration methods: "no manual compression," "minimal vibration," and "significant compression"; video clips of each technique are available online (2013). It is not necessary to generate much vibration when imaging shallow lesions, but greater vibration is needed for deep lesions (Table.1).

- No Manual Compression

Place the probe vertically on the skin without consciously applying any vibration/compression. Keep the probe lightly touching the skin and try not to apply pressure (Barr and Zhang 2012). It is important to keep your hands vertical with no pressure (minimal pre-compression) and still on the skin above a target (Barr and Zhang 2012).

Here the minimal vibration energy of the operator and patient is exploited, so images with good spatial resolution are possible. However, in some cases (large breasts or deep lesions) minimal vibration may be required.

- Minimal vibration

Place the probe vertically on the skin and apply very mild vibration. Do not push too hard. The vibration stroke should be no more than 1 mm. Keep the probe lightly touching the skin, and apply extremely fine vibration with a few cycles/second, as if lifting up the skin with the probe, likening the coupling gel to glue. Vibration should be applied as if you are not moving your hand at all when you observe it. This method can be used for relatively shallow lesions to moderately deep lesions, and it allows elastography imaging of small targets several millimeters in size such as non-mass abnormalities. It can depict the distribution of soft areas (areas with significant strain), and it provides useful diagnostic information (see WFUMB website for examples)

- Significant compression

Place the probe vertically on the skin, and apply fairly significant compression/release (approximately 1-2 mm). This method is similar to the dynamic test in B-mode imaging. As long as the tumor is fairly large, adequate elastography images of lesions at most depths can be obtained (see WFUMB website for examples).

- **Results and Limitations**

Strain

Diagnostic approach and evidence. Some reports suggest the utility of strain imaging is to up-grade or down-grade a lesion ultrasound BI-RADS classification of a lesion (Chiorean 2008, Tan, Teh et al. 2008). Other reports suggest elastography can not only be used to differentiate benign and malignant tumors, but can be effective for evaluation of therapy and for lesions that do form a mass (Nakashima and Moriya 2012)

Utility for differentiating benign and malignant masses. The Tsukuba score (Itoh, Ueno et al. 2006) (Elasticity score), EI/B mode ratio and strain ratio (FLR) have been proposed for characterizing breast masses as benign or malignant (Ueno E 2007).

- Tsukuba score (Elasticity score)

The Tsukuba score (Figure 1) is a five-point scale that visually grades the stiffness of a mass. Its sensitivity, specificity, and accuracy for differentiating between benign and malignant breast masses were reported to be 86.5%, 89.9%, and 88.3% (Itoh, Ueno et al. 2006), respectively. A score from 1 to 5 is assigned based on the color (balance of green and blue) inside the tumor

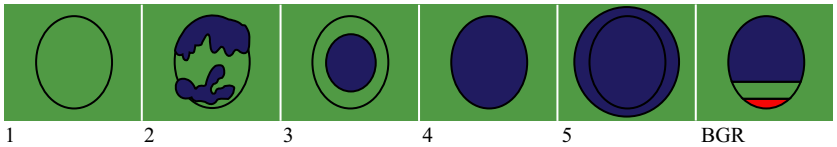


Figure 1. Graphic depiction of the Tsukuba score (Elasticity score) (Itoh, Ueno et al. 2006). This scale combines the size ratio changes and degree of stiffness of the lesion. If the lesion is soft, it is classified as a score of 1; if the lesion has a mixed pattern, it is given a score of 2. A lesion that is hard but smaller on the elastogram is given a score of 3. When the lesion is hard and the same size on elastography as in B-mode, the lesion is given a score of 4. If the lesion is hard and larger on elastography the lesion is classified as 5. It is recommended that lesions with scores of 4 or 5 be biopsied (Itoh, Ueno et al. 2006). Scores of 1 to 3 are classified as probably benign. With some equipment (Hitachi, Toshiba) a tri-laminar appearance of blue, green, and red (BGR) is identified in cysts (tri-color artifact).

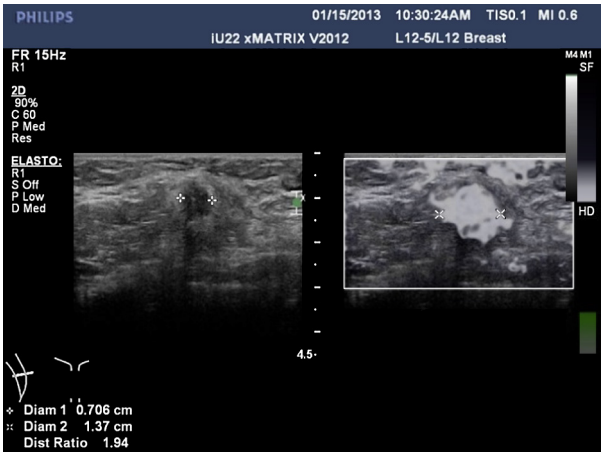


Figure 2. A 45-year-old woman presenting with an abnormality in her right breast on screening mammography. In this Philips image, the SE is present on the right and the B-mode image is presented on the left. By measuring the lesion on the SE image and the B-mode image, the system calculates the EI/B ratio. In this case, the EI/B ratio is 1.94, suggesting a malignant lesion. The final diagnosis is invasive ductal carcinoma.

and the surrounding area, with a higher score indicating a higher diagnostic confidence of malignancy.

Raza S et al.(Raza, Odulate et al. 2010) reported a prospective clinical study using Ito et al.'s elasticity score, and they reported a sensitivity of 92.7% and a specificity of 85.8%.

A ROI that includes various tissue types (fat, fibroglandular tissue, pectorals muscle) in which the lesion accounts for no more than ¼ of the ROI should be chosen. Limitations include the fact that judgment is subjective and that it cannot be used for large tumors because the tumor and the surrounding tissue affect assessment.

Chang JM et al. (Chang, Moon et al. 2011) analyzed factors that affect the accuracy of elasticity scores in a prospective study and determined that the accuracy of elastography differed depending on the depth of the lesion and that accuracy control was necessary.

- EI/B ratio, width ratio, length ratio

Using a real-time dual SE system, Hall (Hall, Zhu et al. 2003) demonstrated that benign lesions are smaller than the corresponding B-mode image while malignant lesions are larger (Figure 2). They proposed utilizing the ratio of the lesion size on elastography to the B-mode size (EI/B-mode ratio) as a diagnostic criterion for benign or malignant. Barr (Barr 2010) in a single center un-blinded trial of 123 biopsy-proven cases using an EI/B-mode ratio of <1.0 as benign and ≥ 1.0 as malignant had a sensitivity of 100% and a specificity of 99% in distinguishing benign from malignant breast lesions. A large multi-center, unblinded trial evaluating 635 biopsy proven cases using Barr's criteria had a sensitivity of 99% and a specificity of 87% (Barr, Destounis et al. 2012). A single center trial of 230 lesions showed a 99% sensitivity, 91.5% specificity, PPV of 90% and a NPV of 99.2% using the EI/B-mode ratio (Destounis, Arieno et al. 2013). The EI/B-mode ratio has been shown to be highly significant between tumor grades of invasive ductal cancers, with the EI/B-mode ratio increasing with tumor grade (Grajo 2013).

Either the lesion length ratio or a lesion area ratio can be used. The lesion is measured in the same position on both the elastogram and B-mode image. The use of a mirror function/copy function is helpful in the measurement technique. Difficulty can occur when measuring the lesion on the elastogram when a fibroadenoma or fibrocystic lesion arises in dense breast tissue. The strain properties of the lesion are similar to the background dense breast tissue. Therefore, one may visualize the combination of the lesion and normal dense breast tissue as one lesion, creating a false positive (Barr 2012). This problem can be avoided by comparing the stiffness of the lesion to surrounding tissue; if it is similar to fibroglandular tissue, it is most likely benign. Using the color scale or LFR may help eliminate this problem. Strain images obtained using the ARFI technique can be interpreted using this technique.

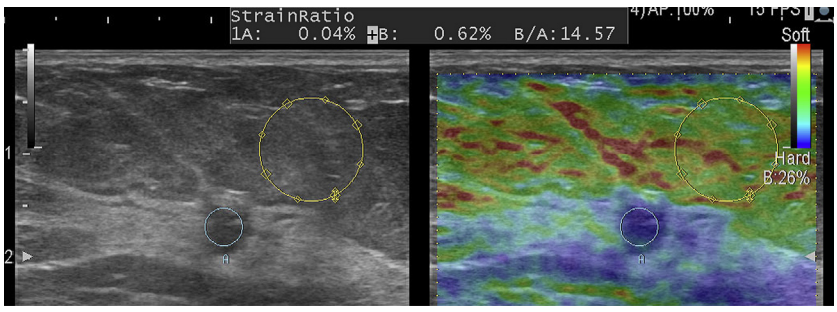


Figure 3. A 69-year-old woman presenting with a 6-mm mass on screening ultrasound. The Hitachi-Aloka SE image is on the right side of the image while the B-mode image is on the left. Regions of interested have been placed in the tumor and in a region of fat. The system calculated the lesion to fat ratio (LFR or Strain Ratio). The Strain Ratio was 14.57 in this case suggestive of malignancy. The mass was diagnosed as an invasive ductal carcinoma (pT1b, pN0, Luminal A type) on core needle biopsy.

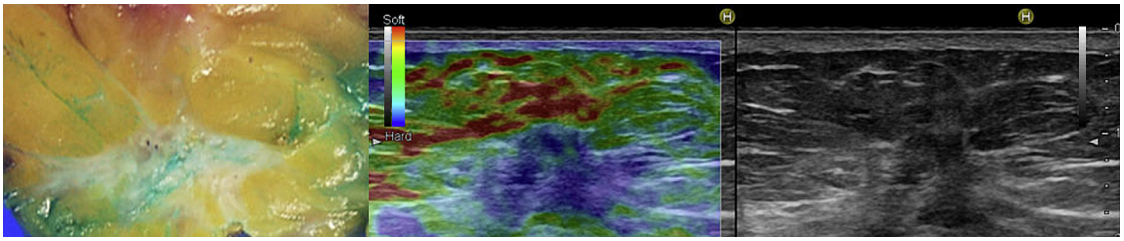


Figure 4. A 55-year-old woman, who presented with a speculated mass on screening mammography. A speculated mass (max length 10 mm) was detected on ultrasound B mode image. The diagnosis was invasive ductal carcinoma (pT2, pN0, Luminal A type) on using core needle biopsy. The Hitachi-Aloka SE image is on the center of the image while the B-mode image is on the right and the pathological image is on the left. The SE's stiff area (blue area) is very similar to the cancer on gross pathology (white area) and is larger than the mass depicted on the B-mode.

- Strain ratio (LFR: lesion to fat ratio)

This diagnostic approach was advocated by Ueno et al. (Ueno E 2007) as a semi-quantitative method of evaluating stiffness. As shown in Figure 3, it is the ratio of the strain in a mass to the strain in subcutaneous fat, and it is a semi-quantitative method for evaluating how much stiffer a mass is compared with fat. The tumor ROI should be placed entirely in the tumor in B-mode. The target ROI for subcutaneous fat should be limited to fat that does not contain fibroglandular breast tissue at a similar depth to the lesion.

Because this method allows evaluation of the stiffness of one specific region of a mass by positioning the ROI, not only is it possible to measure very large tumors, it is also possible to evaluate the stiffness of non-mass abnormalities. This easy to apply approach provides an approximation of tumor stiffness.

Farrokh et al. (Farrokh, Wojcinski et al. 2011) reported a sensitivity of 94.4% and specificity of 87.3% with a cut-off above 2.9 in a prospective study using the strain ratio (FLR). In a study using B-mode, strain pattern (elasticity score), width ratio, and strain ratio, Alhabshi et al. (Alhabshi, Rahmat et al. 2013) reported that width ratio and strain ratio were the most useful methods of lesion characterization, with a cut-off value of 1.1 for width ratio and a cut-off value of 5.6 for strain ratio. Stachs et al. (Stachs, Hartmann et al. 2013) demonstrated the FLR utility in 224 breast masses in 215 patients that the strain ratio was predominantly higher in malignant tumors, i.e., 3.04 ± 0.9 (Mean ± SD) for malignant tumors versus 1.91 ± 0.75 for benign tumors. In a meta-analysis of 2,087 lesions, Sadigh (Sadigh, Carlos et al. 2012) found an overall sensitivity of 88% and specificity of 83% when using strain ratio. Using the length ratio his data showed a sensitivity of 98% and a specificity of 72%.

Estimation of pathological features (diagnosis of non-mass abnormalities and differentiation of pathological features). Many clinicians think SE reflects pathological features relatively well, and there have been many reports of comparisons with resected specimens. A minimal breast cancer elastography image, a macroscopic image of the resected specimen, and an image of hematoxylin and eosin staining are shown in Figure 4. The stiff part (blue) on elastography corresponds to the spread of breast cancer in the radial direction.

In addition, SE subtly depicts not only stiff regions (with little strain) but also soft regions (with much strain), greatly increasing the diagnostic range of ultrasound.

Breast-conserving surgery is the mainstay of breast cancer surgery, but the common widespread intraductal component makes assessment of the extent of resection important. Using elastography to determine tumor spread before breast-conserving surgery, Nakashima et al. (Nakashima and Moriya 2012) reported that it was effective for evaluation of the intraductal component. As elastography was useful for assessing the intraductal component, which is similar to a non-mass abnormality, elastography may also be useful for non-mass abnormalities. Color changes on the elastography of an intraductal component are useful for predicting the pathological features of intraductal progression.

Adamietz et al. (Adamietz, Kahmann et al. 2011) reported that elastography color patterns were useful for comparing and differentiating phyllodes tumors and fibroadenomas.

Recommended imaging techniques. SE supports "no manual compression," "minimal vibration," and "significant compression." It is certainly possible to diagnosis many masses using the "significant compression" approach to elastography, but it is impossible to acquire elastography images in the case of minute lesions such as intraductal lesions using this approach. Therefore, "minimal vibration" is recommended for elastography imaging of minute lesions. In the case of deep lesions, however, "significant compression" may be better for acquiring an adequate elastography image, as the other approaches might not provide sufficient vibration energy.

For beginners, it may be useful to refer to a strain graph that shows in real time the changes in strain over

time to assist deploying these techniques, but experts can usually assess accuracy using the images.

- Displayed Range of Interest (ROI)

Various color or gray scale maps can be used in SE as well as grey scale. To avoid confusion, the scale should always be included in images or discussions. The scale is relative and is based on the range of tissue stiffness in the image. The ROI should partly include subcutaneous tissue and the pectoralis muscle for a more consistent scale range, and it should be expanded to its maximal width to express relative values more accurately. Ribs and lungs should not be included (Barr 2012). In most systems, the color-coding is post processing and the color maps can be changed after acquisition.

- Imaging time

In SE, the color-coding is visualized immediately after the initial vibration (approximately 1 sec), but imaging needs to continue until the color of the entire target is completely stable in order to acquire reliable results. The amount of time required will shorten as your skill improves, so it is recommended that you start by taking plenty of time and continue until the color is stable.

Images and pathological features. The most useful point to remember in everyday practice is that information that can be used to determine benignity without cytology or biopsy can be acquired by differentiating images of cysts, fibroadenomas, and fat islands in patients recalled for closer examination. Elastography also increases confidence that a stiff lesion is a malignancy. Representative images that illustrate the usefulness of elastography for diagnosis are provided elsewhere (see WFUMB website).

- Cystic lesions

There are characteristic SE patterns that can characterize a lesion as cystic.

- Bull's Eye Artifact

A characteristic elastogram, the Bull's Eye Artifact, is observed with benign simple and complicated cysts with some systems (Barr and Lackey 2011). This artifact is characterized by a white central signal within a black outer ring and a bright spot posterior to the lesion. It

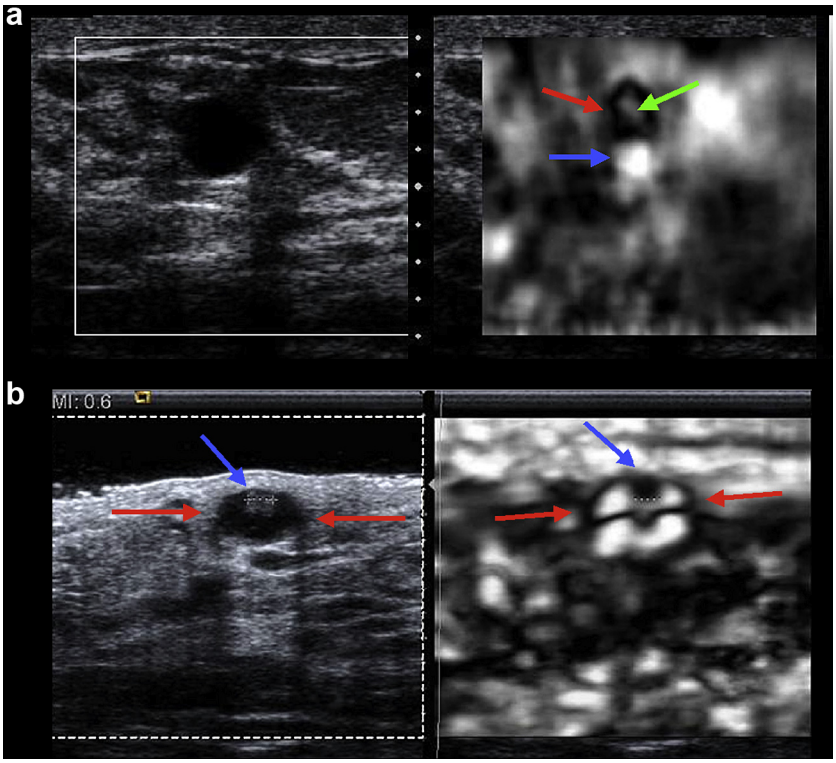


Figure 5. (A) Simple cyst in a 39-year-old woman who presents with a palpable mass. The B-mode image is on the left and the elastogram on the right. The elastogram shows the characteristic "Bull's Eye" artifact, a black area (red arrow) with a central bright spot (green arrow) and posterior bright spot (blue arrow). (B) In this complex mass, the solid component (blue arrow) and the cystic area (red arrow) can be identified in the elastogram. A core biopsy of the solid component demonstrated a 2-mm benign papilloma. Courtesy of Carmel Smith, Queensland Imaging, Brisbane Australia. (Figures with permission from Ultrasound Quarterly (Barr and Lackey 2011)).

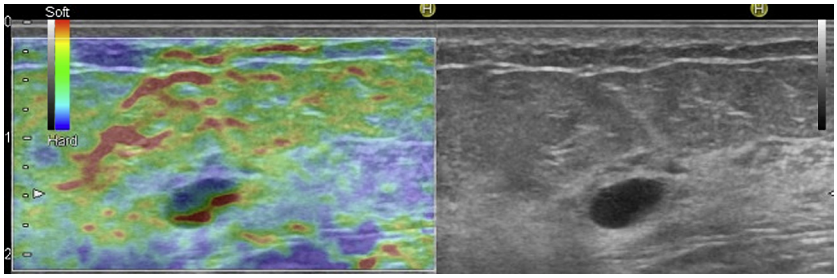


Figure 6. A 45-year-old woman presented with a 10-mm mass on ultrasound screening. On the Hitachi system, the cyst has the BGR artifact, suggesting it is a benign cyst. Diagnosis confirmed by fine needle aspiration cytology.

results from the movement of fluid which causes decorrelation between images (Barr and Lackey 2011) (Figure 5). In a monocentric study, this artifact had a high predictive value for the lesion being a benign cyst. Any solid component in the cyst appears as a solid lesion within the pattern (Figure 5b). Although limited cases have been reported, this artifact is not observed in mucinous or colloid cancers (Barr and Lackey 2011). The artifact can be used to decrease the number of biopsies performed (Barr and Lackey 2011). In one series, 10% of solid lesions on B-mode were in fact complicated cysts (Barr and Lackey 2011). This useful artifact is observed with some equipment (Siemens and Philips) but may not be observed with other equipment.

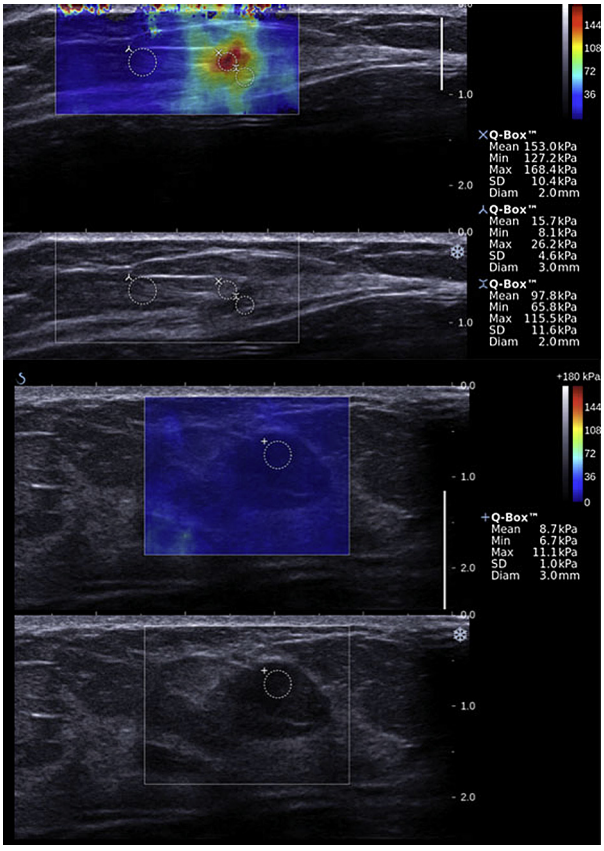


Figure 7. Upper: A 50-year-old woman with an abnormality in her left breast on screening mammography. The upper image is the color-coded SWE image and the B-mode image is below the SWE image. The mass had a high shear wave speed (153 kPa) color-coding red. On biopsy, the lesion was an invasive ductal carcinoma (pT1a, pN0). Lower: A 48-year-old woman who presented with an abnormality in her left breast on screening ultrasound. The mass color-coded blue, having a low shear wave speed (8.7 kPa). On biopsy, the lesion was a fibroadenoma.

- BGR sign

In the case of strain imaging with other vendors' systems, a red band is visualized in the deep part of a lesion that is nearly anechoic. This unique pattern appears when there are no echoes in the mass and increased strain directly deep to it, and it is thought to indicate that the inside of the mass is liquid. It presents as blue, green, and red layers beginning in the shallow area, which is referred to as the BGR sign (Figure 6).

Limitations. Accuracy differs between shallow sites and deep sites due to problems associated with propagation of vibration energy. Further improvement of applications and adjustments to imaging methods are needed.

Reports on the strain ratio have used different cut-off values, so a multicenter study that includes accuracy control is needed.

Summary. There is significant evidence that SE has high sensitivity and specificity for differentiating benign from malignant masses and for non-mass abnormalities. Various methods of interpretation (5 point color scale, length ratio, and lesion to fat ratio) have all been shown to be effective. Currently, there is not enough evidence to suggest that one technique is superior to another.

SWS measurement and imaging

Introduction. With SWE, a quantitative measure of the lesion stiffness can be obtained either in a small fixed ROI (single measurement) or pixel by pixel in a Field-of-View (FOV) box giving a color map. The results are usually coded with red as stiff and blue as soft. The technique

using SE also pertains to SWE, and pre-compression should be avoided.

Recommendations; see strain section
Classification; see strain section
Procedures; see strain section

Results. Based on a recent large multi-center study (BE1) using 2D SWE, a cut-off value of 80 kPa (5.2 m/s) was determined to distinguish BI-RADS category 3 and BI-RADS category 4a lesions with better specificity (Berg, Cosgrove et al. 2012). Examples are presented in Figure 7. Tissue measurements in an ROI can be displayed in speed (m/s) or in pressure/elasticity (kPa). The measurement of stiffness should be obtained from the area of highest stiffness within the lesion or the surrounding tissue. This large multi-center trial demonstrated that when SWS is added to BIRADS classification in B-mode imaging diagnostic accuracy increases (Berg, Cosgrove et al. 2012). The evaluation of SWE signal homogeneity and lesion to fat ratios were the best differentiators of benign and malignant. The addition of SWE increased the characterization of lesion over BI-RADS alone, with a sensitivity and specificity of 93.1% and 59.4% for BI-RADS and 92.1% and 76.4% with the addition of SWE. The authors note that the major value of the addition of SWE is in BI-RADS 3 and 4a lesions where the SWI results are used to upgrade or downgrade the lesion (Berg, Cosgrove et al. 2012, Schaefer 2013). The same study included an analysis of reproducibility, which was very high (Cosgrove, Berg et al. 2012).

The BE1 rules can be summarized as

1. Any of the features analyzed in SWE could improve the diagnostic performance (AUCs) of the BI-RADS score. Thus, SWE features should be combined with B Mode features, and should not be used alone.
2. The best performing SWE features were the quantified maximum stiffness of the lesions (inside or on the periphery), as E Max measurement (Q Box) or visual color assessment (5-level color scale).
3. The publication suggested aggressive and conservative rules (i.e., using different stiffness thresholds) to help assess the level of suspicion of the breast masses, depending on their initial BI-RADS score. In the studied population:

A. All BI-RADS 3 masses with high stiffness (E Max $>$ 160 kPa (7.3 m/s) or E Color = Red with SWE scale set at 180 kPa (7.7 m/s)) could have been upgraded to biopsy. This would have enabled the early management of 4 breast cancers.
B. BI-RADS 4a masses with low stiffness could have been downgraded to follow-up. This would have increased the specificity and PPV for biopsy of the ultrasound diagnosis.
   a. Aggressive rule: low stiffness would be considered with E Max below 80 kPa (5.2 m/s) or E Color light blue or below with SWE scale set at 180 kPa (7.7 m/s).
   b. Conservative rule: low stiffness would be considered with E Max below 30 kPa (3.2 m/s) or E Color dark blue or below with SWE scale set at 180 kPa (7.7 m/s).
   c. The aggressive rule would have enabled a higher improvement in specificity; however, 4 cancers would have been downgraded to follow-up. With the conservative rule, all cancers would have remained in the initial biopsy group, while retaining a significant increase in specificity (Schaefer 2013).

In a study of 158 consecutive patients, Chang (Chang, Moon et al. 2011) found that the mean elasticity values were significantly higher in malignant masses (153 kPa +/- 58) than benign masses (46kPa +/-43) ($P<0.0001$). They determined an optimal cut-off value of 80 kPa (5.2 m/s) which resulted in a sensitivity and specificity of 88.8% and 84.9%, respectively. The area under the ROC curve was 0.898 for conventional US; 0.932 for SWE; and 0.982 for the combined data. In a study of 48 breast lesions, Athanasiou (Athanasiou, Tardivon et al. 2010) found similar results with similar stiffness values for benign lesions (45 +/- 41 kPa) and malignant lesions (147 kPa +/- 40)($P<0.001$). Their results suggest that the addition of SWE to conventional ultrasound could be used to decrease the number of biopsies performed in benign lesions. In a small series Evans (Evans, Whelehan et al. 2010) found the sensitivity and specificity for SWE (97% and 83%) to be better than B-mode alone (87% to 78%). In their series, they used a cutoff value of 50 kPa (4.1 m/s). They also confirmed that the technique is highly reproducible.

Quantitative pSWE with ARFI can be used for characterizing breast masses. In a series of 161 masses, including 43 malignancies, using a SWS cut-off of 3.6 m/s (38 kPa), a sensitivity of 91% and a specificity of 80.6% were achieved (Tozaki, Isobe et al. 2012)

3-D shear wave elastography is in development (Youk, Gweon et al. 2012, Lee, Chang et al. 2013) and no recommendations can be made at this time.

Limitations. When using pSWE (Virtual Touch Quantification™ (VTq) (Siemens Ultrasound)), where a single measurement is obtained from a small ROI, it is not possible to determine where the area of highest stiffness is located on the B-mode image. Multiple measurements within the lesion and surrounding tissue need to be obtained to acquire optimal measurements. The measurement within the tumor often results in "x.xx" signifying that an adequate shear wave for evaluation was not obtained (Barr 2012). Bai (Bai, Du et al. 2012) reported that if a lesion is solid and x.xx is obtained the lesion is most likely a malignancy. With this assumption,

they obtained a sensitivity and specificity of 63.4% and 100%.

Shear waves do not propagate in low viscosity liquids; therefore, simple cysts will not be color-coded. Shear waves are detected using ultrasonic echo signals. Therefore, shear waves cannot be detected in areas with extremely low B-mode signals (anechoic). These regions appear void of signal and are not color-coded. Examples are shadowing from ribs or tumors with significant shadowing (Barr 2012).

Quality Factor. In very stiff lesions such as invasive cancers, shear waves may not propagate so that no results are obtained. The area with no results is not color-coded (Barr 2012) and interpretation is not possible. In general, however, the desmoplastic reaction surrounding the tumor will be stiff and appear as a stiff (red) halo surrounding the lesion. Even if the entire mass is not coded as stiff, heterogeneity of the SWE is part of the criteria for a suspicious lesion. Pre-compression must be avoided as this can create the same appearance in a benign lesion (Barr and Zhang 2012).

In a large number of malignant lesions, the area identified on B-mode as the hypoechoic mass does not code on SWE because a shear wave is not identified or may code with a low c_s. Bai found that 63% of breast malignancies have this finding (Bai, Du et al. 2012). Preliminary evaluation of this phenomenon suggests that shear waves may not propagate as expected in some cancers (Barr 2012) (Figure 8). The shear waves in these tumors demonstrate significant noise that may be incorrectly interpreted as a low SWS by the system. The addition of a quality measure that evaluates the shear waves generated and determines if they are adequate for an accurate c_s measurement will help in eliminating possible false negative cases (Barr 2014, Barr 2012) (Figure 9).

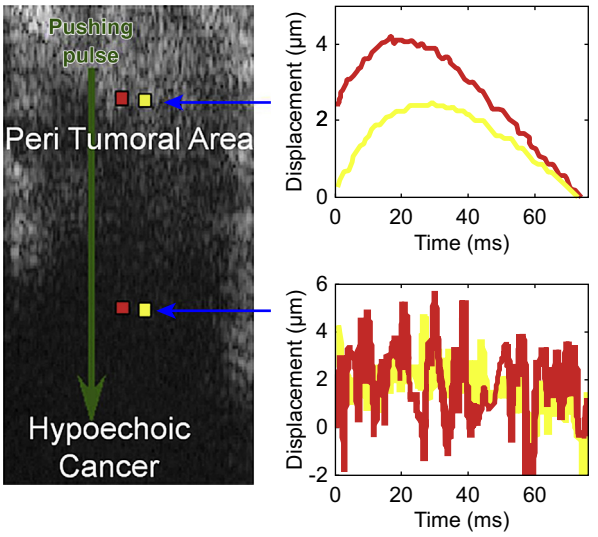


Figure 8. A 57-year-old woman presented with a palpable mass in her right breast. Mammographic and sonographic workup indicates a BI-RADS 4b lesion that proved to be a poorly differentiated invasive ductal cancer on biopsy. The cancer is the hypoechoic mass in the deeper portion of the image. Two waveforms were obtained using the acoustic radiation force impulse technique, one in the tumor and one in the peri-tumoral area. The one taken deeper is from the cancer. The more superficial one is taken in the peritumoral area. The waveform from the cancer is all noise and not interpretable. The waveform in the adjacent peri-tumoral tissue has more noise than in the fat signals but is still interpretable and provides a shear wave speed (with permission from JUM (Barr 2012)).

RECOMMENDATIONS

Should Elastography be performed/interpreted without B-mode?

Elastography is a complimentary technique to B-mode imaging. Elastography (SE or SWE) should be performed and interpreted along with standard B-mode imaging.

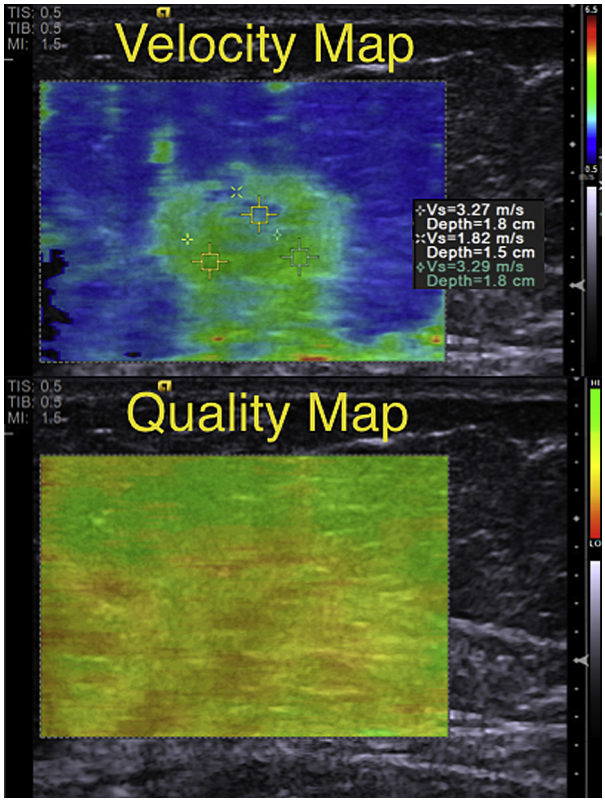
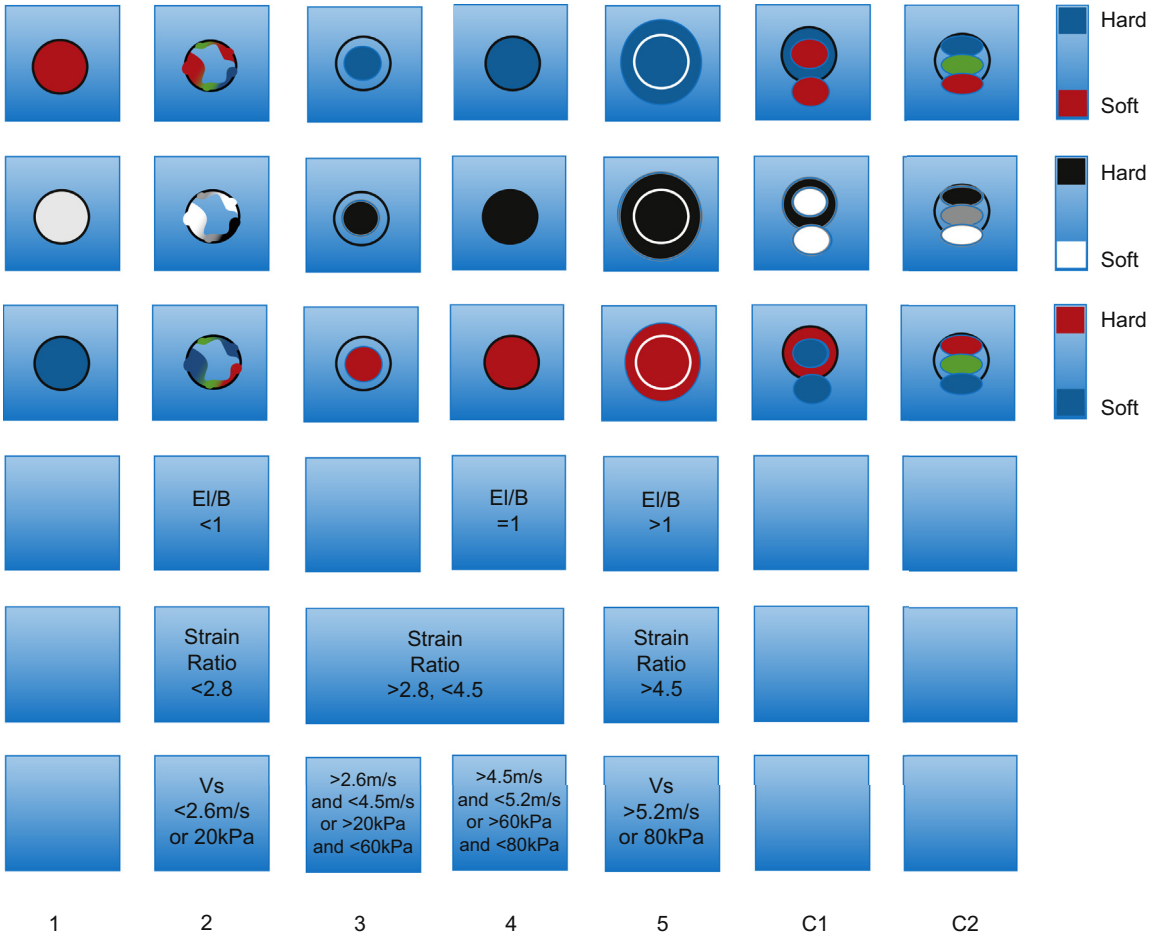


Figure 9. Shear wave elastogram (SWE) of a biopsy proven invasive ductal cancer in a 64-year-old female presenting with a palpable mass. The velocity map in the upper image shows a maximum shear wave speed of 3.27 m/s, suggesting a benign lesion. However, in the Quality Map below, the mass is yellow and red, indicating that the shear waves are not adequate for interpretation. Without the quality map, the lesion could have been classified as a false negative. (Courtesy of Richard G. Barr MD, PhD).

Table 2. Summary of the interpretation methods and their relationships based on a BI-RADS classification system (along the bottom of the table). EI/B - Ratio of the lesion size on elastography to the B-mode size. Strain ratio (fat-lesion ratio (FLR)) - Ratio of target mass stiffness to that of subcutaneous fat (Semi-quantitative value derived from strain elastography (SE)). Vs - Shear wave velocity or shear wave speed (SWS) in units of m/s and stiffness or elasticity in units of kPa are quantitative values in Shear Wave Elastography (SWE) systems.



Should one perform SE or SWE imaging?

Both Strain and SWE have been shown to improve characterization of breast masses. There have been no comparative studies to suggest one technique is better than the other.

How many techniques should be performed on each patient?

No studies have been performed to confirm that one technique is better than the other. Performing more than one technique on a patient may improve confidence in the findings.

Should a benign elastography downgrade a BIRADS 4b, 4c, or 5 lesion to BIRADS 2 or 3?

Downgrading B3 or B4A is reasonable, but downgrading a B4b, B4c, or B5 is not recommended. If a B3 lesion has characteristics of a malignancy on strain or SWE, the lesion should be upgraded to a biopsy. If B-mode or another imaging technique is diagnostic of a B2 (e.g., fat necrosis), elastography should not be used to upgrade a lesion.

Should the Bull's Eye artifact (or BGR Sign) be used to cancel breast biopsies?

The Bull's Eye artifact (seen only with certain strain equipment) has been demonstrated to be highly specific for benign cystic lesions. It is recommended that the accuracy of the finding first be confirmed in the lab before biopsies are cancelled. The BGR artifact (seen with certain equipment) is most likely equivalent to the Bull's Eye artifact, but this has not been biopsy proven.

When should elastography (SE or SWE) be performed?

Elastography should be used to characterize an abnormality identified on conventional B-mode imaging.

Are there situations when elastography should not be used?

Elastography (SE or SWE) should not be used when a lesion is very superficial (<3 mm) from the skin surface. SE should not be used if the lesion is larger than the FOV box.

What are the limitations of elastography in breast imaging?

In addition to those listed above, occasionally a malignant breast lesion may appear soft in shear wave elastography (blue, low *shear wave speed (SWS)*). In these situations, it is important to look at the tissue surrounding the lesion to identify the stiffest part of the lesion. The heterogeneity or increased SWS in surrounding tissues is relevant information and will help characterize the lesion as malignant.

CONCLUSION

There are several methods to obtain and interpret elastography of the breast. No comparative studies have been performed to suggest that one method is better than another.

Table 2 summarizes the various methods of interpretation and how they are related based on a BI-RADS classification system. Elastography systems and the applications themselves continue to evolve, and new tools and new evidence will likely emerge. We anticipate that the direction of development, imaging methods, and diagnostic approaches will change and fragment in the future.

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