

Clinical White Paper

# Breast Elastography™

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# Breast Elastography

## How to Perform and Integrate Into a “Best-Practice” Patient Treatment Algorithm

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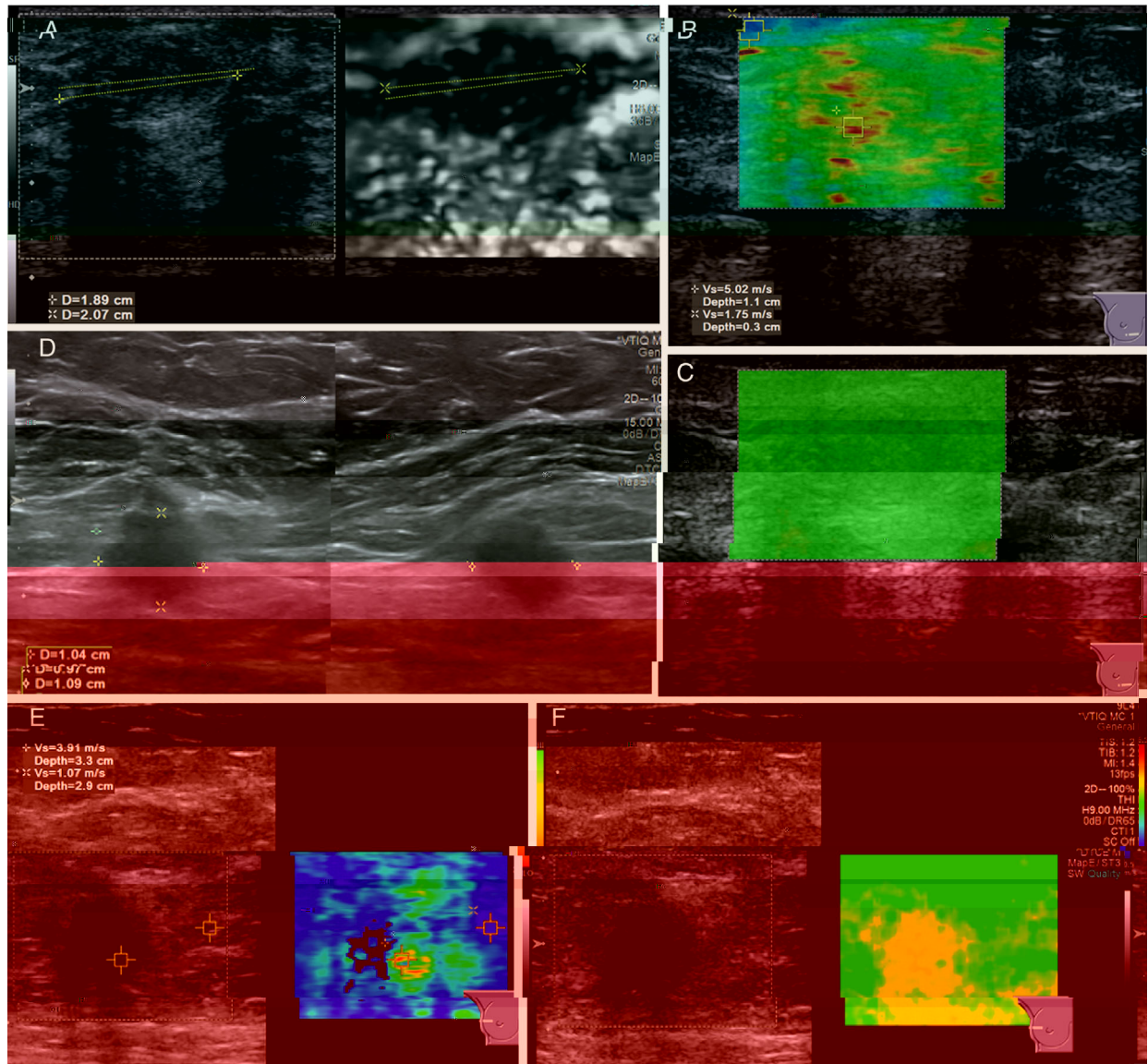
Breast elastography has been available for more than 15 years but is not widely incorporated into clinical practice. Many publications report extremely high accuracy for various breast elastographic techniques. However, results in the literature are extremely variable. This variability is most likely due to variations in technique, a relatively steep learning curve, and variability in methods between

**Figure 1.** The 3 proposed methods for interpretation of breast strain elastography for a 24-year-old patient with a known fibroadenoma. **A,** On the 5-point color scale with blue as stiff and red as soft, the lesion (dotted line) is stiff, whereas the fatty tissue is soft. The lesion appears smaller than the B-mode image. Therefore, this would have a score of 3. **B,** To calculate the strain ratio, an ROI is placed in the lesion and in fatty tissue. In this case, the strain of fat is 0.675, whereas the strain of the lesion is 0.082, giving a ratio of 8.2, suggestive of a malignant lesion. This measurement is highly dependent on the amount of precompression and the specific US vendor. **C,** To calculate the E/B ratio, the lesion is measured on the B-mode image and on the elastogram. The ratio calculated in this case is  $0.69/0.82$ , equal to 0.84, which is suggestive of a benign lesion.



score of 3 when the lesion is stiff and smaller than on the B-mode image, a score of 4 when the lesion is stiff and the same size as on the B-mode image, and a score of 5 when the lesion is stiff and larger than on the B-mode image. Second, a semiquantitative method, the fat-to-lesion ratio, also known as the strain ratio, has been proposed. Since fat in the breast has relatively constant stiffness between patients, it can be used as a reference standard. In this technique,

**Figure 2. A–C,** Images from a 39-year-old patient with a history of bilateral breast reductions who presented with a new palpable mass. Her mammographic findings were negative; however, she had density D breasts. **A,** Elastogram shows that the lesion (dotted line) measures 1.89 cm on B-mode imaging and 2.07 cm on SE, with an E/B ratio of 1.1, suggestive of a malignant lesion. **B,** Two-dimensional SWE of the lesion shows that the maximum stiffness in the lesion is 5.02 m/s, consistent with a malignant lesion. **C,** The quality map corresponding to **B** shows high quality (green) throughout the 2D SWE. The lesion proved to be fat necrosis on biopsy, a known cause of a false-positive result. **D,** B-mode images from a 32-year-old patient with an abnormal mammogram shows a 1.1-cm BI-RADS category 4C lesion. **E,** On 2D SWE, the lesion has a maximum stiffness value of 3.91 m/s, which is suggestive of a benign lesion. However, on the quality map (**F**), the shear wave quality is poor (yellow), so the measurement should not be trusted. In this case, the SE image (not shown) was suggestive of a malignant lesion. The lesion was poorly differentiated invasive ductal cancer, which was estrogen receptor positive, progesterone receptor positive, and human epidermal growth factor receptor 2 negative on biopsy.



category score is assigned to each lesion or area of interest. We then perform both SE and 2D SWE on each lesion or area of concern. Institutional Review Board approval was not required for this report, as it is a review article.

### Strain Elastographic Technique

Ultrasound systems with SE that does not require manual compression/release are used. Strain elastography should be performed with a linear transducer. Most systems have

linear transducers from 9 to 18 MHz that can be used for SE breast imaging. In larger breasts, a lower-frequency transducer may provide better images. Using these systems, simply holding the transducer still will provide high-quality elastograms, with the applied stress coming from patient breathing and heartbeat cardiac pulsations. There are 2 primary signal-processing approaches for generating a strain image: either estimating the strain based on the radiofrequency/quadrature data or estimating the strain based on the (log-magnitude) detected image. The systems (Siemens Medical Solutions [Mountain View, CA], Philips Healthcare [Bothell, WA], and Mindray [Mahwah, NJ]) that we have validated with reproducible results use the radiofrequency/quadrature data to estimate the strain.

We chose to use a grayscale map, as this has been shown to be the most accurate in a meta-analysis.<sup>13</sup> The most important technical factor is not to compress the breast with the transducer.<sup>20</sup> The use of ample coupling gel is helpful. After obtaining the B-mode image, the transducer is lifted until it just barely contacts the skin to ensure that the breast is not compressed by the transducer when the elastogram is obtained. It is helpful to choose and observe a structure in the far field as the transducer is lifted. The object in the far field will move deeper to the skin surface as the transducer is lifted. The elastogram is obtained when the object is as deep in the far field as possible and adequate contact is still maintained. The B-mode image may suffer, but this is important for obtaining an optimal elastogram. With this technique, there should be consistent images on a cine clip from SE, confirming that the appropriate technique is being used. It may be difficult to keep the transducer stable without movement and to maintain the same amount of minimal pressure. Supporting the arm or wrist on the patient is important for controlling the transducer pressure. An elastographic maximum length-to-B-mode maximum length (E/B) ratio is used as a semiquantitative method of analysis. The measurement can be taken in any plane and any location, although the center of the lesion is preferred. The E/B ratio can be up to 3; therefore, taking the measurement in an area of the lesion that is approximately 1 cm is recommended. An E/B ratio lower than 1 is classified as a benign lesion, whereas an E/B ratio of 1 or higher is considered malignant. Low-grade tumors such as mucinous

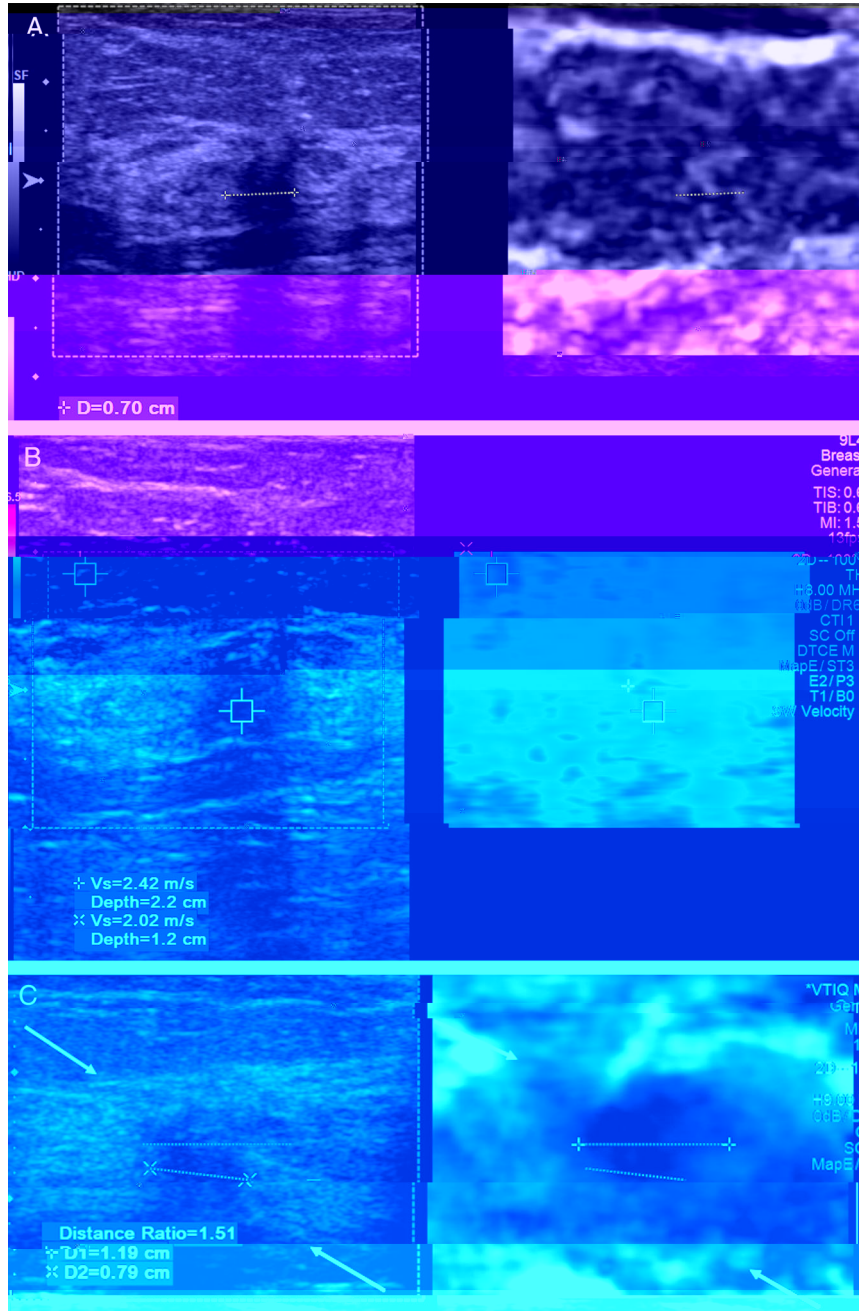
cancers and ductal carcinoma in situ can have ratios close to 1.<sup>21</sup> Three measurements are made, and the one with the highest ratio is used.

When a benign lesion such as a fibroadenoma or fibrocystic change is present in fibroglandular tissue, the stiffness of these benign lesions and fibroglandular tissue is similar. Therefore, identifying the length of the lesion becomes problematic. In this situation, comparing the stiffness with the fibroglandular tissue is helpful. If the lesion is benign, the stiffness is similar to the fibroglandular tissue, whereas if it is malignant, the lesion will be easily identified, as it is substantially stiffer than the fibroglandular tissue (Figure 3).

#### *Two-Dimensional SWE Technique*

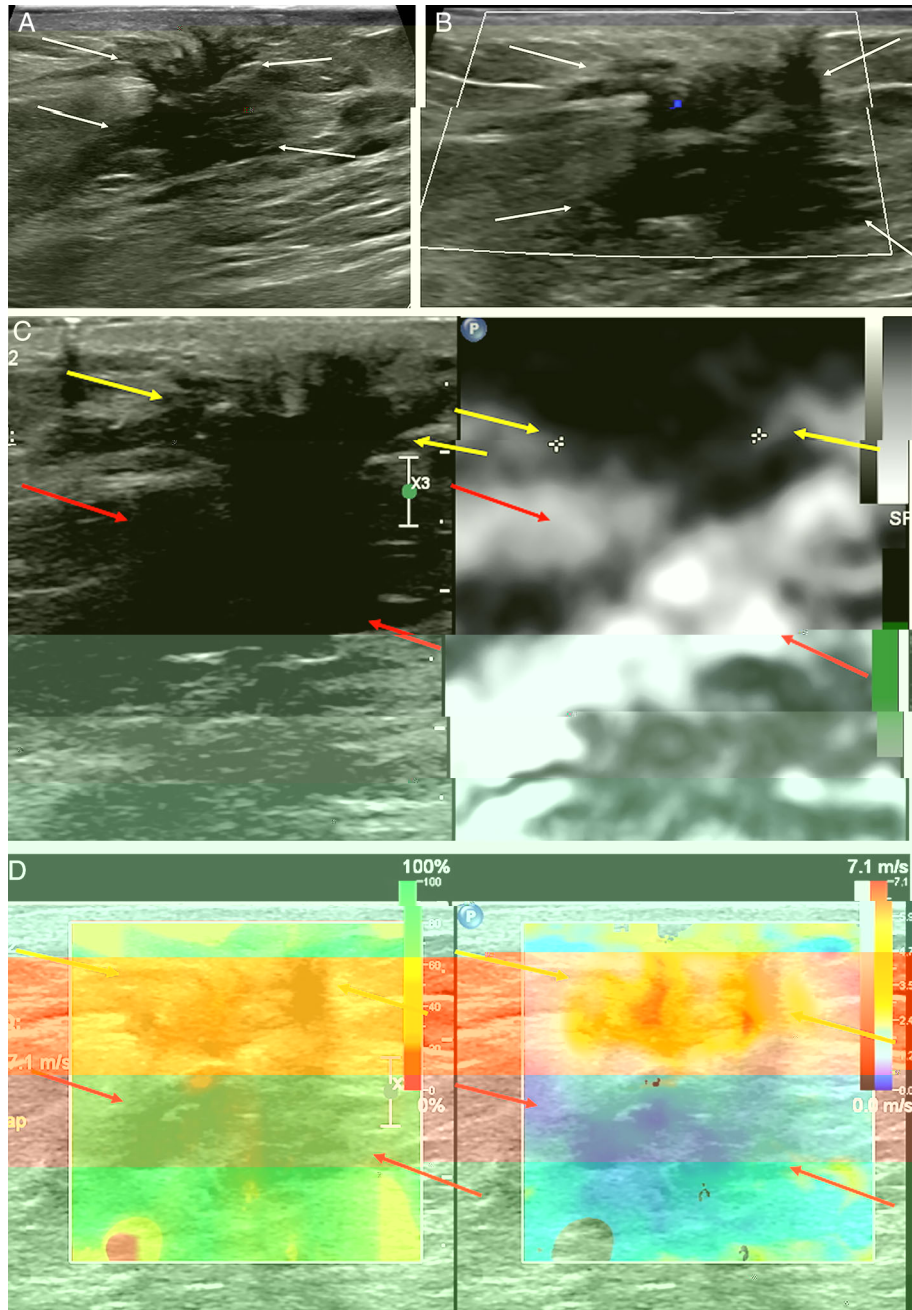
In our experience, the 2D SWE systems from multiple vendors provide similar results with less inter-vendor variability compared with SE. A linear transducer that is optimized for breast elastography should be used. The frequency varies by vendor and can range from 9 to 15 MHz. With a higher-frequency transducer, imaging of denser or large breasts may not provide shear wave results greater than 4 cm deep. As in SE, pressure from the transducer markedly affects the elastographic results. A method of obtaining consistent results has been described.<sup>20</sup> Breast cancers often are not color coded or give false-negative results due to the marked stiffness of breast cancers.<sup>5,17</sup> These are sometimes referred to as “blue cancers” or “soft cancers” (ie, very stiff cancers may look soft on SWE). The use of a quality map is helpful in identifying this artifact. The artifact is discussed in detail elsewhere.<sup>5</sup> We use a cutoff value of 4.5 m/s (60 kPa) to characterize breast lesions based on our previous studies, and this number is applicable for multiple vendors. However, this cutoff is extremely dependent on the amount of pressure applied with the transducer. Each center should have a standard method of controlling the degree of compression, so that all examiners perform the measurements uniformly. Three measurements are taken within the lesion or the surrounding ring if present (3 mm) in the area with the highest stiffness. The ROI should only include the area with the highest stiffness. The stiffest value in the ROI is used. The average of the 3 maximum values is used as the final result.

**Figure 3.** When a benign lesion such as a fibrocystic change is present surrounded by glandular tissue, the stiffness values of both are similar, and it is difficult to identify the lesion on SE. **A**, On this SE image of a 60-year-old patient with a palpable lump and negative mammographic findings, the lesion (dotted line) is seen in the B-mode image (left). On SE, the lesion is difficult to identify. The dotted line on the B-mode image has been copied to the SE image. This is because the lesion has similar stiffness as the surrounding tissue. **B**, However, on 2D SWE, it has benign stiffness with a stiffness value of 2.42 m/s. If the lesion were malignant, it would be stiffer than the surrounding glandular tissue, as in **C**. Note that the white arrows point to the glandular tissue, whereas the dotted line measures the mass on B-mode imaging and SE. The malignant lesion is clearly identified on SE as black; the glandular tissue is light gray; and fat is white. In this case, the E/B ratio is 1.51, concordant with the biopsy result of invasive ductal cancer.





**Figure 5.** Recurrence in a surgical scar can be detected with elastography. The recurrence is stiffer than the surgical scar. This 85-year-old patient had a left lumpectomy 12 years previously and presented with a changing scar on a physical examination. **A**, B-mode image of the postsurgical scar (white arrows). The lesion is an irregular hypoechoic mass. **B**, A Doppler evaluation shows a small amount of flow in the superior portion of the mass. **C**, On SE, the upper third of the scar (yellow arrows) is very stiff, whereas the remainder of the scar is soft (red arrows). **D**, On 2D SWE, the same stiffness pattern is identified, with the superior third having a stiffness value of 7.3 m/s (yellow arrows) and the remainder of the scar having a stiffness value of 2.1 m/s (red arrows). Biopsy of the stiff portion of the scar confirmed recurrence of invasive ductal cancer. It is important to note that elastography can be used to help direct and focus biopsy.



benign lesion, the posttest probability of malignancy is 2%.<sup>13</sup> Breast Imaging Reporting and Data System category 4C and 5 lesions are biopsied even if the elastographic results are suggestive of benign disease. The only false-negative lesion that we have observed is lymphoma. Lymphoma in the breast, whether primary or secondary, presents as a well-circumscribed hypoechoic lesion with markedly increased blood flow on color or power Doppler imaging<sup>24</sup> and is soft on elastography. Lesions with these characteristics of lymphoma are biopsied, especially if the patient has a known diagnosis of lymphoma.

If SE is suggestive of a malignant lesion and 2D SWE is suggestive of a benign lesion, but the 2D SWE results are of poor quality, the lesion is biopsied. These cases reflect the artifact seen in 2D SWE. If the lesion is suggestive of malignancy on SE, biopsy is recommended whether the 2D SWE image is consistent with a benign lesion with high 2D SWE quality or a malignant lesion.

If SE is suggestive of a benign lesion and 2D SWE is suggestive of a malignant lesion, the first thing to do is to confirm that minimal transducer pressure was used when obtaining the 2D SWE image. Also, one should confirm that the stiffness of fat in the image is within the normal range (1.2–1.4 m/s). If high stiffness is confirmed on 2D SWE, the lesion is biopsied. In our experience, this is a rare occurrence.

## Special Cases

### *Bull's Eye Artifact*

With the validated SE vendors, there is an artifact (bull's eye artifact) that is specific for benign cystic lesions, whether simple or complex (Figure 4). This artifact occurs when all of the material within the cyst is mobile. However, it may not occur if the fluid is extremely viscous. If there is a solid component in the cyst, it will appear as a defect in the artifact (Figure 4). This has been validated in a large study using the Siemens system<sup>19</sup> and had 100% sensitivity and 100% specificity for a benign cystic lesion. The artifact does not occur in mucinous or colloid cancers.

### *Postsurgical Scars*

Postsurgical scars are often intermediate in stiffness (below the cutoff value for malignancy). When a

residual or recurrent tumor is present, it will appear as a stiffer area, usually above the cutoff value for malignancy (Figure 5).<sup>22</sup>

### *Architectural Distortion*

If there are areas of architectural distortion or a palpable mass is present, but no B-mode abnormality is identified, elastography is also extremely helpful. If the area is stiff (above the cutoff value for 2D SWE and stiffer than glandular tissue on SE), the area is biopsied. This can be seen in cases of ductal carcinoma in situ and invasive lobular cancer.

These guidelines have been retrospectively applied to a previously published prospectively collected data set of US-guided breast lesions.<sup>5</sup> Applying these criteria to our previously published series,<sup>5</sup> we would have had sensitivity of 100% (95% confidence interval, 94.2%–100%), specificity of 90.3% (83.2%–95.0%), a positive predictive value of 84.9% (74.6%–92.2%), a negative predictive value of 100% (96.4%–100%), a positive likelihood ratio of 10.3 (5.9–17.5), and a negative likelihood ratio of 0 (0–0.6). A multicenter prospective study is needed to fully validate our protocol and patient treatment algorithm.

## Discussion

When high-quality reproducible elastography can be performed on breast lesions, the number of breast biopsies with negative results can be substantially decreased. Since we incorporated elastography in our practice over the last 10 years, our positive biopsy rate has increased from approximately 20%<sup>16</sup> to 80% without missing breast cancers.

It is our observation that SE systems that require manual compression and release have more artifacts and have a substantial learning curve, making their results less accurate and reproducible. We also believe that using color maps in which small stiffness changes translate into large color changes is also problematic. This was also reported in a large meta-analysis of SE for characterization of breast lesions.<sup>13</sup>

Although, to our knowledge, no study comparing the stiffness values of various vendors using 2D SWE has been published, in our experience, there is no notable difference between vendors, although the cutoff values may be slightly different. The World

Federation for Ultrasound in Medicine and Biology guidelines have reviewed the literature and have given general cutoff values.<sup>4</sup> We have noted that there is a slight difference in 2D SWE systems with regard to false-negative cancers, with some systems having a higher number of false-negative cases. This is most likely related to the acoustic radiation force impulse pulse strength.

A multicenter prospective study is needed to validate our protocol. However, based on the results from our center, the number of callbacks, short-interval US follow-ups, and biopsies with negative results can be substantially decreased by using this protocol. We have found the elastographic results from this protocol to be the most sensitive and specific parameters for characterizing breast lesions. If confirmed by larger studies, a requirement for the addition of elastography to the US BI-RADS should be strongly considered.

In conclusion, both high sensitivity and specificity for breast lesion characterization can be obtained by combining results from SE and 2D SWE, which has important implications for patient treatment, with the potential for substantially decreasing the number of breast biopsies with negative results, thereby improving patient care, reducing patient anxiety, and saving health care dollars. Knowledge of false-positive and false-negative lesions also improves the accuracy of interpretation. Careful attention to technique is critical to ensure accurate and reproducible outcomes.

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