REVIEW ARTICLE

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EVALUATION OF ELASTOGRAPHY IN BREAST NODULES: COMPARISON BETWEEN QUANTITATIVE AND SEMI-QUANTITATIVE TECHNIQUES

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ABSTRACT

INTRODUCTION: Since its introduction into clinical practice in the 1970s, ultrasound has been a crucial tool for medical diagnostics. Continuous developments, such as Doppler and elastography, have provided new ways of non-invasive assessment of tissue properties. Elastography, in particular, uses changes in tissue elasticity to offer qualitative and quantitative information for diagnosis. It is of special interest due to its wide availability and relatively low cost.

OBJECTIVE: This study reviews the ultrasound elastography technique, exploring its potential applications in differentiating benign and malignant breast lesions, as well as its limitations.

METHODS: The study is a narrative review of the available literature on breast elastography, analyzing studies that investigated the effectiveness of this technique in characterizing breast lesions. Different scoring systems, criteria, and evaluation methods of elastography are considered, as well as studies that use both strain elastography (SE) and shear wave elastography (SWE) to assess breast lesions.

RESULTS: Breast elastography has proven effective in differentiating between benign and malignant lesions, particularly in cases of indeterminate lesions on conventional ultrasound. The combination of conventional ultrasound with elastography, along with semi-quantitative analyses, has shown significant improvements in diagnostic accuracy.

DISCUSSION: Despite its effectiveness, elastography faces some technical limitations, such as the lack of uniformity in commercial systems and the subjectivity in measurements. However, its promising clinical potential makes it an active area of research in various medical fields.

CONCLUSION: Breast elastography is a useful tool in differentiating between benign and malignant breast lesions, especially in cases of indeterminate lesions on conventional ultrasound. The combination with conventional ultrasound and semi-quantitative analysis can significantly improve diagnostic accuracy. However, elastography may have limitations in lesions classified as BI-RADS 4, and the decision to perform a biopsy should still be based on a comprehensive clinical evaluation.

KEYWORDS: ELASTOGRAPHY, BREAST LESIONS, DIAGNOSTIC ACCURACY.

INTRODUCTION

Ultrasound has been widely used for diagnosis since its introduction into clinical practice in the 1970s. Since then, new ultrasound modalities have been developed, such as Doppler, which provides new information for diagnosis. Elastography was developed in the 1990s[1].

Elastography-based imaging techniques have received substantial attention in recent years for non-invasive assessment of the mechanical properties of tissues. These techniques exploit the alteration of soft tissue elasticity in various pathologies to produce qualitative and quantitative information that can be used for diagnostic purposes. Measurements are acquired in specialized imaging modes that can detect tissue stiffness in response to applied mechanical force (compression or shear wave). Ultrasound-based methods are of particular interest due to their many inherent advantages, such as wide availability, including bedside, and relatively low cost. Several ultrasound elastography techniques using different excitation methods have been developed. In general, these can be classified into strain imaging methods that use internal or external compression stimuli, and shear wave imaging that uses traveling shear waves stimuli generated by ultrasound[2].

Tissue stiffness has long been known as a biomarker of tissue pathology. Ultrasound elastography measures the mechanical properties of tissue by monitoring the tissue's response to acoustic energy. Different elastographic techniques have been applied to various tissues and diseases. Depending on the pathology, patient-based factors, and ultrasound operator-based factors, these techniques vary in accuracy and reliability.[3].

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Breast elastography is an ultrasound technique that provides additional characterization information of breast lesions compared to conventional ultrasound and mammography. This technique provides information about the tension or hardness of a lesion, similar to a clinical palpation exam. Two techniques are now available for clinical use: strain (compression-based elastography) and shear wave elastography. Initial assessment of these techniques in clinical trials suggests that they can substantially improve the characterization of breast lesions as benign or malignant[4].

Furthermore, elastography can help reduce the number of unnecessary biopsies in benign breast lesions, especially in Category IV lesions of the Breast Imaging Reporting and Data System (BI-RADS). Ultrasound elastography is a cheap, readily available, useful, quick, and non-invasive method, but it requires specific training and recognition of technical and pathological factors that can influence it[5].

Breast elastography has been available for over 15 years but is not widely incorporated into clinical practice. Many publications report extremely high accuracy for various breast elastography techniques. However, results in the literature are extremely variable[6].

In this context, this review explores through a review the technique of ultrasound elastography and its limitations.

Ultrasound elastography techniques

The currently available techniques can be classified according to the physical quantity measured: 1) strain imaging and 2) shear wave imaging. Stimulation methods include nearly static displacement induced mechanically by active external compression or passively induced physiological motion (orange), mechanically induced dynamic compression using a probe that "taps" on the tissue surface to generate shear waves (green), and ultrasound-induced dynamic tissue, waves with acoustic radiation force impulse excitation (blue) - figure 1.

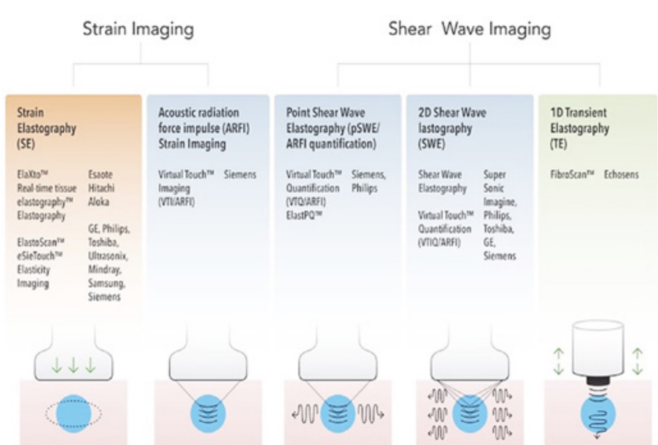

Figure 1 - Differences between techniques.

The successful performance of breast elastography, both strain (SE) and shear wave (SWE), involves several essential technical factors. Below, I summarize the main aspects of the two techniques:

Difference between techniques

1. Strain Elastography (SE)[7]:

Minimum Pre-compression: The application of pre-compression is essential in elastography because when a material is compressed, its stiffness increases. However, in SE, applying significant pre-compression results in noise, while light to moderate pre-compression can produce alternating good and noisy images. Quality images are obtained during the upward compression movement. Applying minimal and consistent pre-compression is crucial.

Maintaining the same image plane: The image plane of the lesion must remain within the field of view (FOV) during data acquisition. The patient should be positioned so that the transducer is perpendicular to the floor, and the patient should be instructed to breathe in a way that moves the lesion within the image plane.

Including different tissues in the FOV: For breast SE, it is important to include various tissues in the FOV, such as fat (softer tissue), fibro-glandular tissue, pectoral muscle, and the lesion. Benign lesions generally have stiffness similar to that of fibro-glandular tissues, while malignant lesions are stiffer than all other tissues.

Choice of color scale: Various color scales can be used in SE, with the grayscale being the most recommended for detecting subtle changes between tissues and identifying noise. It is important to recognize the color scale used, as some display red as rigid, while others use blue to indicate stiffness. Figure 2 illustrates a case of invasive ductal carcinoma using the B-mode and SE technique.

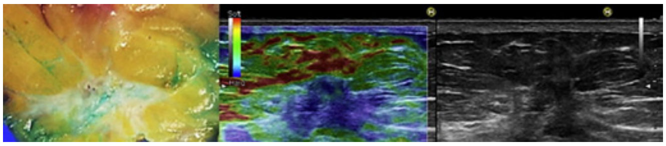

Figure 2 - A 55-year-old woman presented with a spiculated mass on screening mammography. A spiculated mass (maximum length of 10mm) was detected on B-mode ultrasound imaging. The diagnosis was invasive ductal carcinoma (pT2, pN0, luminal A type) confirmed by core needle biopsy. The Hitachi-Aloka SE image is in the center, the B-mode image is on the right, and the pathological image is on the left. The rigid area on the SE (blue area) closely resembles the cancer on macroscopic pathology (white area) and is larger than the mass represented in the B-mode[8].

2. Shear Wave Elastography (SWE)[7]:

Minimal Pre-compression Application: In SWE, the transducer is placed on the breast with minimal pre-compression and held stationary over the area of interest to obtain the measurement. The SWE technique can be either point-based or two-dimensional (2D). Since breast masses, especially malignant ones, tend to be very heterogeneous in terms of stiffness, the 2D-SWE technique is preferred, as the larger FOV can represent stiffness differences and identify the area of greatest stiffness. Figure 3 illustrates two cases using the SWE technique, showing the difference between an invasive ductal carcinoma and a fibroadenoma.

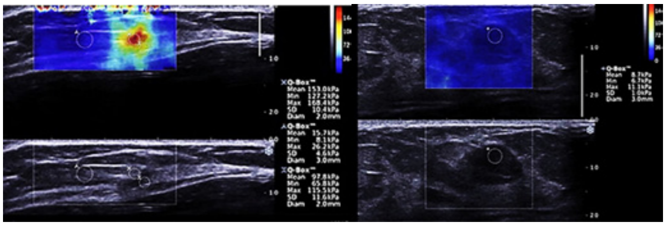

Figure 3 - A 50-year-old woman with an abnormality in the left breast on screening mammography. The left image is the color-coded SWE image, and the B-mode image is below the SWE image. The mass had a high shear wave velocity (153 kPa) coded in red. On biopsy, the lesion was an invasive ductal carcinoma (pT1a, pN0). Right: A 48-year-old woman who presented with an abnormality in the left breast on screening ultrasound. The mass is coded in blue, having a low shear wave velocity (8.7 kPa). On biopsy, the lesion was a fibroadenoma.[8].

The table below lists the main technical factors important in obtaining breast elastography images:

Important Technical Factors

• Minimal pre-compression application for SE and SWE;

• Maintaining the same image plane during acquisition;

• Including various tissues in the FOV, such as fat, fibro-glandular tissue, pectoral muscle, and the lesion;

• Using the appropriate color scale for SE;

• Preferring the 2D-SWE technique to assess the heterogeneity of stiffness in breast masses;

• These technical factors are crucial for obtaining reliable and high-quality elastography images, which are essential for differentiating between benign and malignant breast lesions.

A systematic review with meta-analysis on the use of Shear Wave Elastography (SWE) revealed that SWE has a sensitivity of 0.84 and specificity of 0.87 in the Asian population, while in the Caucasian population, the sensitivity was 0.92 and specificity was 0.89. These results demonstrate that SWE is a valuable tool in identifying malignant breast lesions, regardless of the patients' ethnicity. The diagnostic accuracy of SWE was considerably high in both population groups, with a slight advantage for the Caucasian population (0.95 vs. 0.92). This suggests that SWE is effective in distinguishing between malignant and benign lesions in diverse populations, which is an encouraging finding. The study also compared SWE with another technique, Virtual Touch Tissue Quantification, which showed slightly higher specificity and a superior summary ROC curve compared to SWE. This may indicate that different elastography techniques have their own strengths and that the choice between them may depend on specific clinical needs. The analysis highlighted that maximum stiffness exhibited higher detection sensitivity than mean stiffness (0.91 vs. 0.85). This implies that evaluating maximum stiffness may be particularly useful in identifying malignant lesions, which can guide clinical technique. In conclusion, SWE serves as a precise diagnostic technology in differentiating between benign and malignant breast lesions. This finding is crucial as it suggests that SWE can be widely adopted in clinical practice to increase accuracy in breast cancer diagnosis[9].

Scoring System, Criteria, and Evaluation Methods

Breast elastography uses different scoring systems, criteria, and evaluation methods to differentiate breast lesions and characterize them as likely benign or malignant. These methods are classified into three categories of assessment: qualitative, quantitative, and semi-quantitative[10].

In qualitative evaluation, which is generally less precise, a color map is typically used. The Tsukuba[8] scoring system, which is most commonly used for strain elastography, compares the size of the lesion between B-mode ultrasound and elastographic images. Malignant lesions appear larger on the elastographic image. The stiffness or deformation in the tissue of the lesion is displayed in a black and white or colored image. This system has demonstrated a sensitivity of 87% and specificity of 90% (Figure 4). The system assigns a score of 1-5:

Score 1: Complete deformability of the lesion.

Score 2: Deformability of a large part of the lesion with areas of low stiffness.

Score 3: Presence of a rigid area in the center with peripheral deformability of the lesion.

Score 4: Completely rigid lesion.

Score 5: The entire lesion and surrounding area are rigid. According to this system, elasticity results are considered negative (score 1), equivocal (scores 2-3), and positive (scores 4-5).

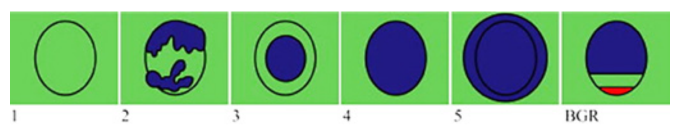

Figure 4. Graphical representation of the Tsukuba score (elasticity score). This scale combines changes in the size ratio and the degree of stiffness of the lesion. If the lesion is soft, it is classified with a score of 1; if the lesion has a mixed pattern, it receives a score of 2. A lesion that is hard but smaller on the elastogram receives a score of 3. When the lesion is hard and the same size on elastography as in B-mode, the lesion receives 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 a score of 4 or 5 be biopsied. Scores 1 to 3 are classified as likely benign. With some equipment (Hitachi, Toshiba), a trilaminar appearance of blue, green, and red (BGR) is identified in cysts (tricolor artifact)[8].

The Italian multicenter study scoring system uses five levels and takes into account both solid and cystic lesions.

Score 1: BGR pattern characteristic of cysts.

Score 2: Mostly elastic.

Score 3: Mostly elastic with some stiff areas.

Score 4: The main lesion is non-deformable.

Score 5: Stiff tissue surrounding a non-deformable lesion.

These scoring methods should always be incorporated into the ultrasound or mammography examination, as they are not sensitive for determining the depth, diameter, or volume of the lesion.

Quantitative assessment:

This method expresses the elasticity of the lesion in units (kPa in shear waves or mm/s in ARFI)[10].

Shear Wave Elasticity Criteria: The color-coded assessment of maximum elasticity is the most useful method in shear wave elastography, which correlates with the maximum elasticity value (kPa). The prognostic value for malignancy is directly proportional to the increase in stiffness, ranging from 0.4% for dark blue to 81.8% for red colors. These are classified into three main categories: Lesions with soft elasticity are represented by dark blue and light blue and considered negative. Lesions with intermediate elasticity are represented by green and orange and considered equivocal. Lesions with high elasticity are represented by red and considered positive. Different cutoff values have been proposed in clinical trials to distinguish benign from malignant lesions.

ARFI Elasticity Criteria: These criteria are used in ARFI quantification. The proposed marginal value for malignant lesions is 4.49-8.22 mm/s, while for benign lesions it is 2.25-3.25 mm/s. An appropriate sensitivity cutoff value of 3.065 mm/s has been recommended.

Semi-quantitative Assessment:[10]:

This assessment uses the strain ratio (SR) to compare the elasticity of the lesion with the surrounding normal breast tissue.

Strain Ratio (SR): The ratio between the average strain in the lesion and the adjacent breast tissue. Malignant lesions have a higher SR than benign lesions. Lesions are considered suspicious for malignancy with an SR greater than [3].

Application of Elastography

In a literature review, a study analyzed the capability of breast elastography to improve the characterization of breast lesions, particularly in cases of indeterminate lesions on conventional ultrasound. The results highlight that ultrasound alone showed high sensitivity (98.1%) in detecting lesions, but with a lower specificity (40.6%). By incorporating elastography, the qualitative analysis demonstrated an increase in specificity (80.2%) and accuracy (81.8%). Notably, the combination of conventional ultrasound with qualitative elastography achieved 100% sensitivity but with 63.2% specificity[11].

Another study evaluated the utility of elastography in characterizing indeterminate breast lesions. Radiologists analyzed both conventional ultrasound and elastography. The results indicate that the combination of elastography and conventional ultrasound led to a significant improvement in sensitivity and specificity compared to conventional ultrasound alone. Semi-quantitative analysis, with measurements such as the strain ratio and width ratio, proved particularly effective in distinguishing between benign and malignant lesions12. Indeterminate breast lesions classified on conventional ultrasound were analyzed. Elastography achieved a sensitivity of 70% and a specificity of 79.6%. The results showed that elastography obtained higher specificity in lesions classified as BI-RADS 3 compared to those classified as BI-RADS 4.

These studies highlight the utility of breast elastography in differentiating benign and malignant lesions, particularly in cases where conventional ultrasound is inconclusive. Qualitative and semi-quantitative elastography analysis has proven effective in improving specificity and diagnostic accuracy. The combination of conventional ultrasound with elastography, along with semi-quantitative assessment, resulted in a high negative predictive value, which may be useful in avoiding unnecessary biopsies in lesions classified as BI-RADS 3. However, elastography alone may not be sufficient to eliminate the need for biopsies in lesions classified as BI-RADS 4, due to its lower specificity. Therefore, the decision to perform a biopsy should still be based on a comprehensive assessment that takes into account all available clinical data[11,12].

Regarding the technique, one study used both SE and SWE to evaluate breast lesions. The analysis of the mean strain elastography ratio (SE) revealed an average value of 4.1, with a cutoff point of 2.86 to differentiate benign from malignant lesions. The area under the ROC curve (AUC) was 0.911 for SE, with a sensitivity of 95.8% and specificity of 89.3%. Regarding SWE, the AUC was 0.929, with a sensitivity of 95.8% and specificity of 85.7%. The results indicate that both SE and SWE are highly effective in distinguishing between benign and malignant lesions. By combining these techniques with B-mode ultrasound, sensitivity can reach 100%, and specificity 96.3%[13].

Another study also employed both SE and SWE in the evaluation of breast lesions. Researchers used multiple variables, including maximum elasticity (Emax), mean elasticity (Emean), standard deviation of elasticity (Esd), lesion-to-fat elasticity ratio, and elastographic classification for analysis. The combination of SWE with SE, incorporating Esd, elasticity ratio, and SWE classification, significantly increased diagnostic efficacy, with an area under the ROC curve (AUC) of 0.89. The study reinforces the effectiveness of combining SWE and SE in differentiating between benign and malignant breast lesions. Specifically, the Esd parameter proved to be a valuable diagnostic factor when used alone or in conjunction with SE and SWE[14].

Both studies emphasize the value of elastography, whether strain elastography (SE) or shear wave elastography (SWE), in differentiating between benign and malignant breast lesions. These techniques provide a detailed analysis of the stiffness of lesions, which can be a crucial indicator of the nature of the lesion.

Limitations of Elastography:

Elastography is affected by technical limitations that hinder the reproducibility of measurements. General ultrasound limitations, such as shadowing, reverberation, and artifacts, can impact elastography. Tissue attenuation with depth limits the accurate assessment of deep tissues. The presence of subcutaneous fat or fluid in the region of interest can affect measurements, especially in cases of obesity or abdominal ascites. System settings and parameters, such as ultrasound frequency and gain, need to be standardized to avoid biased results[15,16].

The lack of uniformity in the design and settings of commercial systems makes comparing measurements between different manufacturers challenging. Measurements in methods that use external stimuli, such as strain elastography, are highly subjective due to the difficulty in controlling applied stress and the variability of physiological motion[15,16].

The selection of the region of interest can be operator-dependent, introducing variability. Assumptions about tissue made by elastography, such as linearity, elasticity, isotropy, and incompressibility, may not be applicable in all clinical situations. Elastography may require more complex models to adequately describe the mechanical properties of tissues, especially in cases of highly heterogeneous tumors[15,16].

Despite its limitations, elastography has promising clinical potential and is widely researched in various medical fields.

FINAL CONSIDERATIONS

The studies indicate that breast elastography is a useful tool in differentiating between benign and malignant lesions, especially in cases of indeterminate lesions on conventional ultrasound. The combination of conventional ultrasound with elastography, along with semi-quantitative analysis, appears to be the most effective approach to improving diagnostic accuracy. However, elastography may have limitations in lesions classified as BI-RADS 4, and the decision for biopsy should still be based on a comprehensive clinical evaluation.

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