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Chapter

Shearwave Elastography in Differentiating Benign and Malignant Breast Lesions

Binafsha Manzoor Syed, Jawaid Naeem Qureshi and Bikha Ram Devrajani

Abstract

Shearwave elastography is a new advance technique of the ultrasound with ultrafast shearwave mode which displays evaluation of the elasticity in real time. As the disease process tend to affect stiffness of the tissue thereby distorting its architecture. This architectural change makes the basic principal of the palpation part of the clinical examination. The shearwave elastography uses the principal of palpation. The output of shearwave is displayed in qualitative mode in the form of color change (ranging from blue to red) and quantitative mode as measure of elasticity in kilopascals (ranging from 0 to 300). The soft tissues are penetrated easily giving a homogenous pattern with blue to green color while cancers show color from red to dark red portraying high elasticity. The scoring system for interpretation of the shearwave results suggest that benign lesions show less (i.e., <200 kPa) elasticity while cancers reach high levels (upto 300 kPa). Shearwave elastography has shown superiority as compared to B-mode ultrasound and mammogram in determining the nature of the breast lesions. It has shown high sensitivity in BIRAD 3 and 4 lesions to downgrade and helps in making accurate diagnosis. It has also shown potential in predicting response of neoadjuvant chemotherapy.

Keywords: breast shearwave elastography, scoring system, breast radiology, ultrasound, breast cancer imaging

1. Introduction

All the tissues of the body have some elasticity due to presence of variable amount of elastic tissue. Pathological insult of the tissues causes change in tissue architecture by disturbing elastic tissue proportion. These pathological insults invariably include chronic inflammatory conditions and cancers as well. Thus the physical examination of the body to make idea of the tissue architecture was the fundamental part of the diagnosis making from the ancient period. Palpation was the sole method of diagnosis in ancient period dates back to more than 5000 years ago during the era of Pharaoh. With advancements in technology, different modes of assessment have been introduced in clinical practice notably imaging techniques. Ultrasound and X-rays are the most commonly used economical, non-invasive and highly reliable techniques in clinical practice. Measurement of the stiffness is quite

old method, the same principal was followed by elastography which measures tissue stiffness and displays it in the output window. Initially strain elastography was introduced where tissue was displaced by applying pressure on tissue by using probe [1].

Shearwave elastography (SWE) is a relatively new (i.e., 2003) advancement of the ultrasound system which uses ultrafast shearwaves for assessment of elasticity of the tissue by using acoustic radiation force excitation and displays in real time [2]. Shearwave elastography has been used in combination with B-mode ultrasound in order to enhance its diagnostic accuracy. A number of studies have been conducted till date showing role of elastography notably assessment of liver fibrosis in chronic hepatitis patients, assessment of thyroid and breast lesions. In all organs it has shown its superiority than conventional B-mode ultrasound in determining the nature of the lesions. In breast diseases it has been studied for its role not only in differentiating benign and malignant lesions, but also investigated in predicting response to neoadjuvant chemotherapy in locally advanced breast cancers. The diagnostic significance of SWE has been studied since its introduction in clinical practice; nevertheless many aspects are still under investigation. In addition, most of the research works done till date has investigated its role in diagnostics; however its role in screening has not been studied yet. This book chapters looks at the basic mechanism of the shearwave elastography, technique of using shearwave elastography in breast, its clinical application in differentiating benign and malignant breast lesions.

2. Mechanism/physics of shearwave elastography

Shearwaves are ultrafast mechanical waves whose propagation is measured while it passes through tissues. The movement of the waves is influenced by the stiffness of the concerned tissue. The mechanism of the shearwaves follows Young's modulus, which has capability to assess difference in the characteristics of different biological tissues and secondly it quantitatively presents tissue stiffness [1]. This reproduction of the stiffness corresponds the palpation of the tissue on clinical examination.

The shearwave elastography is based on two mechanisms including a Mach cone, where different spherical waves in single plane make a Mach cone which allows propagation and rebuilding map of Young's modulus. Secondly the ultrafast mode allows up to 5000–30,000 frames per second depending on the nature of the tissue. In situations of smooth propagation of the waves the real time image generated tends to be clear and homogenous while the areas of stiff tissues show disturbances in the traveling and show high intensity colors with heterogeneous echo pattern. In the areas of extreme hardness the waves do not propagate at all resulting in back area known as *signal void area* or *punched out lesions*. The technique is implanted in Aixplorer (Supersonic Imagine, Aix-en-Province, France) equipment [1]. The equipment has wide acceptance for assessment of liver fibrosis stage in chronic hepatitis patients where this has largely replaced biopsy. However, for breast tissue it has not yet achieved due popularity among clinicians.

3. Elasticity differences of normal and pathological breast tissues

As the normal understanding the elasticity of the tissue varies with the disease progression. The particular diseases like chronic inflammation and cancers have higher tendency to show higher level of stiffness. It is also a general concept that
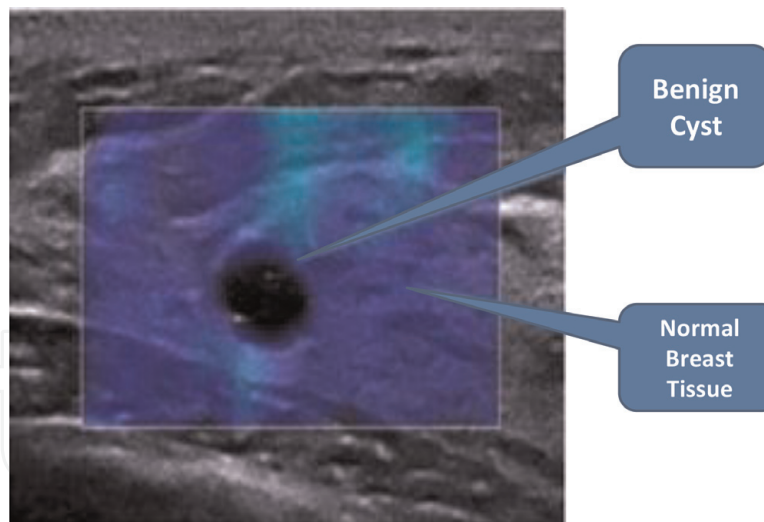
Figure 1.
Qualitative appearance of normal breast tissue and benign cyst on shearwave elastography.
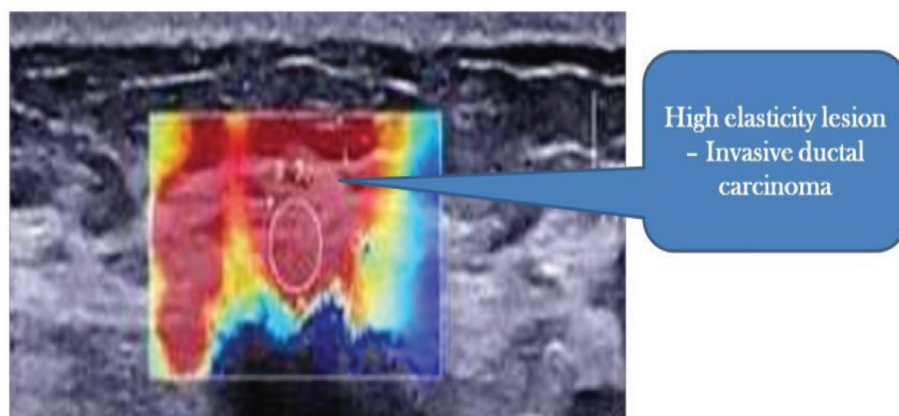

Figure 2.
Invasive ductal carcinoma breast appearance on shearwave elastography.

the cancers tend to be harder than the normal tissue and the benign lesions (**Figures 1** and **2**). Although it is not applicable in all situations as some benign conditions show harder consistency such as a cyst and some cancers show soft consistency like mucinous type. The study conducted on normal tissue showing the soft consistency with averagely blue color on qualitative assessment and normal tissue elasticity of the breast reported to be 30.68 ± 9.11 kPa in the four quadrants while in the nipple areola it was 31.35 kPa [3]. The stiffness shows negative relationship with the age of the patients. As the age advances in particular older women the breast parenchyma is largely replaced by fat. Fat is naturally much softer than the breast parenchyma thus understandably elasticity reduces. In contrast younger patients have more breast parenchyma and firmer breast thus relatively higher elasticity, though within limits of the normal range.

4. Breast shearwave probe and technique

A linear array probe with maximum frequency of 12–14 MHz is used for breast elastography (**Figure 3**). Technique of applying SWE is crucial. The application of probe for SWE is just to place it on the skin, no additional pressure is required. In the experience of the author if pressure is applied on breast tissues it causes false positive results. Thus just placing the probe and holding it perpendicular to the skin

Figure 3.
Linear-array probe used for breast shearwave elastography.
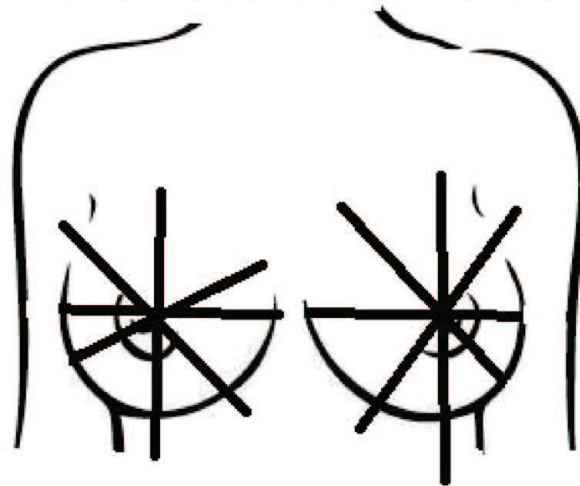

Figure 4.
Clockwise fashion of assessing breast by shearwave elastography.

is just appropriate. However, in deep seated lesions minimal compression may be applied without putting unnecessary pressure on the tumor.

The first stage and important stage is to get good quality homogenous B-mode images. The B-mode provides basis for generation of the SWE. Placing the probe parallel to the duct then moving it in clock wise fashion in all quadrants of the breast allows superficial assessment of whole breast (**Figure 4**). This is the general screening. In case if there is any lesion visible then detailed examination of the lesion is to be done in addition to the general assessment. The initial qualitative assessment is done followed by application of ROI for measurement of the elasticity.

5. Reliability of SWE as imaging modality in breast

5.1 SWE differentiating benign and malignant breast lesions

Since SWE was brought in clinical practice a number of studies have been conducted on its reliability and compared it with the conventional modes of imaging including ultrasound and mammograms. In addition to individual studies a number of meta-analysis has also been done [4–6]. Invariably all the studies showed superiority of SWE over ultrasound and mammograms alone in particular BIRAD 3 and 4 cases. However, SWE did not differentiate among molecular classes of breast cancer, though higher grades were associated with high elasticity [7]. Another study compared ultrasound and combined ultrasound with SWE to differentiate mastitis and malignancy. With addition of SWE specificity was increased from 11.5 to 96% [8].

There were studies available to suggest that SWE stiffness of the breast cancer has been linked with prediction of the poor survival [9, 10]. The harder the tumor, the poorer the survival. This can be biologically explained by having hard aggressive tumors with high grades and solid consistency resulting in poor survival [11]. A

S. No	Author	Name of journal	Year of publication	Sample size	Conclusion
1	Doria [12]	European Journal of Radiology	2019	396	Malignant and benign breast lesions show significant difference in elasticity on SWE. Application of SWE reduces the rate of false positives by 25% in general while for BIRAD category four false negative rate was reduced by 54%
2	Choi [13]	British Journal of Radiology	2019	428	Combined approach with B-mode ultrasound and SWE significantly enhance diagnostic accuracy even in smaller tumors (≤2 cm)
3	Zhang [14]	Breast Cancer Research and Treatment	2019	458	BIRAD category four lesions were evaluated on B-mode Ultrasound and SWE. 90% were downgraded by SWE
4	Lin [15]	Cancer Management Research	2018	2273	Multi-center study compared B-mode ultrasound and SWE and compared with histopathology. SWE was superior in making diagnosis on BIRAD 3 and 4 category
5	Song [9]	Clinical Imaging	2018	209	Breast lesions were compared on B-mode with and without SWE. The addition of SWE improved specificity from 17 to 98%
6	Wang [16]	Ultrasound in Medicine and Biology	2017	126	Addition of SWE to conventional B-mode increases sensitivity and specificity in BIRAD 3 and 4 lesions
7	Choi [17]	European Radiology	2016	116	Non palpable breast lesions were evaluated. Addition of SWE increases sensitivity and specificity of diagnosis and differentiating benign and malignant non palpable breast lesions
8	Kim [18]	Medicine	2015	177	Addition of SWE to B-mode increases diagnostic accuracy in BIRAD 4 category
9	Lee [19]	European Journal of Radiology	2015	140	Complex cystic and solid masses showed that addition of SWE increases the chance of accurate diagnosis in BIRAD 3 and 4 category
10	Youk [20]	Ultrasound in Medicine and Biology	2014	79	Addition of SE or SWE improved the diagnostic performance of B-mode US, potentially reducing unnecessary biopsies
11	Kilic [21]	Journal of Breast Cancer	2014	1 (a case report)	DCIS was detected within the fibroadenoma
12	Lee [22]	Radiology	2014	159	Shearwave increases sensitivity and specificity of US
13	Klotz [23]	Diagnostic and Interventional Imaging	2014	167	Shearwave elastography improves outcome of ultrasound
14	Zhou [24]	Radiology	2014	137	Addition of shearwave with stiff rim setting makes differentiation of the tumors better
15	Park [25]	Ultrasound in Medicine and Biology	2014	64	Excellent reproducibility
16	Mullen [26]	Clinical Radiology	2014	86	In smaller tumors ≤15 cm in size addition of the peri-tumoral rim on SWE in addition to the grayscale measurement make better comparability with the pathological size of the cancer

S. No	Author	Name of journal	Year of publication	Sample size	Conclusion
17	Cebi Olgun [27]	Diagnostic and Interventional Imaging	2014	115	Provides additional valuable quantitative information
18	Choi [11]	Ultrasound in Medicine and Biology	2014	116	Shearwave elastography correlated with the grade and stiffness

Table 1.
Summary of the studies evaluating role of shearwave elastography in differentiating benign and malignant lesions of the breast.

summary of the studies reporting on role of SWE in differentiating benign and malignant lesions is given in **Table 1**.

5.2 SWE predicting response to neo-adjuvant chemotherapy in locally advanced breast cancer

Shearwave elastography was evaluated to assess its potential role in predicting response to chemotherapy in a number of studies (**Table 2**). Each tumor has cellular component and the tumor stroma. When there is compact cellular component the tumor tend to show hardness which appears as high elasticity on SWE. While with the action of the chemotherapy; cells start to die and there comes softness which appears as reduction in elasticity of the tumors. Those tumors show response to chemotherapy present with reduced stiffness earlier in the course of treatment (**Table 2**). Thus invariably all the studies showed that those tumor showing pathological complete response have also shown reduction in the elasticity on SWE earlier [33].

S. No	Author	Name of journal	Year of publication	Sample size	Conclusion
1	Evan [28]	Clinical Radiology	2018	80	Out of 80 patients 26% achieved pathological complete response, which was assessed by reduction in elasticity of the cancer on SWE
2	Wang [29]	British Journal of Radiology	2018	Mouse model	Xenograph mouse models were used. Results showed reduced elasticity of the tumors achieving clinical benefit. This reduction was picked up by SWE
3	Jing [30]	Journal of Ultrasound in Medicine	2016	62	After 2 cycles of neoadjuvant chemotherapy and results showed that the tumors achieving clinical benefit showed reduction in the elasticity with 2 cycles
4	Chamming's [31]	Ultrasound in Medicine and Biology	2016	Mouse model	Xenograph mouse models were used. The SWE evaluation showed significant reduction in tumor stiffness after chemotherapy
5	Lee[32]	Annals of Surgical Oncology	2015	71	The response areas showed reduction in the elasticity while the areas of higher stiffness were corresponding areas with the residual tumors

Table 2.
Summary of the studies showing role of shearwave elastography in predicting response to neoadjuvant chemotherapy in locally advanced breast cancer.
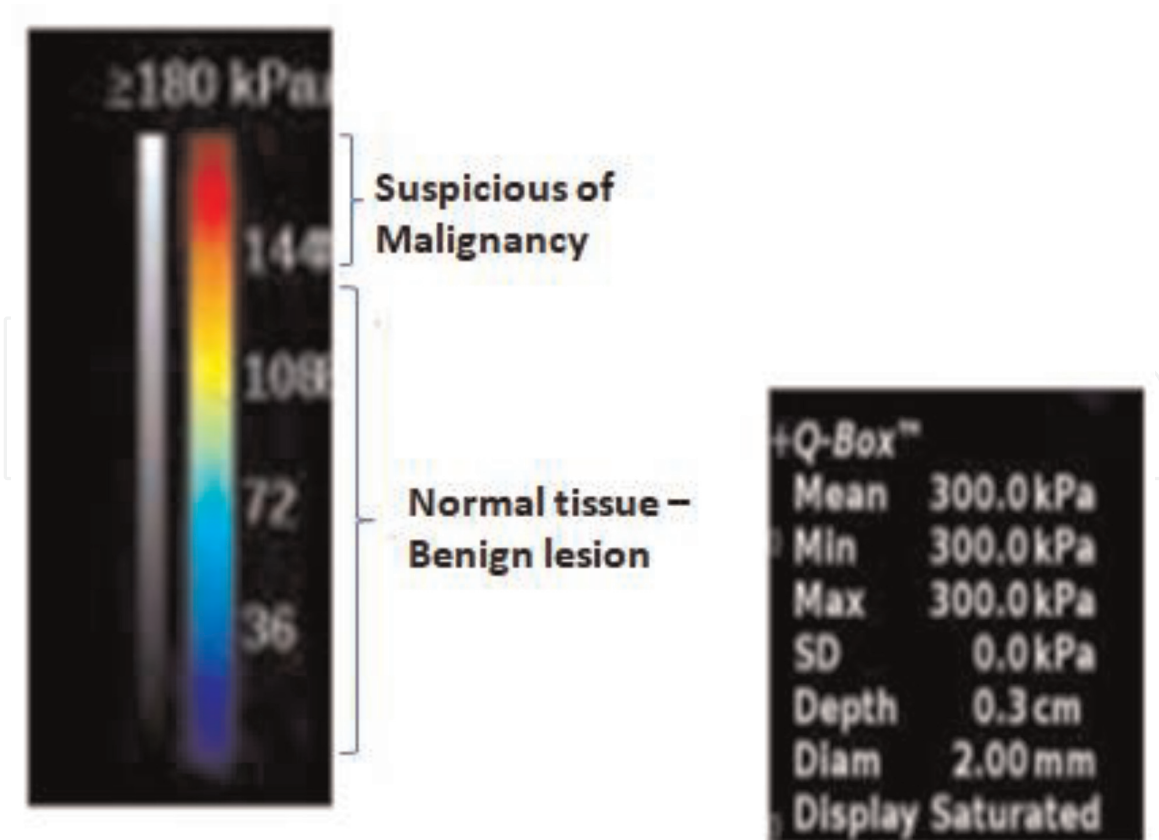
Figure 5.
Qualitative parameter (a) and quantitative parameters (b) of breast lesion assessment on shearwave elastography.

6. Reporting of breast SWE

The probe needs to be placed very gently on the breast without application of any pressure. For breast evaluation clockwise 12 measurements have to be taken. The reporting is to be done by using qualitative as well as quantitative findings of the breast tissue including color of the tissue and maximum elasticity values (**Figure 5a** and **b**). If there is any additional finding such as signal void area then it has to be described along with its location in the breast. The ROI is placed in all the areas with maximum elasticity level are to be taken into account. The size of the ROI is to be adjusted according to the size of the tumor and the proportion of the heterogeneous tissue including hard and soft parts. The cancers show more heterogeneity then the benign lesions. Thus the highest elasticity is taken as well as reading from heterogenous area to take the ratio of the low elasticity and high elasticity. The breast areas are to be reported followed by the detailed report of the lesion. The specific area report should include color, elasticity and the presence of signal void area.

7. Interpretation of shearwave elastography

Shearwaves are ultra-fast waves generated by acoustic force radiation travel transversely into the tissues and display output in qualitative and quantitative mode. The qualitative outcome is displayed in the form of color change that ranges from dark blue (i.e., normal tissue) to yellow, orange (i.e., benign) and finally red and dark red (i.e., malignancy) (**Figures 5a, 6–9**). The corresponding quantitative measurement ranges from 0 to 300 (**Figure 5b**). The tissue elasticity of the breast
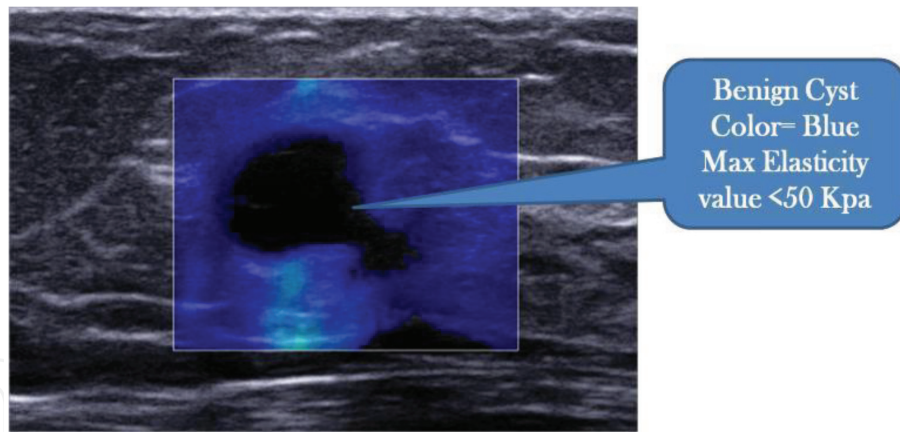
Figure 6.
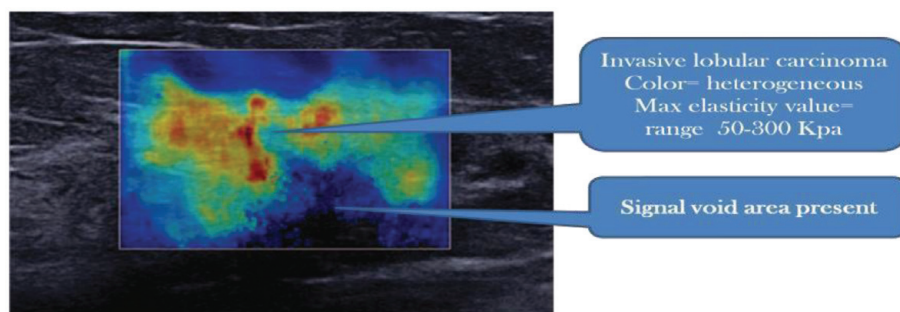*Benign breast cyst on shearwave elastography.*

Figure 7.
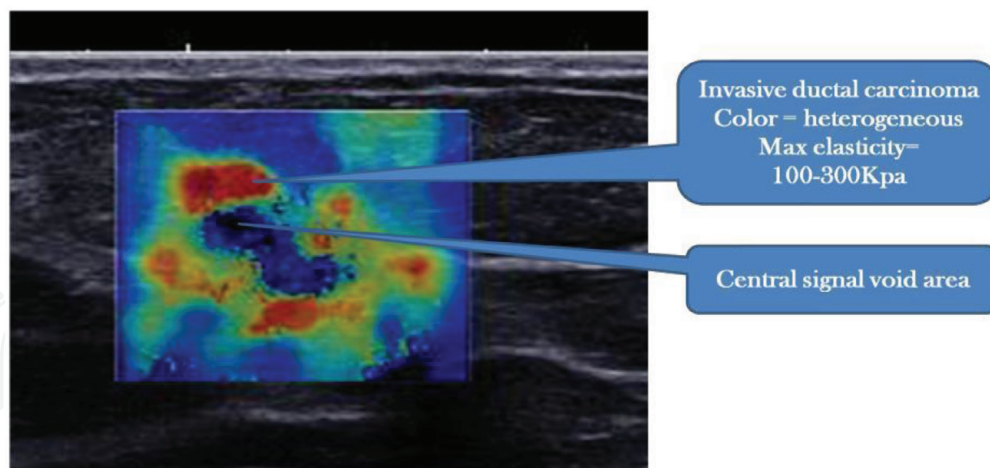*Invasive lobular carcinoma appearance on shearwave elastography.*

Figure 8.
Invasive ductal carcinoma appearance with signal void area on shearwave elastography.

showed negative correlation with the age i.e., as the age advances the tissue elasticity reduces [3]. This can be explained by natural evolution of the breast where with advancing age breast parenchyma replaced by fat tissue. This should always be borne in mind that high resolution good quality images can only be interpreted. In case if there is so much of background noise and the images are not giving a clear description it's better to avoid interpretation of such images. In this regard the best approach is to do a combine approach with B-mode first. With the B-mode imaging identify the lesion and its characteristics then SWE be applied on the lesion in order to avoid influence of artifacts.
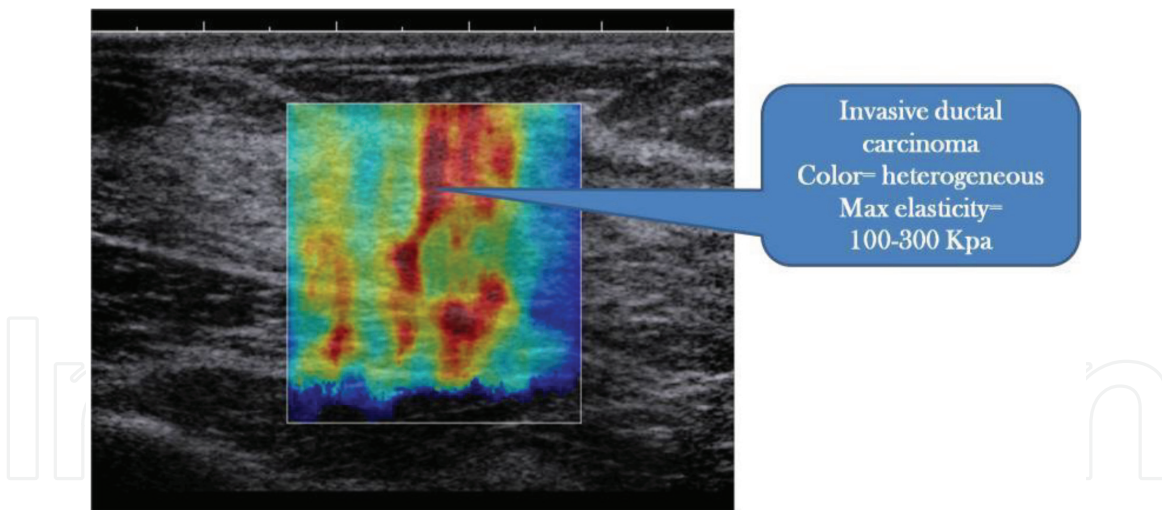
Figure 9.
Invasive ductal carcinoma appearance on shearwave elastography—without signal void area.

As the elasticity increases the kilopascal measurements also rises. However, in certain situations where intrinsic factors of the tumor show false negative results such as in situ cancers. While age of the patients, high risk lesions, tumors closer to the chest wall or overlying skin or deep seated tumors were likely to develop false positives results [13]. The study including 428 smaller tumor (≤2 cm) compared conventional B-mode ultrasound with SWE combined approach. The results showed that SWE combined approach was superior than B-mode alone, however in situ cancers showed false negative results [13]. Another study showed that presence of in situ tumor, calcifications and tumors near the nipple are likely to produce inaccurate results [34]. The study was conducted on non-palpable breast lesions including 79 malignant and 73 benign breast lesions. The smaller size of the lesion was also associated with inaccurate results in the study [34]. The inaccuracies in SWE interpretation could be explained by the nature of the lesion such as the case of in situ cancers, which has not yet produced that high reaction of the surrounding peri-tumoral tissue. The age of the patient and the location of the tumor potentially have influence of the breast tissue elasticity. The study including 1137 tumors to differentiate characteristics of the types of breast cancers on SWE. There was no characteristic difference in different histological types of cancers with exception of tubular type which showed less elasticity [35]. The fibroadenomas on the other hand show false positive expression if they were larger in size [36]. Interestingly lobular carcinoma has potential to display itself as benign or probably benign on B-mode ultrasound or mammogram but SWE showed higher rate of picking up lobular cancers [37].

The characteristics of the benign and malignant lesions were evaluated in a prospective cross-sectional study including 119 women. These patients underwent clinical breast examination, followed by conventional ultrasound then SWE and finally ultrasound guided tissue biopsy. The results showed that the benign lesions tend to be oval or round in shape with homogenous echopattern. Their color ranges from blue to yellow and green but reasonably homogenous with low elasticity. On the other hand malignant lesions were in contrast with irregular margins, heterogeneous echopattern and color from red to dark red in correlation with high elasticity [38].

The debatable issue lies with SWE is the operator dependency which is attached to B-mode ultrasound by default. The application of the probe is crucial with dependency on the operator; however there is less influence on the results if the technique of the probe application is correct.

In this regard, a study compared an operator with 15 years experience with that having 1 year [39]. The reproducibility of the results was high with SWE showing

less dependency on operator experience for interpretation, while intra-observer reproducibility has been reported to be 0.789 on SWE [25].

There are a number of parameters which could be utilized for interpretation such as mean elasticity value, minimum elasticity value and maximum elasticity. Most of the studies showed maximum elasticity value in kilopascals as the most reliable to be considered. However, all parameters need to be observed in cases of highly heterogeneous cancers.

8. Breast lesion scoring system

The authors have developed a scoring system for better diagnostic yield of shearwave elastography by combining qualitative and quantitative characteristics of the breast lesions. The scoring system takes into account the change of color, quantitative measurement of stiffness in kilopascals (kPa) and presence or absence of the signal void area (i.e., punched out lesion). A summary of the scoring system is given in **Table 3**.

Hard solid tumors showed dark color on qualitative measure, while benign soft tumors show natural color including blue, yellow orange. Normal breast tissue is blue in color. Fibrocystic lesion change color from blue to yellow or even orange but none of the benign lesions turn dark red. Similarly all the malignant lesion were red in different shades. Quantitative measurement of the kPa of benign lesions was low with less stiffness while solid tumor and cancers show score >200. Dark red color on qualitative scale and >250 kPa was invariably seen in cancers. When the cancer gets really hard and shear waves fail to penetrate resulting in signal void area punched out lesion. There was an exception of breast abscess which also showed signal void area due to cavity. The differing point of the breast abscess and the malignant breast lesion was based on color and mean kPa score while signal void area was seen in majority of both cases. **Figures 10–12** portray the breast lesion from benign to malignant pathologies.

Parameter	Score 1	Score 2	Score 3
Color	Blue, yellow, orange	Red, dark red	Dark red
Mean kPa range	<200	>200 but <250	>250
Punched out lesion status	Absent	Present	May be present

Table 3.
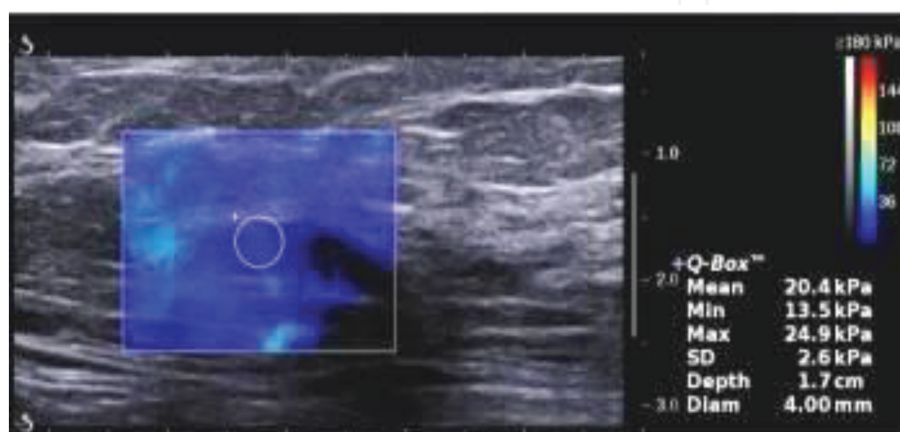*Scoring system to interpret Shearwave elastography findings of breast lesions.*

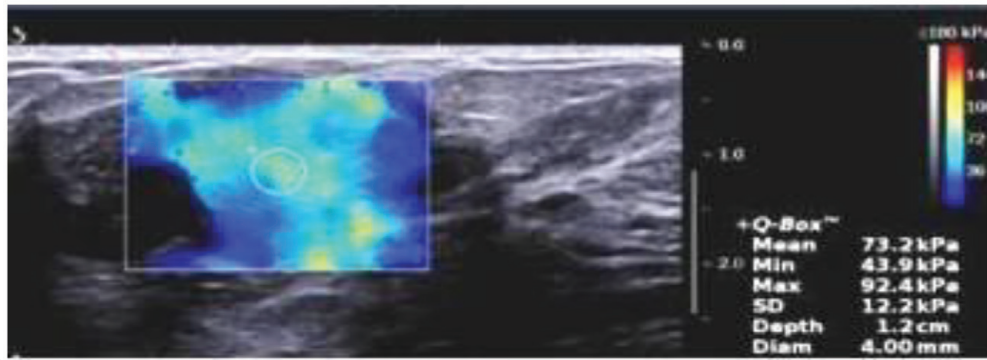**Figure 10.**
Benign breast disease on shearwave elastography.

Figure 11.
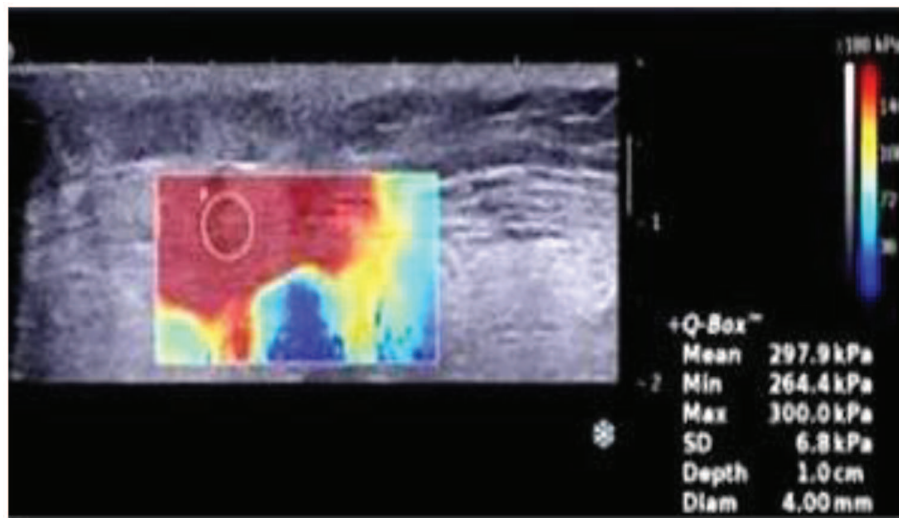*Fibrocystic disease on shearwave elastography.*

Figure 12.
Invasive ductal carcinoma of breast on shearwave elastography.

9. Conclusion

Shearwave elastography is a new advanced technique with ultrafast mode of shearwaves to assess elasticity of the tissue. It has established role in assessment of the liver fibrosis. The available literature favors use of shearwave elastography in combination with B-mode ultrasound to enhance diagnostic accuracy of the conventional ultrasound. However, it has not been widely used in clinical practice. Though it has shown great potential in differentiating BIRAD 3 and 4 categories and successfully avoiding negative biopsies.

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