Independent University **Bangladesh (IUB)**

IUB Academic Repository

Electrical and Electronics Engineering Article

2015

The Journey of Elastography: Background, Current Status and Future Possibilities in Breast Cancer Diagnosis

Faruk, Tasnuva

Elsevier

http://dir.iub.edu.bd:8180/handle/123456789/263

Downloaded from IUB Academic Repository

Accepted Manuscript



The Journey of Elastography: Background, Current Status and Future Possibilities in Breast Cancer Diagnosis

Tasnuva Faruk, Md Kafiul Islam, Sams Arefin, Md Zahurul Haq

PII: S1526-8209(15)00020-8

DOI: 10.1016/j.clbc.2015.01.002

Reference: CLBC 356

To appear in: *Clinical Breast Cancer*

Received Date: 20 October 2014

Accepted Date: 14 January 2015

Please cite this article as: Faruk T, Islam MK, Arefin S, Haq MZ, The Journey of Elastography: Background, Current Status and Future Possibilities in Breast Cancer Diagnosis, *Clinical Breast Cancer* (2015), doi: 10.1016/j.clbc.2015.01.002.

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

ACCEPTED MANUSCRIPT

Review Article

The Journey of Elastography: Background, Current Status and Future Possibilities in Breast Cancer Diagnosis

Tasnuva Faruk[a], Md Kafiul Islam[b*], Sams Arefin[c], and Md Zahurul Haq[d]

[a] Registered Physician, Bangladesh Medical & Dental Council, Dhaka, Bangladesh

[b] Dept. of Electrical and Computer Engineering, National University of Singapore, Singapore

c Dept. of Radiology & Imaging, Dhaka Medical College Hospital, Bangladesh

[d] Dept. of Surgery, Sher-E-Bangla Medical College, Barisal, Bangladesh

[*]Corresponding Author's Contact Details:

Email: kafiul_islam@nus.edu.sg, Phone No. +65-93986197

Address: Blk E4, #08-33, Signal Processing and VLSI Lab, Dept. of ECE, NUS, 4 Eng. Dr. 3, Singapore -117576

ACCEPTED MANUSCRIPT

Review Article

ACCEPTED MANUSCRIPT

The Journey of Elastography: Background, Current Status and Future Possibilities in Breast Cancer Diagnosis

Tasnuva Faruk[a], Md Kafiul Islam[b], Sams Arefin[c] and Md Zahurul Haq[d]

[a] *Registered Physician, Bangladesh Medical and Dental Council*
[b] *Dept. of Electrical and Computer Engineering, National University of Singapore, Singapore*
c Dept. of Radiology & Imaging, Dhaka Medical College Hospital, Bangladesh
d Dept. of Surgery, Sher-E-Bangla Medical College, Barisal, Bangladesh

Received dd/mm/yyyy; accepted dd/mm/yyyy

Abstract

Elastography is a promising way to assess tissue differences in terms of stiffness or elasticity what was historically assessed manually by palpation. Combining with the conventional imaging modality (e.g. ultrasonography), elastography can potentially evaluate the stiffness of a breast lesion and consequently helps to detect the malignant breast tumours from the benign ones. Recent studies show that ultrasound elastography (USE) provides higher image quality compared with the conventional B-mode ultrasonography or mammography during breast cancer diagnosis; which eventually helps to reduce the false positive results (i.e. increased specificity) and therefore is useful in avoiding the breast biopsy. This paper reviews the basics of elastography technique, classifications, diagnosis results obtained from clinical studies to date for differentiating malignant breast tumours from benign lesions and its future possibilities. In addition, this article generalizes different elastography methods, modes and associated imaging modalities in a simpler way, attempts to identify misconceptions and confusions related to existing elastography techniques. It also makes effort to find out the gaps of information needed to be filled so that interested researchers can get an overall idea of elastography based methods in a convenient way to carry out their research on breast elastography for prospective future applications: e.g. breast cancer diagnosis or even in intraoperative breast tumour localization.

Keywords: Elastography; Breast Cancer Diagnosis; Sono-Elastography/Ultrasound Elastography; Breast Cancer Surgery; Shear Wave; Strain Imaging;

INTRODUCTION

Breast cancer is one of the most common malignancies in women and second primary reason of cancer-related death [98]. The matter of hope is that if diagnosed in very early stage, breast cancer can be cured completely. Due to the absence of a known preventable reason of breast cancer, the only most essential factor to lessen the mortality rate and the extent of treatment required is detection at early stage through screening [98]. Due to the advanced screening facilities, thousands of women are diagnosed with breast cancer in the early stage every year even before they start to feel any lump (i.e. impalpable). However, the scenario is relatively different in the developing and third-world countries. Due to high cost of the screening tests, many women cannot afford regular screening, which lead them to die hopelessly since the time the tumour is detected/diagnosed or even the surgery is done, root of the cancer has spread much deeper. Apart from cost effectiveness, there are some other drawbacks of existing screening tools. Due to the sophisticated operation and the need of highly skilled technicians to operate, not every country can afford such systems as they are lack of technically skilled manpower. In addition, the conflict of sensitivity and specificity is also something that matters. Most of the current methods are highly sensitive yet lack in specificity resulting an alarming number of false positive cases. Consequently, the increased false positive results also increase the rate of unnecessary biopsies. Some methods even fail to diagnose *mm* size or cellular level cancers. As a result, despite having regular screening tests, breast cancers can be failed to be diagnosed in early curable stage. Surprisingly these are scenarios from developed countries, not to mention about developing ones. Eventually, in any of the cases, it is troublesome for the patients.

Therefore, the urge for development of a single suitable screening test for breast cancer, is inevitable; which will be highly sensitive as well as specific, easily operable, cost effective, needs no special hardware set up so that the entire world can take the benefits from it regardless of races, continents, economical, developmental, educational solvency. After analyzing above mentioned criteria, elastography seems one of the promising candidates in this regard. Due to the attractive features of elastography as a potential breast cancer diagnostic tool, the research works on elastography for breast cancer diagnosis applications follow an increasing exponential trend since the year 2000[1] till now as shown in Figure 1.

The standard diagnosis process for breast cancer is often termed as *triple assessment* which has three stages: *clinical examination*, *imaging* and *needle biopsy*. The 1st stage involves taking of medical history and clinical examination; followed by imaging of the breast either by ultrasonography or mammography in the 2nd stage and finally laboratory testing of the sample breast tissue obtained using needle biopsy in the last stage. Although mammography and ultrasonography are the two most popular imaging methods in the 2nd stage of the diagnosis process, but both methods suffer from some limitations [30]. As reported in [86], mammography applied in dense breast may sometimes result in false-negatives whereas US has poor

[1] It is important to note that the study of elastography was started almost two decades ago, but from the beginning of 21st century, it has been emerged significantly with several published articles in peer reviewed journals. Hence, we have considered the articles published since the year 2000.

ACCEPTED MANUSCRIPT

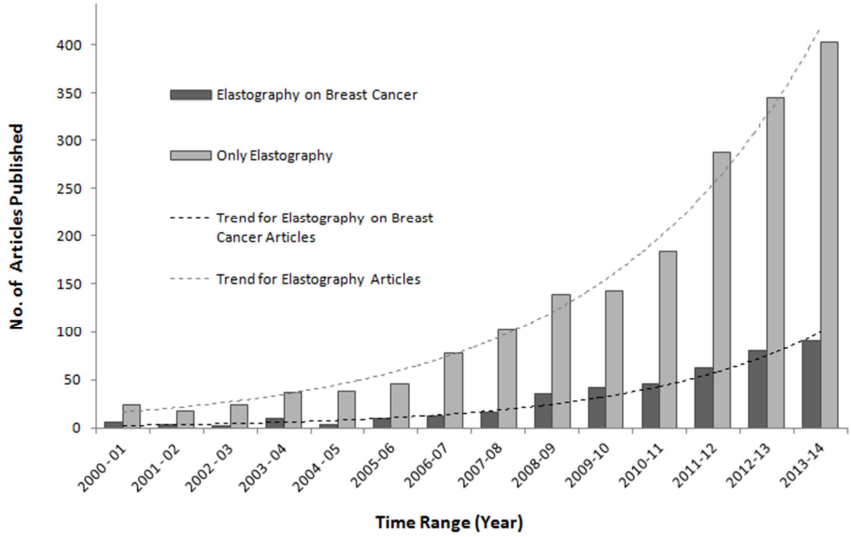


Figure 1. Trend of Elastography research works published in the major journals indexed by *PubMed* since the year of 2000 till date.

specificity as most stiff lesions turn out to be benign. Therefore, breast elastography has been introduced to overcome these limitations and to provide a better breast image for lesion characterization. Besides, breast elastography can act to bridge

Regardless of the fact that the study of elastography is being done for over two decades, most of which were performed almost behind a closed door. So, after two decades of elastography research worldwide, there is a thin connection between the research groups. For example, the current elastography techniques developed in research labs that have already started appearing in the market, it is most likely that most of them are not quantitative or operator independent. In other words, there are no universal standard for scoring and terminologies. Therefore, the term *elastography* can hide very different physical phenomena. Though there are few elastography machines available in the market by different manufacturers, there are still significant amount of confusion, misconception and lack of clarity around the concept of elastography, its implementation and its interpretation for breast tumour assessment.

The purpose of this article is to point-out the commonly encountered confusions, misconception, correlate all the existing methods, classification techniques to provide a better, broader, clearer view to the interested researchers and of course to widely open the window of elastography towards research community. It is high time to understand the underlying mechanisms of different elastography techniques properly in order to make the best use of it in the wide clinical practice.

ELASTOGRAPHY

i) Basic Principle

The concept of elastography was first introduced after 1990 [95] and started to be used in the clinical setting in 1997 [96]. Elastography is a non-invasive imaging technique where the local tissue strains are measured directly (e.g. strain ratio/Young Modulus) or indirectly (e.g. shear wave velocity) after the external stress (static or dynamic) is applied to perturb/compress the tissue. The tissue stiffness can be measured with elastography using a 3-step process [28]:

- Apply a small stress to the tissue.
- Measure the tissue displacement.
- Calculate stiffness based on the tissue displacement.

The basic principle of elastography process is shown in Figure 3. From a physics point of view, elastography aims to quantitatively image the Young's modulus[2], i.e. the physical parameter corresponding to the stiffness. This has two important advantages [29]:

- The Young's modulus, denoted by *E*, reveals key variations between different biological tissues; which makes it ideal for the characterization of different tissues with an excellent contrast.
- This modulus *E* characterizes the stiffness of a tissue, which is nothing but the quantitative representation of a clinician's palpation and thus has relevant diagnostic value.

[2] If F is the amount of force exerted on an object of length L_o through cross-sectional area A_o and the resultant change in length is ΔL then the measurement of elasticity in terms of Young's modulus, E is calculated as follows:

$$E \equiv \frac{tensile\ stress}{tensile\ strain} = \frac{F/A_o}{\Delta L/L_o} = \frac{FL_o}{A_o \Delta L}$$

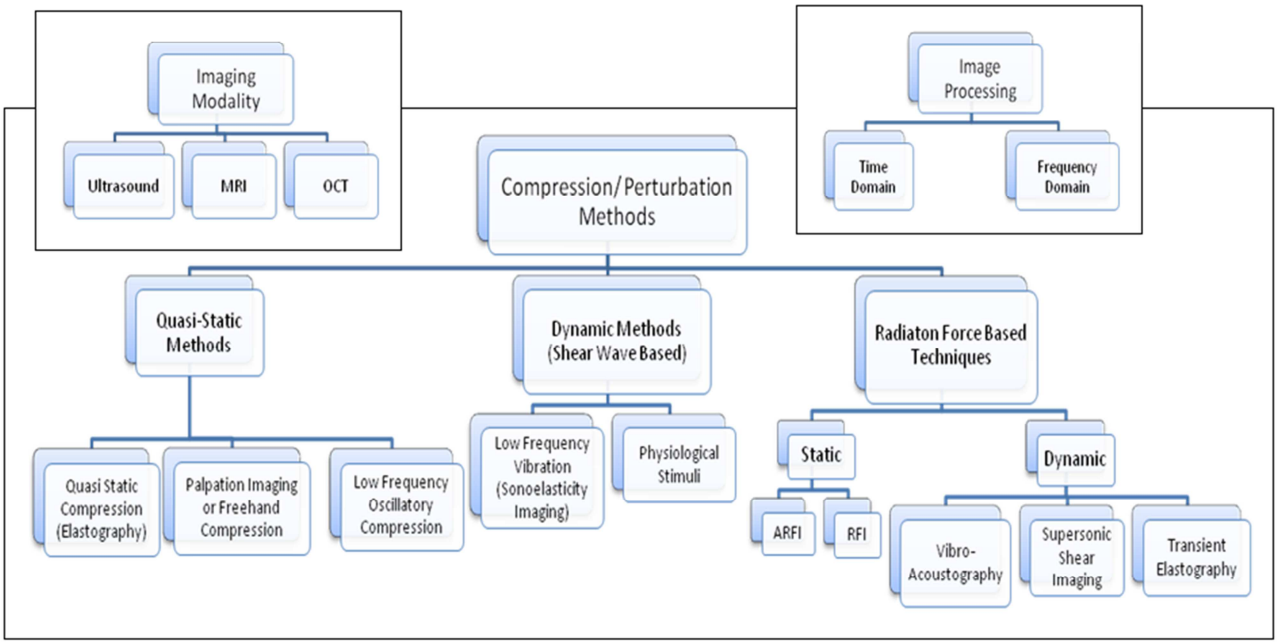


Figure 2. Different methods for strain imaging used in elastogrpahy as described in [27]

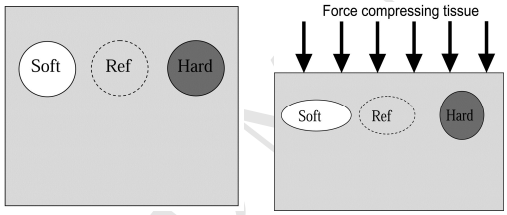


Figure 3. The basic principle of elastography relies on the stiffness of the tissue. The figure illustrates the effect of compression for three types of tissue before (left) and after (right) a same force is applied on them.

Different methods of overall elastography process starting from tissue compression to imaging are shown in Figure 2. as reported in [27].

ii) Compression Methods

The first step of any elastography process is to apply external stress to compress/perturb tissue based on which there are different methods available. The different ways of applying mechanical stimuli for tissue compression are discussed below:

❖ *Quasi-static Method*

The Young's modulus is given via the Hooke's law, which links stress and strain in a purely elastic medium. However, due to the unavailability of quantitative value of applied stress, only the relative strain is shown in the form of a map that is sometimes called *elastogram*. This method is easy to implement but cannot give a quantitative value for the Young's modulus since only the strain can be estimated, and the applied stress is not known. It is, therefore, impossible to recover the Young's modulus using Hooke's law [29]. An example of static elastography based compression process is shown in Figure 4.

The algorithms used for Quasi-static method are:

a. Cross-Correlation [67]
b. Phase shift correlation [69]
c. Phase-root seeking [70]
d. Block-matching methods [71, 72]
e. De-correlation methods [68, 73]
f. Envelope processing [74]
g. Envelope + RF [75]

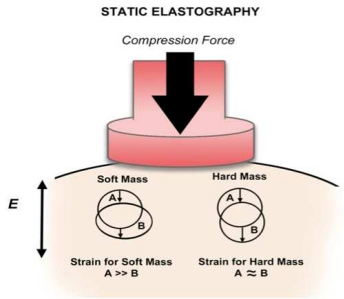


Figure 4. Strain/static elastography measures tissue displacement as a consequence of an applied initial compression. Tissue displacement is larger in soft tissue than hard tissue. This figure is adopted from [28].

❖ *Dynamic Method*

In biological tissues, which are almost incompressible, the Young's modulus can be approximated as three times the shear modulus. Dynamic elastography techniques, which rely on shear wave propagation, can produce quantitative and higher resolution Young's modulus map compared to quasi-static methods. However, it requires a more complex system to be able to generate the shear wave (mechanical vibrator or ultrasound radiation pressure) and to image the small displacements induced by the shear wave (ultrafast or stroboscopic ultrasound) [29]. The illustration of compression process used in shear-wave elastography is shown in Figure 5.

Shear wave elastography (SWE) is applicable to soft tissue [55], and it provides highly reproducible results compared to static (strain) elastography [56, 57]. This reproducibility is considered as a main problem and can compromise the patient outcomes. Therefore, it is required to have more research in the future to study the utility of SWE [55].

❖ *Radiation Force Based Technique*

ARFI: In acoustic radiation force impulse (ARFI) imaging, an initial ultrasonic pulse is transmitted at diagnostic intensity level to acquire a baseline signal for comparison afterwards. A short duration (~ 0.3 sec), high-intensity acoustic 'pushing pulse' is subsequently transmitted followed by a series of diagnostic intensity pulses, that are used to track the tissue displacement due to the pushing pulse [52-54]. The tissue response due to the radiation force is seen using conventional B-mode imaging pulses and the shear-wave velocity (Vs; m/s) for ARFI displacement is possible to display quantitatively. This is because the velocity of shear-wave is proportional to the square root of stiffness/elasticity of the tissue. Therefore, it is feasible to apply ARFI technology to elastography. However, so far according to the studies found in the literature, this particular method has been only applied for liver fibrosis applications, not on breast cancer applications.

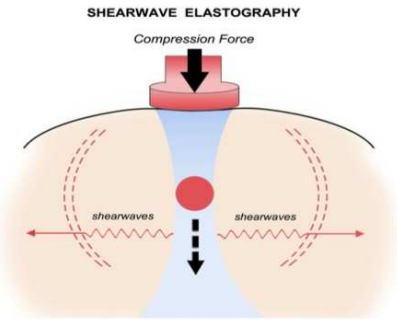


Figure 5. Dynamic or Shear-wave elastography assess the speed of the transverse oriented shear-waves which travel faster through hard tissue than soft tissue. This figure is adopted from [28].

iii) Imaging Modality

Elastography itself is insufficient and can't be directly applied for imaging breast tissue. It requires an imaging modality as a complementary tool to make the whole process complete and fully functional. However, the choice of imaging modality plays a vital role in elastography techniques since both resolution and penetration depth depends on it. For example, the typical resolution of ultrasound elastography (USE) is 125-200 µm, while resolution in MRI elastography is usually of mm scale [58]. An illustration of different imaging modalities comparing their resolution and penetration depth is shown in Figure 6. while the comparison between their contrast mechanisms is shown in Figure 7.

❖ *Ultrasound*

Ultrasonography is a widely used imaging technique which has been in the clinical practice for almost 50 years. The advantages of using ultrasound are ease of use, real-time capability, portability and low-cost. This method allows the

construction of morphological images of organs/tissue based on the propagation of mechanical waves and more particularly on high-frequency compression waves (also known as ultrasound).

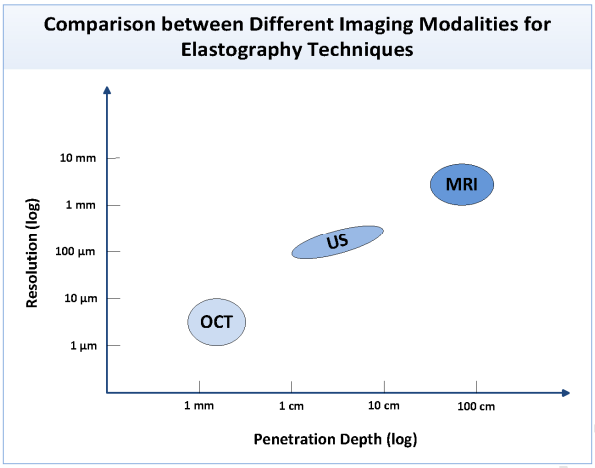


Figure 6. Comparison between different imaging modalities in terms of their resolution vs. penetration depth.

However, it lacks fundamental and quantitative information on tissue elastic properties since the propagation of ultrasound is almost homogeneous in the different biological tissues and does not depend on tissue elasticity [29, 60].

❖ *MRI*

MRI-based elastography acquires information about tissue stiffness by measuring the propagation of mechanical waves through the tissue with a special MRI technique which involves three steps as follows [61]:

(1) Generating shear waves in the tissue,
(2) Obtaining MR images that represent the propagation of induced shear waves, and
(3) Processing shear wave images to generate quantitative maps of tissue stiffness, which is called elastograms.

❖ *OCT*

Optical coherence tomography (OCT)–based elastography, which is expressed as optical coherence elastography (OCE) [63], shows great potential for micron and submicron imaging applications because it benefits from the high resolution of OCT [64] while additionally providing the elastic properties of the sample [62]. This advantageous high-resolution, non-invasive imaging modality allows OCE to evaluate the mechanics of intact tissue on a scale that cannot be offered by elastography produced by the competing imaging modalities of ultrasound or MRI (magnetic resonance imaging) [62].

iv) Image Processing

In order to display breast images, image processing is performed during the final stage in either time domain or frequency domain. FFT-based techniques (i.e. frequency domain) provide better accuracy than time domain based processing, but it has higher computational time compared to its counterpart.

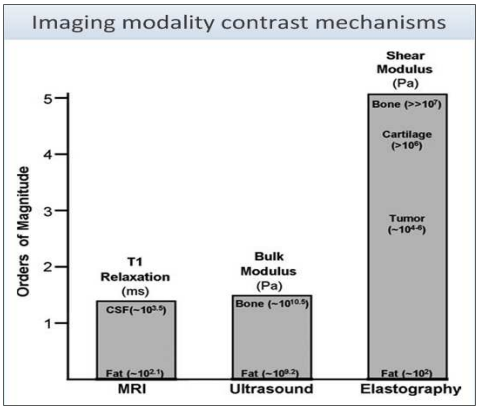


Figure 7. Illustration of different imaging modalities and the spectrum of their contrast mechanisms. The shear modulus is found to have the biggest variation among various physiological states of normal and pathologic tissues. The figure is adopted from [61] with little modification.

ACCEPTED MANUSCRIPT

BREAST ELASTOGRAPHY

Breast ultrasonography (US) has been acknowledged as a valuable diagnostic tool for both palpable and non-palpable breast masses. However, [78] reports that sonologists often find it a bit challenging to precisely distinguish isoechoic lesions from surrounding fat with conventional US. Therefore, it may result in false-negative interpretations and eventually causing a delayed diagnosis of the cancer. Other limitations of US include: failure to detect cellular level carcinomas, unable to image areas deep inside the breast, failure to show micro-calcifications, sometimes may have trouble to distinguish cancer from other pathologies, etc. In order to identify isoechoic lesions surrounded with fat by using breast US, it requires careful evaluation with B-mode US in correlation with mammography. However, it is essential to consider the location of lesion, surrounding tissue, and lesion characteristics (including size, shape, and internal contents), for measuring correlation between mammography and US. For evaluating the isoechoic breast lesions, the complementary tools to B-mode US comprise: spatial compound imaging, tissue harmonic imaging, US elastography, Contrast agent enhancement, color or power Doppler imaging, and power Doppler vocal fremitus imaging [79].

Breast biopsy followed by specimen radiography can be useful in evaluating the competence of tissue sampling. Moreover, such specimen radiography can help in assessing the correctness for targeting and localizing lesion, also in evaluations that increase confidence in the detections from tissue acquisition [79].

Table 1. Classification and comparison of different elastography techniques followed by available manufacturers [78]

Classification by Technical Method		**Classification by Interpretation**				
Method	Manufacturer Company	Method	Comparison	Diagnosis	Diagnostic Approach	Manufacturer Company
Strain Elastography	Hitachi Aloka, GE Healthcare, Philips Healthcare, Siemens, Toshiba	1(Scoring)/ Color Pattern Diagnosis	Color Images From Elastography	Based on Assessed Score	Elasticity Score	Hitachi Aloka Medical, GE Healthcare, Philips Healthcare, Siemens, Toshiba Medical
					Tsukuba score	
					Strain pattern	
					Tozaki's score	N/A
ARFI Imaging	Siemens	2 (Ratio)	grayscale images from elastography are compared with B-mode images	size ratio of the target lesion:	E/B Ratio	Philips Healthcare, Siemens, GE Healthcare
					Width Ratio	
					Length Ratio	
Shear wave Elastography	SuperSonic Imagine, Siemens	3 (Tissue Elasticity)	numerical value to the stiffness	tissue elasticity	Strain ratio	Hitachi Aloka Medical, GE Healthcare, Philips Healthcare, Toshiba Medical, Siemens
					fat–lesion ratio (FLR)	
					kPa (unit of stiffness),	SuperSonic Imagine, Siemens
					m/s (unit of sound velocity	

i) Evaluation criteria

Two most important characteristics of breast nodules are considered for US elastography based evaluation of breast lesions: size and stiffness [30, 77]. For example, stiff lumps will appear bigger in elastogram in US that result in the difference in dimension and this difference is expressed as a size ratio after comparing with conventional B-mode imaging. Sometimes, numerical values of tissue stiffness or elasticity are available (e.g. in shear wave elastography) as criteria for breast evaluation. Regarding the stiffness criteria, different scoring systems are proposed in the literature which evaluates the presence, distribution and surrounding areas of abnormal stiffness of tissue obtained from colour elastogram. An example of such scoring system proposed by [1] is shown in Table 1. Here, benign lesions are characterized as lesions with a low score (i.e. score 1–2) in the colour map and the most critical point for differentiating benign from malignant masses lies at the boundary of score 3-4. Because of low compressibility, often being hard and low deformable lesions, cysts are commonly represented as blue pattern in colour map with high strain ratio [59] as shown in Table 2.

ACCEPTED MANUSCRIPT

There are several artifacts present in both form of elastography: strain and shear-wave elasticity imaging. Those artifacts need to be understood and corrected in order to interpret the real diagnostic information. An effort is made by [39] to describe typically encountered artifacts found in US elastography that is summarized in Table 3.

ii) B-mode US vs. US Elastography

A comparison of salient features between conventional B-mode US and US elastography images that are usually found for different types of breast lesions is shown in Table 4.

iii) Mammography vs. Elastography

A comparison of scoring system for evaluation of breast lesion characterization between conventional mammography and elastography is shown in Table 5.

Table 2. Elastography Score for Breast Cancer Classification [1]

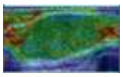
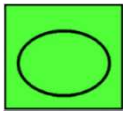
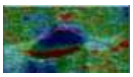
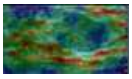
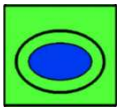
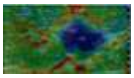
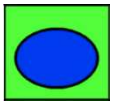
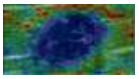
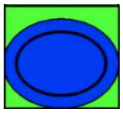
Score	Image	Color	Description	Class
1			Entire area is evenly shaded green, as is surrounding tissue	**Benign**
2			Lesion area shows a mosaic pattern of green and blue.	
3			Central part of the area is blue (stiff), and peripheral part is green (soft).	**Intermediate** (Probably Benign)
4			Entire area is blue (stiff).	**Malignant**
5			Entire area and its surrounding area are blue (stiff).	

Table 3. Comparative analysis of artifacts present in the sonographic breast elastography images for both strain-based and shear-wave based elasticity imaging [39]

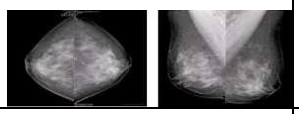
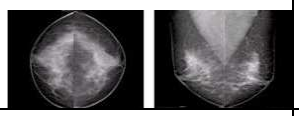
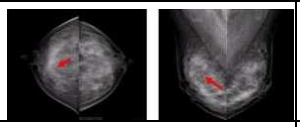
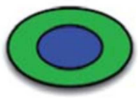
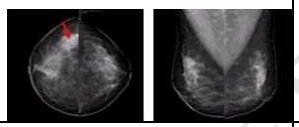
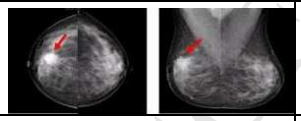
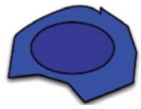
Strain Elasticity Imaging					**Shear Wave Elasticity Imaging**				
Artifact	***Description***	***Indication***	***Correction***	***Clinical Information***	***Artifact***	***Description***	***Indication***	***Correction***	***clinical information***
sliding artifact	White ring/ waves around lesion	Tumour moving in and out of imaging plane	i) Using less compression ii) Reposition iii) Holding breath	lesion is freely moveable (most likely benign)	**Areas are not color coded**	i) defined desmoplastic reaction ii) No red halo surrounding the lesion	shear wave cannot propagate	Using minimal precompression	very hard lesions (invasive cancers)
noise	pattern of large moving areas (worm pattern)	substantial precompression	using minimal precompression	no clinical information				**Not mentioned**	Benign lesion, Simple Cyst
bull's eye artifact	i) decorrelation between images ii) solid component in cyst will appear solid lesion within pattern	fluid inside the tumour is moving,	**Not mentioned**	cystic lesions, (benign simple / complicated cyst) **not seen in mucinous or colloid cancers**		areas in B-mode image show extremely low signal	echo signal is too low for successful detection	**Not mentioned**	i) areas with marked shadowing (ribs, calcification) ii) tumors with substantial shadowing

ACCEPTED MANUSCRIPT

Table 4. Difference in Imaging Features between B-mode US and US Elastography [77]

Type of Lesion	Imaging Modality	
	Conventional B-mode US	**US Elastography**
Invasive Ductal Carcinoma	Hypoechoic speculated/ microtubular branching mass	Increased stiffness, larger lesion than B-mode
Fibroadenoma	Oval well defined, homogenous hypoechoic area	Area of greater stiffness smaller than lesion boundaries
Cyst	Round/ oval anechoic lesion with clear transmission	Bull's-eye appearance with brighter posterior wall
Malignant Lymph Node	Rounded, enlarged lesion, loss of fatty hilum	Low strain, larger than B-mode image
Hematoma	Appearance varies from anechoic to separate cystic	Similar to cysts. May be stiff, measure less than on B-mode

Table 5. Comparative Study of Existing Scoring System of Mammography Vs Elastography [99, 100]

Mammography			Elastography	
	Category 0	Incomplete Assessment		
	Category 1	Negative for Malignancy	Score 1	
	Category 2	Benign Findings	Score 2	
	Category 3	Probably Benign Findings	Score 3	
	Category 4	Suspicious for Malignancy	Score 4	
	Category 5	Highly Suspicious for Malignancy	Score 5	
	Category 6	Known Biopsy Proven Malignancy		

DIAGNOSIS RESULTS AND COMPARATIVE STUDY

After going through several articles [1-25, 97, 98], it is obvious that the ultrasound elastography can provide additional diagnostic information for characterizing breast lesions and has high potential to improve the specificity. The features of elastography including shape, size ratios, homogeneity and their quantitative analysis might be complimentary to conventional ultrasound for the complete analysis of breast lesions [28]. A summarized diagnostic outcome from US elastography compared with normal B-mode Sonography and mammography is provided in Table 6.

We have also accumulated the breast lesion classification results in terms of mean sensitivity vs. mean specificity from all of 27 articles [1-25, 97, 98] and compared with two techniques: Digital Infrared Thermal Imaging (DITI) and Electrical Impedance Scanning (EIS) for average ROC curve as shown in Figure 8. [26]. It is obvious that US elastography

outperforms the other techniques by well margin with an average sensitivity of almost 87% and an average specificity of 80%.

Some recent studies in the year 2014 [55, 88-94] show that shear-wave elastography (SWE) has excellent diagnostic performance in terms of both increased sensitivity and specificity in differentiating malignant breast masses from benign ones.

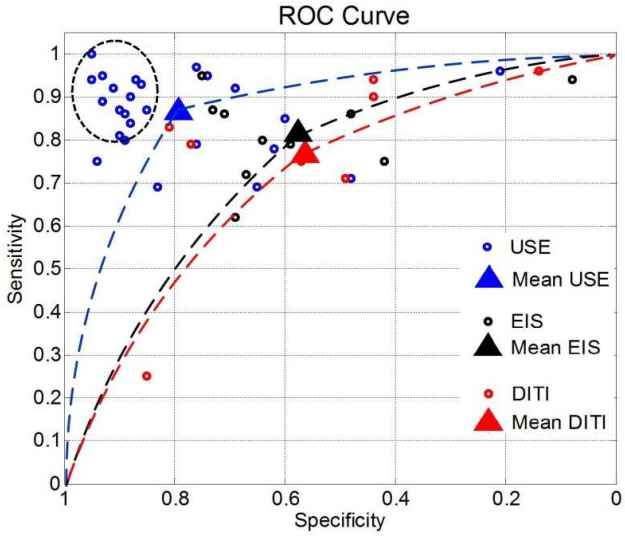


Figure 8. Comparative ROC curves of Ultra-Sound Elastography (USE), Digital Infrared Thermal Imaging (DITI) and Electrical Impedance Scanning (EIS) are plotted in blue, red and black dash-lines respectively with their average values are marked by triangle. Each point in the plot represents a published article as cited in [26]. The dash ROC curves are estimated from the dots using curve-fitting technique. It is obvious from the ROC curves that USE outperforms the other two in diagnosing of breast cancer. Please note that most of the USE performance points (as circled by black dash line) situate near the top left corner of ROC plot that supports its efficacy compared with other techniques.

DISCUSSION

i) The Mist of Confusion: Obstacles to Understand Elastography Better

Though it is the third decade the world has been familiar with the term *elastography*, the language of elastography is yet to be properly understood by the researchers worldwide! There are so much confusion regarding the terminologies used by individual research teams and manufacturers that sometimes they sound similar yet express different meaning, sometimes vice versa. E.g. the term *strain imaging* has been referred to all types of elastography techniques as described in [27] and according to which Figure 2. is plotted. However, in some other places, *strain imaging* is referred as one of the two types of elastography techniques for estimation of tissue stiffness where the second type is referred as *shear-wave imaging* [66]. Another example is that the term *USE* refers *ultrasound elastography*; however, it may also sometimes refer to *ultrasound strain elastography* which is a specific type of elastography that makes use of strain ratio for scoring. The term *transient elastography* denotes as one of the radiation force based dynamic techniques (as shown in Figure 2.) in some places, but it is also denoted as one of the shear-wave based methods in another place. In fact, the word '*transient*' refer to the applied force to be transient in nature, so it can either belong to mechanical vibration or belong to radiation force based perturbation methods.

Also, there is some confusion in the scoring method for classification between benign and malignant tissues since different manufacturers define it in different ways. Strain and shear-wave elastography are two different techniques and imaging features that differ across different manufacturers. Some manufacturers provide a black-and-white elastogram, others provide a colour elastogram. The colour coding may be adjusted according to the individual operator's preference. Currently as there is no benchmark in the colour elastogram assignment, stiff lesions might be seen as red while soft lesions as blue or vice versa [28].

ii) Current Status

Currently, there are several US machines that can provide breast elastography with reasonable image quality [80]. However, use of elastogram can be a bit more challenging for some sonologists as they have reported to find it less useful than conventional B-mode US. The problem in interpreting images might be because of not using the highest quality elastograms that are available [80]. It is important to mention that the target of breast elastography not only is to diagnose cancers but also to classify the doubtful lesions on the ultra-sonogram confidently as benign. This will eventually reduce the

ACCEPTED MANUSCRIPT

Table 6. Breast cancer diagnostic results of US Elastography claimed in different published works [1-25, 97, 98] compared to conventional B-mode Sonography and Mammography[3].

Article/Year	# Benign/ malignant Size	Technique Used	Sensitivity TPR (%)	Specificity TNR (%)	Accuracy (%)	PPV / NPV (%)
[1] Itoh et al./2006	59/52 <30 mm	Free Hand US Elastography	86.5	89.8	88.3	-
[2] Gong et al./2011	30/198 -	Free Hand US Elastography	95	93.3	94.7	76.5 / 73.7
[3] Raza et al. /2010	127/61 <26 mm	Free Hand US Elastography	92.7	85.8	88.3	76 / 96
		B-mode Sonography	98.4	66.9	--	58.8 / 98.8
[5] Fischer et al./2011	85/116 -	Free Hand USE (SR)	95	74	86	83 / 91.3
		B-mode Sonography	85	60	-	
		Mammography	78	62	-	
[6] Wojcinski et al./ 2010	419/360 < 30 mm	Sonoelastography	81.2	89.5	-	86.8 / 84.8
		B-mode ultrasound	95	76.1	-	77.2 / 94.7
		Mammography	87.2	82.9		
[7] Hatzung et al./ 2010	66/31 -	Sonoelastography	71	48	-	39 / 78
		Mammography	84	89	-	79 / 92
		B-mode US	97	82	-	71 / 98
[8] Yerli et al./ 2011	62/16	US Elastography (SR)	75	94	89.7	75 / 93.5
[9] Lee et al./ 2011	267/48	US Elastography (SR)	68.75	64.8	65.4	26 / 92
[10] Kumm et al./ 2010	223/87	US Elastography (SR)	79	76	77	56.5 / 90.4
[28] Zhi et al./ 2010	415/144	US Elastography (SR)	92	91	91.4	78.2 / 97.2
[29] Cho et al./ 2010	79/20	US Elastography (SR)	95	75	78.8	48.7 / 98.3
[13] Farrokh et al./2010	63/54	US Elastography (SR)	94	87	90.6	86.4 /94.8
[14] Thomas et al. / 2010	113/114	US Elastography (SR)	90	88	89.4	88.8 / 90
[15] Moon et al. / 2009	113/68	US Elastography (SR)	84	88	86.2	80.3 / 90
[16] Barr et al. / 2010	197/54	US Elastography (LR)	100	95	96	84.4 / 100
[17] Leong et al. / 2010	84/26	US Elastography (LR)	92	69	74.5	48 / 96.7
[18] Regner et al. / 2006	38/51	US Elastography (LR)	96	21	64	62 / 80
[19] Parajuly et al./ 2010	-	USE Elasticity Score	94	95	-	-
[20] Zhu et al. / 2008	-	USE Elasticity Score	86	89	-	-
[21] Regini et al./ 2010	-	USE Elasticity Score	89	93	-	-
[22] Navarro et al./2011	-	USE Elasticity Score	69	83	-	-
[23] Guiseppetti et al./2005	-	USE Elasticity Score	80	89	-	-
[24] Chang et al./2011	-	USE Elasticity Score	87	85	-	-
[25] Schaefer et al./2009	-	USE Elasticity Score	97	76	-	-
[98] Nesreen et al./2014	81/33 < 90 mm	Mammography	72.7	86.4	82.5	-
		US	69.7	72.8	71.9	-
		USE	69.7	95.1	81.7	-
		Combined US + UE	90.9	95.1	93.8	-
[97] Zhi et al./2007	209/87 < 100.6 mm	Mammography	72.4	87.1	82.7	70.0 /88.3
		US (B-mode)	71.2	73.2	72.6	52.5 / 86.0
		USE	70.1	95.7	88.2	87.1 / 88.5
		US + USE	89.7	95.7	93.9	89.7 / 95.7

[3]The shaded rows of the table represent the articles that have provided mammography's diagnostic performance along with B-mode US and USE. The rest of the articles provided diagnostic results of only B-mode US and USE, not mammography.

no. of biopsies of benign lesions [80]. In this regard, as reported by articles [25, 84-86], breast elastography has shown excellent area under the ROC curve having values of around 88% to 95% for classification between benign and malignant breast masses [80].

Recently, apart from the enhancement of elastography by quantification of stiffness either by strain-ratio measurement [81] or by ARFI imaging and shear-wave velocity estimation [82], a new technique is reported by [83] named *axial shear strain elastography* (ASSE). This technique is expected to be helpful to improve the capability of elastography in separating benign from malignant masses. Since ASSE can show how strongly any lesion is attached with its surrounding tissues, therefore the images can be easy to interpret compared with normal elastograms and consequently can be useful in deciding on equivocal cases [80].

According to the current medical policy, Oct 2014, stated by Health Net, Inc. [87], breast elastography performed either by US or MRI is considered to be investigational. Even though several studies and clinical trials are going on, there is not adequate proof in the peer-reviewed medical literature to support the effectiveness of breast elastography. Therefore, extensive clinical trials of this technology are required by addressing proper patient selection and diagnostic parameters in order to get approval for widespread clinical use.

iii) Limitations of Breast Elastography

While breast elastography is a promising technique in lesion detection, it also has several limitations, largely due to the structural characteristics of the breast itself and its nodule. There are also some issues related to elastographic technique and due to its vague knowledge as mentioned in the first part of this section. The other limitations are listed below [28, 59]:

- Different expression of gland components found within the population studied
- Absence of the capsule that could allow to contain the compressing tissues
- It is hard to distinguish lesions with high variability and with features of benignity or malignancy that may not match to their elasticity (e.g. cysts, necrosis, etc.).
- The ambiguity on reference parameters, especially the requirement of sufficiently surrounded share of healthy parenchyma that must be localized at equal depth of lesions for getting a right contrast.
- The variability of transducer pressure can affect the quality of elastograms and hence sometimes the stiffness of benign and malignant tissues may overlap. E.g. some cancers lack a considerable desmoplastic reaction and may be soft, thus results in false negative elastograms.
- Some benign lesions might be seen as stiff including hyalinized fibroadenomas, fat necrosis and fibrosis.
- Posterior breast masses can be also tricky to assess with elastography as the compression force is unable to displace deep tissue less than superficial tissue.
- It is difficult to image extremely large tumor (>3 cm) as all tissues in the range of vision are stiff and normal tissue may not be incorporated for examination.
- Absence of standard color-coding or scoring.

FUTURE POSSIBILITIES

As mentioned earlier that US elastography has already been proven to have enormous potential to improve both specificity and sensitivity significantly in separating between benign and malignant breast lesions. The future possibilities of elastography combined with other techniques can be really exciting of which some examples are given in this section.

i) Detection and Diagnosis

The features of elastography including size ratios, homogeneity, and lesion stiffness may be useful to characterize masses that appear on conventional breast ultrasound. Careful correlation of B-mode ultrasound, mammography and elastography is essential as not every cancer appears stiff on elastography. If all elastography features are found to be benign, it is probably wise to downgrade from BI-RADS 4A to BI-RADS 3 or from BI-RADS 3 to BI-RADS 2, although large prospective clinical studies are required for validation [28]. Some possible future uses of elastography as mentioned in [28] are as follows:

- Characterization of small incidental masses as observed during screening breast US
- Detection of malignant auxiliary lymph nodes
- Detection of subtle masses during targeted US after MRI
- Recognition of more suspicious part of the lesion to facilitate guiding during US biopsy

ACCEPTED MANUSCRIPT

Shear wave based techniques have been demonstrated to have significant advantages over quasi-static techniques: they are better in reproducibility, quantitative, depend on automated shear wave generation and provide good contrast in elasticity. These benefits will potentially allow SWE imaging for new applications in the future not only for diagnosis but also for follow-up. In addition, the real-time imaging ability of some of SWE techniques also permits the development of 3D elastography imaging which may facilitate some of the routine clinical practices of detection, therapy planning and monitoring for breast cancer [29].

ii) Intraoperative Tumor Detection

While the primary focus of this article is breast cancer diagnosis, and so far the research or use of elastography-based techniques limited to diagnosis purpose, we believe that it can also be a potential tool for surgical guidance in future. In the case of the impalpable breast tumor, the treatment of choice is surgery. In the past, only surgical option was *mastectomy*, but nowadays, with the availability of advanced surgical procedure, *lumpectomy* or *breast conserving surgery* (BCS), is the first preference from patient's point of view. However, it is quite troublesome from the surgeon's perspective to accurately locate the tumor during surgery when it is impalpable. The existing tools for intraoperative localization of breast tumors have respective drawbacks. Especially, in case of detecting *mm* size tumors or cellular seedling of cancers, all of the tools fail invariably. Without any doubt, if a survey from breast surgeons could have been performed, BCS would rank the most technically challenging due to the shortcomings of the existing solutions. Some limitations of available intraoperative breast cancer detection tools are given in Table 7.

Table 7. Limitations of the current intraoperative detection tools

Current Intraoperative Detection Tools	**Limitations**
Wire Guided Localization **(WGL)**	Scheduling problem Dislocation, burning, breakage of wire Hard to locate when tumour is far away for skin Difficult to identify tumour margin
Radio Guided Occult Lesion Localization **(ROLL)**	Radioactive hazards to both surgeon & patient Scheduling problem Start/stop disadvantage due to gamma probe
Radioactive Seed Localization **(RSL)**	
Intraoperative ultrasound **(IOUS)**	Failure to detect isoechoic, small sized lesions Start/stop disadvantage

In pursue of finding a solution to the above mentioned limitations, elastography can be a better alternative to all these methods to aid intraoperative detection of impalpable mm size, cellular seedlings of breast tumors. With an appropriate tissue compression technique and a high quality imaging modality suitable for real-time imaging, elastography is expected to be useful in intraoperative applications. In order to achieve such, state-of-the-art image processing will also play an important role. Further research in this regard can open a gateway to make elastography device portable, wireless, easy to handle, and mostly to aid real-time imaging to continue breast-conserving surgery with maximum possible perfection.

CONCLUSION

Elastography is an emerging research field with lots of possibilities. It provides a unique way to assess tissue stiffness and finds out that tissue elasticity is of great significance for diagnosis. Ultrasound elastography is proved to be effective for breast lesion characterization and is an easier, cheaper method. It is also more specific than mammography or US alone. However, it is operator dependent. It is suggested that the radiologists should be more careful in identifying the difference between different types of USE since they differ from one manufacturer to another; especially there is lack of universal colour-coding standard. Hence, stiff lesions may appear red, while soft lesions may appear blue, or vice versa depending on the manufacturer. It is essential to study the underlying physics of each elastography method to find out their pros and cons for use in clinical practice. In addition, in order to understand different elastography techniques and their imaging modalities, standard terminologies are indeed required. The research teams should co-operate to validate the prospects of elastography and then the manufacturers would be able to bring the elastography technology in market with standard display and universal classification scores for early and better diagnosis of breast cancer along with other cancers as well (e.g. liver, prostrate, etc.), even for application as surgical guidance in the future.

ACCEPTED MANUSCRIPT

APPENDIX

Abbreviation	Definition
US	Ultrasonography / Sonography
USE	Ultrasound Elastography / Sono-Elastography; Ultrasound Strain Elastography
USB	B-mode Ultrasound
SWE	Shear-wave Elastography
ROC	Receiver Operating Characteristic
RTE	Real-time Elastography
ARFI	Acoustic Radiation Force Impulse (imaging)
ASSE	Axial Shear Strain Elastography
MRE	Magnetic Resonance Elastography
SSI	Supersonic Shear Imaging
VCTE^{TM}	Vibration-Controlled Transient Elastography
TPR / FPR	True Positive Rate / False Positive Rate
PPV / NPV	Positive Prediction Value / Negative Prediction Value
BI-RADS	Breast Imaging-Reporting and Data System
OCT / OCE	Optical Coherence Tomography / Optical Coherence Elastography
BCS	Breast Conserving Surgery
SR	Strain Ratio
LR	Likelihood Ratio
DITI	Digital Infrared Thermal Imaging
EIS	Electrical Impedance Scanning

References

[1] Itoh A, Ueno E, Tohno E, et al. Breast disease: clinical application of US elastography for diagnosis. Radiology 2006;239:341–50.

[2] Gong X, Xu Q, Xu Z, et al. Real-time elastography for the differentiation of benign and malignant breast lesions: a meta-analysis. Breast Cancer Research and Treatment 2011;130(1):11–8.

[3] Raza S, Odulate A, Ong EM, et al. Using real-time tissue elastography for breast lesion evaluation: our initial experience. Journal of Ultrasound in Medicine2010;29(4):551–63.

[4] Sadigh G, Carlos RC, Neal CH, et al. Accuracy of quantitative ultrasound elastography for differentiation of malignant and benign breast abnormalities: a meta-analysis. Breast Cancer Research and Treatment 2012;134:923–31.

[5] Fischer T, Peisker U, Fiedor S et al (2011) Significant differentiation of focal breast lesions: raw data-based calculation of strain ratio. Ultraschall Med. doi:10.1055/s-0031-1273222

[6] Wojcinski S, Farrokh A, Weber S, Thomas A, Fischer T, Slowinski T, Schmidt W, Degenhardt F. et al. Multicenter study of ultrasound real-time tissue elastography in 779 cases for the assessment of breast lesions: improved diagnostic performance by combining the BI-RADS®-US classification system with sonoelastography. Ultraschall Med. 2010 Oct; 31(5):484-91. doi: 10.1055/s-0029-1245282. Epub 2010 Apr 20.

[7] Hatzung G, Grunwald S, Zygmunt M, Geaid AA, Behrndt PO, Isermann R, Kohlmann T, Ohlinger R. et al. Sonoelastography in the diagnosis of malignant and benign breast lesions: initial clinical experiences. Ultraschall Med. 2010 Dec; 31(6):596-603. doi: 10.1055/s-0029-1245526. Epub 2010 Jul 7.

[8] Yerli H, Yilmaz T, Kaskati T, Gulay H (2011) Qualitative and semiquantiative evaluations of solid breast lesions by sonoelastography. J Ultrasound Med 30:179–186

[9] Lee JH, Kim SH, Kang BJ, Choi JJ, Jeong SH, Yim HW et al (2011) Role and clinical usefulness of elastography in small breast masses. Acad Radiol 18(1):74–80

[10] Kumm TR, Szabunio MM (2010) Elastography for the characterization of breast lesions: initial clinical experience. Cancer Control 17:156–161

[11] Zhi H, Xiao XY, Yang HY, Ou B, Wen YL, Luo BM (2010) Ultrasonic elastography in breast cancer diagnosis: strain ratio vs. 5-point scale. Acad Radiol 17(10):1227–1233

[12] Cho N, Moon WK, Kim HY, Chang MJ, Park SH, Lyou CY (2010) Sonoelastographic strain index for differentiation of benign and malignant nonpalpable breast masses. J Ultrasound Med 29:1–7

[13] Thomas A, Degenhardt F, Farrokh A, Wojcinski S, Slowinski T, Fischer T et al (2010) Significant differentiation of focal breast lesions: calculation of strain ratio in breast sonoelastography. Acad Radiol 17(5):558–563

[14] Hiltawsky KM, Kruger M, Starke C, Heuser L, Ermert H, and Jensen A, Freehand ultrasound elastography of breast lesions: clinical results, Ultrasound Med Biol. 27 (11), 1461-1469., 2001

[15] Cho N, Moon WK, Park JS (2009) Real-time US elastography in the differentiation of suspicious microcalcifications on mammography. Eur Radiol 19(7):1621–1628

[16] Barr RG (2010) Real-time ultrasound elasticity of the breast: initial clinical results. Ultrasound Q 26(2):61–66

[17] Leong LC, Sim LS, Lee YS, Ng FC, Wan CM, Fook-Chong SM et al (2010) A prospective study to compare the diagnostic performance of breast elastography versus conventional breast ultrasound. Clin Radiol 65(11):887–894

[18] Regner DM, Hesley GK, Hangiandreou NJ, Morton MJ, Nordland MR, Meixner DD et al (2006) Breast lesions: evaluation with US strain imaging—clinical experience of multiple observers. Radiology 238(2):425–437

[19] Parajuly SS, Lan PY, Yan L, Gang YZ, Lin L (2010) Breast elastography: a hospital-based preliminary study in China. Asian Pac J Cancer Prev 11(3):809–814

[20] Zhu QL, Jiang YX, Liu JB, Liu H, Sun Q, Dai Q et al (2008) Real-time ultrasound elastography: its potential role in assessment of breast lesions. Ultrasound Med Biol 34(8):1232–1238
[21] Regini E, Bagnera S, Tota D, Campanino P et al (2010) Role of sonoelastography in characterising breast nodules. Preliminary experience with 120 lesions. Radiol Med (Torino) 115:551–562
[22] Navarro B, Ubeda B, Vallespi M, Wolf C et al (2011) Role of elastography in the assessment of breast lesions: preliminary results. J Ultrasound Med 30:313–321
[23] Giuseppetti G M, an B D Cioccio A M and Baldassarre S 2005 Elastosonography in the diagnosis of the nodular breast lesions: preliminary report Radiologia Med. 110 69–76
[24] Chang JM, Moon WK, Cho N, Kim SJ (2011) Breast mass evaluation: factors influencing the quality of US elastography. Radiology 259:59–64
[25] Schaefer FK, Heer I, Schaefer PJ, Mundhenke C et al (2009) Breast ultrasound elastography-Results of 193 breast lesions in a prospective study with histopathologic correlation. Eur J Radiol 77:450–456
[26] Thomas D. Vreugdenburg, Cameron D. Willis, Linda Mundy and Janet E. Hiller: A systematic review of elastography, electrical impedance scanning and digital infrared thermography for breast cancer screening and diagnosis. Breast Cancer Res Treat (2013) 137:665–676.
[27] Tomy Varghese. Imaging Elastographic Properties of Soft Tissues Using Ultrasound: http://www.aapm.org/meetings/04AM/pdf/14-2318-43703.pdf
[28] https://iame.com/online/breast_elastography/content.php
[29] J. L. Gennisson, T. Deffieux, M. Fink and M. Tanter. Ultrasound elastography: Principles and techniques. Diagnostic and Interventional Imaging (2013) 94, 487—495
[30] A. Goddi, M. Bonardi, S. Alessi. Breast elastography: A literature review. Journal of Ultrasound (2012) 15, 192e198
[31] Regina J. Hooley, Leslie M. Scoutt, and Liane E. Philpotts. Breast Ultrasonography: State of the Art. Radiology: Volume 268: Number 3, September 2013.
[32] Paolo Ricci, Elena Maggini, Ester Mancuso, Pietro Lodise, Vito Cantisani and Carlo Catalano. Clinical application of breast elastography: State of the art. European Journal of Radiology, Volume 83, Issue 3, Pages 429–437, March 2014.
[33] Marvin M. Doyley and Kevin J. Parker. Elastogrpahy: General Principles and Clinical Applications. Ultrasound Clin 9 (2014) 1–11
[34] K. M. Hiltawsky, W. Khaled, A. Lorenz, C. Perrey, A. Pesavento, U. Scheipers, S. Siebers, M. Vogt and H. Ermert. Principle, Applications and Limitations of Ultrasound Elastography. W Arnold and S. Hirsekorn (eds.). Acoustical Imaging, 503-510. 2004 Kluwer Academic Publishers.
[35] C. Balleyguiera, S. Canale, W. Ben Hassen, P. Vielh, E.H. Bayou, M.C. Mathieu, C. Uzan, C. Bourgier, and C. Dromain. Breast elasticity: Principles, technique, results: An update and overview of commercially available software. European Journal of Radiology 82 (2013) 427– 434
[36] Katsumi Ikeda, Yoshinari Ogawa, Mamiko Takii, Kenji Sugano, Tetsuro Ikeya, Shinya Tokunaga, Yukio Nishiguchi and Teruyuki Ikehara. A role for elastography in the diagnosis of breast lesions by measuring the maximum fat lesion ratio (max-FLR) by tissue Doppler imaging. Breast Cancer (2012) 19:71–76
[37] Sughra Raza, Ayodule Odulate, Eugene M. W. Ong, Sona Chikarmane and Chad W. Harston. Using Real-time Tissue Elastography for Breast Lesion Evaluation. J Ultrasound Med 2010; 29:551–563
[38] Richard G. Barr, Stamatia Destounis, Logan B. Lackey II, William E. Svensson, Corinne Balleyguier and Carmel Smith. Evaluation of Breast Lesions Using Sonographic Elasticity Imaging. J Ultrasound Med 2012; 31:281–287
[39] Richard G. Barr. Sonographic Breast Elastography. J Ultrasound Med 2012; 31:773–783
[40] Kevin J. Parker, Dongshan Fu, Sheryl M. Graceswki, Fai Yeung, and Stephen F. Levinson. Vibration Sonoelastography and the Detectability of Lesions. Ultrasound in Med. & Biol., Vol. 24, No. 9, pp. 1437–1447, 1998
[41] Garra BS. Imaging and estimation of tissue elasticity by ultrasound. Ultrasound Q [Internet]. 2007 Dec;23(4):255-68.
[42] Barr RG. Sonographic breast elastography: A primer. J Ultrasound Med [Internet]. 2012 May;31(5):773-8.
[43] Athanasiou A, Tardivon A, Tanter M, Sigal-Zafrani B, Bercoff J, Deffieux T, Gennisson JL, Fink M, Neuenschwander S. Breast lesions: Quantitative elastography with supersonic shear imaging--preliminary results. Radiology [Internet]. 2010 Jul;256(1):297-303.
[44] Berg WA, Cosgrove DO, Dore CJ, Schafer FK, Svensson WE, Hooley RJ, Ohlinger R, Mendelson EB, Balu-Maestro C, Locatelli M, Tourasse C, Cavanaugh BC, Juhan V, Stavros AT, Tardivon A, Gay J, Henry JP, Cohen-Bacrie C, BE1 Investigators. Shear-wave elastography improves the specificity of breast US: The BE1 multinational study of 939 masses. Radiology [Internet]. 2012 Feb;262(2):435-49.
[45] Fleury Ede F, Fleury JC, Piato S, Roveda D,Jr. New elastographic classification of breast lesions during and after compression. Diagn Interv Radiol [Internet]. 2009 Jun;15(2):96-103.
[46] Tozaki M, Fukuma E. Pattern classification of Shear Wave elastography images for differential diagnosis between benign and malignant solid breast masses. Acta Radiol [Internet]. 2011 Dec 1;52(10):1069-75.
[47] Barr RG, Lackey AE. The utility of the "bull's-eye" artifact on breast elasticity imaging in reducing breast lesion biopsy rate. Ultrasound Q [Internet]. 2011 Sep;27(3):151-5.
[48] Cho N, Moon WK, Chang JM, Kim SJ, Lyou CY, Choi HY. Aliasing artifact depicted on ultrasound (US)-elastography for breast cystic lesions mimicking solid masses. Acta Radiol [Internet]. 2011 Feb 1;52(1):3-7.
[49] Evans A, Whelehan P, Thomson K, McLean D, Brauer K, Purdie C, Baker L, Jordan L, Rauchhaus P, Thompson A. Invasive breast cancer: Relationship between shear-wave elastographic findings and histologic prognostic factors. Radiology [Internet]. 2012 Jun;263(3):673-7.
[50] Cosgrove DO, Berg WA, Dore CJ, Skyba DM, Henry JP, Gay J, Cohen-Bacrie C, BE1 Study Group. Shear wave elastography for breast masses is highly reproducible. Eur Radiol [Internet]. 2012 May;22(5):1023-32.
[51] Hirokazu Takahashi1 et al. (2011) Acoustic Radiation Force Impulse Elastography: A Non-Invasive Alternative to Liver Biopsy. Liver Biopsy, InTech
[52] Nightingale KR, Palmeri ML, Nightingale RW, Trahey GE. On the feasibility of remote palpation using acoustic radiation force. J Acoust Soc Am 2001.110: 625–34.
[53] Palmeri ML, Frinkley KD, Zhai L, Gottfried M, Bentley RC, Ludwig K, Nightingale KR. Acoustic radiation force impulse (ARFI) imaging of the gastrointestinal tract. Ultrason Imaging. 2005;27:75–88.
[54] Dahl JJ, Pinton GF, Palmeri ML, Agrawal V, Nightingale KR, Trahey GE.. A parallel tracking method for acoustic radiation force impulse imaging. IEEE Trans Ultrason Ferroelectr Freq Control. 2007;54:301–12.
[55] Deniz Çebi Olgun, Bora Korkmazer, Fahrettin Kılıç, Atilla Süleyman Dikici, Mehmet Velidedeoğlu, Fatih Aydoğan, Fatih Kantarcı, Mehmet Halit Yılmaz. Use of shear wave elastography to differentiate benign and malignant breast lesions. Diagn Interv Radiol DOI 10.5152/dir.2014.13306
[56] Evans A, Whelehan P, Thomson K, et al. Quantitative shear wave ultrasound elastography: initial experience in solid breast masses. Breast Cancer Res 2010; 12:R104.
[57] Cosgrove DO, Berg WA, Doré CJ, et al. Shear wave elastography for breast masses is highly reproducible. Eur Radiol 2011; 22:1023–1032.
[58] http://biophotonics.illinois.edu/technology/elas/index.html
[59] Rebekah Moan. Breast elastography: the pros and cons. Appeared in European Journal of Radiology. http://medicalphysicsweb.org/cws/article/research/53994
[60] A. Sarvazyan, A.R. Skovoroda, S. Emelianov, J.B. Fowlkes Biophysical bases of elasticity imaging Acoust Imag, 21 (1995), pp. 223–241
[61] Yogesh K. Mariappan, Kevin J. Glaser, And Richard L. Ehman. Magnetic Resonance Elastography: A Review. Clinical Anatomy 23:497–511 (2010)

[62] Cuiru Sun, Beau Standish, and Victor X. D. Yang. Optical coherence elastography: current status and future applications. Journal of Biomedical Optics 16(4), 043001 (April 2011)
[63] K. Han-Jo, T. Wei, R. A. Stack, and S. A. Boppart, "Optical coherence elastography of developing biological tissues," Proc. SPIE 5690, 187–194 (2005).
[64] V. Yang, N. Munce, J. Pekar, M. Gordon, S. Lo, N. Marcon, B. Wilson, and I. Vitkin, "Novel micromachined array tip for multifocus fiber-based optical coherence tomography," Opt. Lett. 29, 1754–1756 (2004).
[65] Raquel Constantino Pardal, António Fernando Lagem Abrantes, Luís Pedro Vieira Ribeiro, Rui Pedro Pereira Almeida, Kevin Barros Azevedo, Teresa Leonor Figueiredo and Sónia Isabel Rodrigues. Screening of breast lesions: a comparative study between mammography, B-mode ultrasonography, sonoelastography and histological results. Radiol Bras. 2013 Jul/Ago;46(4):214–220
[66] Ji Hyun Youk, Hye Mi Gweon, Eun Ju Son, Jeong-Ah Kim and Joon Jeong. Shear-wave elastography of invasive breast cancer: correlation between quantitative mean elasticity value and immunohistochemical profile. Breast Cancer Res Treat (2013) 138:119–126
[67] J Ophir, I Cespedes, H Ponnekanti, Y Yazdi, X Li. Elastography: a quantitative method for imaging the elasticity of biological tissues. Ultrasonic imaging, 1991 – Elsevier
[68] T Varghese, J Ophir, I Cespedes. Noise reduction in elastograms using temporal stretching with multicompression averaging - Ultrasound in medicine & biology, 1996 – Elsevier
[69] M O'Donnell. Real□time adaptive array processing for medical ultrasound imaging. *The Journal of the Acoustical Society of America* 90 (4), 2288-2288
[70] A Pesavento, A Lorenz, S Siebers and H Ermert. New real-time strain imaging concepts using diagnostic ultrasound. *Phys. Med. Biol*. 45 1423
[71] P Chaturvedi, MF Insana, TJ Hall. Ultrasonic and elasticity imaging to model disease-induced changes in soft-tissue structure - *Medical image analysis*, 1998 – Elsevier
[72] LN Bohs, BH Friemel, GE Trahey. Experimental velocity profiles and volumetric flow via two-dimensional speckle tracking - *Ultrasound in medicine & biology*, 1995 – Elsevier
[73] DS Bell, JC Bamber, RJ Eckersley. Segmentation and analysis of colour Doppler images of tumour vasculature - *Ultrasound in medicine & biology*, 1995 – Elsevier
[74] T Varghese, J Ophir. An analysis of elastographic contrast-to-noise ratio - *Ultrasound in medicine & biology*, 1998 – Elsevier
[75] SK Alam, J Ophir, Reduction of signal decorrelation from mechanical compression of tissues by temporal stretching: Applications to elastography - *Ultrasound in medicine & biology*, 1997 – Elsevier
[76] http://contech.suv.ac.kr/contech/research/mammography.htm
[77] Ginat DT, Destounis SV, Barr RG, Castaneda B, Strang JG, Rubens DJ.Deborah J. Rubens. US Elastography of Breast and Prostate Lesions. *Radiographics*. 2009 Nov;29(7):2007-16
[78] Kazutaka Nakashima, Tsuyoshi Shiina, Masaru Sakurai, Katsutoshi Enokido, Tokiko Endo, Hiroko Tsunoda, Etsuo Takada, Takeshi Umemoto and Ei Ueno. JSUM ultrasound elastography practice guidelines: breast. *J Med Ultrasonics* 2013
[79] Ophir, J., Alam, K.,Garra, B., Kallel, F., Konofagou, E., Krouskop, T., Varghese T., Elastography: Ultrasonic estimation and imaging of the elastic properties of tissues, Invited Paper & Review, *Proc. Inst. Mech. Eng., Part H J Engg. Med.*, Vol. 213, pp. 203-233,1999
[80] Brian S. Garra. Elastography: Current Status, Future Prospects, and Making It Work for You. *Ultrasound Quarterly* 2011; 27:3; pp.177-186
[81] Zhi H, Xiao XY, Yang HY, et al. Semi-quantitating stiffness of breast solid lesions in ultrasonic elastography. *Acad Radiol*. 2008;15(11):1347-1353.
[82] Bercoff J, Chaffai S, Tanter M, et al. In vivo breast tumor detection using transient elastography. *Ultrasound Med Biol*. 2003;29:1387-1396.
[83] Thitai-Kumar A, Garra BS, Ophir J. Visualization of bonding at an inclusion boundary using axial-strain elastography: a feasibility study. *Phys Med Biol*. 2007;52(9):2615.
[84] Hall TJ, Zhu Y, Spalding CS. In vivo real-time freehand palpation imaging. *Ultrasound Med Biol*. 2003;29(3):427Y435.
[85] Burnside ES, Hall TJ, Sommer AM, et al. Differentiating benign from malignant solid breast masses with US strain imaging. *Radiology*. 2007;245:401Y410.
[86] Saarenmaa I, Salminen T, Geiger U, Heikkinen P, Hyva¨rinen S, Isola J, et al. The effect of age and density of the breast on the sensitivity of breast cancer diagnostic by mammography and ultrasonography. *Breast Cancer Res Treat* 2001; 67:117e23.
[87] Breast Elastography by National Medical Policy provided by *Health Net, Inc.* found in https://www.healthnet.com/static/general/unprotected/pdfs/national/policies/BreastElastography.pdf
[88] Au FW, Ghai S, Moshonov H, et al. Diagnostic performance of quantitative shear wave elastography in the evaluation of solid breast masses: determination of the most discriminatory parameter. *AJR Am J Roentgenol.* 2014 Sep;203(3):W328-36.
[89] Chen L, He J, Liu G, et al. Diagnostic performances of shear-wave elastography for identification of malignant breast lesions: a meta-analysis. *Jpn J Radiol.* 2014 Sep 7.
[90] Lee SH, Chang JM, Kim WH, et al. Added Value of Shear-Wave Elastography for Evaluation of Breast Masses Detected with Screening US Imaging. *Radiology*. 2014 Oct;273(1):61-9.
[91] Lee SH, Cho N, Chang JM, et al. Two-View versus Single-View Shear-Wave Elastography: Comparison of Observer Performance in Differentiating Benign from Malignant Breast Masses. *Radiology*. 2013 Oct 28:130561.
[92] Mullen R, Thompson JM, Moussa O, et al. Shear-wave elastography contributes to accurate tumour size estimation when assessing small breast cancers. *Clin Radiol.* 2014 Sep 17.
[93] Plecha DM, Pham RM, Klein N, et al. Addition of Shear-Wave Elastography during Second-Look MR Imaging-directed Breast US: Effect on Lesion Detection and Biopsy Targeting. *Radiology*. 2014 Sep;272(3):657-64.
[94] Youk JH, Son EJ, Park AY, Kim JA. Shear-wave elastography for breast masses: local shear wave speed (m/sec) versus Young modulus (kPa). *Ultrasonography*. 2014 Jan;33(1):34-9.
[95] K.J. Parker, R.M. Lerner. Sonoelasticity of organs: shear waves ring a bell. *J Ultrasound Med*, 11 (August (8)) (1992), pp. 387–392
[96] B.S. Garra, E.I. Cespedes, J. Ophir et al. Elastography of breast lesions: initial clinical results. *Radiology*, 202 (January (1)) (1997), pp. 79–86
[97] Zhi H, Ou B, Luo BM, Feng X, Wen YL, Yang HY. Comparison of ultrasound elastography, mammography, and sonography in the diagnosis of solid breast lesions. *J Ultrasound Med.* 2007 Jun;26(6):807-15.
[98] Nesreen Mohey, Tamir A. Hassan. Value of mammography and combined grey scale ultrasound and ultrasound elastography in the differentiation of solid breast lesions. *The Egyptian Journal of Radiology and Nuclear Medicine* (2014) 45, 253–261
[99] Raquel et al. Screening of breast lesions: a comparative study between mammography, B-mode ultrasonography, sonoelastography and histological results. *Radiol Bras* vol.46 no.4 São Paulo July/Aug. 2013.
[100] http://contech.suv.ac.kr/contech/research/mammography.htm

All in-text references underlined in blue are linked to publications on ResearchGate, letting you access and read them immediately.