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PRINCIPLES OF ULTRASOUND ELASTOGRAPHY

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Abstract

Tissue stiffness has long been known to be a biomarker of tissue pathology. Ultrasound elastography measures tissue mechanical properties by monitoring the response of tissue to acoustic energy. Different elastographic techniques have been applied to many different tissues and diseases. Depending on the pathology, patient based factors and ultrasound operator based factors, these techniques vary in accuracy and reliability. In this review, we discuss the physical principles of ultrasound elastography, discuss differences among various ultrasound elastographic techniques, and review the advantages and disadvantages of these techniques in clinical practice.

Keywords

Ultrasound; elastography; shear wave; strain

INTRODUCTION

Since time immemorial, physicians have gained insight into tissue biology through diagnostic palpation, the physical examination technique by which mechanical tissue property changes are detected. Changes in tissue mechanics typically accompany common disease processes, including fibrosis, inflammation and neovascularization. These changes can be assessed with new advanced ultrasound techniques, termed ultrasound elastography.

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Elastography Physics

Elastography is the set of techniques by which tissue stiffness is estimated as a physical property termed the Young's modulus (E). The Young's modulus is a proportionality constant that relates applied force per unit area or stress, and the resultant relative change in tissue dimension, or strain. Ultrasound elastography methods may be divided into two categories: quasi-static, or strain based, and dynamic, or shear wave based.

The nature of the external mechanical stimulus defines these methods. In strain-based elastography, force is applied by the application of probe pressure or through endogenous mechanical force (e.g. carotid pulsation). In shear-wave based elastography, a tissue shear-wave is induced by the imaging system. In both approaches, the response of tissue to these mechanical stimuli is used to estimate tissue mechanical properties. Strain imaging uses the direct relationship $E= \sigma/\varepsilon$ (Hooke's Law) in which σ represents externally applied stress, and ε represents strain[1,2]. Young's modulus is usually not computed with clinical strain imaging systems, as the applied force on the tissue of interest is usually not known. Shear wave imaging systems compute Young's modulus using the relationship $E=3\rho c_s^2$ in which ρ represents tissue density, and c_s represents shear wave speed[1,2]. Most of the vendors provide automatic calculation systems and ultrasound operator can convert kPa to m/s and m/s to kPa. Secondly at the end of the ultrasound exam, most ultrasound systems show a table that indicates stiffness values both in kPa and m/s.

STRAIN ELASTOGRAPHY (SE)

SE measures tissue stiffness by applying external tissue pressure[3]. Tissue dimensions change due to the applied pressure; this deformation is termed strain. Stiffer lesions deform less, and have correspondingly lower strain and higher Young's modulus. The strain ratio can be computed as the ratio between strain in a region of tissue and strain in a reference region of tissue. Computation of the strain ratio does not require knowledge of the applied force. For this reason, strain ratio is commonly used in clinical practice, and is mathematically equivalent to the Young's modulus ratio between two tissue regions, assuming applied force is equivalent across these regions.

Strain elastography can be further divided into two groups by the method of tissue excitation(external manual excitation or excitation with internal physiological movement) [1]. Excitation with manual pressure measures elasticity in superficial tissues. A disadvantage of this excitation method is that manual stress is not efficiently transmitted to deeper tissues. Excitation from natural physiologic motion, such as cardiac pulsation and respiration, is another mechanism of generating tissue stress. Deep organs can be assessed with this method[1]. A variety of strain elastography implementations are available on clinical ultrasound systems, including ElaXto™, Real-time tissue elastography™, ElastoScan™, eSieTouch™, and Elasticity Imaging by the manufacturers Esaote, Hitachi, GE, Philips, Toshiba, Ultrasonix, Mindray, Samsung and Siemens[1,2]. A strain image example, in comparison with conventional ultrasound image, is indicated in figure 1. In Virtual Touch™Imaging (VTI), strain elastography is performed with the help of an acoustic push pulse, eliminating the need for an external/internal excitation method[2].

In strain imaging, tissue displacement is calculated by processing radiofrequency (RF) datasets obtained before and after compression[4]. Translucent colored elastograms (strain images) can be superimposed on B-mode images to provide complementary anatomic information. It is common to display the strain map as colored pixels on a red/blue scale or gray scale[5]. Unfortunately, inter-manufacturer display scale variability is substantial, limiting inter-vendor comparability of strain elastography images.

Parameters commonly used in strain elastography include:

- Strain ratio measures tissue deformation compared between two regions of interest (ROI). Strain ratio >1, is an indicator of relatively low strain, high stiffness[2].
- Elasticity scores or grading systems are qualitative systems that have been used in a wide spectrum of disease processes, including breast imaging, to assess lesions[5]. These systems typically classify elastography patterns in a range between benign and malignant[1,5]
- Fat to lesion strain ratio is the strain ratio between fat and a lesion[6].
- Elastography-to-B-mode size ratio is an index of the maximum size of a lesion on elastogram to that on a corresponding B-mode image[7].

Generally, in deep organs such as the liver and kidney, tissue stress is obtained with the help of cardiac/arterial or respiratory motion. In superficial organs like the thyroid, tissue stress is obtained with the help of manual compression. A strain image example of a lesion in comparison with conventional ultrasound image, is presented in figure 1.

SHEAR WAVE ELASTOGRAPHY (SWE)

The compressive acoustic waves used for conventional B mode image generation travel at high speeds through soft tissue (1450–1550 m/s). By contrast, mechanical shear waves used for shear wave elastography travel relatively slowly (1–10 m/s). Shear wave propagation velocity depends on tissue stiffness[2,4]. In commercially available shear wave elastography systems, compressive acoustic waves are used both to induce and track shear waves. Acoustically induced shear waves travel perpendicular to compressive waves; tissue motion induced by these shear waves is monitored at multiple locations along the ultrasound probe, permitting shear wave velocity estimation[4]. Young’s modulus can be algebraically derived from the shear wave speed (SWS).

SWS can be used in many different tissues for a variety of applications including hepatic lesion characterization[8], renal lesion characterization[9], diffuse liver and renal disease evaluation[10,11], breast mass diagnosis[12,13], prostate cancer detection[14], thyroid lesion characterization[15] and tendon imaging[16].

Transient Elastography (TE)

A low frequency (50 Hz) mechanical push is generated by a mechanical actuator and a resulting shear wave is generated and evaluated[17,18]. With this technique, parameters like anisotropy, viscosity or elastic non-linearity can also be obtained[19]. Shear wave

propagation velocity is proportional to tissue stiffness, which increases with fibrosis[20]. 1D transient elastography is marketed under the trade name FibroScan®. TE measures tissue stiffness over a 1 cm diameter-4 cm length region of tissue, which is 100 times larger than that evaluated with liver biopsy. If the pulse is not transmitted and recorded successfully, the software does not provide a reading[21]. Stiffness values are presented in kPa. Controlled Attenuation Parameter (CAP), is a technology that quantifies hepatic steatosis by measuring the energy loss as the sound wave passes through the medium. Total attenuation at 3.5MHz is expressed in $dB.m^{-1}$ and steatosis is estimated using the same radiofrequency data as elastography, in the same location that stiffness is measured[22] (Figure 2).

Point Shear Wave Elastography (pSWE)

Focused ultrasound results in focal tissue displacement, a process termed acoustic radiation force impulse (ARFI) imaging. The resultant shear waves are tracked, yielding a shear wave speed estimate that is an algebraic function of tissue stiffness. Point SWE is available on the Siemens VirtualTouch™Quantification (VTQ/ARFI) system and on the Philips ElastPQ™ system[2]. An example of pSWE application on a phantom, is presented in figure 3.

2D Shear Wave Elastography

In this technique, acoustic radiation force is used to displace tissue at multiple points. The resultant shear wave front is more readily detectable with high frame rate imaging, which is used to monitor propagation of the shear waves in real time at multiple points in the image[24]. A quantitative elasticity image (elastogram) is presented as a colorized display map, with quantitative results available as shear wave propagation speed in m/sec or as the algebraically derived Young's modulus in kPa[25]. Real time tissue stiffness color maps added on the B-mode image allows the operator to avoid confounding anatomic structures such as blood vessels[26]. Maximum elastogram sizes are 2–3 cm in side length with a linear probe, and 9 × 4 cm with a convex probe[24]. This technique is available on multiple ultrasound systems including VirtualTouch™Imaging Quantification (VTIQ/ARFI) by Siemens, Shear Wave Elastography by Philips, Shear Wave™ Elastography by SuperSonic Imagine, 2D-SWE by GE Healthcare and Acoustic Structure Quantification™ (ASQ) by Toshiba [2]. An example of 2D-SWE application on a phantom, is presented in figure 4.

CLINICAL APPLICATIONS

1) Liver

Strain elastography—The liver fibrosis index (LFI)[27,28] has been shown to be an accurate technique to distinguish fibrosis stages with AUROC (Area under receiver operating characteristic) values of 0.82 for fibrosis stage F0–1 vs F2–4 and 0.87 for fibrosis stage F0–3 vs F4[27]. Koizumi et al. reported that a different strain parameter, termed 'elastic ratio' (the strain distribution value, intrahepatic venous small vessels/value in the hepatic parenchyma), was highly correlated with biopsy proven fibrosis stage (Spearman correlation 0.82, $p<0.001$) with AUROC values to diagnose F≥2 (0.89), F≥3 (0.94) and F=4 (0.95)[29]. SE can also be used to evaluate liver masses, with significant differences reported between benign and malignant lesions ($p<0.0001$)[30].

Transient elastography can be used in the diagnosis of liver fibrosis due to multiple etiological factors including chronic viral infection and excessive alcohol intake[31–33]. In a meta-analysis including chronic liver disease due to multiple etiological factors, TE showed summary sensitivity and specificity values of 0.79 (95% CI 0.74–0.82) and 0.78 (95% CI 0.72–0.83) for F2 stage and 0.83 (95% CI 0.79–0.86) and 0.89 (95% CI 0.87–0.91) for cirrhosis[34]. TE does not use B-mode anatomic imaging to define the tissue from which stiffness information is obtained. The operator uses A-Mode US to define a measurement location away from vascular structures[2]. Therefore, an operator is not able to select the same liver region for serial TE measurements over time. Obtaining reliable acquisitions requires, 1) at least 10 valid measurements, 2) valid measurements/total measurements ratio ≥60% and 3) interquantile range (IQR) less than 30% of median value. A short training period is typically required for TE operators [2,35]. TE has been shown to be reproducible with inter-operator intraclass correlation coefficient (ICC) of 0.98 and intra-operator ICC of 0.98[36]. CAP, is an integrated technology which can be used simultaneously with liver fibrosis quantification in FibroScan system. An image example of transient elastography is demonstrated in Figure 5.

pSWE can be used in HBV, HCV, hepatic toxicity, alcoholic liver disease, and autoimmune hepatitis related liver fibrosis[37–39]. It can also be used as a screening tool for fibrosis detection at early stages[40], although evidence of benefit in this setting is limited. pSWE has been shown to be useful in detection of liver fibrosis. In a recent meta-analysis of 23 studies, Hu et al. reported AUROC values to distinguish liver fibrosis stages ranging from 0.649 to 0.934 for F≥2, 0.848 to 0.97 for F≥3 and 0.723 to 0.98 for F4[41]. Using point SWE technique on both the liver and spleen has greater discriminative power than assessment of the liver alone[42]. Setting the ROI away from the liver capsule is recommended, as this choice results in more reliable shear wave speed values[43]. pSWE is a reproducible and reliable liver stiffness assessment technique, with ICC values of 0.89 (95% CI, 0.85–0.92) for intra-observer and 0.85 (95%CI,0.76–0.90) for inter-observer agreement[44]. An image example of pSWE is demonstrated in Figure 5.

2D-SWE is a useful and feasible technique for fibrosis staging in both pediatric and adult patients[10, 45]. 2D-SWE has good performance for fibrosis staging. For example, for the diagnosis of fibrosis stage F≥2, AUROC value is 0.862, and for early cirrhosis diagnosis, AUROC value is 0.926[46]. Using a cut-off value 7.29 kPa, this technique reaches a sensitivity of 95.4% for fibrosis stage ≥2 [47]. Although the diagnostic ability of the techniques are similar, shear wave speed values obtained from 2D-SWE may show higher stiffness values[48]. An image example of 2D-SWE is shown in Figure 5.

2) Kidney

Strain Elastography—Chronic kidney disease (CKD) patients show higher strain index (ratio) values when compared to healthy volunteers ($p<0.0001$)[49]. SE can also be used to detect renal graft interstitial fibrosis, a manifestation of organ rejection as a long-term complication of renal transplantation. Early diagnosis of graft fibrosis may play a useful role in treatment decisions concerning immunosuppressive agents[50].

pSWE—Renal fibrosis and diabetic renal disease can be evaluated with pSWE techniques. pSWE can detect renal fibrosis with a sensitivity of 86.3% and specificity of 83.3%[51]. Yu et al. reported a correlation of 0.773 ($p<0.05$) between urinary albumin to creatinine ratio (diabetic kidney disease marker) and shear wave speed determined by VTQ, implying pSWE may server as a marker for diabetic kidney disease[52]. pSWE has been shown as a reproducible technique with intraclass correlation coefficient(ICC) values of 0.71 in the right kidney and 0.69 in the left kidney[53]. Age ($p=0.006$) and gender ($p=0.03$) can influence the SWS measurements acquired from the kidney[54]. The etiology of CKD may be different between adults and pediatric population, and vesicoureteral reflux is accepted as the most common etiology in children[55].

2D-SWE can be used to diagnose chronic kidney disease. CKD patients show higher stiffness values[9.4kPa] when compared with healthy volunteers[4.4kPa]($p=0.002$)[11]. 2D-SWE can also be used in the diagnosis of diabetic kidney disease (DKD). Hassan et al. reported a significant difference in cortical stiffness values of DKD patients and healthy subjects(23.7kPa vs. 9.02, $p<0.001$). Furthermore, significant differences between CKD grades have been reported[56]. An image example of 2D-SWE use in renal tissue is demonstrated in Figure 6.

3) Breast

Several *strain elastography* features have been proposed, including strain ratio, elasticity score (Tsukuba score), and elastography-to-B-mode size ratio[57]. In a meta-analysis with 25 studies focusing on elasticity score and strain ratio, overall mean sensitivity and specificity values to distinguish malignant breast lesions were reported as 0.834 (95%CI, 0.814–0.853) and 0.842 (95%CI, 0.829–0.854), respectively, for elasticity score and 0.883(95%CI,0.844–0.916) and 0.814 (95%CI, 0.786–0.839) respectively, for strain ratio[58]. Furthermore, tumor grade can also be distinguished using an elasticity imaging/B-mode ratio[59]. It has been shown that the addition of strain elastography to a conventional grey-scale ultrasound based classification system - Breast Imaging Reporting and Data System (BI-RADS) – yields an AUROC of 0.875 in cancer detection with the ability to characterize lesions < 2 cm[60]. Breast lesion size prediction has been reported to be more accurate on elastographic images than conventional gray-scale images when compared with the reference standard of the surgical excision specimen[61].

pSWE—Li et al. reported the diagnostic performance of pSWE to differentiate malignant and benign lesions in a meta-analysis of 11 studies, finding an overall sensitivity of 0.84 (95%CI, 0.81–0.87) and specificity of 0.94 (95%CI, 0.91–0.94)[62]. 2D-SWE and pSWE had similar performance to detect malignancy in breast tissue. In a different meta-analysis of 9 studies comparing 2D-SWE and pSWE, overall sensitivity and specificity values were reported as 0.91 (95%CI, 0.88–0.94) and 0.82 (95%CI, 0.75–0.87) for 2D-SWE and 0.89 (95%CI, 0.81–0.94) and 0.91 (95%CI, 0.84–0.95) for pSWE, respectively[63].

2D-SWE is useful for differentiating benign and malignant breast lesions with reported AUROC values ranging from 0.74 to 0.98[64]. The addition of 2D-SWE to conventional B-

mode ultrasound can improve diagnostic performance by reducing the need for follow up exams of patients with BI-RADS 3 breast lesions[61].

4) Prostate

Conventional screening and diagnostic methods for prostate evaluation include Prostate-Specific antigen (PSA) assessment, digital rectal exam (DRE) and transrectal ultrasound (TRUS) guided biopsy. However, due to invasiveness and low diagnostic performance, elastographic techniques are gaining popularity[65]. Elastographic techniques can be used to assess both benign prostatic hyperplasia (BPH) and prostate cancer (PC).

In *strain elastography*, images are obtained with slight transrectal manual compression. An inflatable endorectal balloon may be used to generate endorectal prostate elastography images[61]. Although SE guided prostate biopsy shows higher sensitivity when compared to conventional grey scale US guided biopsy to detect prostate cancer (60.8% vs 15%, respectively), only relying on SE results is not recommended[66]. Strain elastography has been shown to have a sensitivity of 58.8% and specificity of 43.3% to identify the prostate cancer index lesion (the main lesion that is responsible for possible metastasis)[61,67]. An image example of strain elastography for prostate cancer diagnosis is shown in Figure 7.

In *pSWE*, malignancy shows higher SWS values than BPH and normal prostate tissue(2.37m/s, 1.98m/s and 1.34m/s, respectively)[68]. pSWE can be used to differentiate BPH and malignancy with an AUROC value of 0.86. SWS differences between the transition and peripheral zones of the prostate are possible in both BPH and cancer. When compared to DRE, pSWE shows higher diagnostic accuracy to detect malignancy, with AUROC value of 0.86 (vs. 0.67 for DRE)[68]

2D-SWE has been shown to be useful for differentiating benign and malignant lesions in the peripheral zone[69]. Using a cutoff stiffness value of 35 kPa to differentiate benign and malignant lesions yields sensitivity and specificity values of 96% and 85%, respectively[70]. 2D-SWE is a reproducible technique with ICC value of 0.876[71]. In a recent meta-analysis with 7 studies, Sang et al. reported pooled sensitivity and specificity values of 0.844 (95%CI, 0.69–0.92) and 0.86 (95%CI,0.79–0.908) (AUROC value of 0.91) to differentiate malignant prostate lesions[72]. A different research group, Woo et al., reported similar results in their recent meta-analysis with 8 studies, pooled sensitivity value of 0.83 (95%CI, 0.66–0.92) and specificity value of 0.85 (95%CI,0,78–0.9)[73]. 2D-SWE can also be used to assess BPH. Unlike most prostate malignancies, BPH develops from the transition zone of the prostate. Stiffness values of the transition zone can be measured via transrectal elastography. 2D-SWE can diagnose BPH with an AUROC value of 0.826 (95%CI, 0.717–0.934). Elasticity values higher than 32.4kPa can be an indicator of BPH[74].

5) Thyroid

Strain elastography requires external manual compression or physiological motion such as carotid pulsation[75]. The reported sensitivity of different strain imaging features for diagnosis of thyroid carcinoma ranges from 82%–100%, with specificity ranging from 81.1%–100%[76]. Although most studies indicate higher accuracy for thyroid cancer detection with strain elastography than conventional grey scale US, there is presently

insufficient agreement among research groups regarding diagnostic criteria, and elastography is thought to be insensitive to some malignant tumor types[61,76–78].

Malignant thyroid nodules show higher SWS values when compared to benign nodules, either with pSWE or 2D-SWE[61]. *pSWE* can differentiate benign and malignant thyroid nodules. In a meta-analysis with 16 studies, pSWE has been reported to have an overall AUROC value of 0.91[79]. In the assessment of diffuse chronic thyroid disease, pSWE is also useful to differentiate subjects with Graves disease and autoimmune thyroiditis from healthy subjects[80]. However, current knowledge on this evaluation is based on preliminary results and more studies are needed.

2D-SWE is an effective technique to diagnose thyroid malignancies with AUROC values of 0.73 in nodules <10mm, 0.88 in nodules 11–30mm and 0.82 in nodules >30mm[81]. 2D-SWE has also been shown to potentially be able to differentiate benign and malignant follicular thyroid nodules, a clinically relevant finding that cannot be accomplished with FNA[15]. An image example of 2D-SWE use in thyroid tissue is indicated in Figure 8. Use of these elastographic methods in combination with B mode ultrasound is recommended[82]. Addition of CEUS can also increase diagnostic performance[83].

6) Pancreas

Either strain or shear wave elastography can be used in the evaluation of the pancreas. Strain elastography is performed by using an endoscopic ultrasound system, in which aortic pulsation is used as the excitation method. Strain elastography with endoscopic ultrasound is not preferable due to invasiveness, inadequate quality of images from the head and tail of the pancreas, and atherosclerotic changes that can affect aortic pulse excitation. However, initial strain elastography studies have been used to assess malignancy and pancreatic parenchymal diseases[84].

Strain Elastography—In a recent study of 149 patients, Rustemovic et al. proposed the strain ratio cut-off value of 7.59 to distinguish malignancies[100%sensitivity, 95%specificity][85]. However, previous studies reported different results, which may be caused by the invasiveness and operator dependence of endoscopic ultrasound[84]. In a large mixed study population with 555 subjects that included healthy subjects, patients with chronic pancreatitis and patients with pancreatic cancer, Kim et al. reported strain ratio values of 3.78, 8.21 and 21.8, respectively. Sensitivity and specificity to distinguish malignancy were similar as Rustemovic et al.'s results [95.6% and 96.3%, respectively, cut-off 8.86][86]. In their study with 191 patients with chronic pancreatitis, Iglesias-Garcia et al. reported sensitivity and specificity values of 91.2% and 91%, to detect chronic pancreatitis[AUROC value of 0.949], which are higher than Kim et al.'s values[87].

pSWE can be used with cutaneous approach and it can detect stiffness differences between a lesion and background pancreatic parenchyma[88]. D'Onofrio et al. reported significant differences between SWS values obtained in adenocarcinoma and normal pancreatic parenchyma[89]. Patients with chronic pancreatitis may show higher stiffness values with pSWE when compared to healthy controls[4.3kPa vs. 2.8kPa, $p<0.001$][90]. Current knowledge on elastography of pancreas is limited to strain elastography and pSWE. Studies

comparing elastography methods in the diagnosis of pancreatic masses and parenchymal diseases are also limited[91].

7) Spleen

Portal hypertension and increased hepatic venous pressure gradient(HVPG), are critical indicators of end stage chronic liver disease. At this stage, patient can develop variceal bleeding, ascites and hepatic encephalopathy which increases the mortality rates drastically[2]. Accurate and fast detection of portal hypertension and the resulting esophageal varice, is critical to preclude these clinical complications, in which elastography techniques may fulfil this need. As mentioned above strain elastography needs an excitation/pressure method. Spleen is in relatively deep location and stiffness assessment with strain elastography can be performed with endoscopic ultrasound. However, physical compression with endoscopic ultrasound is difficult and strain elastography is not preferable for spleen stiffness evaluation[61].

Transient elastography probe can be put on spleen with using the same procedure methods as liver. It is known that TE can successfully detect stiffness of spleen in patients with cirrhosis, and it correlates with HVPG which can be predictive for esophageal varices. Spleen stiffness value 3.3m/s has been proposed as the cut-off value to rule esophageal varices, however more studies are encouraged[93]. In studies comparing TE application in liver and spleen to diagnose portal hypertension, diagnostic performance of TE in liver was reported higher than in spleen(AUROC's 0.95 vs 0.85, respectively)[2]. Use of transient elastography in combination with conventional ultrasound may help operators to locate the most reliable location[61].

pSWE has also been studied in cirrhotic patients. To diagnose clinically significant portal hypertension, pSWE technique gave AUROC value of 0.943 with cut-off value 3.36m/s, and to detect presence of esophageal varices, pSWE technique gave AUROC value of 0.933 with cut-off value 3.30m/s [103,104]. Recently, research groups reported studies with 2D-SWE to predict esophageal varices and portal hypertension[105–107]. Elkrief et al. evaluated the performance of TE and 2D-SWE to detect portal hypertension by measuring liver stiffness and spleen stiffness, and reported higher AUROC value for liver stiffness measurements when compared to spleen stiffness(0.87vs0.64, p=0.003). They also reported superior technical success rate of 2D-SWE when compared to TE, in assessment of liver and spleen stiffness[107]. These results show that measuring liver and spleen stiffness in combination, may result in more reliable values. Although cut-off values of elastography methods to detect portal hypertension or esophageal varices through evaluation of spleen stiffness are similar, more studies are encouraged to verify these cut-off values.

In this review we tried to include principles of elastography technologies and clinical applications of these methods. Summary and classification of all elastographic techniques are indicated in Figure 9. Strong features and limitations of these techniques are summarized in Figure 10 and Figure 11.

CONCLUSION

Ultrasound elastography comprises a set of techniques that non-invasively measure tissue stiffness. Use of these techniques has blossomed with recognition that many disease processes affect tissue stiffness, providing a new imaging target for assessment of disease biology. In this review, we have provided a brief introduction to the physical concepts that underpin ultrasound elastography, and have discussed several different commercially available ultrasound elastography systems with evidence of their efficacy in different biologic settings. With the help of guidelines, meta-analysis reports and studies with large study populations, various cut-off values are determined. However, there may be specific differences between measurements with different ultrasound systems. Researchers and clinicians should liaise with manufacturers regarding the cut-off values in specific elastography applications.

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References

1. Shiina T, Nightingale KR, Palmeri ML, Hall TJ, Bamber JC, Barr RG, Castera L, Choi BI, Chou YH, Cosgrove D, Dietrich CF, Ding H, Amy D, Farrokh A, Ferraioli G, Filice C, Friedrich-Rust M, Nakashima K, Schafer F, Sporea I, Suzuki S, Wilson S, Kudo M. WFUMB Guidelines and Recommendations for Clinical Use of Ultrasound Elastography: Part 1: Basic Principles and Terminology. Ultrasound in Medicine & Biology. 2015; 41(5):1126–47. DOI: 10.1016/j.ultrasmedbio.2015.03.009 [PubMed: 25805059]
2. Sigrist RMS, Liau J, Kaffas AE, Chammas MC, Willmann JK. Ultrasound Elastography: Review of Techniques and Clinical Applications. Theranostics. 2017; 7(5):1303–1329. DOI: 10.7150/thno.18650 [PubMed: 28435467]
3. Ophir J, Cespedes I, Ponnekanti H, Yazdi T, Li X. Elastography: a quantitative method for imaging the elasticity of biological tissues. Ultrasonic Imaging. 1991; (2):111–34. [PubMed: 1858217]
4. Garra BS. Elastography: history, principles, and technique comparison. Abdominal Imaging. 2015; 40(4):680–97. DOI: 10.1007/s00261-014-0305-8 [PubMed: 25637125]
5. Itoh A, Ueno E, Tohno E, Kamma H, Takahashi H, Shiina T, Yamakawa M, Matsumura T. Breast Disease: Clinical Application of US Elastography for Diagnosis. Radiology. 2006; 239:341–350. [PubMed: 16484352]
6. Zhou J, Zhou C, Zhan W, Jia X, Dong Y, Yang Z. Elastography ultrasound for breast lesions: fat-to-lesion strain ratio vs gland-to-lesion strain ratio. Eur Radiol. 2014; 24:3171–3177. DOI: 10.1007/s00330-014-3366-8 [PubMed: 25182624]
7. Barr RG. Real-time ultrasound elasticity of the breast: initial clinical results. Ultrasound. 2010; (2): 61–6. DOI: 10.1097/RUQ.0b013e3181dc7ce4
8. Guibal A, Boularan C, Bruce M, Vallin M, Pilleul F, Walter T, Scoazec JY, Boublay N, Dumortier J, Lefort T. Evaluation of shearwave elastography for the characterisation of focal liver lesions on ultrasound. Eur Radiol. 2012; 23:1138–1149. DOI: 10.1007/s00330-012-2692-y [PubMed: 23160662]
9. Lu Q, Wen JX, Huang BJ, Xue LY, Wang WP. Virtual Touch quantification using acoustic radiation force impulse(ARFI) technology for the evaluation of focal solid renal lesions: preliminary findings. Clin Radiol. 2015; 70(12):1376–81. DOI: 10.1016/j.crad.2015.08.002 [PubMed: 26375726]

10. Samir AE, Dhyani M, Vij A, Bhan AK, Halpern EF, Méndez-Navarro J, Corey KE, Chung RT. Shear-Wave Elastography for the Estimation of Liver Fibrosis in Chronic Liver Disease: Determining Accuracy and Ideal Site for Measurement. Radiology. 2015; 274:888–896. DOI: 10.1148/radiol.14140839 [PubMed: 25393946]
11. Samir AE, Allegretti AS, Zhu Q, Dhyani M, Anvari A, Sullivan DA, Trottier CA, Dougherty S, Williams WW, Babitt JL, Wenger J, Thadhani RI, Lin HY. Shear wave elastography in chronic kidney disease: a pilot experience in native kidneys. BMC Nephrology BMC Nephrology. 2015; : 1–9. DOI: 10.1186/s12882-015-0120-7
12. Hong S, Woo OH, Shin HS, Hwang S-Y, Cho KR, Seo BK. Reproducibility and diagnostic performance of shear wave elastography in evaluating breast solid mass. Clinical Imaging Elsevier Inc. 2017; 44:42–45. DOI: 10.1016/j.clinimag.2017.03.022
13. Park SY, Choi JS, Han BK, Ko EY, Ko ES. Shear wave elastography in the diagnosis of breast non-mass lesions: factors associated with false negative and false positive results. European Radiology. 2017; (9):3788–3798. DOI: 10.1007/s00330-017-4763-6 [PubMed: 28168373]
14. Boehm K, Salomon G, Beyer B, Schiffmann J, Simonis K, Graefen M, Budaeus L. Shear Wave Elastography for Localization of Prostate Cancer Lesions and Assessment of Elasticity Thresholds: Implications for Targeted Biopsies and Active Surveillance Protocols. Journal of Urology Elsevier Ltd. 2015; 193:794–800. DOI: 10.1016/j.juro.2014.09.100
15. Samir AE, Dhyani M, Anvari A, Prescott J, Halpern EF, Faquin WC, Stephen A. Shear-Wave Elastography for the Preoperative Risk Stratification of Follicular-patterned Lesions of the Thyroid: Diagnostic Accuracy and Optimal Measurement Plane. Radiology. 2015; 277:565–573. DOI: 10.1148/radiol.2015141627 [PubMed: 25955578]
16. DeWall RJ, Slane LC, Lee KS, Thelen DG. Spatial variations in Achilles tendon shear wave speed. Journal of Biomechanics. 2014; 47:2685–2692. DOI: 10.1016/j.jbiomech.2014.05.008 [PubMed: 24933528]
17. Catheline S, Thomas JL, Wu F, Fink MA. Diffraction field of a low frequency vibrator in soft tissues using transient elastography. IEEE Trans Ultrason Ferroelectr Freq Control. 1999; (4): 1013–9. DOI: 10.1109/58.775668 [PubMed: 18238506]
18. Sandrin L, Tanter M, Gennison JL, Catheline S, Fink M. Shear Elasticity Probe for Soft Tissues with 1-D Transient Elastography. IEEE Trans Ultrason Ferroelectr Freq Control. 2002; (4):436–46. [PubMed: 11989699]
19. Gennisson JL, Deffieux T, Fink M, Tanter M. Ultrasound elastography: Principles and techniques. Diagnostic and Interventional Imaging. 2013; 94:487–495. DOI: 10.1016/j.diii.2013.01.022 [PubMed: 23619292]
20. Babu AS, Wells ML, Teytelboym OM, Mackey JE, Miller FH, Yeh BM, Ehman RL, Venkatesh SK. Elastography in Chronic Liver Disease: Modalities, Techniques, Limitations and Future Directions. Radiographics. 2016; 36(7):1987–2006. DOI: 10.1148/rg.2016160042 [PubMed: 27689833]
21. Castera L, Forns X, Alberti A. Non-invasive evaluation of liver fibrosis using transient elastography. Journal of Hepatology. 2008; 48:835–847. DOI: 10.1016/j.jhep.2008.02.008 [PubMed: 18334275]
22. Sasso M, Beaugrand M, de Ledinghen V, Douvin C, Marcellin P, Poupon R, Sandrin L, Miette V. Controlled attenuation parameter (CAP): a novel VCTE™ guided ultrasonic attenuation measurement for the evaluation of hepatic steatosis: preliminary study and validation in a cohort of patients with chronic liver disease from various causes. Ultrasound Med Biol. 2010; 36(11):1825–35. DOI: 10.1016/j.ultrasmedbio.2010.07.005 [PubMed: 20870345]
23. Sandrin L, Fourquet B, Hasquenoph JM, Yon S, Fournier C, Mal F, Christidis C, Ziol M, Poulet B, Kazemi F, Beaugrand M, Palau R. Transient elastography: a new noninvasive method for assessment of hepatic fibrosis. Ultrasound Med Biol. 2003; (12):1705–13. [PubMed: 14698338]
24. Bamber J, Cosgrove D, Dietrich C, Fromageau J, Bojunga J, Calliada F, Cantisani V, Correas JM, D'Onofrio M, Drakonaki E, Fink M, Friedrich-Rust M, Gilja O, Havre R, Jenssen C, Klauser A, Ohlinger R, Săftoiu A, Schaefer F, Sporea I, Piscaglia F. EFSUMB Guidelines and Recommendations on the Clinical Use of Ultrasound Elastography. Part 1: Basic Principles and Technology. Ultraschall in Med. 2013; 34:169–184. DOI: 10.1055/s-0033-1335205 [PubMed: 23558397]

25. Bercoff J, Tanter M, Fink M. Supersonic Shear Imaging: A New Technique for Soft Tissue Elasticity Mapping. IEEE Trans Ultrason Ferroelectr Freq Control. 2004; (4):396–409. [PubMed: 15139541]
26. Ferraioli G, Tinelli C, Dal Bello B, Zicchetti M, Filice G, Filice C. on behalf of the Liver Fibrosis Study Group. Accuracy of real-time shear wave elastography for assessing liver fibrosis in chronic hepatitis C: A pilot study. Hepatology. 2012; 56:2125–2133. DOI: 10.1002/hep.25936 [PubMed: 22767302]
27. Fujimoto K, Kato M, Kudo M, Yada N, Shiina T, Ueshima K, Yamada Y, Ishida T, Azuma M, Yamasaki M, Yamamoto K, Hayashi N, Takehara T. Novel Image Analysis Method Using Ultrasound Elastography for Noninvasive Evaluation of Hepatic Fibrosis in Patients with Chronic Hepatitis C. Oncology. 2013; 84:3–12. DOI: 10.1159/000345883 [PubMed: 23428852]
28. Yada N, Kudo M, Morikawa H, Fujimoto K, Kato M, Kawada N. Assessment of Liver Fibrosis with Real-Time Tissue Elastography in Chronic Viral Hepatitis. Oncology. 2013; 84:13–20. DOI: 10.1159/000345884 [PubMed: 23428853]
29. Koizumi Y, Hirooka M, Kisaka Y, Konishi I, Abe M, Murakami H, Matsuura B, Hiasa Y, Onji M. Liver Fibrosis in Patients with Chronic Hepatitis C: Noninvasive Diagnosis by Means of Real-time Tissue Elastography—Establishment of the Method for Measurement. Radiology. 2011; (2):610–7. DOI: 10.1148/radiol.10100319
30. Onur MR, Poyraz AK, Ucak EE, Bozgeyik Z, Ozercan IH, Ogur E. Semiquantitative Strain Elastography of Liver Masses. J Ultrasound Med. 2012; (7):1061–7. [PubMed: 22733855]
31. Li Y, Huang YS, Wang ZZ, Yang ZR, Sun F, Zhan SY, Liu XE, Zhuang H. Systematic review with meta-analysis: the diagnostic accuracy of transient elastography for the staging of liver fibrosis in patients with chronic hepatitis B. Aliment Pharmacol Ther. 2016; 43:458–469. DOI: 10.1111/apt.13488 [PubMed: 26669632]
32. Ying HY, Lu LG, Jing DD, Ni XS. Accuracy of transient elastography in the assessment of chronic hepatitis C-related liver cirrhosis. Clin invest med. 2016; 39(5):E150–E160. [PubMed: 27805898]
33. Pavlov CS, Casazza G, Nikolova D, Tsochatzis E, Gluud C. Systematic review with meta-analysis: diagnostic accuracy of transient elastography for staging of fibrosis in people with alcoholic liver disease. Aliment Pharmacol Ther. 2016; 43:575–585. DOI: 10.1111/apt.13524 [PubMed: 26791825]
34. Tsochatzis EA, Gurusamy KS, Ntaoula S, Cholongitas E, Davidson BR, Burroughs AK. Elastography for the diagnosis of severity of fibrosis in chronic liver disease: a meta-analysis of diagnostic accuracy. J Hepatol. 2011; 54(4):650–9. DOI: 10.1016/j.jhep.2010.07.033 [PubMed: 21146892]
35. Wong VW, Chan HL. Transient Elastography. J Gastroenterol Hepatol. 2010; (11):1726–31. DOI: 10.1111/j.1440-1746.2010.06437.x [PubMed: 21039833]
36. Fraquelli M, Rigamonti C, Casazza G, Conte D, Donato MF, Ronchi G, Colombo M. Reproducibility of transient elastography in the evaluation of liver fibrosis in patients with chronic liver disease. Gut. 2007; 56:968–973. [PubMed: 17255218]
37. Kiani A, Brun V, Lainé F, Turlin B, Morcet J, Michalak S, Le Gruyer A, Legros L, Bardou-Jacquet E, Gandon Y, Moirand R. Acoustic radiation force impulse imaging for assessing liver fibrosis in alcoholic liver disease. WJG. 2016; 22(20):4926–35. DOI: 10.3748/wjg.v22.i20.4926 [PubMed: 27239119]
38. Tachi Y, Hirai T, Kojima Y, Miyata A, Ohara K, Ishizu Y, Honda T, Kuzuya T, Hayashi K, Ishigami M, Goto H. Liver stiffness measurement using acoustic radiation force impulse elastography in hepatitis C virus-infected patients with a sustained virological response. Aliment Pharmacol Ther. 2016; 44:346–355. DOI: 10.1111/apt.13695 [PubMed: 27291657]
39. Cao W, Zhou Y, Niu Y, Zhu X, Song Y, Guo R. Quantitative Analysis of Hepatic Toxicity in Rats Induced by Inhalable Silica Nanoparticles Using Acoustic Radiation Force Imaging. Journal of Ultrasound in Medicine. 2017; 36(9):1829–1839. DOI: 10.1002/jum.14219 [PubMed: 28471058]
40. Bert F, Stahmeyer JT, Rossol S. Ultrasound Elastography Used for Preventive Non-Invasive Screening in Early Detection of Liver Fibrosis. J Clin Med Res. 2016; 8:650–655. DOI: 10.14740/jocmr2625w [PubMed: 27540438]

41. Hu X, Qiu L, Liu D, Qian L. Acoustic Radiation Force Impulse (ARFI) Elastography for non-invasive evaluation of hepatic fibrosis in chronic hepatitis B and C patients: a systematic review and meta-analysis. Med Ultrason. 2017; 19:23–31. DOI: 10.11152/mu-942 [PubMed: 28180193]

42. Cabassa P, Ravanelli M, Rossini A, Contessi G, Almajdalawi R, Maroldi R. Acoustic radiation force impulse quantification of spleen elasticity for assessing liver fibrosis. Abdominal Imaging. 2015; (4):738–44. DOI: 10.1007/s00261-014-0306-7 [PubMed: 25425490]

43. Jaffer OS, Lung PFC, Bosanac D, Patel VM, Ryan SM, Heneghan MA, Quaglia A, Sidhu PS. Acoustic radiation force impulse quantification: repeatability of measurements in selected liver segments and influence of age, body mass index and liver capsule-to-box distance. BJR. 2012; 85:e858–e863. DOI: 10.1259/bjr/74797353 [PubMed: 22763032]

44. Balakrishnan M, Souza F, Muñoz C, Augustin S, Loo N, Deng Y, Ciarleglio M, Garcia-Tsao G. Liver and Spleen Stiffness Measurements by Point Shear Wave Elastography via Acoustic Radiation Force Impulse. Journal of Ultrasound in Medicine. 2016; 35:2373–2380. [PubMed: 27663656]

45. Dhyani M, Gee MS, Misdraji J, Israel EJ, Shah U, Samir AE. Feasibility study for assessing liver fibrosis in paediatric and adolescent patients using real-time shear wave elastograph. J Med Imaging Radiat Oncol. 2015; 59(6):687–94. DOI: 10.1111/1754-9485.12388 [PubMed: 26503488]

46. Zheng J, Guo H, Zeng J, Huang Z, Zheng B, Ren J, Xu E, Li K, Zheng R. Two-dimensional Shear-Wave Elastography and Conventional US: The Optimal Evaluation of Liver Fibrosis and Cirrhosis. Radiology. 2015; 275:290–300. DOI: 10.1148/radiol.14140828 [PubMed: 25575116]

47. Dhyani M, Grajo JR, Bhan AK, Corey K, Chung R, Samir AE. Validation of Shear Wave Elastography Cutoff Values on the Supersonic Aixplorer for Practical Clinical Use in Liver Fibrosis Staging. Ultrasound in Medicine & Biology Elsevier Inc. 2017; 43:1125–1133. DOI: 10.1016/j.ultrasmedbio.2017.01.022

48. Woo H, Lee JY, Yoon JH, Kim W, Cho B, Choi BI. Comparison of the Reliability of Acoustic Radiation Force Impulse Imaging and Supersonic Shear Imaging in Measurement of Liver Stiffness. Radiology. 2015; 277:881–886. DOI: 10.1148/radiol.2015141975 [PubMed: 26147680]

49. Menzilcioglu MS, Duymus M, Citil S, Avcu S, Gungor G, Sahin T, Boysan SN, Altunoren O, Sarica A. Strain wave elastography for evaluation of renal parenchyma in chronic kidney disease. BJR. 2015; 88:20140714–6. DOI: 10.1259/bjr.20140714 [PubMed: 25806412]

50. Orlacchio A, Chegai F, Del Giudice C, Anselmo A, Iaria G, Palmieri G, Di Caprera E, Tosti D, Costanzo E, Tisone G, Simonetti G. Kidney Transplant: Usefulness of Real-Time Elastography (RTE) in the Diagnosis of Graft Interstitial Fibrosis. Ultrasound Med Biol. 2014; (11):2564–72. DOI: 10.1016/j.ultrasmedbio.2014.06.002 [PubMed: 25218454]

51. Cui G, Yang Z, Zhang W, Li B, Sun F, Xu C, Wang K. Evaluation of acoustic radiation force impulse imaging for the clinicopathological typing of renal fibrosis. Exp Ther Med. 2014 Jan; 7(1):233–235. [PubMed: 24348796]

52. Yu N, Zhang Y, Xu Y. Value of virtual touch tissue quantification in stages of diabetic kidney disease. J Ultrasound Med. 2014 May; 33(5):787–92. DOI: 10.7863/ultra.33.5.787 [PubMed: 24764333]

53. Bob F, Bota S, Sporea I, Sirli R, Petrica L, Schiller A. Kidney shear wave speed values in subjects with and without renal pathology and inter-operator reproducibility of acoustic radiation force impulse elastography (ARFI)--preliminary results. PLoS One. 2014; 9(11):e113761. [PubMed: 25426849]

54. Bota S, Bob F, Sporea I, Şirli R, Popescu A. Factors that influence kidney shear wave speed assessed by acoustic radiation force impulse elastography in patients without kidney pathology. Ultrasound Med Biol. 2015; 41(1):1–6. [PubMed: 25438855]

55. Wang L. Applications of acoustic radiation force impulse quantification in chronic kidney disease: a review. Ultrasonography. 2016; 35(4):302–8. [PubMed: 27599890]

56. Hassan K, Loberant N, Abbas N, Fadi H, Shadia H, Khazim K. Shear wave elastography imaging for assessing the chronic pathologic changes in advanced diabetic kidney disease. Ther Clin Risk Manag. 2016; 12:1615–1622. [PubMed: 27853373]

57. Barr RG, Nakashima K, Amy D, Cosgrove D, Farrokh A, Schafer F, Bamber JC, Castera L, Choi BI, Chou YH, Dietrich CF, Ding H, Ferraioli G, Filice C, Friedrich-Rust M, Hall TJ, Nightingale

KR, Palmeri ML, Shiina T, Suzuki S, Sporea I, Wilson S, Kudo M. WFUMB guidelines and recommendations for clinical use of ultrasound elastography: Part 2: breast. Ultrasound Med Biol. 2015 May; 41(5):1148–60. DOI: 10.1016/j.ultrasmedbio.2015.03.008 [PubMed: 25795620]

58. Gong X, Xu Q, Xu Z, Xiong P, Yan W, Chen Y. Real-time elastography for the differentiation of benign and malignant breast lesions: a meta-analysis. Breast Cancer Res Treat. 2011; (1):11–8. DOI: 10.1007/s10549-011-1745-2
59. Grajo JR, Barr RG. Strain elastography for prediction of breast cancer tumor grades. J Ultrasound Med. 2014 Jan; 33(1):129–34. DOI: 10.7863/ultra.33.1.129 [PubMed: 24371107]
60. Zhi H, Xiao XY, Ou B, Zhong WJ, Zhao ZZ, Zhao XB, Yang HY, Luo BM. Could ultrasonic elastography help the diagnosis of small (≤2 cm) breast cancer with the usage of sonographic BI-RADS classification? Eur J Radiol. 2012 Nov; 81(11):3216–21. DOI: 10.1016/j.ejrad.2012.04.016 [PubMed: 22608397]
61. Cosgrove D, Piscaglia F, Bamber J, Bojunga J, Correas JM, Gilja O, Klauser A, Sporea I, Calliada F, Cantisani V, D'Onofrio M, Drakonaki E, Fink M, Friedrich-Rust M, Fromageau J, Havre R, Jenssen C, Ohlinger R, Săftoiu A, Schaefer F, Dietrich C. EFSUMB Guidelines and Recommendations on the Clinical Use of Ultrasound Elastography. Part 2: Clinical Applications. Ultraschall in Med. 2013; 34:238–253. DOI: 10.1055/s-0033-1335375 [PubMed: 23605169]
62. Li DD, Guo LH, Xu HX, Liu C, Xu JM, Sun LP, Wu J, Liu BJ, Liu LN, Xu XH. Acoustic radiation force impulse elastography for differentiation of malignant and benign breast lesions: a meta-analysis. Int J Clin Exp Med. 2015; 8(4):4753–4761. [PubMed: 26131049]
63. Li G, Li DW, Fang YX, Song YJ, Deng ZJ, Gao J, Xie Y, Yin TS, Ying L, Tang KF. Performance of shear wave elastography for differentiation of benign and malignant solid breast masses. PLoS One. 2013; (10)doi: 10.1371/journal.pone.0076322
64. Liu B, Zheng Y, Huang G, Lin M, Shan Q, Lu Y, Tian W, Xie X. Breast lesions: Quantitative diagnosis using ultrasound shear wave elastography-A systematic review and meta-analysis. Ultrasound Med&Biol. 2016; (42):835–847. DOI: 10.1016/j.ultrasmedbio.2015.10.024 [PubMed: 26778289]
65. Woo S, Kim SY, Cho JY, Kim SH. Shear wave elastography for detection of prostate cancer: a preliminary study. Korean J Radiol. 2014; (3):346–55. [PubMed: 24843239]
66. Brock M, von Bodman C, Palisaar RJ, Loppenberg B, Sommerer F, Deix T, Noldus J, Eggert T. The impact of real-time elastography guiding a systematic prostate biopsy to improve cancer detection rate: a prospective study of 353 patients. J Urol. 2012; 187:2039–2043. DOI: 10.1016/j.juro.2012.01.063 [PubMed: 22498211]
67. Walz J, Marcy M, Pianna JT, Brunelle S, Gravis G, Salem N, Bladou F. Identification of the prostate cancer index lesion by real-time elastography: considerations for focal therapy of prostate cancer. World J Urol. 2011; 29:589–594. DOI: 10.1007/s00345-011-0688-x [PubMed: 21614469]
68. Zheng X, Ji P, Mao H, Hu J. A comparison of virtual touch tissue quantification and digital rectal examination for discrimination between prostate cancer and benign prostatic hyperplasia. Radiol Oncol. 2012; 46(1):69–74. DOI: 10.2478/v10019-011-0026-3 [PubMed: 22933982]
69. Rouvière O, Melodelima C, Dinh AH, Bratan F, Pagnoux G, Sanzalone T, Crouzet S, Colombel M, Mège-Lechevallier F, Souchon R. Stiffness of benign and malignant prostate tissue measured by shear-wave elastography: a preliminary study. European Radiology. 2017; 27(5):1858–1866. DOI: 10.1007/s00330-016-4534-9 [PubMed: 27553936]
70. Correas JM, Tissier AM, Khairoune A, Vassiliu V, Méjean A, Hélénon O, Memo R, Barr RG. Prostate Cancer: Diagnostic Performance of Real-time Shear-Wave Elastography. Radiology. 2015; 275:280–289. DOI: 10.1148/radiol.14140567 [PubMed: 25599156]
71. Woo S, Kim SY, Lee MS, Cho JY, Kim SH. Shear wave elastography assessment in the prostate: an intraobserver reproducibility study. Clin Imaging. 2015; 39(3):484–7. DOI: 10.1016/j.clinimag.2014.11.013 [PubMed: 25481218]
72. Sang L, Wang XM, Xu DY, Cai YF. Accuracy of shear wave elastography for the diagnosis of prostate cancer: A meta-analysis. Sci Rep. 2017; (1):1949.doi: 10.1038/s41598-017-02187-0 [PubMed: 28512326]

73. Woo S, Suh CH, Kim SY, Cho JY, Kim SH. Shear-Wave Elastography for Detection of Prostate Cancer: A Systematic Review and Diagnostic Meta-Analysis. AJR Am J Roentgenol. 2017; (4): 806–814. DOI: 10.2214/AJR.17.18056 [PubMed: 28796546]
74. Zhang M, Fu S, Zhang Y, Tang J, Zhou Y. Elastic modulus of the prostate: a new non-invasive feature to diagnose bladder outlet obstruction in patients with benign prostatic hyperplasia. Ultrasound Med Biol. 2013 Jul; 40(7):1408–13. 2014. DOI: 10.1016/j.ultrasmedbio.2013.10.012
75. Dighe M, Bae U, Richardson ML, Dubinsky TJ, Minoshima S, Kim Y. Differential Diagnosis of Thyroid Nodules with US Elastography Using Carotid Artery Pulsation. Radiology. 2008; 248:662–669. DOI: 10.1148/radiol.2482071758 [PubMed: 18539888]
76. Bojunga J, Herrmann E, Meyer G, Weber S, Zeuzem S, Friedrich-Rust M. Real-Time Elastography for the Differentiation of Benign and Malignant Thyroid Nodules: A Meta-Analysis. Thyroid. 2010; 20:1145–1150. DOI: 10.1089/thy.2010.0079 [PubMed: 20860422]
77. Moon HJ, Sung JM, Kim EK, Yoon JH, Youk JH, Kwak JY. Diagnostic performance of gray-scale US and elastography in solid thyroid nodules. Radiology. 2012; 262:1002–1013. DOI: 10.1148/radiol.11110839 [PubMed: 22357900]
78. Azizi G, Keller J, Lewis M, Puett D, Rivenbark K, Malchoff C. Performance of Elastography for the Evaluation of Thyroid Nodules: A Prospective Study. Thyroid. 2013; 23:734–740. DOI: 10.1089/thy.2012.0227 [PubMed: 23136893]
79. Zhan J, Jin JM, Diao XH, Chen Y. Acoustic radiation force impulse imaging (ARFI) for differentiation of benign and malignant thyroid nodules--A meta-analysis. Eur J Radiol. 2015; 84(11):2181–6. DOI: 10.1016/j.ejrad.2015.07.015 [PubMed: 26259701]
80. Sporea I, Sirli R, Bota S, Vlad M, Popescu A, Zosin I. ARFI elastography for the evaluation of diffuse thyroid gland pathology: Preliminary results. World J Radiol. 2012; 4(4):174–8. DOI: 10.4329/wjr.v4.i4.174 [PubMed: 22590672]
81. Liu B, Liang J, Zheng Y, Xie X, Huang G, Zhou L, Wang W, Lu M. Two-dimensional shear wave elastography as promising diagnostic tool for predicting malignant thyroid nodules: a prospective single-centre experience. Eur Radiol. 2015; 25:624–634. DOI: 10.1007/s00330-014-3455-8 [PubMed: 25298171]
82. Zhang F, Zhao X, Han R, Du M, Li P, Ji X. Comparison of Acoustic Radiation Force Impulse Imaging and Strain Elastography in Differentiating Malignant From Benign Thyroid Nodules. J Ultrasound Med. 2017; doi: 10.1002/jum.14302
83. Deng J, Zhou P, Tian SM, Zhang L, Li JL, Qian Y. Comparison of diagnostic efficacy of contrast-enhanced ultrasound, acoustic radiation force impulse imaging, and their combined use in differentiating focal solid thyroid nodules. PLoS One. 2014; (3):e90674.doi: 10.1371/journal.pone.0090674 [PubMed: 24594879]
84. Kawada N, Tanaka S. Elastography for the pancreas: Current status and future perspective. World J Gastroenterol. 2016; 22(14):3712–24. DOI: 10.3748/wjg.v22.i14.3712 [PubMed: 27076756]
85. Rustemović N, Kalauz M, Grubelić Ravić K, Iveković H, Bilić B, Ostojić Z, Opačić D, Ledinsky I, Majerović M, Višnjić A. Differentiation of Pancreatic Masses via Endoscopic Ultrasound Strain Ratio Elastography Using Adjacent Pancreatic Tissue as the Reference. Pancreas. 2017; (3):347–351. DOI: 10.1097/MPA.0000000000000758 [PubMed: 28099260]
86. Kim SY, Cho JH, Kim YJ, Kim EJ, Park JY, Jeon TJ, Kim YS. Diagnostic efficacy of quantitative endoscopic ultrasound elastography for differentiating pancreatic disease. J Gastroenterol Hepatol. 2017; (5):1115–1122. DOI: 10.1111/jgh.13649 [PubMed: 27862278]
87. Iglesias-Garcia J, Domínguez-Muñoz JE, Castiñeira-Alvariño M, Luaces-Regueira M, Lariño-Noia J. Quantitative elastography associated with endoscopic ultrasound for the diagnosis of chronic pancreatitis. Endoscopy. 2013; (10):781–8. DOI: 10.1055/s-0033-1344614 [PubMed: 24019131]
88. Park MK, Jo J, Kwon H, Cho JH, Oh JY, Noh MH, Nam KJ. Usefulness of acoustic radiation force impulse elastography in the differential diagnosis of benign and malignant solid pancreatic lesions. Ultrasonography. 2014; 33:26–33. DOI: 10.14366/usg.13017 [PubMed: 24936492]
89. D'Onofrio M, De Robertis R, Crosara S, Poli C, Canestrini S, Demozzi E, Mucelli RP. Acoustic radiation force impulse with shear wave speed quantification of pancreatic masses: A prospective study. Pancreatology. 2016; 16:106–109. DOI: 10.1016/j.pan.2015.12.003 [PubMed: 26746355]

90. Pozzi R, Parzanese I, Baccarin A, Giunta M, Conti CB, Cantù P, Casazza G, Tenca A, Rosa R, Gridavilla D, Casella G, Conte D, Fraquelli M. Point shear-wave elastography in chronic pancreatitis: A promising tool for staging disease severity. Pancreatology. 2017 pii: S1424-3903(17)30856-6.
91. Mateen MA, Muheet KA, Mohan RJ, Rao PN, Majaz HM, Rao GV, Reddy DN. Evaluation of ultrasound based acoustic radiation force impulse (ARFI) and eSie touch sonoelastography for diagnosis of inflammatory pancreatic diseases. JOP. 2012; 13(1):36–44. [PubMed: 22233945]
92. Kim HG, Park MS, Lee JD, Park SY. Ultrasound Elastography of the Neonatal Brain: Preliminary Study. J Ultrasound Med. 2017; 36(7):1313–1319. DOI: 10.7863/ultra.16.06079 [PubMed: 28304105]
93. Ferraioli G, Filice C, Castera L, Choi BI, Sporea I, Wilson SR, Cosgrove D, Dietrich CF, Amy D, Bamber JC, Barr R, Chou YH, Ding H, Farrokh A, Friedrich-Rust M, Hall TJ, Nakashima K, Nightingale KR, Palmeri ML, Schafer F, Shiina T, Suzuki S, Kudo M. WFUMB guidelines and recommendations for clinical use of ultrasound elastography: Part 3: liver. Ultrasound Med Biol. 2015; (5):1161–79. DOI: 10.1016/j.ultrasmedbio.2015.03.007 [PubMed: 25800942]
94. Shiina T. JSUM ultrasound elastography practice guidelines: basics and terminology. J Med Ultrason (2001). 2013; 40(4):309–23. DOI: 10.1007/s10396-013-0490-z [PubMed: 27277449]
95. Barr, Richard G. Principles of Elastography. In: Barr, RG., editor. Elastography: A Practical Approach. 1. Thieme; New York: 2017. p. 6-24.
96. Arena U, Vizzutti F, Corti G, Ambu S, Stasi C, Bresci S, Moscarella S, Boddi V, Petrarca A, Laffi G, Marra F, Pinzani M. Acute viral hepatitis increases liver stiffness values measured by transient elastography. Hepatology. 2008; 47:380–384. [PubMed: 18095306]
97. Stevenson M, Lloyd-Jones M, Morgan MY, Wong R. Non-invasive diagnostic assessment tools for the detection of liver fibrosis in patients with suspected alcohol-related liver disease: a systematic review and economic evaluation. Health Technol Assess. 2012; 16:1–194. DOI: 10.3310/hta16040
98. de Ledinghen V, Vergniol J, Foucher J, El-Hajbi F, Merrouche W, Rigalleau V. Feasibility of liver transient elastography with FibroScan® using a new probe for obese patients. Liver Int. 2010; 30:1043–1048. DOI: 10.1111/j.1478-3231.2010.02258.x [PubMed: 20492500]
99. Barr RG, Zhang Z. Effects of precompression on elasticity imaging of the breast: development of a clinically useful semiquantitative method of precompression assessment. J Ultrasound Med. 2012 Jun; 31(6):895–902. [PubMed: 22644686]
100. Hong Y, Liu X, Li Z, Zhang X, Chen M, Luo Z. Real-time ultrasound elastography in the differential diagnosis of benign and malignant thyroid nodules. J Ultrasound Med. 2009; 28:861–867. [PubMed: 19546328]
101. Early H, Aguilera J, Cheang E, McGahan J. Challenges and Considerations When Using Shear Wave Elastography to Evaluate the Transplanted Kidney, With Pictorial Review. J Ultrasound Med. 2017; 36(9):1771–1782. DOI: 10.1002/jum.14217 [PubMed: 28471017]
102. Popescu A, Bota S, Sporea I, Sirli R, Danila M, Racean S, Suseanu D, Gradinaru O, Siegfried CI. The Influence of Food Intake on Liver Stiffness Values Assessed by Acoustic Radiation Force Impulse Elastography-Preliminary Results. Ultrasound in Medicine & Biology Elsevier Ltd. 2013; 39:579–584. DOI: 10.1016/j.ultrasmedbio.2012.11.013
103. Takuma Y, Nouso K, Morimoto Y, Tomokuni J, Sahara A, Takabatake H, Matsueda K, Yamamoto H. Portal Hypertension in Patients with Liver Cirrhosis: Diagnostic Accuracy of Spleen Stiffness. Radiology. 2016; 279(2):609–19. DOI: 10.1148/radiol.2015150690 [PubMed: 26588019]
104. Takuma Y, Nouso K, Morimoto Y, Tomokuni J, Sahara A, Toshikuni N, Takabatake H, Shimomura H, Doi A, Sakakibara I, Matsueda K, Yamamoto H. Measurement of spleen stiffness by acoustic radiation force impulse imaging identifies cirrhotic patients with esophageal varices. Gastroenterology. 2013; (1):92–101.e2. DOI: 10.1053/j.gastro.2012.09.049
105. Grgurevic I, Bokun T, Mustapic S, Trkulja V, Heinz R, Banic M, Puljiz Z, Luksic B, Kujundzic M. Real-time two-dimensional shear wave ultrasound elastography of the liver is a reliable predictor of clinical outcomes and the presence of esophageal varices in patients with compensated liver cirrhosis. Croat Med J. 2015; 56:470–81. DOI: 10.3325/cmj.2015.56.470 [PubMed: 26526884]

106. Kim TY, Kim TY, Kim Y, Lim S, Jeong WKJ, Son JH. Diagnostic Performance of Shear Wave Elastography for Predicting Esophageal Varices in Patients With Compensated Liver Cirrhosis. J Ultrasound Med. 2016; 35:1373–1381. [PubMed: 27208198]

107. Elkrief L, Rautou PE, Ronot M, Lambert S, Burgio MD, Francoz C, Plessier A, Durand F, Valla D, Lebrec D, Vilgrain V, Castera L. Prospective comparison of spleen and liver stiffness by Using shear-Wave and Transient elastography for Detection of Portal hypertension in cirrhosis. Radiology. 2015; 275(2):589–98. DOI: 10.1148/radiol.14141210 [PubMed: 25469784]

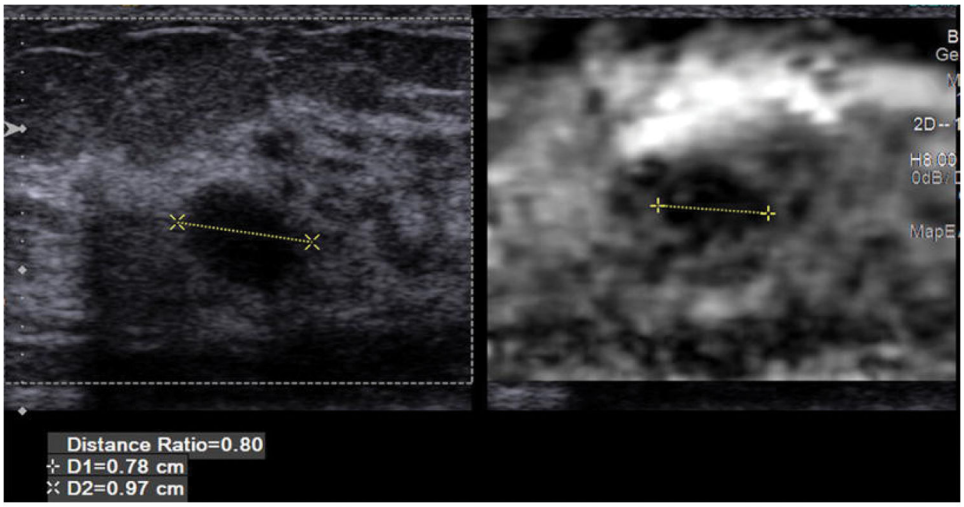

Figure 1.

Palpable breast mass from 24year old woman proven to be a benign fibroadenoma. A Conventional B mode image on the left, and a map of relative tissue stiffness in the same region of interest on the right. On the elastogram, bright areas depict tissue that is less stiff than tissue in the dark areas. Images were acquired using a L9 probe on a Siemens S2000 US system with manual strain (Courtesy of Dr. Richard Barr, MD, PhD).

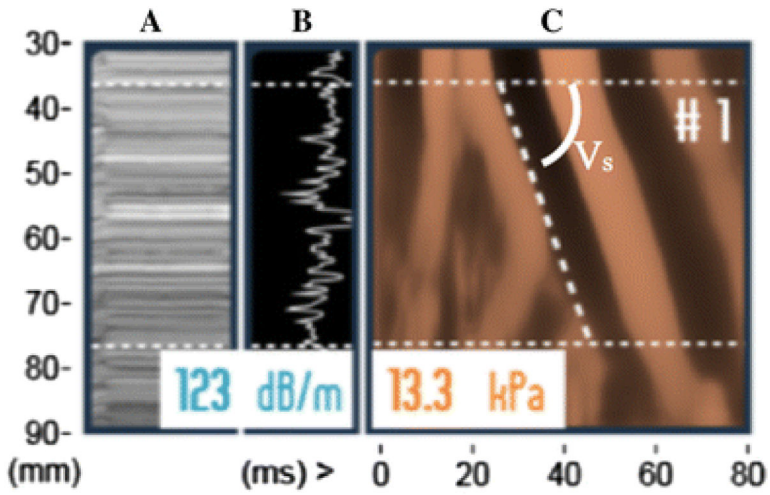

Figure 2.

Transient elastography acquisition on a phantom. **a)**Time-motion(TM) mode **b)**Amplitude(A) mode. TM and A modes are used to locate ideal liver part. **c)**Shear wave propagation image. y-axis is distance from skin, x-axis is time. Slope of the dashed line is shear wave speed(V_s)[23]. Tissue stiffness value is indicated in kPa. In the left panel, controlled attenuation parameter(CAP) value, which quantifies steatosis level is indicated in dB/m.

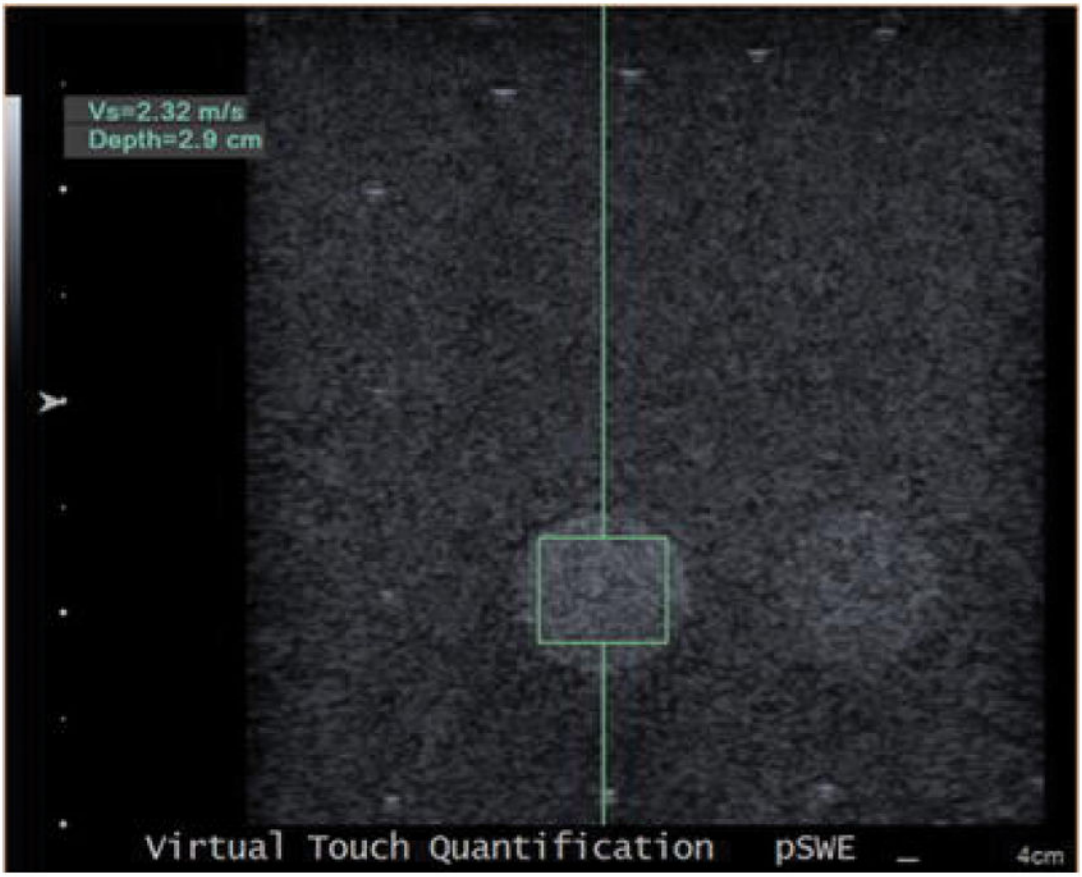

Figure 3.
pSWE acquisition on a phantom. Green box is the focus of ARFI excitation. Shear wave speed value is indicated in left panel.

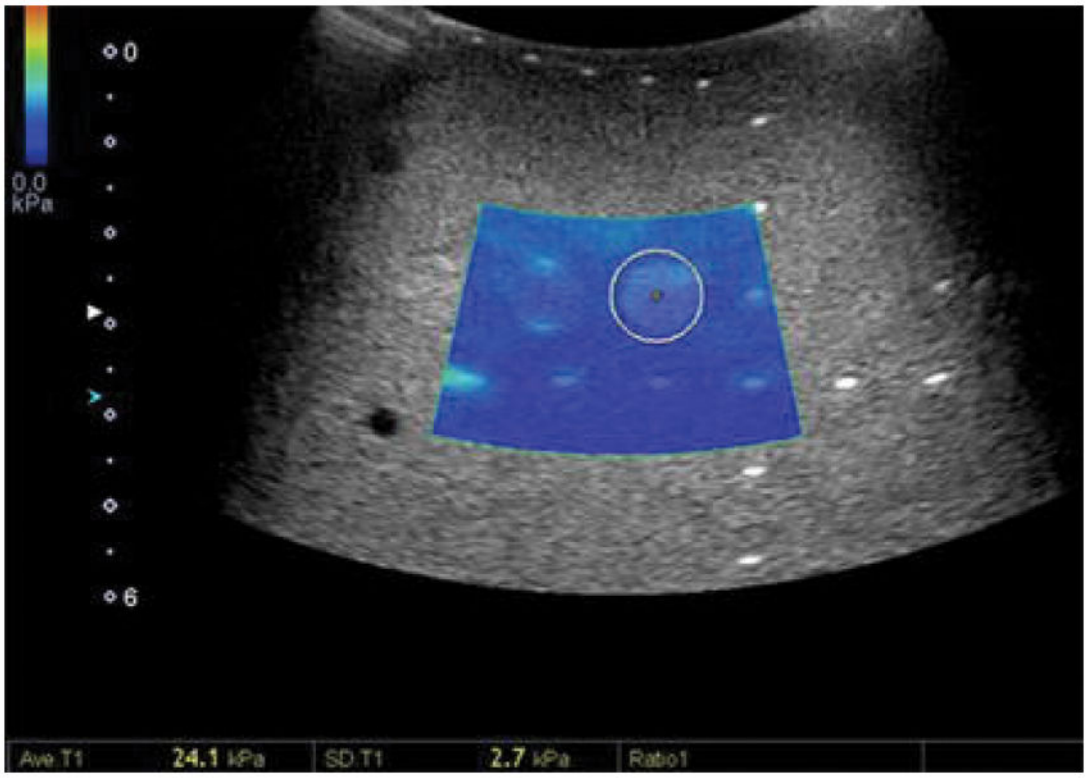

Figure 4.

2D-SWE acquisition on a phantom. Blue box denotes elastographic field of view (FOV) and circle decodes region of interest. Tissue stiffness in kPa, is indicated at the bottom of the image. The color scale can be adjusted by the user. Blue areas are less stiff than red areas.

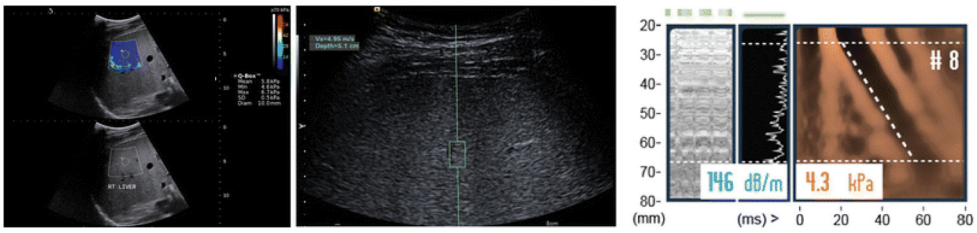

Figure 5.

Liver elastography image examples; 1)2D-SWE acquisition of liver with Supersonic Aixplorer. Color coded elastogram with color scale on right top. SWS values are indicated below the scale. 2)pSWE acquisition of liver with Siemens ACUSON S3000. ARFI induced technique measures SWS in the center area. 3) Transient Elastography measurement example with FibroScan.

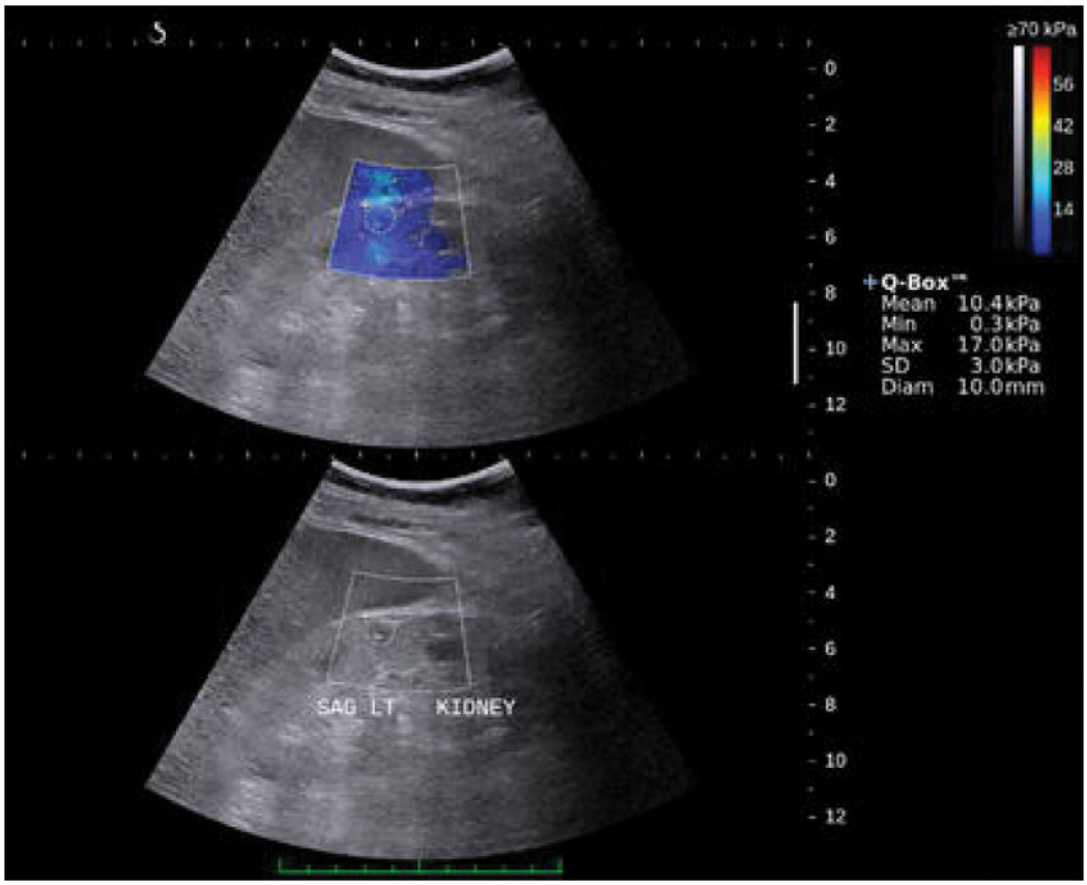

Figure 6.

2D-SWE image of kidney. Mean stiffness is 10.4kPa for this patient, likely reflecting elevated renal stiffness due to CKD –related fibrosis [11].

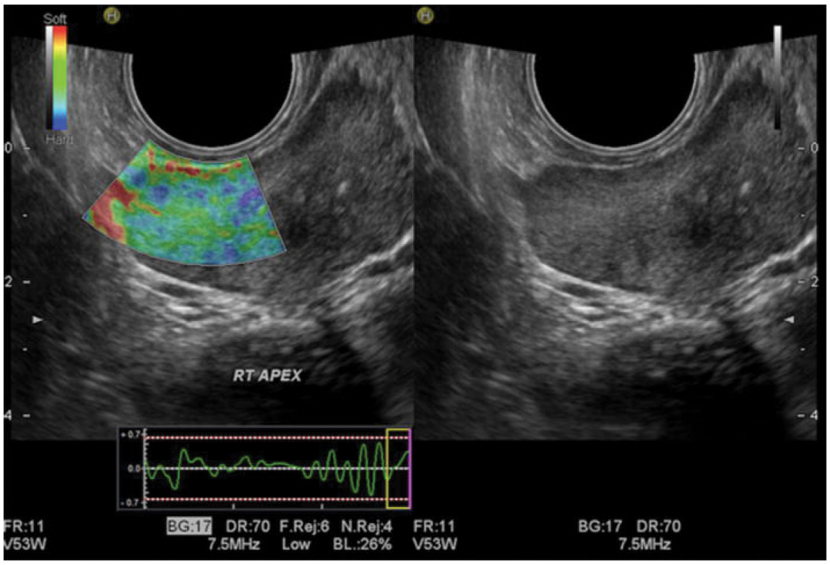

Figure 7.

Strain image of prostate with distribution of stress in color coded map(transrectal approach) Blue color represents hard tissue. Red color represents soft tissue. Real time display of compression is indicated at bottomside.

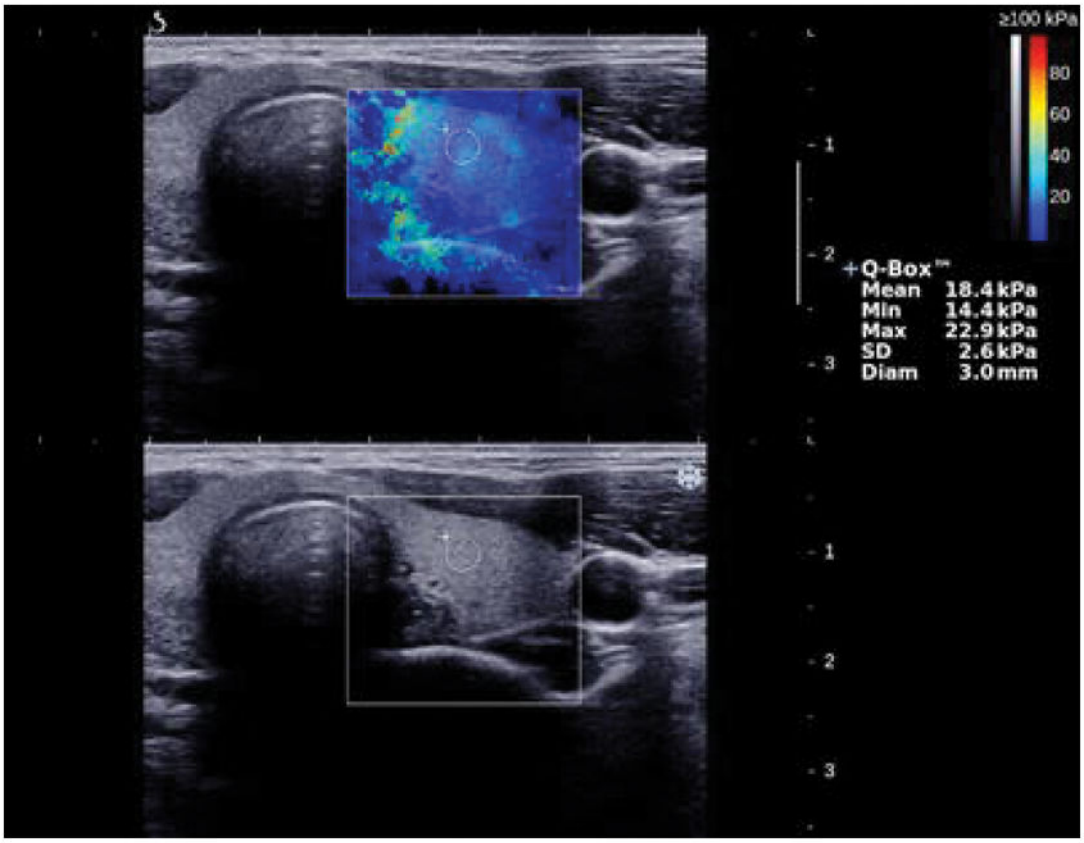

Figure 8.
2D-SWE image of thyroid. Quantitative SWS value is indicated in right side of the image

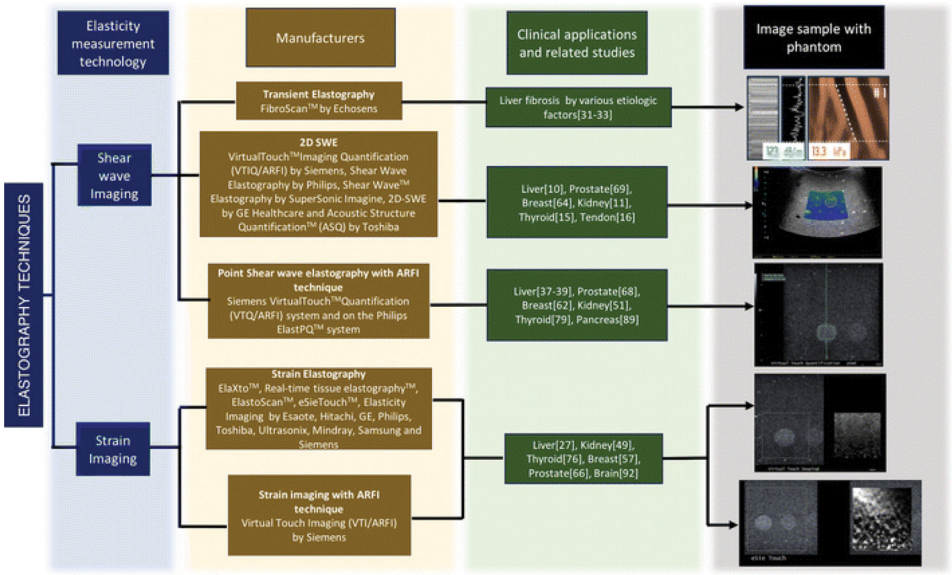

Figure 9.
Summary and classification of elastography techniques

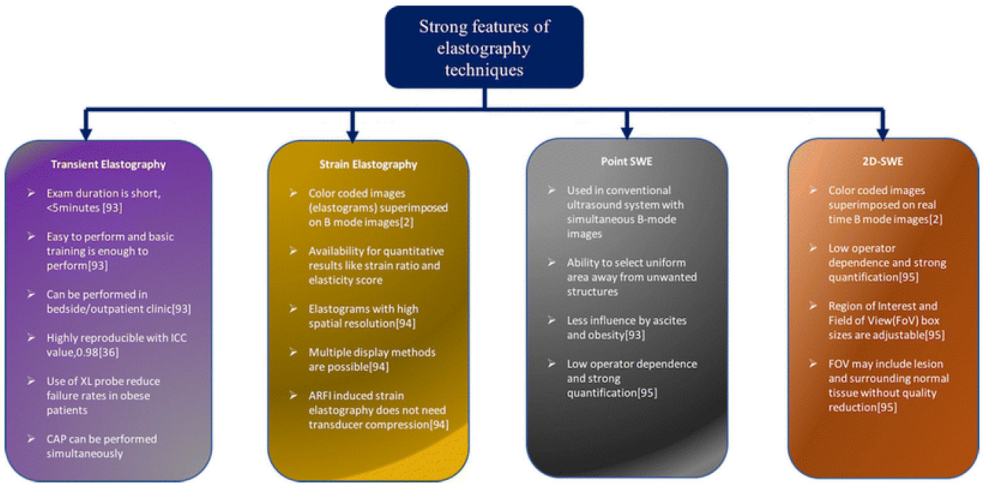

Figure 10.
Strong features of elastography techniques

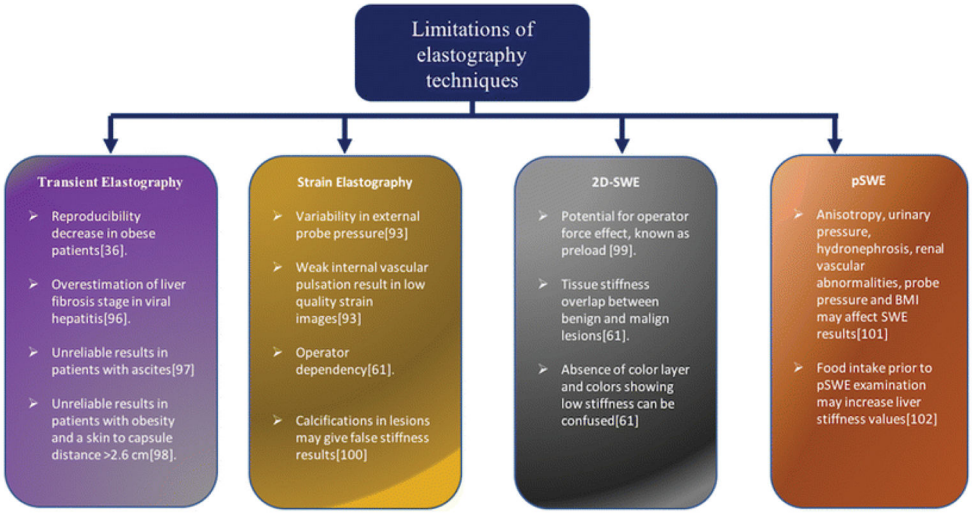

Figure 11.
Limitations of elastography techniques