Review Article

# Ultrasound elastography of liver: How Radiologist can help.

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**Abstract**

Conventional Ultrasonography imaging does not provide information on mechanical properties of body tissues. Advances in ultrasound like contrast enhanced ultrasound, multiplaner 3D ultrasound and elastography have improved the performance of ultrasound in detection and characterization of pathologies and also has added a new dimension to conventional imaging technique. At this time, the use of elastography is not recommended for characterization of focal liver lesions, however in diffuse liver diseases Ultrasound elastography finds a role in identifying, classifying and grading fibrosis. Liver biopsy has been regarded as the gold standard to detect and classify liver fibrosis. However, due to high cost, inherent complications, invasive nature and its observer and sampling inadequacy, alternative methods to biopsy like Ultrasound elastography might have a role to play in detecting and grading liver fibrosis. This review focuses on the type of elastography and its role and applicability in various liver pathologies.

**Key words:** Elastography, Liver fibrosis, Stiffness, Ultrasonography

## Introduction

Ultrasound imaging plays important role in the diagnosis, monitoring and therapeutic decisions of myriad of liver diseases. Though ultrasound has been criticized for many of its limitations, it still is the initial imaging modality for most pathology due to its inexpensive nature and versatility. Advances in ultrasound like contrast enhanced ultrasound, multiplaner 3-dimensional ultrasound and elastography have improved the performance of ultrasound in detection and characterization of pathologies and also has added a new dimension to conventional imaging technique.

Conventional USG imaging does not provide information on mechanical properties of body tissues and detection of lesion or pathology requires distortion of echotexture, internal architecture and/or shape of the normal liver. The sensitivity of the conventional technique is thus low for evaluation of early stage of disease particularly fibrosis, which can be detected early on by elastography techniques when the disease is more curable and fibrosis is reversible. Also evaluation of tissue stiffness has been used to characterize focal lesions: softer ones being benign lesion and stiffer being at the malignant end of the spectrum. However focal liver masses have a variable appearance on elastography, with a large overlap in the stiffness of benign and malignant lesions making their differentiation problematic.[1]

## Types of USG elastography for imaging of liver:

### 1. Strain elastography (SE) imaging:

SE determines the elasticity of tissue correlative strain within a field-of-view (FOV).[2] The more an organ deforms when force is applied, the higher the strain and the softer the tissue. SE can be performed on ultrasound equipment that evaluates the differences in deformation in tissue when a force (stress) is applied. The force can be from patient movement, such as breathing, heartbeat, or external compression with rhythmic motion of the ultrasound transducer as the source of the movement.

The real-time SE image is displayed with a scale based on the relative strain of the tissues within the FOV.[2]

Results are displayed in gray-scale or with various color displays; preference is often determined by the user's exposure to elastography and preference in interpretation. In the gray-scale map, soft is coded white, while hard is coded black. Several factors affecting the elastogram are important in performing SE, including what tissues are included in the FOV, amount of pre-compression, and tissue movement.[2, 3]

**2. Elastography using Acoustic radiation force impulse (ARFI) imaging: imaging tissue displacement induced by radiation force.**

The use of a low-frequency ultrasound ARFI pulse (push pulse) can be used as a source of tissue displacement. This technique is called ARFI.[4, 5] This push pulse generates both axial displacement and shear waves. Acoustic radiation force can create a localised displacement of a few microns in the ultrasound axial direction, which decays in a few milliseconds.[6] Sufficient force for this purpose can be generated with a standard ultrasound scanner at depths of many centimeters by a sequence of rapid bursts of long (tens of microseconds) focused ultrasound pulses.[4] The displacement is measured at a known time after cessation of the push and displayed as a qualitative elastogram within a small box.[7] As the ultrasound beam creates the displacements, they are less user-dependent than those in hand-induced strain imaging. When the axial displacement is measured, the technique is similar to SE called Virtual Touch Imaging (VTI; Siemens Ultrasound).[8]

**3. Point shear-wave elastography (pSWE): shear-wave speed measurement at a location using acoustic radiation force.**

The type of localized transient displacement generated by ARFI creates a transient shear-wave propagating away from the pushing-beam's axis and focus, being strongest at the depth of the pushing-beam's focus.The shear displacement is along the ultrasound imaging beam, allowing the use of correlation tracking or Doppler to measure the small displacements of the shear-wave and detect its time of arrival at lateral positions.

The speed can be measured to depths of up to about 8 cm[9] and is reported in units of m/s or converted to Young's modulus (kPa). Although ultrasound imaging is used to guide placement of the region of interest (ROI), no elasticity images are produced. Commercial systems by Siemens and Philips are based on this technique.[8]

An important application is in characterizing diffuse liver disease where, unlike TE, there are no problems with propagating through ascites, and potentially fewer problems with obese patients and with patients with dysmorphic livers, given the guidance of conventional ultrasound.[8, 10]

**4. Shear-wave elastography: shear-wave speed imaging (2D-SWE) using acoustic radiation force.**

SWE can be utilized to produce two- or three-dimensional quantitative images of shear wave speed with a useful field of view. Super-Sonic Imagine USG implements one such technique. The acoustic radiation force focus is swept down the acoustic axis faster than the shear-wave speed, so as to generate tissue displacements (tens of μm) at all positions along the acoustic axis almost simultaneously. This produces a shear-wave in the shape of a cone with a shallow angle, known as a Mach cone, that travels away from the push line, which spreads less and thus decays less rapidly with distance than that from a single pushing focus.An ultrafast scanner achieves an ultrasound frame rate of up to 20 kHz by transmitting a plane wave and focusing only on receive, so that each ultrasound echo image is created with a single transmit pulse. This high frame rate allows the shear-waves to be followed in real time, and echo tracking over a grid of points produces a displacement movie from which a small map of shear-wave time-of-arrival can be created. The process is repeated for a number of different push lines to create a final quantitative elasticity image in a box, which is presented as a color overlay on the B-mode image in units of m/s or converted to Young's modulus in kPa.[6, 8, 10]

**5. Transient elastography (TE): shear-wave speed measurement using a surface impulse.**

This method is known as transient elastography even though all of the dynamic methods use transient excitations. It employs a brief push (a small "thump") applied with an automated movement of the ultrasound transducer, which acts like a piston at the skin surface. The strongest shear-wave arises from the edge of the piston: thus a disc-shaped piston approximates a ring source. A component of the wave from this ring converges on the ultrasound axis and after some distance travels down the axis at a speed close to the shear-wave

speed.The shear displacement (in the ultrasound axial direction) versus depth may then be measured and the speed of the wave is obtained.[8, 10]

## USG elastography in Liver pathology:

### 1. Focal Liver Lesions

Both SE and SWE can be used to evaluate focal liver lesions.[1, 11-13]Because SE is qualitative, a lesion can be compared with "normal" liver to determine if the lesion is harder or softer than the background liver. However, this technique is limited in that the background liver may have variable stiffness depending on the degree of steatosis or fibrosis. In addition, both benign and malignant lesions can be soft or hard compared with normal liver. With SWE, a stiffness measurement is obtained; however, because of the wide variability of a given pathologic abnormality's stiffness, characterization of a lesion as benign or malignant is problematic.

In a series by Yu et al[1], five hemangioma had a shear wave velocity range of 0.87 to 4.01 m/s with an average of 0.71 m/s, whereas hepatocellular carcinoma (HCC) had a range of 0.77 to 4.34 m/s with an average of 1.01 m/s. Overall, the difference in shear wave velocity of malignant 2.57 ± 1.01 m/s and benign lesions 1.73 ± 0.8 was statistically significant (P<0.01).

Guibal[11] used SWE for evaluation of various focal hepatic lesions. For the 139 lesions successfully evaluated, SWE values were (in kPa), for the 10 adenomas 9.4±4.3, for the 22 haemangiomas 13.8±5.5, for the 16 focal nodular hyperplasias (FNH) 33±14.7, for the 26 HCCs 14.86±10, for the 53 metastasis 28.8±16, and for the 7 cholangiocarcinomas 56.9±25.6. In their study, FNH had significant differences in stiffness compared with adenomas ($P=0.0002$). Fifty percent of the FNHs had a radial pattern of elevated elasticity. A significant difference was also found between HCCs and cholangiocarcinomas elasticity ($P=0.0004$).

However, the large overlap of elasticity values between benign and malignant makes the technique unreliable for focal liver mass characterization in any given case. At this time, the use of elastography is not recommended for characterization of focal liver lesions and large elastography studies along with biopsy correlation of the lesions will be required before it can be applied in clinical practice.[3, 10]

### 2. Diffuse Liver Disease

Liver fibrosis is a significant worldwide problem. As fibrosis progresses, there is increasing loss of liver function and higher risk of liver cancer. This chronic liver disease is characterized by the deposition of fibrous tissue within the liver. The stage of liver fibrosis is important to determine prognosis, surveillance, and treatment options. Early-stage fibrosis is reversible, whereas the disease that has progressed to cirrhosis is likely irreversible. Presently, the only method of staging fibrosis has been by liver biopsy.[14, 15]

Liver biopsy is considered the gold standard for fibrosis assessment and stage classification and is also able to grade necro-inflammatory activity. In addition to being invasive with potential complications that can be severe in up to 1% of cases.[15] A liver biopsy represents roughly only 1/50,000 of the liver volume, and there is interobserver variability at microscopic evaluation.[16] Therefore, noninvasive methods for liver fibrosis assessment have been an intense field of research, including elastographic methods using ultrasound and magnetic resonance imaging.

With increasing fibrosis, the liver becomes stiffer, which can be monitored using SWE.[10, 17, 18] With this technique, ROI is placed in a region of the liver taking care not to include large vasculature (Figure 1). Elasticity value of liver increases in liver fibrosis and progresses as the grade of fibrosis increases, thus helping in diagnosis and grading fibrosis (Figure 2). An intercostal approach in segment VIII of the liver has been shown to provide morphology accurate results. Serial measurements are taken while the patient suspends respiration. The average of these measurements is used to estimate degree of liver fibrosis. All vendors recommend taking serial measurements and using a mean value for making clinical decisions. The number of measurements recommended varies in the literature from 5 to 10. Values that are obviously inaccurate are discarded. The inaccurate values can be due to transducer movement or patient movement during the data acquisition.[19]

Suh et al[20] found that the elasticity values of biopsy proven normal liver was 4.4±0.9 kPa. Reference range of normal hepatic elasticity was 2.6– 6.2 kPa. With 6.2 kPa as a cutoff value, the sensitivity and specificity for the diagnosis of hepatic fibrosis were 91% (20 of 22 subjects) and 95.9% (188 of 196 subjects), respectively. The potential confounding factors like age, sex, body

mass index, steatosis had negligible effects on the elasticity values.

Friedrich et al used ARFI for determining the variation of elasticity between healthy individuals and patients with liver fibrosis. In healthy individuals the mean shear wave velocity was 1.13±0.23 m/s (elasticity value in Young's modulus was 3.89 kPa). Mean shear wave velocity in patients with severe hepatic fibrosis (stage F4) was 2.38±0.74 m/sec, 16.99 kPa). They concluded that the shear wave velocity in patients with histologically proven hepatic fibrosis were significantly higher than normal individuals and ARFI imaging was a promising USG-based method for assessing liver fibrosis in chronic viral hepatitis.[21]

Cutoff values of 1.21 to 1.34 m/s have been shown to predict significant fibrosis.[22, 23]For diagnosis of cirrhosis, SWE cutoff values range from 1.55 to 2.0 m/s. [17, 23, 24] Recommendations are that pSWE and 2D-SWE can be used to assess the severity of liver fibrosis in patients with chronic viral hepatitis, especially with chronic hepatitis-C virus (HCV) infection. Cutoff values between different shearwave methodologies and for different brands of scanners vary using the same methodology.[18]

In a meta-analysis that included nine studies, the optimal cutoff values were 1.34, 1.55, and 1.80 meters per second, respectively for staging clinically significant fibrosis, severe fibrosis, and cirrhosis.[25] In a series of 102 consecutive patients with chronic HCV, it has been shown that healthy volunteers show significantly lower values of both pSWE and TE compared with patients with nonsignificant fibrosis.[26]

## Recommendations

The Society of Radiologists in Ultrasound (radiology consensus)[18] convened a panel of specialists from radiology, hepatology, pathology, and basic science and physics to arrive at a consensus regarding the use of elastography in the assessment of liver fibrosis in chronic liver disease. The recommendations in this statement are based on analysis of current literature and common practice strategies and are thought to represent a reasonable approach to the noninvasive assessment of diffuse liver fibrosis.

The panel suggested that TE and ARFI (pSWE and 2D SWE) techniques were at least equivalent, with a few studies showing that ARFI techniques may bemore accurate.[27, 28] Patients can be grouped into three categories (Table 1): those with normal elastography values who have a low likelihood of cirrhosis (stage F0 or F1) and may not require additional follow-up, those with high elastography values who have a high likelihood of cirrhosis, and those in between who have moderate to severe fibrosis (stages F2 and F3) and are at risk for progression of the fibrosis, depending on the origin of the fibrosis.

**Table 1.Consensus of Suggested Thresholds in Patients with Hepatitis C for significant liver fibrosis.[18]**

| Device | No clinically significant fibrosis-Unlikely to need follow-up | Advanced fibrosis and/or cirrhosis-clinically significant fibrosis |
|---|---|---|
| Transient Elastography[29-31] | < 7kPa (1.5 m/s) | >15 kPa (2.2 m/s) |
| Point shear wave elastography (Siemens)[25, 30] | <1.2 m/s (5.6 kPa) | >2.2 m/s (>15 kPa) |
| Point shear wave elastography (Philips)[26] | < 7kPa (1.5 m/s) | >2.2 m/s (>15 kPa) |

## Conclusion

There is limited role of USG elastography for differentiating various focal lesions or grouping them as benign or malignant. However USG elastography might have an important role in diffuse liver disease especially in detecting and quantitating fibrosis. The literature indicates that USG elastography is extremely useful to distinguish patients with no or minimal fibrosis and differentiate them from those with severe fibrosis or cirrhosis. Intermediate group between these cutoff values requires additional studies in future to determine follow-up. Further research in USG elastography is required in the areas of population differences, disease differences, spleen measurement, steatosis, focal hepatic lesions and incidence of HCC related to liver fibrosis grade. For developing country like Nepal, biopsy

of liver for diagnosis of liver fibrosis and response to treatment will be limited due to lack of expertise and cost issue. Due to factors like high cost and inherent complications of biopsy, noninvasive method like USG elastography might have a role to play in management of such patients.

## Conflict of interest: None declared

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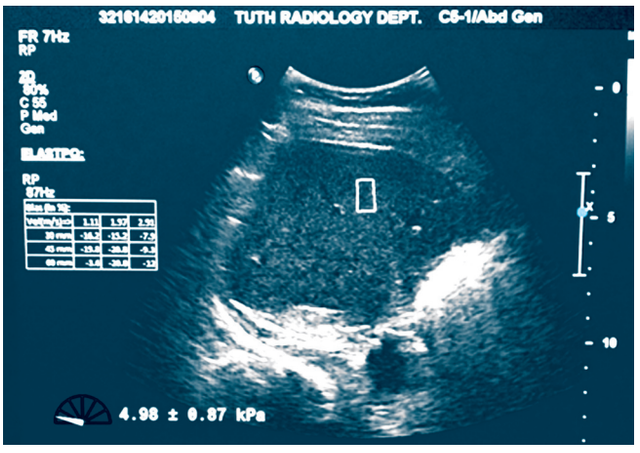


**Figure 1. Point shear wave elastography of normal liver shows elasticity value of 4.98 ± 0.87 kPa.**

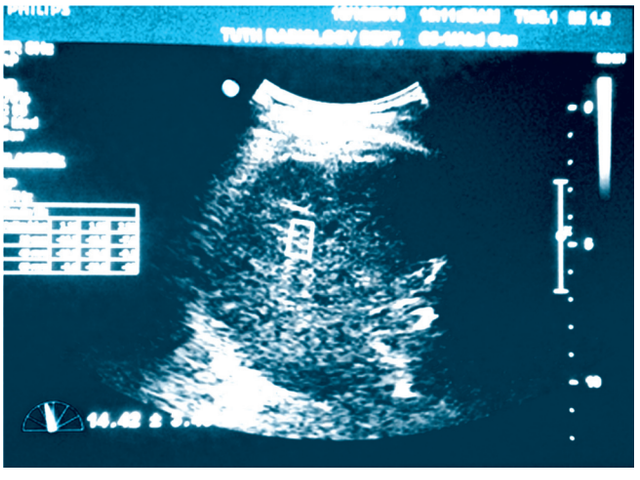

**Figure 2. A case of extrahepatic portal vein thrombosis with cirrhosis of liver. Ultrasonography shows coarse increased hepatic echotexture with irregular nodular surface. Point shear wave elastography shows increased liver stiffness with elasticity value of 14.42 ±3.45 kPa, suggestive of advanced fibrosis and cirrhosis of liver.**