US and Diffuse Liver Diseases
Diffuse Liver Diseases

Acute hepatitis

Chronic hepatitis

Cirrhosis
Sonography is often the first imaging procedure performed in the evaluation of individuals with suspected liver disease.
Acute Viral Hepatitis

In patients with Acute Hepatitis sonography is not useful for the specific diagnosis, but only for differential diagnosis with other liver diseases.
Acute Hepatitis

There are no specific US findings in acute hepatitis
Acute Hepatitis

- Hepatomegaly
- Splenomegaly
- Enlarged lymph nodes at hepatic hilum
- Thick gallbladder wall
Acute Hepatitis
NAFLD and US

- **High sensitivity**
- **Low specificity**
  - None of the radiological features distinguished between NASH and other types of NAFLD.
  - The presence of >33% fat on liver biopsy was optimal for detecting steatosis on radiological imaging.

*Saadeh S et al. Gastroenterology 2002*
Bright Liver
FATTY LIVER

- Usually is diffuse
- Sometimes steatosis can involve only a part of the liver
- This phenomenon is known as “focal fatty change”
- Tipically, such fat infiltration has irregular margins and it does not cause “mass effect” on the surrounding structures
Focal steatosis: CEUS
• Immediate
• Reproducible
• Operator independent
• Machine independent
• Same ROI of Fibroscan
• Only liver
• Volume explored is 100 times greater than that of LB
Chronic Hepatitis and Cirrhosis

- There are no specific US signs for Chronic Hepatitis.
- Sometimes, also in patients with Cirrhosis, liver sonography can be completely normal.
- Sonography is a very useful tool for FOLLOW-UP and early diagnosis of COMPLICATIONS in Chronic Hepatitis and Liver Cirrhosis.
CHRONIC HEPATITIS

- Normal liver echotexture
- Possible lymph node enlargement in the hepatoduodenal ligament

Perihepatic lymphadenopathy in chronic hepatitis C: a complementary diagnostic element?

Enlargement of perihepatic lymph nodes in relation to liver histology and viraemia in patients with chronic hepatitis C.

Volume controls: $2.2 \pm 2.2 \text{ ml}$

$5.8 \pm 2.2 \text{ ml}$ Mild – Moderate CH

$18.1 \pm 10.4 \text{ ml}$ Severe CH

$22.8 \pm 18.8 \text{ ml}$ Cirrhosis

No correlation with genotype and liver function tests

In conclusion:

enlargement of perihepatic lymph nodes is predictive for severe inflammation activity.

Total perihepatic lymph node volume changes according to the antiviral response and leads to progressive normalization in the perihepatic lymph node volume in sustained virologic responders. A decrease in the perihepatic lymph node volume is associated with an improvement in liver histology.
Among **Chronic Liver Diseases**, only **Cirrhosis** can be diagnosed by **US** with high sensitivity and specificity, so that **Liver Biopsy** can often be avoided.
Liver becomes nodular due to cell death, fibrosis and regenerative nodules.

Increased liver echogenicity and distorted parenchyma with decreased penetration of the US beam.

Cirrhosis
Diffuse Liver Diseases
US Evaluation

- Margins
- Echotexture
- Segments
- Vessels
Liver Margins

Smooth

Nodular
Liver Echotexture
Coarse nodular pattern
The only pathologic changes of liver parenchyma that can be easily shown by US are "STEATOSIS" and "FIBROSIS" although not always US are able to correctly differentiate them, that’s why………………

…………..Clinical Approach besides

The Imaging is important.
Liver Segments

Caudate lobe > 0.65
Right liver

Sensitivity, 38.2
Specificity, 99.5

Giorgio A et al. Radiology 1986
Segment 4 (the quadrate lobe):
A barometer of cirrhotic liver disease at US

Segment 4 mean diameter

Controls: 43 mm ± 8

Patients: 28 mm ± 9

Lafortune M et al. Radiology 1998
Liver Cirrhosis: US Findings

Regional changes in hepatic morphology

- Enlargement of the left lobe
- Hypertrophy of the caudate lobe
- Shrinkage of the right lobe
- Decreased size of segment 4 diameter

C/RL Ratio
Vessels
Sonography of Diffuse Liver Disease

- Sonography is of limited usefulness in acute hepatitis.
- Increased parenchymal echogenicity is a reliable criterion for diagnosing fatty liver.
- Cirrhosis can be diagnosed in the correct clinical setting when the following are present:
  - nodular liver surface
  - increased C/RL ratio
  - indirect evidence of portal hypertension

Tchelepi H et al. JUM 2002
Portal Hypertension

Main sonographic features:

- Dilated portal vein
- Dilated splenic vein
- Dilated superior mesenteric vein
- Splenomegaly
- Presence of collateral vessels
- Ascites
Portal vein diameter

Normal up to 12-14 mm
Dilated portal vein

Diameter 17 mm
Dilated splenic vein

Normal, \( \leq 10\) mm
Dilated superior mesenteric vein
Spleen

17 cm
Cirrhosis: Ascites

Morison’s pouch

Pouch of Douglas
PORTAL VEIN THROMBOSIS
PORTAL VEIN
THROMBOSIS
PORTAL VEIN
CAVERNOMA
Vena porta: Flusso epatofugo

Scansione intercostale
Collateral vessels
Paraumbilical vein
Circolo collaterale spleno-renale
Sonography is useful for **FOLLOW-UP** and early diagnosis of **THE MOST IMPORTANT COMPLICATION OF CIRRHOSIS (PORTAL HYPERTENSION AND HCC)**
HCC

- L’ecografia è largamente accettata come metodica di imaging nella sorveglianza del paziente cirrotico
- Le caratteristiche ecografiche dell’HCC sono aspecifiche
HCC: Valutazione Doppler
Further, in our own experience, not only is there variation of stiffness measurements within masses with the same diagnosis, there may also be variation of stiffness measurements from within the margins of a single focal mass, as well.
HCC
HCC

56.4% larger in size

(Chen MH et al. Clin Radiol 2007)
Infiltrative HCC
Perfusion Quantification Softwares

They enable assessment of perfusion using curve-fitting models, and generation of parametric images by synthesizing perfusion information at the pixel level.

The quantification of the tumor microcirculation can detect changes in hemodynamic parameters for effective monitoring of tumor treatment.
Assessment of signal intensity versus time from a region of interest
ROI 1 = 14.53 dB
(Smoothing=On, Log)
Echo Mean = 14.53 dB
Echo Mean Min/Max/Mean = 0.00/16.27/8.17 dB
Echo Std Dev = 16.79 dB

Curve Fit - Echo Mean - LDRW WWO
Derived Clinical Parameters
Rise time = 23.76 sec
Peak Intensity = 15.62 dB
Mean transit time = 47.86 sec
Area under the curve = 1471.74 dB sec
Time from peak to one half = 63.29 sec
Wash in slope = 0.58 dB/sec
Time to peak = 41.60 sec
R² = 0.9477
Chi² = 1957.11
(Motion Compensation is ON)

ROI Area = 822.20 mm²
Quantitative Evaluation of Tumor Response to Chemotherapy
US and SonoElastography of the liver:

The clinical point of view

Carlo Filice

Ultrasound Unit, Infectious Disease Department, Fondazione IRCCS Policlinico S. Matteo
University of Pavia - Italy
CH CorB & HIV/AIDS
Dual or triple Hepatitis
  • HBV- HDV
  • HBV- HCV
  • HCV- HBV- HDV

HCV
Parenchimopatie Diffuse
NAFLD
Hepatosteatosis NASH (25%)
Autoimmuni
Cirrosi Biliare Primitiva
Colangite Sclerosante
Overlap Syndrome
Farmaci
  • Cortisonici
  • antiblastici
  • antiipertensivii
  • ART

HBV
Emocromatosi
Alcool
NAFLD
Hepatosteatosis NASH (25%)
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  • ART

US Diagnosis in Chronic Hepatitits
CH with hepatomegaly

Diffuse Steatosis

Irregular borders

Peri hepatic lymph node

Coarse echo pattern

Ultrasound and diffuse liver disease
Diagnostic Accuracy: 82-88%

Low specificity for diagnosing staging in intermediate stage
SonoElastography

Non invasive imaging technique for assessing the stiffness of tissues

Main applications

Liver  Breast  Thyroid  MSK

• Liver
• Pancreas
• Prostate
• Breast
• Lymph Nodes
• Thyroid
• Salivary Glands
• Heart
• MSK
• Uterus
• Kidney
SonoElastography and Liver

PubMed search results for "elastography liver" show 820 results.

Further searches for "transient elastography liver" show 534 results.

Search for "real time elastography liver" shows 78 results.
From Imaging Journals to... Clinical Journals


Assessment of impact factors on shear wave based liver stiffness measurement.
Ling W, Lu Q, Quan J, Ma L, Luo Y.
Department of Ultrasound, West China Hospital of Sichuan University, Chengdu 610041, China. lingwenwubing@163.com


Performance of liver stiffness measurements by transient elastography in chronic hepatitis.
Giovanna Ferraioli, Mabel Zicchetti, Raffaella Lissandrini, Carlo Filice, Elisabetta Above, Gianluigi Poma, Marta Di Gregorio, Ultrasound Unit, Department of Infectious Diseases, Fondazione IRCCS Policlinico San Matteo, Medical School University of Pavia, 27100 Pavia, Italy.


Accuracy of real-time shear wave elastography for assessing liver fibrosis in chronic hepatitis C: a pilot study.


Real-time tissue elastography in the assessment of liver stiffness.
Ferraioli G, Lissandrini R, Filice C.
Ultrasound Unit - Infectious Diseases Department, Fondazione IRCCS Policlinico San Matteo - Medical School.
Transitent Elastography

Clinical Practice Guidelines

EASL Clinical Practice Guidelines: Management of hepatitis C virus infection

European Association for the Study of the Liver

Clinical Practice Guidelines

Transient elastography (TE) can be used to assess liver fibrosis in patients with chronic hepatitis C, provided that consideration is given to factors that may adversely affect its performance such as obesity, age, and biochemical necroinflammatory activity. TE results should be evaluated relative to interquartile range and to the success rate of measurements. TE performs better at detecting cirrhosis than lesser degrees of fibrosis [65,66].
Elastography Guidelines

Ultraschall Med, 2013

May 2 - 5, 2013, Sao Paulo (Brazil)
Elastography in Liver Disease, why?

- Chronic liver disease affects millions of people worldwide
- Long-lasting disease
- Patients need many clinical evaluations every year
- Biopsy is not a perfect gold standard for detecting liver fibrosis
Biopsy limits

- Invasive procedure
- Poor compliance
- Complications (5.9%)
- Sampling errors
- Small portion of liver tissue
- Intra- and inter-observer variability
- Not easy to repeat
- Costs
Elastography: Open Questions

- Is elastography useful in the evaluation of chronic liver disease?
- Is the method a reproducible one?
- Do strain elastography and shear wave elastography show the same accuracy in the evaluation of diffuse liver disease?
- What are the main limitations of strain elastography and shear wave elastography?
- Is liver biopsy still needed in the assessment of diffuse liver disease?
- To what extent real-time elastography can replace liver biopsy?
Can Elastosonography replace liver biopsy?
CAN YOU DO IT?

YES I CAN!
WFUMB Elastography Consensus

Liver: Shear Wave Elastography

Carlo Filice
Giovanna Ferraioli

Ultrasound Unit, Infectious Disease Department, Fondazione IRCCS Policlinico S. Matteo
University of Pavia - Italy
Our Aims for WFUMB Guidelines on Liver Elastography

For each technique (procedure, reproducibility, results, limitations, recommendations)

Questions and Answers

(Based on Expert opinion and international peer-review papers)

Official meetings in:

Informal meeting in New York – AIUM 2013
WFUMB Guidelines for the use of US Shear Wave Elastography in Liver Disease

Ferraioli G (Italy), Kudo M (Japan), Castera L (France), Choi BI (Korea), Sporea I (Romania), Wilson S (Canada), Cosgrove D (UK), Filice C (Italy)
Procedure*

- **Fasting conditions**;
- **Dorsal decubitus positioning, with the right arm elevated above the head for optimal intercostal access**;
- **Resting respiratory position (breath-hold without deep inspiration)**;
- **Minimal scanning pressure applied by the operator**;
- **ROI placement beneath Glisson’s capsule by 1.5-2.0 cm to avoid reverberation artifacts**;
- **ROI placement to avoid large liver vessels**.

*General procedures, valid for all techniques*
Reproducibility

**Virtual Touch Tissue Quantification VTTQ®**  
ICC: 0.84 - 0.87

**Shear Wave Elastography Imaging (SWEI)**  
ICC: 0.93 - 0.95

**ElastPQ®**  
ICC: 0.97

*Intraclass Correlation Coefficient (ICC):*
- Poor (ICC = 0.00 to 0.20)
- Fair to good (ICC = 0.40-0.75)
- Excellent (ICC > 0.75)
**Results**

*Healthy Subjects*

\[ \text{VTTQ} : < 1.2 \text{ m/sec} \]

\[ \text{SWEI} : 4.37 \text{ kPa} \]

\[ \text{ElastPQ} : 3.5 \text{ kPa} \]
## Results

### Subjects with Chronic Viral Hepatitis

<table>
<thead>
<tr>
<th></th>
<th>( F&gt;2 )</th>
<th>( F&gt;3 )</th>
<th>( F=4 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>( V_{TTQ} ) (m/sec)*</td>
<td>1.33-1.5</td>
<td>1.43-1.81</td>
<td>1.36-2.13</td>
</tr>
<tr>
<td>( SWEI ) (kPa)^</td>
<td>7.1</td>
<td>8.7</td>
<td>10.4</td>
</tr>
<tr>
<td>( ElastPQ ) (kPa)#</td>
<td>5.6</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* 27 studies  
^ 1 study  
# 1 study (abstract)
Results

Other Etiologies
(Liver cirrhosis, NAFLD)

Several studies using VTTQ, that is the first available technique in the market, have been published.

The results need to be validated in larger series.
Limitations

- SWEI accuracy assessed only in the right lobe. Interlobe variations of liver stiffness have been reported with PSWE. Body habitus (obesity, narrow intercostal spaces) may hamper the results.

- Because of the frequency dependency of elasticity properties of tissue, great care and consideration must be used when comparing quantitative results among these techniques.

- Results in kiloPascal are not comparable between SWEI, PSWE and TE.

- The majority of the studies were performed in patients with chronic hepatitis C, thus the cutoffs are not applicable to other viral etiologies and to NAFLD. Only small series of patients with NAFLD have been studied, thus the cutoffs in these patients need to be further assessed.

- Value may be higher in patients with ALT levels greater than five times the upper limit of normal, thus the effect of necro-inflammation should be taken into account, and the results should always be evaluated in clinical settings.
Conclusions

- **VTTQ, SWEI, and ElastPQ** can be used to assess the severity of liver fibrosis in patients with chronic viral hepatitis, especially with hepatitis C.
- Nonetheless, the weight of evidence that is available is still limited.
- Like TE, shear wave elastography is more accurate in detecting cirrhosis rather than significant fibrosis.
WFUMB Guidelines and Recommendations on Clinical Use of Ultrasound Elastography.
Part 3: Liver

Ferraioli G (Italy), Kudo M (Japan), Castera L (France), Choi BI (Korea), Sporea I (Romania), Wilson S (Canada), Cosgrove D (UK), Filice C (Italy)

These recommendations are written based on the international literature and on the WFUMB experts group.
1. Is elastography useful in the evaluation of diffuse liver disease?

Liver elastography is useful for the evaluation of diffuse liver diseases with a high level of evidence. The duration of clinical application differs as some methods have been used for more than ten years and others are more recently introduced resulting in large difference in the number of reports. The majority of the studies have evaluated patients with viral chronic hepatitis.

The results obtained in this framework cannot be applicable to other clinical indications. As a matter of fact the cutoffs are strongly dependent on the etiologies.

It is also worth mentioning that values obtained with shear wave based elastography techniques or index obtained with strain techniques vary between manufacturers.

Therefore the cutoffs are both system and etiology dependent.
Elastography is capable of distinguishing significant fibrosis (F2 or more) from non significant (F0 - F1) fibrosis.

However, more data are needed to confirm its use to distinguish between consecutive stages within earlier fibrosis stage.

It is also important to note that every technology may give different values expressed in different units (meter per second, kilopascals) or index.

Several confounding factors have been identified such as liver inflammation, liver congestion and biliary obstruction.

Elastography results shall be interpreted in the full clinical context of the patient taking into account the technological characteristics of the method used to obtain the results.

Elastography can be used to follow patients with chronic liver diseases.
2. Is the method a reproducible one?

Generally, reproducibility of elastography techniques is good. However manufacturer recommendations shall be strictly respected.

Dedicated training is required for all elastography methods.
3. What is the accuracy and (comparison if there is) of the technique covering every indication (every pathologies and clinical framework, liver transplant, NASH, Hepatitis C and others)

Accuracy of elastography methods increases with the severity of fibrosis.

The most studied etiology is chronic viral hepatitis. The body of evidence is highly dependent on the method for other etiologies.
4. What are the limitations?

Obesity is a common limitation of all ultrasound based elastography methods.

Other limitations are the narrow intercostals space and, for transient elastography, the presence of ascites.

Most methods show increased values in the presence of elevated amino-transferases.

Some manufacturers do not recommend the use of liver elastography in pregnancy.
5. **To what extend elastography can reduce liver biopsies?**

In some countries, where liver elastography is used in clinical practice, the number of liver biopsies significantly decreased. When elastography results are consistent with other clinical findings, liver biopsy may be avoided.

6. **Can Elastography provide additional information for focal liver lesions?**

At this moment, the body of evidence regarding the use of elastography in focal liver lesions is still not strong enough to recommend its use in clinical practice.
EFSUMB Guidelines and Recommendations on the Clinical Use of Ultrasound Elastography. 
Part 1: Basic Principles and Technology. Ultraschall 2013
Part 2: Clinical Applications. Ultraschall 2013

WFUMB Elastography Guidelines Presentation:
May 4, 2013, Sao Paulo (Brazil)
The liver guidelines are in agreement with that issued by EFSUMB
4th INTERNATIONAL MEETING on
SONO-ELASTOGRAPHY
EFSUMB Endorsed Hands-On Course

PRELIMINARY PROGRAM

Castrovillari (CS) - 25th - 26th - 27th JUNE 2014