Fibrosis Quantification: MR Elastography

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Disclosure

• I do not have any relevant financial relationships with any commercial interest
Chronic Liver Diseases

- Multiple etiologies - viral, alcohol, NAFLD
- Chronic, progressive destruction and regeneration of liver leading to fibrosis/cirrhosis.
- A major health problem worldwide - ~ 1 billion affected
  - 400 million hepatitis B
  - 170 million with hepatitis C
  - NAFLD is most common cause in US
    - >30% US population is obese!
- 20-40% develop advanced fibrosis and cirrhosis
- > 1.3 million deaths/ year in 2010 worldwide*

Chronic Liver Disease

- New effective antiviral drugs
- Regression of fibrosis
- Complete resolution
Detection and Staging Fibrosis

- Early treatment
- Assess response to treatment
- Follow up strategies in advanced fibrosis

- Stage 0: Minimal/Early fibrosis
- Stage 1: Significant Fibrosis
- Stage 2: Advanced Fibrosis
- Stage 3: Advanced Fibrosis
- Stage 4: Advanced Fibrosis
Liver collagen content in CLD

Normal <1%
2-8mg/g

Cirrhosis
>30mg/g


Fibrosis content change with treatment

Goodman et al.  
Hepatology 2009; 50:1738-49
Diagnosis of Liver Fibrosis

- Liver biopsy - invasive, sampling error, poor interobserver variability
- Liver function tests
- Conventional imaging
- Advanced imaging - DWI, MRS - promising
- Elastography techniques
  - Sensitive, Accurate

Not sensitive for mild to moderate fibrosis
MR Elastography of Liver

MRI based elastography technique.

Most accurate non-invasive technique for detection and staging liver fibrosis.

“imaging gold standard for liver fibrosis”
MR Elastography of Liver

- Newer Technique
- FDA approved in 2009
- All 3 major MRI vendors
- ~600 sites worldwide
- Easily integrated into existing clinical scanner
Principle of MRE

1. Propagation of waves (60Hz)
2. MRE sequence
3. Inversion

Passive Driver

Conventional MR Image

Displacement (µm)

Wave image

Shear stiffness (kPa)

Elastogram
Liver stiffness 8.5 kPa

Liver stiffness 2.3 kPa
Liver Fibrosis and Stiffness

<table>
<thead>
<tr>
<th>Stage</th>
<th>Stiffness (kPa)</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>2.1</td>
</tr>
<tr>
<td>F2</td>
<td>3.1</td>
</tr>
<tr>
<td>F3</td>
<td>4.8</td>
</tr>
<tr>
<td>F4</td>
<td>10.8</td>
</tr>
<tr>
<td>Normal</td>
<td></td>
</tr>
</tbody>
</table>
Liver stiffness $\uparrow$ s with fibrosis stage

Chronic Hepatitis C

- Ichikawa S et al. MRM 2012; 11(4): 798-98

Chronic Hepatitis B


Alcohol


NAFLD

12 studies, 697 patients

Etiology: HBV (11.6%), HCV (47.1%), NAFLD (16.5%), alcoholic liver disease (3.0%), autoimmune hepatitis (4.6%), cholestatic liver diseases (5.9%), and miscellaneous (11.3%)
Magnetic resonance elastography for staging liver fibrosis in non-alcoholic fatty liver disease: a diagnostic accuracy systematic review and individual participant data pooled analysis

Siddharth Singh¹ · Sudhakar K. Venkatesh² · Rohit Loomba³ · Zhen Wang³ · Claude Sirlin⁴ · Jun Chen⁴ · Meng Yin⁴ · Frank H. Miller⁶ · Russell N. Low⁶ · Tarek Hassanein⁷ · Edmund M. Godfrey⁷ · Patrick Asbach⁸ · Mohammad Hassan Murad⁹ · David J. Lomas⁹ · Jayant A. Talwalkar¹ · Richard L. Ehman⁷
MRE correlates w. collagen content

Determinants of Liver Stiffness

- Fibrosis
- Inflammation
- Portal pressure
- Venous congestion
- Infiltrative processes
- Cellular contractility

Always consider clinical setting and data when interpreting MRE
MRE of Liver

- Repeatable, reproducible and has excellent interobserver agreement.
- MRE is proven to superior for fibrosis staging
  - Liver function tests
  - Ultrasound based elastography (TE, ARFI, SWE)
  - Morphological features
  - Diffusion weighted MRI
  - Gadoxetate (Eovist) enhanced scans
  - MR Spectroscopy

Hines et al 2008
Huart et al 2008, Huwart et al 2007,
Venkatesh SK et al 2012, Rustogi et al 2010,
Venkatesh SK et al 2014, Yoon JH et al 2015,
Choi YR et al 2013, Godfrey EM et al 2012
MRE of Liver- advantages

Obesity

Ascites

Catheters
No significant effect of Fat on Stiffness

Liver Stiffness (kPa)

Fat / Water Ratio

Liver Patient

- Normal
- Stage 0
- Stage 1
- Stage 2
- Stage 3
- Stage 4

0.68
MRE in NAFLD

Simple steatosis vs. NASH >0.90

Chen J et al Radiology 2010
Limitations of MRE

- Confounding factors for fibrosis
  - Inflammation-acute and chronic
  - Passive congestion
- Technical failure
  - Extreme obesity
  - Iron overload
Iron overload livers and solution!

Mariappan YK, Venkatesh SK, Glaser K, McGee K, Ehman RL. ISMRM 2013
Beyond detection/staging fibrosis

- Differentiate Simple steatosis from NASH
- Longitudinal clinical follow up
- Assess treatment response
- Cirrhosis
  - Stratify the risk of clinical progression
  - Prediction of decompensation of disease
- Characterization of focal liver lesions
Longitudinal F/U

54/F  PBC

MRE can detect fibrosis even in the absence of morphological (nodularity, lobar atrophy/hypertrophy) changes in the liver.
Longitudinal F/U

76/F

2008
Stage 3-4, Gr 3

2012

6.1 ± 1.5 kPa
2.1 ± 0.2 kPa
Assessment of Treatment Response

Two patients with Chronic Hepatitis C received antiviral treatment.

Improvement

Progression

4.2 kPa

6.3 kPa

2.8 kPa

4.2 kPa

3 years
Stiffness distribution and etiology

- Chronic hepatitis C
- Primary biliary cirrhosis
- Primary sclerosing cholangitis
- Autoimmune hepatitis
MRE in Cirrhosis

Baseline liver stiffness may be useful in

• Prediction of progression Child-Pugh A to B
  • > 8.2kPa has PPV of 83.3%
  • Non responders to treatment and Child-Pugh score of 6 were associated with progression

Takamura et al JMRI 2016
Prediction of decompensation

- Decompensated livers are stiffer (6.8kPa vs. 5.2kPa)
- Baseline stiffness independently associated with decompensated cirrhosis

Compensated Livers on follow up

Hazard of decompensation is 1.42/ unit stiffness

4.96 (95% CI 1.4-17.0, p=0.019) for a subject with liver stiffness $\geq$ 5.8kPa

Emerging Indications For MRE

- Portal hypertension
- Recurrence CLD in Transplants
- Occult fibrosis
  - Resectability of liver neoplasms
  - Chemotherapy associated steatohepatitis (CASH)
  - Liver donors- silent fibrosis
Conclusions

• MRE is an accurate and reproducible technique for evaluation of liver fibrosis

• MRE is useful
  • Clinical follow up for fibrosis progression/regression
  • Assessment of therapeutic response

• Clinical indications for liver MRE continue to emerge.