Magnetic Resonance Elastography (MRE) of Liver Disease

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1. Overview of MRE Imaging

MRE is a magnetic resonance imaging (MRI)-based technology for non-invasively characterizing the biomechanical properties of tissues and may serve as a potential surrogate to invasive liver biopsies for diagnosing and staging liver fibrosis. MRE can be used to quantitatively image the direct consequence of liver fibrosis—increased stiffness of the hepatic tissue. MRE is performed following three basic steps: 1) using a vibration source to generate low frequency mechanical waves in tissue, 2) imaging the propagating waves using a phase contrast MRI technique and then 3) processing the wave information to generate quantitative images (elastograms) showing the mechanical properties, i.e. stiffness, of the tissue.

2. Liver MRE Acquisition

2.1 Generating Mechanical Waves

To implement MRE imaging, a subject lies on the scanner table in the supine position and a disc-shaped acoustic passive driver is placed on the abdomen as shown in Figure 1 [1,2]. The driver is placed against the right anterior chest wall overlaying the right lobe of the liver with its center at the level of the xiphisternum as shown in Figure 2. The passive driver is then secured in place with an elastic belt. The passive driver is connected, via flexible polyvinylchloride (PVC) tubing, to an acoustic speaker system located outside of the scanner room. The acoustic speaker produces vibrations of approximately 60 Hz, which are transmitted to the passive driver via the tube. Commercially available MRE systems typically contain the necessary hardware (drivers and tubing) as well as specialized software for acquisition and processing.
Figure 1. Diagram of the MRE driver system setup for a clinical whole-body MRI scanner. 1: patient table, 2: patient, 3: passive MRE driver, 4: MRI scanner bore, 5: flexible PVC tube, 6: acoustic speaker. Figure taken from Chen et al. [1].

Figure 2. Diagram demonstrating how the mechanical driver is positioned over the right lobe of the liver. The center of the driver is typically centered at the level of the xiphisternum. Accurate positioning of the driver ensures that the largest cross-section of the liver is directly under the passive driver allowing good illumination of liver. Figure is from Venkatesh et al. [2].

2.2 MRE Sequence

MRE can be readily implemented on a conventional MR system with added hardware and software. For liver imaging, the MRE sequence that is most commonly implemented for clinical hepatic application is a modified gradient-recalled echo (GRE) sequence with a motion-encoding gradient (MEG) imposed along the longitudinal axis of the body [2]. Figure 3 provides a two-dimensional gradient echo-based MRE sequence. Typically, between two to four axial image sections are imaged through the widest transverse
dimension of the liver. As recommended by Ehman group [2] the following sequence parameters are used during MRE acquisition:

- TR/TE = 50/20 ms
- FOV = 30-48 cm
- Matrix = 256 x 64
- NEX = 1
- Phase offsets = 4
- Band width = 33
- Slice thickness = 6-10mm

Using parallel imaging with acceleration factor of 2, each section can be acquired with an acquisition time of 16 seconds. The MRE can be implemented on scanners from 1.5 to 7T.

**Figure 3.** Two-dimensional gradient echo-based MRE sequence. MEGs (shown in pink) that are synchronized with the applied vibration are added during the image acquisition. The MEGs sensitize the sequence to cyclic tissue motion in x, y, or z directions. The phase relationship (θ) between the MEGs and the applied waves can be adjusted in steps to acquire wave images at different phases of the cyclic motion. Figure is from Venkatesh et al. [2].
2.3 Generating Elastograms

The third step of MRE is to us to generate images of hepatic stiffness. These elastograms are calculated using direct inversion of the differential equations describing the wave propagation. A review of the MRE methodology and associated equations are provided by Glaser et al. [3]. With commercially available systems, the wave images are automatically processed by the scanner to generate the quantitative images depicting stiffness (units of kilopascals [kPA]). These elastograms can be displayed in either gray scale or color scale. The inversion algorithms can also be configured to provide confidence maps to aid in identifying regions of reliable stiffness data [4]. Representative magnitude and wave images and elastograms are shown in Figure 4.

![Figure 4](image_url)

**Figure 4.** Images acquired from MRE imaging. The left panel is a magnitude image that shows some signal loss and blurring due to the effects of the applied MEGs. The image aids in identifying anatomical locations on the corresponding elastogram (right panel). The center panel is the corresponding wave image which shows the pattern of propagating waves. The right panel is the elastogram (obtained by processing the wave information) which provides the stiffness measurements (0 to 8 kPa). The stiffness values reported by the elastogram are valid for regions with sufficient MRI signal, as seen in the magnitude image, and sufficient wave amplitude, as seen in the wave image. Figure is from Venkatesh et al. [2].

3. Review and Analysis of Elastograms

Elastograms can be reviewed for quantitative assessment of liver stiffness. The clinically relevant cut-off value for distinguishing between nonfibrotic and fibrotic liver tissue is a stiffness value of approximately 3 kPa; stiffness measurements above this cut-off indicate abnormal or diseased liver tissue [1].

In order to evaluate liver stiffness, the reader must review several images. The MR magnitude and phase images (Figure 4) are reviewed to confirm that blood vessels and boundary effects are excluded when defining regions of interest (ROIs) and that there is good wave quality in each two-dimensional slice [5]. If the color wave is acquired with cine mode, then the wave map can also aid in identifying ROIs that are free of wave interference [4]. Additionally, the reader can review the confidence map (Figure 5),
which displays crosshatched areas representing stiffness measurements that are less reliable (i.e. below 95% confidence), to confirm and optimize ROI selection [4,5]. The reader also reviews the elastogram for artifacts, i.e. hot/cold spots indicating wave interference or oblique wave propagation. Such artifacts are noted and excluded when defining the ROIs. In general, ROIs are placed in areas of the liver with adequate wave amplitude and usually do not extend closer than one-half wavelength to the liver margin as to avoid edge effects [2]. Additionally, ROIs are typically not placed over the left lobe of the liver since cardiac palpations can cause motion artifacts [4]. The mean stiffness within each ROI is then calculated using the elastogram image. This procedure is a manual process that is repeated for each slice acquired during MRE imaging. Algorithms aimed at automating the process of defining artifact-free ROIs and calculating liver stiffness have been created by the Ehman group at the Mayo Clinic [5].

![Figure 5](image.png)

**Figure 5.** Confidence maps aid in defining regions to analyze on elastograms. The left panel shows an elastogram with a 0 to 8 kPa stiffness scale. The right panel shows a confidence map overlaid on the elastogram. A threshold of 0.95 is applied in the confidence map and the black crosshatches represent regions with less valid measurements. When defining ROIs, regions with crosshatches should be avoided. Figure modified from Venkatesh et al. [4].

4. VirtualScopics Analysis of MRE Images

MRE is now being implemented in clinical trials due to its non-invasive nature and reliable ability to evaluate liver fibrosis. Given our expertise in MR imaging and the capabilities of our proprietary image analysis platform, which provides radiologists the necessary tools for viewing images and identifying ROIs, we are able to automatically extract mean stiffness measurements to facilitate liver fibrosis assessments to meet clinical trial goals and objectives. Additionally, our working relationship with the Ehman group, the pioneers of MRE imaging, further facilitates our ability to provide reliable MRE data to our sponsors.
5. References


