MR Elastography – Pearls and Pitfalls

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Introduction

Obesity is one of the most common lifestyle diseases in many countries and has led to a dramatic increase in patients diagnosed with non-alcoholic fatty liver disease (NAFLD). Within just half a decade, prevalence of NAFLD among a general population in the United States increased from 15% in 2005 to 25% in 2010 [1]. The picture is even more dramatic in the obese population with the reported prevalence ranging from 30–37% [2].

The clinical appearance of NAFLD encompasses a broad spectrum ranging from mild fatty liver disease, steatosis, inflammation, fibrosis, cirrhosis, and, finally, to hepatocellular carcinoma. Early detection and grading of fibrosis, therefore, has important implications for the management of patients with NAFLD to retard the progression to more severe stages of liver disease.

Percutaneous liver biopsy and histopathological analysis used to be the standard method to confirm and classify nonalcoholic steatohepatitis (NASH). This has now been widely replaced by noninvasive tests such as Ultrasound Elastography and MR Elastography (MRE) of the liver. In several comparison studies of MRE with different Ultrasound Elastography techniques, and MRE with functional MR imaging, MRE has been shown to exceed all other techniques in terms of diagnostic accuracy, sensitivity, specificity, and organ coverage [3–5].

Commercially available solutions for MRE allow the assessment of liver stiffness to be seamlessly integrated into a normal MR examination, including automated processing of the data1.

How does MRE work? MRE depicts motion of mechanical shear waves in tissue using motion-sensitized sequences, followed by ‘inverting’ the wave pattern to deduce tissue stiffness. External motion is induced by an acoustic driver system (Resoundant Inc., Rochester, MN, USA). MRE requires additional hardware, and mechanical wave propagation varies inter-individually, so in practical application MRE does have some pitfalls, which if ignored, may lead to e.g., improper tissue actuation, offset slice positioning, and, ultimately, suboptimal results. Another challenge is posed by patients with marked iron deposits in the liver: In these cases, T2*-mediated signal loss can make it impossible to sufficiently capture the shear wave propagation through tissue using MRI. According to the literature, the technical failure rate is about 10% for conventional GRE-based MRE [6].

Alternative ways to overcome this problem include the use of fractional encoding [7] to allow a shorter echo time (TE) and the use of spin-echo-based MRE sequences [8].

Therefore, it is essential to set up the MRE equipment carefully, prepare patients properly, and choose the right MRE sequence for the given case. And ensure that the evaluation of stiffness values follows established procedures. This article provides some practical guidance and tips on how to perform MRE successfully in daily clinical practice.

Figure 1:
Sequence scheme for conventional GRE MRE (1A) and rapid fractional MRE (1B).

1 WIP, the product is currently under development and is not for sale in the US and in other countries. Its future availability cannot be ensured.
**MRE sequence improvements tailored to different use cases**

**Rapid MRE**

In the original version, MRE is performed with a phase-contrast gradient recalled echo (GRE) sequence, which applies motion-encoding gradients (MEGs) in synchronization with a 60 Hz external shear wave induced to the abdomen (Fig. 1A). This scheme is repeated every 50 ms with alternating polarity of the MEGs, resulting in a total acquisition time of about 20 seconds per slice, depending on the spatial resolution [9].

With rapid GRE (RF-GRE, [9]) this scheme is optimized as follows: Instead of applying MEGs with different polarity every 50 ms in the same phase of the mechanical excitation, the MEGs are played out with the same polarity every 25 ms, matching with opposite phases of the mechanical excitation (Fig. 1B).

The 50% shorter TRs dramatically reduce the required breath-hold duration. This means that patients have to hold their breath for just ~10 seconds rather than ~20 seconds, positively impacting the robustness of the method.

**Fractional MRE encoding**

Motion encoding is normally done with a gradient waveform matching the mechanical wave period, i.e. a “1-2-1” MEG of 16.6 ms duration at 60 Hz driver frequency. This puts a lower limit on the achievable minimum TE, which may be too long for livers with iron overload, or at 3T. Alternatively, shortened, ‘fractional’ MEGs can be used. These have a lower motion-encoding strength, but the resulting shorter TE makes the GRE sequence less prone to T2*-induced signal loss, giving a net benefit for the final MRE result [10].

**Spin Echo EPI MRE**

As an alternative to a GRE-type sequence for MRE, a Spin Echo (SE) sequence with a fast Echo-planar imaging (EPI) readout can also be used for MRE [8]. Due to the rapid readout, all required k-space data for several slices can typically be acquired within a 10–12 second breath-hold. Other advantages of the SE-EPI based approach are a higher robustness in patients with iron overload and a higher signal-to-noise ratio of the wave images compared with GRE-based MRE. SE-EPI MRE can also be combined with fractional encoding.

<table>
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<tr>
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<th>Conventional GRE</th>
<th>RF-GRE</th>
<th>SE-EPI</th>
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<tbody>
<tr>
<td>Breath-hold duration</td>
<td>~20 sec</td>
<td>~10 sec</td>
<td>~10 sec</td>
</tr>
<tr>
<td>Measureable area of liver stiffness</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Robustness against iron overload</td>
<td>+</td>
<td>++</td>
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1Rapid MRE is available with the syngo MR E11C software version.
2Rapid and fractional gre-MRE are available with syngo MR E11C. (There are no new protocols in the Siemens tree, but recommended protocols are available from application support.)
3Spin Echo MRE is available with the syngo MR E11E software version. The product is still under development and not commercially available yet. Its future availability cannot be ensured.

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*Figure 2:*

41-year-old woman with NAFLD. Magnitude, wave, and liver stiffness maps with 95% confidence masks (left to right) for GRE (2A-C), RF-GRE (2D-F), and SE-EPI (2G-I) demonstrating largest area of measurable liver stiffness for the RF-GRE sequence with ROI areas of 15 mm², 27 mm², and 24 mm², respectively. Figure reprinted from [11], with friendly permission of ER Felker and American Journal of Roentgenology (AJR).
MR Elastography workflow

Elastography can be performed at the beginning or end of a routine liver examination, this is a site preference.

1. Prior to positioning the patient turn on the Active Driver (Figure 3 – found in the equipment room). Note: The Active Driver goes into sleep mode after approximately one hour of inactivity.

2. Position the patient for an abdominal examination. Position the black Velcro Band directly underneath the liver.

3. Place the paddle (Passive Driver) on patient’s right upper abdomen so that 1/4 of the paddle is over midline and 1/3 of the paddle is below the bottom of the rib cage (Fig. 4). Note: The tubing from the paddle can be placed coming from head or feet depending on scan room configuration.

4. Secure the paddle on the patient using the black Velcro Band. Please ensure that the entire paddle has good contact with the upper abdomen and is flat against the body surface. If the paddle has improper contact or is rocking back and forth try to adjust the position slightly for better contact. Note: Please make sure that the black Velcro Band is secured very tight on patient and paddle.

5. Prepare the patient mentally for the examination.
   a. Inform the patient that Elastography is performed at end expiration.
   b. Notify the patient, that she/he will feel pressure coming from the paddle during the examination.

6. Place the Body Array coil on the patient for a liver examination.

7. Register the patient and select the appropriate abdominal imaging protocol.

8. As indicated before, MRE can either be performed at the beginning or in the end of the abdominal examination. Note: Please make sure, that the localizer images / images used for planning the MRE exam are acquired in end expiration.

9. Planning of MRE scans: Position the MRE acquisition slice in the mid of the liver as indicated in the images (Fig. 5).

Comparison of methods

A recently published study [11] has compared conventional GRE, RF-GRE, and SE-EPI for MRE. While the study found no equivalent measures of liver stiffness for all techniques, significant differences in terms of failure rates and measureable areas of liver stiffness were found: Both RF-GRE and SE-EPI yielded larger measureable areas than conventional GRE, with RF-GRE having the largest measureable areas. Among patients with iron overload, there was a trend toward a larger measurable area of liver stiffness with SE-EPI. A corresponding example is shown in Figure 2.

Given that liver fibrosis is often spatially heterogeneous, the volume of liver sampled is considered one of the key advantages of MR Elastography compared with liver biopsy and ultrasound elastography. Therefore, RF-GRE appears to be the best choice in patients with normal iron concentrations in the liver, while SE-EPI appears to be superior for patients with iron overload.
10. Instruct the patient again, that during the exam vibrations will be felt from the paddle.

11. Apply MR Elastography sequence. Perform the breath-holds in the exam at the end expiratory state.

12. Load and review images in Viewing Task Card to assess image quality. The following four series will be displayed (clockwise order):

   **Magnitude image:** standard MRI image to evaluate general image quality such as breath-hold quality or SNR.

   **Stiffness Map / Elastogram:** The elastogram is calculated from the shear wave images and represents the relative shear stiffness of tissue. The color scale indicates shear stiffness values in kPa ranging from 0–8 kPa.

   **Stiffness Map with 95% confidence mask overlay (hatched areas):** With the confidence mask, areas where the calculated relative shear wave stiffness values are unreliable, are hashed out. This allows exclusion of areas of insufficient data quality.

   **Wave images:** Wave images illustrate the propagation of shear waves through tissue with different speed and wave length. Based on this information, the Stiffness Maps are automatically calculated by the software (Fig. 6).

   a. Check if the patient held the breath properly.
   b. Check if the signal quality is sufficient, i.e. signal drops, inhomogeneities.
      • Is the liver very dark?
      • Is there a lot of lung tissue, but not much liver tissue in the FOV?
   Note: If the quality is sub-optimal repeat the acquisition after checking proper slice positioning and reminding the patient to follow the instructions carefully.

14. Depending on the local preferences, repeat the MRE acquisition in different locations of the liver in H-F direction.
   Note: Typically, 3–4 contiguous slices near the center of the liver are used.

15. Image analysis / post-processing: Select the Stiffness 95% Map and draw an ROI inside the grid area, avoiding meshed areas. Ensure that the ROI is drawn in liver tissue only. To draw an ROI select the “Tools” subtask card in the Viewing Task Card. Select the Circle ROI or Freehand ROI tool (Fig. 7).
16. Draw an ROI as described above. The displayed “Mean Value” divided by 100 shows the Relative Shear Stiffness in kPA in the ROI (Fig. 8).

17. Repeat this process for all acquired slices and average the resulting stiffness values.

**Image quality troubleshooting tips**

Anatomical Masking Failure – occurs when signal levels in the liver are lower than other structures in the slice. Review the GRE Magnitude image.
- Is there tissue that has brighter tissue then the liver (see Figure 9)?
- Does the tissue in the posterior peripheral tissue have brighter signal intensity then the liver does?
- Is the patient’s stomach full?
- Tip: Repeat series with Sat band over bright signal (Fig. 9).
- If the entire liver is rejected by the confidence mask, shear waves may be missing in the tissue.
- Is the Active Driver turned off or in sleep mode?
- Did one of the hoses come undone?

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