“I was happy to learn that my liver is healthy - and to find that out without experiencing any pain.”
INTRODUCTION TO MAGNETIC RESONANCE ELASTOGRAPHY

Many disease processes cause profound changes in the mechanical properties of tissues. MR Elastography (MRE) is an MRI-based technique for quantitatively assessing tissue stiffness. It was first introduced as an FDA-cleared product in the US in 2009 and since then it has been made available by several manufacturers as an upgrade to their MRI systems. The main application of MRE at this time is non-invasive assessment of liver fibrosis. As of 2018, over 1,000 MRI systems around the world had been equipped for MRE.

MRE is based on the physical principle that the propagation characteristics of mechanical waves within various materials are determined by their mechanical properties. The technique consists of three steps: (1) generating mechanical waves in the region of interest, (2) imaging propagating mechanical waves, and (3) processing the information to calculate the mechanical properties. For assessing liver disease, mechanical waves are typically generated at 60 Hz in the upper abdomen with a flat disk-shaped vibration source that is placed against the body wall. During imaging, synchronous cyclic motion-sensitizing gradients are used with a modified phase-contrast MRI pulse sequence to acquire snapshots of the propagating waves, depicting displacements as small as fractions of microns. The acquired data are then automatically processed with an inversion algorithm to generate cross-sectional images showing the mechanical properties of tissues (i.e., shear stiffness) on a color scale.
The MRE acquisition is performed during breath-holding at end expiration and takes 12-15 seconds for each slice. This acquisition is typically repeated four times, for a total acquisition time of less than one minute. MRE is usually added to a conventional abdominal MRI protocol (either full or limited) and adds little additional time to the overall examination. Another option is to perform a very limited exam consisting only of MRE and a ~30 second proton density fat fraction sequence, which would provide quantitative estimates of fat fraction, iron content, and liver stiffness in an exam that could be accomplished in less than 10 minutes of scanner time and at a very low cost.

HOW LIVER MRE IS PERFORMED

A simple, drum-like driver generates acoustic waves within the tissue of interest.

A special MRI technique images tiny displacements of the tissue that result from wave propagation.

An advanced mathematical algorithm generates maps of tissue stiffness, known as “elastograms.”

After 1-3 minutes of automatic processing, the scanner produces color-scaled quantitative images (“elastograms”) depicting tissue shear stiffness in units of kiloPascals (kPa). In addition, the algorithm provides anatomic images corresponding to each of the elastograms and “confidence images” that provide a measure of the reliability of the tissue stiffness measurement at each image location.
Rarely seen, but always heard.

Sitting in the room adjacent to the MRI suite, the Resoundant system’s Active Driver safely produces the 60Hz vibrations that work with the proprietary MRE software to uncover even the most subtle changes in tissue stiffness.

Mayo Clinic patient K.A. describes herself as “a 43-year-old fairly healthy mother of two.” She commented on her experience in having an MRE exam:

“Part of me just wanted to know how exactly someone could vibrate my liver...the other part of me wanted to know why my liver enzymes are always a little high, something my family physician assures me is nothing to be concerned about.”

“MRE is an experience like no other, and I do mean that in a good way. No needles, no poking and prodding, just a small circular device (much like the surface of a drum) that was placed against my abdomen before I was moved into the MRI machine. Once in the machine, I was asked to inhale, exhale and then hold my breath. The ‘drum’ literally vibrated in different drum beats which then helped the physician see a better scan of my liver. It was pretty amazing.”
GLOBAL PARTNERSHIPS WITH LEADERS IN IMAGING

Resoundant, Inc. is proud to collaborate with leading imaging manufacturers to make MRE available around the world. With more than 1,000 units installed worldwide, MRE is widely available for patients and providers.

MRE is an add-on option for most new MR scanner purchases, or MRE can be added to nearly any existing 1.5T or 3T MR scanner by contacting one of our partners.
Hepatic elastography addresses a long-recognized need for a non-invasive alternative to liver biopsy for diagnosing and staging liver fibrosis. Liver biopsy has a risk of morbidity and mortality, is affected by sampling error, and subjective histologic interpretation. Additionally, it is much more expensive than imaging, including MRI.

At Mayo Clinic, the most common indication for MRE is to assess possible hepatic fibrosis in patients who have conditions that are known to lead to this problem, such as fatty liver disease and chronic viral hepatitis.

Other indications include follow-up of previously diagnosed fibrosis, staging patients with known cirrhosis, and evaluating patients with unexplained portal hypertension. Because the MRE acquisition can be added to a conventional abdominal MRI protocol with little or no impact on examination time, it does not require a high threshold of suspicion to be included in the protocol.
Since 2006, there have been dozens of published studies assessing the diagnostic performance of MRE in detecting and staging hepatic fibrosis, using biopsy as the reference standard. An MRE-based measurement of hepatic stiffness that is in the normal range (< 2.5 kPa) has a very high negative predictive value for ruling out hepatic fibrosis of any stage. Excellent diagnostic performance for staging hepatic fibrosis has been reported in multiple studies.

For instance, a recent meta-analysis concluded that the sensitivity, specificity, and AUROC of MRE for diagnosing advanced hepatic fibrosis and cirrhosis (≥F3) from less-advanced disease are 0.92, 0.96, and 0.98, respectively. These metrics are probably at the limit of what is realistic to achieve, given the known limitations of using biopsy as a “gold standard.” Another pooled meta-analysis of 12 published studies encompassing 697 patients found that the sensitivity, specificity, and AUROC diagnostic performance for diagnosing stage F3 fibrosis and higher are 0.85, 0.85, and 0.93 respectively.
In a pooled analysis of data from individual participants with NAFLD in 3 independent studies, MRE demonstrated a significantly higher diagnostic accuracy than TE for the detection of individual stages of fibrosis using liver biopsy as a reference.\textsuperscript{9,10}

**CASE STUDY**

MRE provides highly sensitive and comprehensive assessment to treatment response, something previously not possible with traditional MR imaging.

**A 57-YEAR-OLD MALE PATIENT WITH CHRONIC HEPATITIS C**

Baseline liver stiffness = 4.2 kPa ± 0.88

3-year follow-up liver stiffness = 2.80 kPa ± 0.69

Decreasing liver stiffness indicating response to treatment
The FDA-cleared MRE products from GE, Siemens, and Philips all use the same mechanical driver hardware, the same default shear wave frequency of 60 Hz, comparable pulse sequences, and the same data processing algorithm to compute tissue stiffness. They all report the magnitude of the complex shear modulus (i.e., tissue stiffness), use the same color scale in the images, and a default 0-8 kPa display. Testing in phantoms and human volunteers has provided confirmation that liver stiffness data obtained on systems from these three vendors can be compared on a valid basis. MRE-based measurements of phantom stiffness have also been demonstrated to compare favorably with TE-based measurements.

More than 10 published studies have assessed the test-retest repeatability of MRE in liver imaging. In general, they have shown that differences in MRE-derived liver stiffness of greater than 19% represent meaningful longitudinal changes. This is a useful level of repeatability because the difference in mean stiffness between normal liver and significant fibrosis is approximately 100% and for advanced fibrosis it is approximately 200%.
MRE has the same potential confounding factors as quantitative ultrasound-based elastography. Liver stiffness is affected by chronic and acute inflammation. The presence of chronic inflammation can cause considerable overlap in stiffness values between patients with stage F0 and stage F1 fibrosis. Acute hepatitis can be associated with very high liver stiffness values without any degree of fibrosis. Portal hypertension, hepatic venous congestion, and malignant cellular infiltrates can elevate liver stiffness independent of the presence of fibrosis.

The most common reason for technical failure of MRE has been hepatic iron overload, which is not uncommon in patients with liver disease. With conventional gradient echo MRE sequences, very high liver iron content may cause the signal intensity of the liver to be too low to visualize the mechanical waves, resulting in a failure rate of ~4% in clinical populations. The newly-introduced SE-EPI MRE sequences are much less sensitive to iron overload, making these technical failures much less common.

Clinical experience has shown that the technical success of MRE is not affected by obesity, unless the patient cannot fit in the scanner. The presence of ascites, common in patients with liver disease, does not affect the technical success rate of MRE.

Quantitative Imaging Biomarkers Alliance

“In adults with NAFLD and a higher risk of cirrhosis, MRE is suggested, rather than VCTE, for detection of cirrhosis”


“MRE is excellent for identifying varying degrees of fibrosis in patients with NAFLD. VCTE or MRE are clinically useful tools for identifying advanced fibrosis in patients with NAFLD.”

The Diagnosis and Management of Nonalcoholic Fatty Liver Disease: Practice Guidance From the American Association for the Study of Liver Diseases (2017)

“MR elastography is the most accurate method for diagnosing liver fibrosis non-invasively because it assesses the whole liver and can stage liver fibrosis.”

American College of Radiology Appropriateness Criteria®: Chronic Liver Disease (2017)
Figures listed are estimates for illustrative purposes only. Please refer to resoundant.com/mre-connect for up to date listings.

With over 1,000 clinical installations, MR Elastography is widely available. To find a location near you, go to: resoundant.com/mre-connect.

If you don’t yet have a local imaging center equipped with MRE, you can go to resoundant.com/mrenearme to help us bring MRE to your area.
Our vision
Contrary to popular belief, Lorem Ipsum is not simply random text. It has roots in a piece of classical Latin literature from 45 BC, making it over 2000 years old. Richard McClintock, a Latin professor at Hampden-Sydney College in Virginia.

The well-documented value of MR elastography as an alternative to liver biopsy in diagnosing hepatic fibrosis has prompted the transition of MR elastography from the laboratory to a widely-available clinical diagnostic tool. Further technical developments, especially advances in pulse sequences and processing algorithms for 3D MRE are opening up new applications. Among the abdominal imaging applications, MRE seems to be particularly promising for assessing pancreatic disease.

The application that is most likely to become the next well-documented indication for MRE is preoperative assessment of meningiomas and skull base tumors,\(^{19-20}\) MRE provides a range of novel quantitative imaging biomarkers that will merit exploration for many years to come.

CONCLUSION

The well-documented value of MR elastography as an alternative to liver biopsy in diagnosing hepatic fibrosis has prompted the transition of MR elastography from the laboratory to a widely-available clinical diagnostic tool. Further technical developments, especially advances in pulse sequences and processing algorithms for 3D MRE are opening up new applications. Among the abdominal imaging applications, MRE seems to be particularly promising for assessing pancreatic disease.

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References


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About Resoundant, Inc.

Resoundant, Inc. was founded by Mayo Clinic and is the developer and manufacturer of Magnetic Resonance Elastography (MRE), a revolutionary imaging technology that quantitatively maps the mechanical properties of tissue almost anywhere in the body. With MRE, physicians can assess changes in these novel biomarkers that occur in conditions like fibrosis, inflammation, and cancer, obtaining information painlessly and noninvasively that previously may have required a biopsy.

The software and hardware needed for MRE is available as an upgrade for many 1.5T or 3T MRI systems from GE Healthcare, Philips Healthcare or Siemens Healthineers. MRE was invented by Mayo Clinic physicians and researchers in a program continuously program funded by the National Institutes of Health since 1995. MRE has been commercially-available as an FDA-cleared diagnostic technology since 2009 and is used in clinical practice on over 1,000 MRI systems around the world. MRE has been recognized as a standard of clinical care for liver fibrosis staging by a number of professional medical societies and serves as a key biomarker for liver fibrosis for numerous NAFLD/NASH clinical trials. In the United States, a new Current Procedural Terminology (CPT) code was recently approved, advancing its role as a standalone, rapid and cost-effective diagnostic test of liver health.