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Guidance for Sponsors
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Magnetic Resonance Elastography: A Quantitative Endpoint for Liver Fibrosis Trials

By Benjamin E. Tubb, M.D., Ph.D., Board Certified Radiologist · Updated for 2026 by Intrinsic Imaging

Magnetic resonance elastography (MRE) measures liver stiffness without a needle, and it has become one of the most accurate imaging tools available for staging liver fibrosis. Now that the FDA has approved the first therapies for metabolic dysfunction-associated steatohepatitis (MASH), sponsors developing the next generation of liver therapies need endpoints that are quantitative, repeatable and acceptable to patients. Combined with MRI proton density fat fraction (MRI-PDFF) in a single liver MRI exam, MRE provides exactly that: a one-minute acquisition that stages fibrosis and tracks how it changes over the course of a trial.

Magnetic Resonance Elastography

MRE is an MRI technique that provides sensitive, quantitative assessment of tissue stiffness. First described in 1995 and cleared by the FDA in 2009, it has emerged as an important tool for detecting and staging liver fibrosis in patients with known or suspected chronic liver disease.[1] Liver fibrosis is the central pathologic process that leads to cirrhosis, liver failure and liver cancer.

The need has never been greater. In 2023, the major international liver societies renamed nonalcoholic fatty liver disease (NAFLD) as metabolic dysfunction-associated steatotic liver disease (MASLD), and nonalcoholic steatohepatitis (NASH) as MASH.[2] MASLD is now estimated to affect 32.5% of U.S. adults, and its prevalence is projected to reach 41.4% by 2050.[3] Chronic viral hepatitis and alcohol-related liver disease remain important causes of fibrosis as well.

Monitoring these patients for the development and progression of inflammation, fibrosis and cirrhosis usually combines physical examination, laboratory testing and imaging. Yet conventional ultrasound, CT and MRI may remain normal during the early stages of disease. The liver does not show gross morphological abnormalities such as a nodular contour or segmental atrophy until fibrosis is advanced, and complications such as portal hypertension, splenomegaly and ascites also signal advanced disease. For this reason, liver biopsy has long been the reference standard. Biopsy, however, is invasive, costly and carries procedural risk. It also suffers from sampling error and reader variability, and its limitations as a standard of truth are increasingly recognized.[1]

MRE was developed by Dr. Richard Ehman and colleagues at the Mayo Clinic as a noninvasive way to measure tissue stiffness. Their work and that of others has shown that liver stiffness rises progressively with fibrosis, and that MRE can detect and quantify this change years before the liver's size and shape become abnormal on other imaging modalities.

The technique is straightforward. At the start of the exam, the technologist places a small passive driver over the patient's upper abdomen. Connected by a flexible tube to an active driver outside the scanner room, it delivers gentle low-frequency vibrations, typically at the standard frequency of 60 Hz, without discomfort to the patient.[1] These vibrations generate shear

waves within the liver, which phase-contrast MR sequences capture. As liver tissue becomes stiffer, the shear waves lengthen. Dedicated software converts these wave images into color-coded stiffness maps (elastograms) and reports stiffness in kilopascals (kPa) across the liver or within defined regions of interest. The entire acquisition takes about one minute, adding negligible time to a standard liver MRI.

Detection and Staging of Fibrosis

MRE provides highly reliable measurements with little test-retest variation. Normal liver tissue measures consistently soft, with a mean stiffness of about 2.2 kPa. In the original Mayo Clinic validation study, a cut-off of 2.93 kPa distinguished any stage of fibrosis from normal liver with 98% sensitivity and more than 99% specificity.[4]

Two decades of subsequent research have confirmed these findings at scale. Most head-to-head comparisons conclude that MRE has the highest diagnostic performance among available tests for staging liver fibrosis.[1] In pooled analyses in MASLD, MRE achieves an area under the curve of about 0.92 for advanced fibrosis, with commonly cited cut-offs as follows:[5]

Fibrosis stage	MRE cut-off
Significant fibrosis (≥F2)	≈3.14 kPa
Advanced fibrosis (≥F3)	≈3.53 kPa
Cirrhosis (F4)	≈4.45–4.76 kPa

Sponsors should note that optimal thresholds vary between studies. Across 12 studies, the reported threshold for advanced fibrosis ranged from 2.9 to 4.8 kPa, largely because of differences in the patient populations studied.[1] Thresholds should therefore be pre-specified in the protocol and imaging charter, not borrowed after the fact.

MRE in Today's MASH Trials

When the first edition of this issue was written, there were no approved therapies for NASH. That has changed. In March 2024, the FDA granted accelerated approval to Rezdiffra (resmetirom), the first treatment for noncirrhotic MASH with moderate to advanced fibrosis.[6] In August 2025, the FDA approved Wegovy (semaglutide) for the same population.[7] Both approvals rested on liver biopsy endpoints, and dozens of further agents are in development.

The field is now working to reduce its reliance on repeat biopsy. A 2026 review of noninvasive surrogate endpoints in MASH trials found that baseline values and longitudinal changes in liver stiffness, measured by MRE or transient elastography, correlate with histological stage and predict liver-related events. Among these tools, MRE offers superior accuracy and repeatability, although trial-level evidence is still accumulating before formal qualification.[8] Researchers have also identified MRE-based liver stiffness as the most important single imaging biomarker for at-risk MASH (stage F2 fibrosis or higher), while MRI-PDFF is the leading biomarker of liver fat.[1] Measured together in one exam, they give sponsors a complete, quantitative picture of the two processes that matter most.

Guidance for Sponsors

Building MRE into a liver trial

- **Qualify sites and scanners first.** Confirm MRE hardware, software and driver setup before the first patient. Keep each participant on the same scanner throughout the study wherever possible.
- **Standardize acquisition.** Require a 4-hour fast, because liver stiffness can rise by as much as 40% after a meal.[1] Also standardize breath-hold instructions, slice placement and sequence parameters.
- **Choose sequences that minimize failures.** Spin-echo echo-planar MRE sequences perform reliably at 3 T and in moderate iron overload, bringing technical failure rates to 2% or less.[1]
- **Pair MRE with MRI-PDFF.** Measuring stiffness and fat in the same visit adds minutes, not visits.
- **Pre-specify analysis.** Define region-of-interest methods, stiffness thresholds and change criteria in the imaging charter, with blinded central review and quality control at every timepoint.

Summary

MRE has matured from a promising research technique into a validated, FDA-cleared tool with the strongest diagnostic performance of any noninvasive test for liver fibrosis. As MASH therapies multiply and the field moves toward noninvasive endpoints, MRE will play a central role in screening participants, enriching enrollment for at-risk disease and measuring treatment response. Its value to sponsors depends on rigor: consistent acquisition across sites, validated analysis and central reading that holds up to regulatory review.

About the Author

Dr. Tubb, a board-certified radiologist, wrote the original edition of this issue at Intrinsic Imaging. He completed his radiology residency at Johns Hopkins Hospital after finishing the combined MD-PhD program at Baylor College of Medicine in Houston, Texas, where his PhD research in Molecular and Cellular Biology produced multiple peer-reviewed publications. During residency, he received a one-year RSNA Resident Research Award for a project involving targeted MRI contrast agents and high-resolution pancreatic imaging, and he served as chief resident. He then completed a one-year MRI fellowship at the University of Pennsylvania, with broad experience in body and oncologic, breast, spine and musculoskeletal imaging. His work has focused on the design and implementation of imaging components in clinical trials and on applying new imaging technologies, such as MR elastography, to liver disease.

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Contact

Intrinsic Imaging, LLC
580 Main Street, Suite 210
Bolton, MA 01740
Tel: +1 978-616-4650
Contact@IntrinsicImaging.com
www.IntrinsicImaging.com