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No matter how you look at it, MR Elastography can provide new information and options – and it’s here today

By Vinod S. Palathinkara, PhD, Lloyd Estkowski, and David W. Lee, PhD

While MR Elastography (MRE) is an innovative technology, an investment in MRE can bring immediate clinical value to patients. MRE gives referring physicians a powerful new option for liver assessment. It is a new tool that provides diagnostic information without the discomfort and risk of complications due to invasive procedures, enabling more frequent evaluation when closer monitoring is needed. By creating a vivid visual representation of liver tissue stiffness, MRE lets radiologists deliver a more confident diagnosis. MRE enables diagnostic procedures at a lower cost than previous techniques. Both comprehensive and non-invasive, the technique can appeal to patients and referring physicians, and can help expand the role of radiology into new areas. More than anything else, MRE holds the promise of better outcomes at lower costs to the overall healthcare system.

Chronic liver disease and cirrhosis are major public health problems worldwide. In 2004, these conditions were associated with nearly 40,000 deaths and a cost of at least $1.4 billion for medical services in the U.S. alone.¹ ² These figures are expected to increase due to aging, obesity, and end-stage liver disease caused by chronic hepatitis C infection. The major biological process responsible for clinical liver disease is progressive hepatic fibrosis.
Liver biopsy is the current gold standard for detecting hepatic fibrosis. There are, however, limitations with the technique that include poor acceptance by patients, measurement errors, and cost.³,⁴ Current non-invasive alternatives to liver biopsy are serum-based testing,⁵ which is not reliable for detecting early disease, and transient ultrasound elastography,⁶ which has technical limitations in patients with obesity and conditions such as ascites.

MRE, a technique developed by Richard Ehman, MD, and colleagues at Mayo Clinic (Rochester, MN), uses low-frequency mechanical waves to probe the elastic properties of tissue. These mechanical waves are generated in the body through an external acoustic driver, which are then imaged using a special phase-contrast MR sequence. Using a sophisticated mathematical algorithm, the mechanical wave data collected by the MR is then used to generate an “elastogram,” – a diagnostic image that depicts tissue stiffness.

In its spirit of bringing the latest technology to clinicians, in July 2009, GE Healthcare commercially launched MR-Touch, an MR-Elastography (MRE) application, available on the Optima MR450w and Signa HDxt systems. GE Healthcare is currently working to expand its availability to other 1.5T systems.

Clinical value of MRE

Yin et al. evaluated the diagnostic performance of an optimized MR elastography protocol for assessing hepatic fibrosis among patients with diverse causes of chronic liver disease and in normal individuals.⁸ The summary of mean values and variance of liver stiffness from the 35 normal volunteers and 48 patients with chronic liver disease are shown in Figure 1.

When assessed by stage of fibrosis, the mean liver stiffness value increased systematically with excellent correlation between histologic fibrosis and shear stiffness obtained with MR elastography ($R^2 = 0.94, P < 0.001$) (Figure 1). The study results supported the hypothesis that MR elastography is effective for distinguishing normal, soft-liver tissue from stiff fibrotic liver tissue with a very high negative predictive value. The severity of increased stiffness was shown to allow moderate to severe fibrosis to be distinguished non-invasively from mild fibrosis (Figures 1 and 2).

It is important to assess the accuracy of MRE in relation to the accuracy of liver biopsy. A review of the available data on the accuracy of needle liver biopsy to define the stage of fibrosis reveals that significant sampling and interpretive error affects the assessment of liver biopsy. Needle liver biopsy assesses only about 1/50,000 of the volume of the liver and so it may be affected by substantial sampling error.⁹ Autopsy and laparoscopy studies that have evaluated the accuracy of liver biopsy for staging fibrosis and diagnosing cirrhosis have clearly shown that cirrhosis is missed on a single blind liver biopsy in 10% to 30% of cases.¹⁰,¹¹,¹²,¹³,¹⁴ The majority of this error is due to the

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In liver biopsies, the absence of key findings does not rule out a suspected diagnosis.

under-staging of disease. Both the size of the biopsy and number of biopsies taken have a major effect on accuracy. Abdi et al. report that the correct diagnosis of cirrhosis with a single biopsy increased from 80% to 100% when three specimens were analyzed. Similarly, in a study that evaluated the agreement between three biopsies taken at a single setting, Maharaj reported that cirrhosis was identified in all three biopsies in only 50% of the cases.

Rockey et al. suggest that sampling variability appears to be one of the major limitations of liver biopsy. In a study of 124 patients with chronic HCV infection who underwent laparoscopy-guided left and right lobe liver biopsies, 33% of cases had discordant results by at least one histological stage. A smaller but substantial proportion of biopsies were discordant by at least two stages. Similarly, a single liver biopsy specimen may fail to distinguish steatohepatitis from simple steatosis and may mis-stage the disease by one (or less frequently, two stages if the specimen is much smaller than 2 cm. The authors caution that although even small biopsy specimens may be sufficient for diagnostic purposes in certain situations, the possibility that sampling variability exists must be recognized, so that the absence of key findings does not rule out a suspected diagnosis. By showing information about liver stiffness over one or more cross sections of the entire liver, MR elastography provides a more comprehensive view than before available.

### Health care system costs

Given the novelty of the MRE technology, peer-reviewed academic or medical literature evaluating the potential cost-effectiveness of this non-invasive testing strategy in the diagnosis and management of liver fibrosis is currently limited. There is, however, evidence to suggest that MRE has the potential to lower the overall costs in the management of liver diseases.

Carlson et al. used data originally reported by Wong et al. and adjusts for inflation using Consumer Price Index to arrive at an estimated cost of liver biopsy of $1,255*, but this estimate underestimates the true costs of a liver biopsy because it excludes procedure-related morbidities. Myers et al. used administrative databases from a large Canadian Health Region to identify percutaneous liver biopsies performed between 1994 and 2002. The study found that between 1994 and 2002, 3,627 patients had 4,275 liver biopsies. Thirty-two patients (0.75%) had significant biopsy related complications. The median direct cost of a hospitalization for complications was $4,579 Canadian (range $1,164-$29,641).

As a new technology, MRE is currently not reimbursed with its own CPT code*. Because the acquisition time is very short, the addition of MRE for liver evaluation into a conventional MRI examination protocol adds very little to the typical examination time of 30 to 45 minutes. If MRE is not reimbursed any more than a typical abdominal MRI

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*Figures associated with US rates of reimbursement. Not globally applicable.
MRE is effective for distinguishing stiffness ... with very high negative-predictive value.

scan, the reimbursement for a valid MRE scan would be similar to the 2010 national Medicare average payment rate for an abdominal MRI, i.e., $628 (CPT code 74183). At this stage, there is no way to predict the willingness of payers to cover the procedure and the level of reimbursement.

MRE has the potential to significantly reduce cost as a triage for liver biopsy. The information MRE provides could be used to assess if and when a patient should undergo liver biopsy. If one assumes that the cost of a liver biopsy is $1,255 and the cost of an MRE would be $628, then MRE would lower costs by at least 15% if it successfully avoids approximately two-thirds of unnecessary biopsies (Figure 3). Yin et al. showed that MRE has high predictive value in distinguishing stiffness associated with normal liver tissue.8 Even though liver biopsy is accurate in identifying fibrosis, due to its basis as a sampling technique, absence of evidence of fibrosis from biopsy does not rule out fibrosis. MRE may also be a useful tool that helps guide clinicians in localizing the area of biopsy. If MRE achieves a 65% success rate in triaging, it would reduce the total costs by approximately 15%. With a negative-predictive value of 97% (95% CI, 83.8%-99.8%), the threshold of 65% for MRE is far less than the combined true positive, false positive, and false negative rates for MRE.

Conclusion

MRE is non-invasive and provides tissue stiffness information for the entire liver and avoids the discomfort and risk of complications associated with other invasive procedures. In addition, elastograms avoid sampling errors and provide richer information that could assist in diagnosis. Studies show that the technique has excellent sensitivity in differentiating stiffness associated with normal liver tissue and fibrotic tissue. Stiffness of normal liver tissue is comparable to that of subcutaneous fat; studies have also not reported any influence of steatosis on tissue stiffness. In summary, the evidence supports the use of MRE as a triaging option for liver biopsy. The accuracy, lower costs, and the noninvasive nature of the technology offer the promise that MRE could improve outcomes at lower costs.
