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Ultrasound Elastography and MR Elastography for Assessing Liver Fibrosis: Part 2, Diagnostic Performance, Confounders, and Future Directions

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OBJECTIVE. The purpose of the article is to review the diagnostic performance of ultrasound and MR elastography techniques for detection and staging of liver fibrosis, the main current clinical applications of elastography in the abdomen.

CONCLUSION. Technical and instrument-related factors and biologic and patient-related factors may constitute potential confounders of stiffness measurements for assessment of liver fibrosis. Future developments may expand the scope of elastography for monitoring liver fibrosis and predict complications of chronic liver disease.

Keywords: elasticity, elastography, liver fibrosis, MR elastography (MRE), MRI, ultrasound, viscosity

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In abdominal imaging, liver stiffness estimated by elastography techniques may be used as a quantitative imaging biomarker for detection, staging, and monitoring of liver fibrosis [1–3]. Liver stiffness is used to evaluate the severity of the underlying chronic liver disease, guide treatment decision, assess disease outcome, and evaluate response to therapy [4].

In this second article of a two-part series [5], we will discuss the clinical applications in the liver. We will focus on diagnostic performance of ultrasound elastography and MR elastography techniques for detection, staging, and monitoring of liver fibrosis, the main current clinical applications of elastography in the abdomen. We will discuss potential confounders of stiffness measurements for assessment of liver fibrosis, which include technical and instrument-related factors (location and depth of measurements, wave frequencies, and device dependencies) and biologic and patient-related factors (concomitant hepatic steatosis, inflammation, cholestasis; breathing; right heart failure and hepatic venous congestion; and fasting vs postprandial state). Finally, we will briefly discuss future directions and technical innovations in this field of research.

As will be shown in this article, elastography techniques integrated to clinical ultrasound and MR systems now provide the capability to examine by imaging what once could be examined only by direct palpation, which is likely to open new opportunities to noninvasively diagnose disease, guide management, and improve outcomes.

Key Learning Points

First, the main current clinical indications for abdominal elastography techniques are detection and staging of liver fibrosis. In general, elastography techniques provide good-to-excellent diagnostic accuracy for the detection of advanced fibrosis but have more modest performance for detection of early or mild fibrosis. Most studies to date have been in adults; performance characteristics in children are less well known. Research is needed to better understand the performance of elastography for monitoring longitudinal changes in fibrosis. Emerging indications of elastography include detection of hepatic inflammation, assessment of portal hypertension, characterization of focal liver lesions, and evaluation of other abdominal organs.

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TABLE 1: Summary of Meta-Analyses: Pooled Diagnostic Performance of Elastography Techniques for Staging of Liver Fibrosis

Technique, Study	No. of Studies (No. of Patients) Included	Implementation	Fibrosis Stage ≥ 1				Fibrosis Stage ≥ 2				Fibrosis Stage ≥ 3				Fibrosis Stage 4			
			Cutoff	AUC	Sensitivity	Specificity	Cutoff	AUC	Sensitivity	Specificity	Cutoff	AUC	Sensitivity	Specificity	Cutoff	AUC	Sensitivity	Specificity
Ultrasound elastography																		
Talwalkar et al. [23]	9 (2083)	1D transient elastography	—	—	—	—	—	0.8701	0.70	0.84	—	—	—	—	—	0.9567	0.87	0.91
Friedrich-Rust et al. [1]	50 (8433)	1D transient elastography	—	—	—	—	7.65 kPa	0.84	—	—	—	0.89	—	—	13.01 kPa	0.94	—	—
Tsochatzis et al. [24]	40 (7723)	1D transient elastography	—	—	—	—	7.0 kPa	—	0.70	0.81	9.5 kPa	—	0.80	0.85	12.0 kPa	—	0.86	0.88
Friedrich-Rust et al [3].	8 (518)	Point shear-wave elastography	—	—	—	—	1.34 m/s	0.87	0.79	0.85	1.55 m/s	0.91	0.86	0.86	1.80 m/s	0.93	0.92	0.86
Bota et al. [25]	13 (1163)	1D transient elastography	—	—	—	—	—	0.87	0.78	0.84	—	—	—	—	—	0.93	0.89	0.87
		Point shear-wave elastography	—	—	—	—	1.30 m/s	0.85	0.74	0.83	—	—	—	—	1.80 m/s	0.93	0.87	0.87
MR elastography																		
Wang et al. [2]	5 (398)	Magnitude of complex shear modulus	—	0.95	—	—	—	0.98	0.94	0.95	—	0.98	0.92	0.96	—	0.99	—	—
Singh et al. [26]	12 (697)	Complex (G′, G″)	3.45 kPa	0.84	73	79	3.66 kPa	0.88	0.79	0.81	4.11 kPa	0.93	0.85	0.85	4.71 kPa	0.92	0.91	0.81

Note—Fibrosis was staged on a 5-point scale 0 (none) to 4 (cirrhosis) in the meta-analysis. Dash indicated not available. G′ = storage modulus, G″ = loss modulus.

Second, potential confounders when using stiffness for assessment of liver fibrosis include technical and instrument-related factors and biologic and patient-related factors. The former include location and depth of measurements, wave frequencies, and device dependencies. The latter include concomitant hepatic steatosis, inflammation, and cholestasis; breathing; right heart failure and hepatic venous congestion; and fasting versus postprandial state.

Third, measured stiffness is frequency dependent: in general, measured stiffness increases as the frequency of the shear waves increases. Different techniques use different frequencies; hence, observed stiffness values are technique dependent.

Fourth, various elastography techniques have advantages and limitations, and no single technique currently can be recommended as optimal for all indications and circumstances. Depending on the indication (screening, diagnosis, or monitoring of liver fibrosis), different modalities may be preferred. Ultrasound elastography techniques are relatively inexpensive, portable, increasingly available, and generally provide good diagnostic accuracy for advanced fibrosis. Nevertheless, they sample relatively small portions of the liver and they may be unreliable in obese patients and those with narrow intercostal spaces. MR elastography samples larger portions of the liver and offers excellent diagnostic accuracy that probably slightly exceeds that of ultrasound-based techniques, but quality may be degraded in patients with marked iron deposition. Availability of the required hardware or software remains comparatively limited.

Finally, elastography techniques integrated to clinical ultrasound and MRI systems can assess mechanical properties in vivo. Radiologists should be familiar with these exciting new technical capabilities to examine by imaging what once could be examined only by direct palpation.

Clinical Applications in the Liver

Clinical applications of elastography in the liver include noninvasive assessment of fibrosis and characterization of focal lesions [6–9]. This article will focus on assessment of liver fibrosis. Most studies to date have been in adults. The performance characteristics of elastography techniques in children are less well known and require further study [10–15].

The clinical adoption of elastography techniques for assessment of liver fibrosis is based on the observation that liver stiffness increas-

es with higher fibrosis stages [16–18]. The central concept is that collagen deposition and other microstructural changes associated with fibrosis impart parenchymal rigidity. Although fibrosis stages are categorized by pathologists using ordinal scores, typically from stage 0 to stage 4, the imaging literature has focused on the classification of patients into dichotomized fibrosis stages, mostly for the diagnosis of significant (stage ≥ 2) or advanced (stage ≥ 3) fibrosis. As opposed to dichotomized classification (e.g., stage 0–1 vs stages 2–4), prediction of exact fibrosis stage has not been explored in depth.

Histologically determined fibrosis stage is a semiquantitative assessment of cumulative liver injury based on the location and amount of excess collagen as well as associated remodeling of liver architecture [19, 20]. Because the location of collagen and the presence of remodeling contribute to the fibrosis stage, the fibrosis stage is not dictated solely by the total amount of collagen, and the relationship of fibrosis stage to total collagen content is not linear [21, 22]. Instead, as the fibrosis stage increases from stage 0 (no abnormal fibrosis) to higher stages, the total collagen content remains fairly stable until an advanced fibrosis stage is reached and then the total collagen content increases exponentially. It is likely that elastography is a more direct marker of total collagen content than fibrosis stage. Hence, we should not expect a linear relationship between stiffness and fibrosis stage, and clinical studies consistently have shown a curvilinear (exponential) relationship between fibrosis stage and stiffness. A corollary is that stiffness estimates tend to overlap in the lower fibrosis stages but to be separated in the higher fibrosis stages.

Diagnostic Performance

Several meta-analyses have been published on the diagnostic performance of 1D transient elastography [1, 23–25], point shear-wave elastography [3, 25], and MR elastography [2, 26] for noninvasive staging of liver fibrosis. These studies relied on histopathology as the reference standard. Although some studies have reported the diagnostic performance of shear-wave elastography [27, 28], other studies did not have liver biopsy as an independent reference standard for all patients [29, 30]. The pooled diagnostic performance and thresholds for staging of dichotomized liver fibrosis in the meta-analyses are summarized in Table 1 for ultrasound elastography and MR elastography techniques.

The estimates of diagnostic performance (AUC, sensitivity, and specificity) for ultrasound elastography techniques were similar in the three meta-analyses of 1D transient elastography and the meta-analysis of point shear-wave elastography. The two meta-analyses on the diagnostic performance of MR elastography reported higher AUCs, although the sensitivity and specificity were similar to those of ultrasound elastography techniques.

Comparison of Elastography Techniques

A few studies have directly compared different elastography techniques cross-sectionally with histopathology as the independent reference standard. Most studies that have compared ultrasound elastographic methods (point shear-wave elastography vs 1D transient elastography) have reported similar diagnostic performance for fibrosis staging in patients with chronic liver disease [31–34], chronic viral hepatitis [35], and nonalcoholic fatty liver disease [36, 37]. However, some of these studies have reported higher rates of technical failure or invalid measurements with 1D transient elastography than with point shear-wave elastography [31, 37, 38].

Two studies have reported higher diagnostic accuracy of ultrasound-based methods that generate shear waves using acoustic radiation-force impulses (point shear-wave elastography or shear-wave elastography) than with external vibration (1D transient elastography). A study by Rizzo et al. [38] in patients with chronic hepatitis C found higher accuracy with point shear-wave elastography than 1D transient elastography for the diagnosis of significant (stage ≥ 2) and severe (stage ≥ 3) fibrosis ($p = 0.024$ and $p = 0.002$, respectively). Similarly, a study by Ferraioli et al. [39] in patients with chronic hepatitis C found higher accuracy with shear-wave elastography than 1D transient elastography for staging significant fibrosis (stage ≥ 2) ($p = 0.002$); the diagnostic accuracy, as estimated by AUCs, was similar for staging of severe fibrosis (stage ≥ 3) and cirrhosis (stage 4) [39].

Studies that have compared MR elastography with ultrasound elastography methods have found different results depending on the techniques compared. A cross-sectional study by Huwart et al. [18] reported a higher technical success rate with an investigational form of MR elastography (94%) than with 1D transient elastography (84%). The AUC was significantly superior for MR elastography (0.994 for stage ≥ 2, 0.985 for stage ≥ 3, and 0.998 for stage 4) than for 1D transient elastography (0.837 for stage ≥ 2, 0.906 for stage ≥ 3, and 0.930 for stage 4).

Recently, Yoon et al. [40] compared the fibrosis staging accuracy of shear-wave elastography with MR elastography in patients undergoing liver biopsy for suspicion of chronic liver disease before liver transplantation and before hepatectomy or liver donation. The technical failure rates were similar for shear-wave elastography (2.33%) and MR elastography (4.65%). Among patients who had reliable results on both techniques, the AUCs were similar for detection of significant fibrosis (stage ≥ 2) (0.852 for shear-wave elastography and 0.853 for MR elastography).

Confounders of Stiffness Measurements

The accuracy of elastography techniques for assessment of fibrosis may be influenced by technical and instrument-related factors and biologic and patient-related factors. Some confounding factors may be technique or instrument specific, but it is reasonable to assume that the physiologic underpinning of several biologic and patient-related confounding factors should be equally applicable to ultrasound elastography and MR elastography.

Technical Confounders

Left Versus Right Lobe Measurements

In several studies, higher liver stiffness measurements were observed in the left than in the right liver lobe with ultrasound elastography techniques [31, 41–44]. Moreover, better accuracy and a lower rate of invalid measurements were observed by the intercostal approach in the right lobe [37, 45]. It has been hypothesized that liver compression by the transducer, heart, or stomach may contribute to higher stiffness measurements in the left lobe. Hence, right lobe measurements by the intercostal approach, unaffected by the effect of probe compression against the liver parenchyma, are preferred.

Depth of Measurements

Higher stiffness measurements were observed close to the liver surface compared with deeper measurements performed with ultrasound elastography techniques [42, 46]. Correlation between liver stiffness and fibrosis stage is higher for measurements made at 1–3 cm below the liver capsule than for superficial measurements performed between 0 and 1 cm below the liver capsule [47]. On the basis of these observations, stiffness

measurements acquired at least 1 cm below the liver capsule are advocated.

Wave Frequencies

The liver has been shown to display dispersive (i.e., frequency-dependent) behavior [48]. Hence, the choice of excitation frequency is critical in liver elastography to obtain the frequency-dependent viscoelastic properties of liver tissue. However, it is currently unclear which shear-wave frequency will provide the optimal discrimination ability for fibrosis staging.

Prior studies relied on different excitation frequencies depending on imaging technique and study subjects. For example, 1D transient elastography uses a lower excitation frequency of 50 Hz [17], whereas point shear-wave elastography and shear-wave elastography typically use higher frequencies [49, 50]. The choice of frequency used in those studies was partly dictated by technical constraints, such as transducer configuration and depth of tissue studied, because a higher frequency would result in wave amplitude dissipation and signal-to-noise ratio decrease. Commercial MR elastography typically uses a frequency of 60 Hz, although frequencies between 40 and 200 Hz have been investigated for clinical liver imaging [51–55].

Device Dependencies

Shear-wave speed measurement is not yet standardized across modalities, scanners, and transducers. These inconsistencies do not invalidate published results; rather, they make comparison of diagnostic cutoffs difficult, limit generalizability of results, and complicate the implementation of published cutoffs into individual practice. With time, we expect the terminology and the parameters to be standardized, which will facilitate meta-analysis, pooling of results, direct comparison of diagnostic cutoffs, and implementation of these techniques into clinical practice and clinical trials.

Because of the lack of standardization in terminology, shear-wave frequency, reported parameters, and other technical factors comparing different elastographic techniques can be challenging. The reported diagnostic thresholds for a specific condition, such as liver fibrosis, are technique dependent. This translates into a wide range of published elastographic thresholds for the staging of liver fibrosis [1–3, 56]. In particular, because shear-wave speed is related to the square root of the stiffness-related moduli (Young modulus, complex shear modulus), techniques that report shear-wave speed will appear to provide more closely spaced results than techniques that report a modulus. This should not be misinterpreted as signifying that techniques that report shear-wave speed are more limited as tissue classifiers.

Biologic Confounders

Hepatic Steatosis

The effect of steatosis on liver stiffness remains controversial. A clinical study evaluating point shear-wave elastography in patients with nonalcoholic fatty liver disease found lower stiffness in patients with simple steatosis but not fibrosis compared with healthy volunteers [36]. However, some MR elastography studies that assessed fat fraction on MRI did not find an effect of liver fat on liver stiffness [57–59]. Further studies are needed to determine definitively whether liver steatosis affects liver stiffness and if so whether the effect is frequency dependent.

Inflammation

Elastographic imaging techniques, which measure the elasticity (springlike behavior) and viscosity (dashpot-like behavior) of soft tissues, suggest that both elasticity and viscosity increase markedly with fibrosis, moderately with inflammation, and mildly with steatosis [36, 50, 60, 61]. Inflammation causes edema, which increases both elasticity and viscosity [62].

Cholestasis

Liver stiffness is also influenced by extrahepatic cholestasis. A clinical study evaluating liver stiffness in patients with extrahepatic bile duct obstruction showed elevated liver stiffness irrespective of fibrosis before ERCP and decreased liver stiffness 3–12 days after successful biliary drainage [63]. The relationship between liver stiffness and extrahepatic cholestasis was reproduced in a pig model of bile duct ligation [64]. Therefore, liver stiffness should be interpreted with caution in patients with biliary obstruction.

Breathing

Elastography measurements are acquired during breath-holding to minimize liver motion. Deep inspiration has been shown to increase stiffness measurements compared with resting expiratory position [65]. Hence, breath-hold at expiration is preferable to obtain consistent liver position between acquisitions and to avoid overestimation of liver stiffness.

Right Heart Failure

Liver stiffness is affected by central venous pressure as shown in an experimental animal study [64]. A clinical study has also confirmed higher liver stiffness in patients with decompensated heart failure at admission than after correction at discharge [66]. The presence of heart failure as a potential confounding factor should therefore be taken into consideration when measuring liver stiffness as a biomarker of liver fibrosis.

Hepatic Venous Congestion

Similarly, hepatic venous congestion also contributes to liver stiffness elevation. Serial measurements before and after treatment of venous stenosis either in the setting of an experimental murine model through partial ligation of the inferior vena cava [67] or in the setting of human liver transplantation have shown the potential confounding effect of hepatic venous congestion on liver stiffness [68].

Fasting Versus Postprandial State

Elastography measurements should be acquired in the fasting state because the postprandial state may increase liver stiffness in patients with chronic liver disease, as assessed by ultrasound elastography [69, 70] and MR elastography [71]. However, in one MR elastography study, postprandial status did not significantly alter liver stiffness in healthy subjects [72].

Future Directions

Liver elastography is an active area of research. Indications beyond cross-sectional assessment of liver fibrosis are emerging. Liver elastography has been proposed for liver stiffness monitoring, prognostication of hepatic complications, assessment of cirrhosis, and detection of inflammation and portal hypertension.

Monitoring

Several studies have proposed elastography techniques for monitoring liver stiffness. However, many of these studies have not included paired biopsies for validation of elastographic changes. A study that evaluated paired liver biopsy and 1D transient elastography in the follow-up of patients for recurrent hepatitis C after transplantation showed that liver stiffness changes in parallel with recurrent hepatitis C [73]. However, when stiffness changes are observed, it is currently unclear whether stiffness changes are related to fibrosis changes, inflammatory changes, venous congestion, or other factors. The

biologic meaning of longitudinal stiffness changes requires further study.

Prognostication

Elastography has prognostic value for overall survival and survival without liver-related death over a 5-year period in patients with chronic hepatitis C virus infection [74]. Elastography may also be used to predict the risk of hepatic complications, including features of decompensation (variceal hemorrhage, ascites, hepatic encephalopathy, jaundice, hepatorenal syndrome, and spontaneous bacterial peritonitis), liver transplantation, and mortality in patients with chronic liver disease [75, 76]. A study suggested that liver stiffness predicts future decompensation better than fibrosis stage [74]. Some studies [76–78] but not all [79] suggested that stiffness predicts future development of hepatocellular carcinoma.

Assessment of Cirrhosis

The clinical and pathophysiologic spectrum of patients with cirrhosis (which ranges from asymptomatic with normal or near-normal liver function to debilitated terminally ill end-stage liver dysfunction) is greater than the clinical and pathophysiologic spectra of patients with all precirrhotic stages of fibrosis combined because these patients are usually asymptomatic and have normal liver function. Yet current histologic staging systems do not subclassify patients once they advance to cirrhosis, in part because biopsy is not performed in patients with known cirrhosis because of the greater risk associated with this procedure in patients with cirrhosis and in part because until now cirrhosis has been considered irreversible and no treatments were available. Elastography offers promise for monitoring patients with cirrhosis. This will be important as treatments for cirrhosis emerge.

Detection of Inflammation

Currently, both fibrosis and inflammation may contribute to stiffness [61]. An area of active investigation is to separate the contributions of fibrosis and inflammation [60]. If this investigation is successful, elastography could permit identification of patients with inflammation who have not yet progressed to fibrosis and could additionally be used for monitoring the effects of intervention on each component separately.

Portal Hypertension

Some studies have suggested that spleen stiffness may be a marker of portal hypertension [80, 81]. Additionally, spleen stiffness may help predict the presence of esophageal varices and the risk of bleeding [82]. More research in this area is needed before these indications can be considered because of the limited accuracy of spleen stiffness estimation for diagnosis of esophageal varices in patients with cirrhosis when compared with esophagogastroduodenoscopy as the reference standard [83].

Interpretation of Stiffness and Other Mechanical Properties

As experience and knowledge with elastographic imaging accrue, we anticipate that stiffness and other mechanical properties will develop an intrinsic meaning without requiring translation to histologic markers, such as fibrosis stage. For example, at some point, a stiffness value of 4.5 kPa on 2D MR elastography will connote advanced liver disease at risk for decompensation without requiring the intermediate translation to the corresponding expected fibrosis stage. Similarly, it is conceivable that patients may be classified on the basis of elastographic measurements rather than histology.

Other Emerging Applications

Other emerging indications for abdominal elastography include characterization of focal liver lesions [6, 7, 9] and evaluation of other solid organs [84–86].

Technical Innovations

Several innovations may further refine liver tissue characterization by elastographic techniques. This includes 3D measurement of tissue displacement, multifrequency elastography, standardization of terminology, and calibration of measurements obtained by different elastography techniques.

Three-Dimensional Implementations

Commercially available ultrasound elastography and MR elastography implementations sample wave propagation in only one or two dimensions. Future 3D implementations may permit assessment of a larger liver volume and measurement of tissue displacement fields using ultrasound [87, 88] or MRI [89]. This will enable analysis of more and thinner slices. In theory, this should help improve colocalization across time points, monitoring for longitudinal change, and more complete representation of wave propagation.

Multifrequency Elastography

To account for frequency-dependent mechanical properties of both healthy and pathologic liver, multifrequency shear waves may be used to characterize liver across a frequency range. An extension to the shear-wave elastography technique has been used to acquire shear-wave spectroscopy at a wide frequency range from 75 to 500 Hz to account for the dispersive behavior of liver parenchyma at higher frequencies [90]. Multifrequency MR elastography excitation has also been reported in a frequency range from 25 to 62.5 Hz [91]. In addition to liver stiffness (elasticity), a multifrequency acquisition scheme also permits calculation of viscosity [51], which conceivably may help in the separation of fibrosis from inflammation. However, preliminary results indicate that multifrequency MR elastography does not provide higher accuracy than optimum single-frequency MR elastography for staging hepatic fibrosis [92].

Terminology and Technique Standardization

The medical community has not standardized the relevant terminology, which has been adapted inconsistently from engineering and physics. Different clinical investigators have used terms inconsistently, including using the same term to refer to different parameters and different terms to refer to the same parameters.

The European Federation of Societies for Ultrasound in Medicine and Biology [93] has proposed terminology to reduce the number of commercial names for ultrasound-based techniques. In addition to generic terms to describe shear-wave techniques, there is a need to harmonize the terminology used to describe the mechanical properties and parameters in the field of elastography.

In 2008, the Radiological Society of North America created the Quantitative Imaging Biomarkers Alliance (QIBA) to advance quantitative imaging and the use of imaging-based biomarkers in clinical practice and clinical trials. The Ultrasound Modality Committee formed in 2012 performed an interlaboratory study of shear-wave speed estimation on phantoms [94]. The study revealed little difference between operators but significant differences in shear-wave speed estimates related to depth of measurements and between systems. An MR elastography QIBA working group was launched in January 2015. Ultimately the hope is that a kilopascal measured on one device will equal that measured on another device, assuming the same mechanical parameter (e.g., Young modulus) is being reported at the same frequency.

Conclusion

The main clinical application for elastography techniques in the abdomen is noninvasive detection and staging of liver fibrosis. Both ultrasound elastography and MR elastography techniques report very good to excellent diagnostic performance for diagnosis of advanced fibrosis. Radiologists who interpret elastography examinations should be aware of several technical and biologic confounding factors that may affect the feasibility or fibrosis classification accuracy of these techniques. We envision future standardization of elastography techniques so that quantitative parameters obtained by clinical systems from different vendors may provide similar results. This will ultimately improve reproducibility of elastography measurements, facilitate comparison of diagnostic thresholds, and improve patient care.

References

1. Friedrich-Rust M, Ong MF, Martens S, et al. Performance of transient elastography for the staging of liver fibrosis: a meta-analysis. *Gastroenterology* 2008; 134:960–974
2. Wang QB, Zhu H, Liu HL, Zhang B. Performance of magnetic resonance elastography and diffusion-weighted imaging for the staging of hepatic fibrosis: a meta-analysis. *Hepatology* 2012; 56:239–247
3. Friedrich-Rust M, Nierhoff J, Lupsor M, et al. Performance of acoustic radiation force impulse imaging for the staging of liver fibrosis: a pooled meta-analysis. *J Viral Hepat* 2012; 19:e212–e219
4. Martinez SM, Crespo G, Navasa M, Forns X. Noninvasive assessment of liver fibrosis. *Hepatology* 2011; 53:325–335
5. Tang A, Cloutier G, Szeverenyi NM, Sirlin CB. Ultrasound elastography and MR elastography for assessing liver fibrosis. Part 1. Principles and techniques. *AJR* 2015; 206:(in press)
6. Venkatesh SK, Yin M, Glockner JF, et al. MR elastography of liver tumors: preliminary results. *AJR* 2008; 190:1534–1540
7. Ronot M, Di Renzo S, Gregoli B, et al. Characterization of fortuitously discovered focal liver lesions: additional information provided by shear-wave elastography. *Eur Radiol* 2015; 25:346–358
8. Davies G, Koenen M. Acoustic radiation force impulse elastography in distinguishing hepatic haemangiomata from metastases: preliminary observations. *Br J Radiol* 2011; 84:939–943
9. Cho SH, Lee JY, Han JK, Choi BI. Acoustic radiation force impulse elastography for the evaluation of focal solid hepatic lesions: preliminary findings. *Ultrasound Med Biol* 2010; 36:202–208
10. Nobili V, Vizzutti F, Arena U, et al. Accuracy and reproducibility of transient elastography for the diagnosis of fibrosis in pediatric nonalcoholic steatohepatitis. *Hepatology* 2008; 48:442–448
11. Kim S, Kang Y, Lee MJ, Kim MJ, Han SJ, Koh H. Points to be considered when applying FibroScan S probe in children with biliary atresia. *J Pediatr Gastroenterol Nutr* 2014; 59:624–628
12. Binkovitz LA, El-Youssef M, Glaser KJ, Yin M, Binkovitz AK, Ehman RL. Pediatric MR elastography of hepatic fibrosis: principles, technique and early clinical experience. *Pediatr Radiol* 2012; 42:402–409
13. Hanquinet S, Rougemont AL, Courvoisier D, et al. Acoustic radiation force impulse (ARFI) elastography for the noninvasive diagnosis of liver fibrosis in children. *Pediatr Radiol* 2013; 43:545–551
14. Tutar O, Beser OF, Adaletli I, et al. Shear wave elastography in the evaluation of liver fibrosis in children. *J Pediatr Gastroenterol Nutr* 2014; 58:750–755
15. Xanthakos SA, Podberesky DJ, Serai SD, et al. Use of magnetic resonance elastography to assess hepatic fibrosis in children with chronic liver disease. *J Pediatr* 2014; 164:186–188
16. Yeh WC, Li PC, Jeng YM, et al. Elastic modulus measurements of human liver and correlation with pathology. *Ultrasound Med Biol* 2002; 28:467–474
17. Sandrin L, Fourquet B, Hasquenoph JM, et al. Transient elastography: a new noninvasive method for assessment of hepatic fibrosis. *Ultrasound Med Biol* 2003; 29:1705–1713
18. Huwart L, Sempoux C, Vicaut E, et al. Magnetic resonance elastography for the noninvasive staging of liver fibrosis. *Gastroenterology* 2008; 135:32–40
19. Theise ND. Liver biopsy assessment in chronic viral hepatitis: a personal, practical approach. *Mod Pathol* 2007; 20(suppl 1):S3–S14
20. Kleiner DE, Brunt EM, Van Natta M, et al. Design and validation of a histological scoring system for nonalcoholic fatty liver disease. *Hepatology* 2005; 41:1313–1321
21. Calvaruso V, Burroughs AK, Standish R, et al. Computer-assisted image analysis of liver collagen: relationship to Ishak scoring and hepatic venous pressure gradient. *Hepatology* 2009; 49:1236–1244
22. Xu S, Wang Y, Tai DC, et al. qFibrosis: a fully-quantitative innovative method incorporating histological features to facilitate accurate fibrosis scoring in animal model and chronic hepatitis B patients. *J Hepatol* 2014; 61:260–269
23. Talwalkar JA, Kurtz DM, Schoenleber SJ, West CP, Montori VM. Ultrasound-based transient elastography for the detection of hepatic fibrosis: systematic review and meta-analysis. *Clin Gastroenterol Hepatol* 2007; 5:1214–1220
24. Tsochatzis EA, Gurusamy KS, Ntaoula S, Cholongitas E, Davidson BR, Burroughs AK. Elastography for the diagnosis of severity of fibrosis in chronic liver disease: a meta-analysis of diagnostic accuracy. *J Hepatol* 2011; 54:650–659
25. Bota S, Herkner H, Sporea I, et al. Meta-analysis: ARFI elastography versus transient elastography for the evaluation of liver fibrosis. *Liver Int* 2013; 33:1138–1147
26. Singh S, Venkatesh SK, Wang Z, et al. Diagnostic performance of magnetic resonance elastography in staging liver fibrosis: a systematic review and meta-analysis of individual participant data. *Clin Gastroenterol Hepatol* 2015; 13:440–451
27. Ferraioli G, Tinelli C, Dal Bello B, Zicchetti M, Filice G, Filice C. Accuracy of real-time shear wave elastography for assessing liver fibrosis in chronic hepatitis C: a pilot study. *Hepatology* 2012; 56:2125–2133
28. Cassinotto C, Lapuyade B, Mouries A, et al. Noninvasive assessment of liver fibrosis with impulse elastography: comparison of supersonic shear imaging with ARFI and FibroScan. *J Hepatol* 2014; 61:550–557
29. Bavu E, Gennisson JL, Couade M, et al. Noninvasive in vivo liver fibrosis evaluation using supersonic shear imaging: a clinical study on 113 hepatitis C virus patients. *Ultrasound Med Biol* 2011; 37:1361–1373
30. Sporea I, Bota S, Jurchis A, et al. Acoustic radiation force impulse and supersonic shear imaging versus transient elastography for liver fibrosis assessment. *Ultrasound Med Biol* 2013; 39:1933–1941
31. Boursier J, Isselin G, Fouchard-Hubert I, et al. Acoustic radiation force impulse: a new ultrasonographic technology for the widespread noninvasive diagnosis of liver fibrosis. *Eur J Gastroenterol Hepatol* 2010; 22:1074–1084
32. Ebinuma H, Saito H, Komuta M, et al. Evaluation of liver fibrosis by transient elastography using acoustic radiation force impulse: comparison with Fibroscan(®). *J Gastroenterol* 2011; 46:1238–1248
33. Rifai K, Cornberg J, Mederacke I, et al. Clinical feasibility of liver elastography by acoustic radiation force impulse imaging (ARFI). *Dig Liver Dis* 2011; 43:491–497
34. Sporea I, Sirli R, Popescu A, Danila M. Acoustic radiation force impulse (ARFI): a new modality for the evaluation of liver fibrosis. *Med Ultrason* 2010; 12:26–31
35. Friedrich-Rust M, Wunder K, Kriener S, et al. Liver fibrosis in viral hepatitis: noninvasive assessment with acoustic radiation force impulse imaging versus transient elastography. *Radiology* 2009; 252:595–604
36. Yoneda M, Suzuki K, Kato S, et al. Nonalcoholic fatty liver disease: US-based acoustic radiation force impulse elastography. *Radiology* 2010; 256:640–647
37. Friedrich-Rust M, Romen D, Vermehren J, et al. Acoustic radiation force impulse-imaging and transient elastography for non-invasive assessment of liver fibrosis and steatosis in NAFLD. *Eur*

J Radiol 2012; 81:e325–e331

38. Rizzo L, Calvaruso V, Cacopardo B, et al. Comparison of transient elastography and acoustic radiation force impulse for non-invasive staging of liver fibrosis in patients with chronic hepatitis C. *Am J Gastroenterol* 2011; 106:2112–2120
39. Ferraioli G, Tinelli C, Dal Bello B, et al. Accuracy of real-time shear wave elastography for assessing liver fibrosis in chronic hepatitis C: a pilot study. *Hepatology* 2012; 56:2125–2133
40. Yoon JH, Lee JM, Joo I, et al. Hepatic fibrosis: prospective comparison of MR elastography and US shear-wave elastography for evaluation. *Radiology* 2014; 273:772–782
41. Toshima T, Shirabe K, Takeishi K, et al. New method for assessing liver fibrosis based on acoustic radiation force impulse: a special reference to the difference between right and left liver. *J Gastroenterol* 2011; 46:705–711
42. D'Onofrio M, Gallotti A, Mucelli RP. Tissue quantification with acoustic radiation force impulse imaging: measurement repeatability and normal values in the healthy liver. *AJR* 2010; 195:132–136
43. Horster S, Mandel P, Zachoval R, Clevert DA. Comparing acoustic radiation force impulse imaging to transient elastography to assess liver stiffness in healthy volunteers with and without Valsalva manoeuvre. *Clin Hemorheol Microcirc* 2010; 46:159–168
44. Karlas T, Pfrepper C, Wiegand J, et al. Acoustic radiation force impulse imaging (ARFI) for noninvasive detection of liver fibrosis: examination standards and evaluation of interlobe differences in healthy subjects and chronic liver disease. *Scand J Gastroenterol* 2011; 46:1458–1467
45. Goertz RS, Zopf Y, Jugl V, et al. Measurement of liver elasticity with acoustic radiation force impulse (ARFI) technology: an alternative noninvasive method for staging liver fibrosis in viral hepatitis. *Ultraschall Med* 2010; 31:151–155
46. Kaminuma C, Tsushima Y, Matsumoto N, Kurabayashi T, Taketomi-Takahashi A, Endo K. Reliable measurement procedure of virtual touch tissue quantification with acoustic radiation force impulse imaging. *J Ultrasound Med* 2011; 30:745–751
47. Sporea I, Sirli RL, Deleanu A, et al. Acoustic radiation force impulse elastography as compared to transient elastography and liver biopsy in patients with chronic hepatopathies. *Ultraschall Med* 2011; 32(suppl 1):S46–S52
48. Klatt D, Friedrich C, Korth Y, Vogt R, Braun J, Sack I. Viscoelastic properties of liver measured by oscillatory rheometry and multifrequency magnetic resonance elastography. *Biorheology* 2010; 47:133–141
49. Muller M, Gennisson JL, Deffieux T, Tanter M, Fink M. Quantitative viscoelasticity mapping of human liver using supersonic shear imaging: preliminary in vivo feasibility study. *Ultrasound Med Biol* 2009; 35:219–229
50. Chen S, Sanchez W, Callstrom MR, et al. Assessment of liver viscoelasticity by using shear waves induced by ultrasound radiation force. *Radiology* 2013; 266:964–970
51. Asbach P, Klatt D, Schlosser B, et al. Viscoelasticity-based staging of hepatic fibrosis with multifrequency MR elastography. *Radiology* 2010; 257:80–86
52. Chen J, Talwalkar JA, Yin M, Glaser KJ, Sanderson SO, Ehman RL. Early detection of nonalcoholic steatohepatitis in patients with nonalcoholic fatty liver disease by using MR elastography. *Radiology* 2011; 259:749–756
53. Huwart L, Sempoux C, Salameh N, et al. Liver fibrosis: noninvasive assessment with MR elastography versus aspartate aminotransferase-to-platelet ratio index. *Radiology* 2007; 245:458–466
54. Klatt D, Asbach P, Rump J, et al. In vivo determination of hepatic stiffness using steady-state free precession magnetic resonance elastography. *Invest Radiol* 2006; 41:841–848
55. Yin M, Chen J, Glaser KJ, Talwalkar JA, Ehman RL. Abdominal magnetic resonance elastography. *Top Magn Reson Imaging* 2009; 20:79–87
56. Stebbing J, Farouk L, Panos G, et al. A meta-analysis of transient elastography for the detection of hepatic fibrosis. *J Clin Gastroenterol* 2010; 44:214–219
57. Yin M, Talwalkar JA, Glaser KJ, et al. Assessment of hepatic fibrosis with magnetic resonance elastography. *Clin Gastroenterol Hepatol* 2007; 5:1207e2–1213e2
58. Lee DH, Lee JM, Han JK, Choi BI. MR elastography of healthy liver parenchyma: normal value and reliability of the liver stiffness value measurement. *J Magn Reson Imaging* 2013; 38:1215–1223
59. Venkatesh SK, Wang G, Teo LL, Ang BW. Magnetic resonance elastography of liver in healthy Asians: normal liver stiffness quantification and reproducibility assessment. *J Magn Reson Imaging* 2014; 39:1–8
60. Salameh N, Larrat B, Abarca-Quinones J, et al. Early detection of steatohepatitis in fatty rat liver by using MR elastography. *Radiology* 2009; 253:90–97
61. Palmeri ML, Wang MH, Rouze NC, et al. Noninvasive evaluation of hepatic fibrosis using acoustic radiation force-based shear stiffness in patients with nonalcoholic fatty liver disease. *J Hepatol* 2011; 55:666–672
62. Iredale JP. Models of liver fibrosis: exploring the dynamic nature of inflammation and repair in a solid organ. *J Clin Invest* 2007; 117:539–548
63. Millonig G, Reimann FM, Friedrich S, et al. Extrahepatic cholestasis increases liver stiffness (FibroScan) irrespective of fibrosis. *Hepatology* 2008; 48:1718–1723
64. Millonig G, Friedrich S, Adolf S, et al. Liver stiffness is directly influenced by central venous pressure. *J Hepatol* 2010; 52:206–210
65. Karlas T, Pfrepper C, Troeltzsch M, Wiegand J, Keim V. Acoustic radiation force impulse liver stiffness measurement: interlobe differences demand standardized examination procedures. (letter) *Eur J Gastroenterol Hepatol* 2010; 22:1387
66. Colli A, Pozzoni P, Berzuini A, et al. Decompensated chronic heart failure: increased liver stiffness measured by means of transient elastography. *Radiology* 2010; 257:872–878
67. Simonetto DA, Yang HY, Yin M, et al. Chronic passive venous congestion drives hepatic fibrogenesis via sinusoidal thrombosis and mechanical forces. *Hepatology* 2015; 61:648–659
68. Wang HK, Lai YC, Tseng HS, et al. Hepatic venous congestion after living donor liver transplantation: quantitative assessment of liver stiffness using shear wave elastography—a case report. *Transplant Proc* 2012; 44:814–816
69. Mederacke I, Wursthorn K, Kirschner J, et al. Food intake increases liver stiffness in patients with chronic or resolved hepatitis C virus infection. *Liver Int* 2009; 29:1500–1506
70. Berzigotti A, De Gottardi A, Vukotic R, et al. Effect of meal ingestion on liver stiffness in patients with cirrhosis and portal hypertension. *PLoS ONE* 2013; 8:e58742
71. Yin M, Talwalkar JA, Glaser KJ, et al. Dynamic postprandial hepatic stiffness augmentation assessed with MR elastography in patients with chronic liver disease. *AJR* 2011; 197:64–70
72. Hines CD, Lindstrom MJ, Varma AK, Reeder SB. Effects of postprandial state and mesenteric blood flow on the repeatability of MR elastography in asymptomatic subjects. *J Magn Reson Imaging* 2011; 33:239–244
73. Rigamonti C, Donato MF, Fraquelli M, et al. Transient elastography predicts fibrosis progression in patients with recurrent hepatitis C after liver transplantation. *Gut* 2008; 57:821–827
74. Vergniol J, Foucher J, Terrebonne E, et al. Noninvasive tests for fibrosis and liver stiffness predict 5-year outcomes of patients with chronic hepatitis C. *Gastroenterology* 2011; 140:1970–1979
75. Corpechot C, Carrat F, Poujol-Robert A, et al. Noninvasive elastography-based assessment of liver fibrosis progression and prognosis in primary biliary cirrhosis. *Hepatology* 2012; 56:198–208
76. Pang JX, Zimmer S, Niu S, et al. Liver stiffness by transient elastography predicts liver-related complications and mortality in patients with chronic liver disease. *PLoS ONE* 2014; 9:e95776
77. Merchante N, Rivero-Juarez A, Tellez F, et al. Liver stiffness predicts clinical outcome in human immunodeficiency virus/hepatitis C virus-coinfected patients with compensated liver cirrhosis. *Hepatology* 2012; 56:228–238
78. Shin SH, Kim SU, Park JY, et al. Liver stiffness-based model for prediction of hepatocellular carcinoma in chronic hepatitis B virus infection: comparison with histological fibrosis. *Liver Int*

2015; 35:1054–1062

79. Anaparthy R, Talwalkar JA, Yin M, Roberts LR, Fidler JL, Ehman RL. Liver stiffness measurement by magnetic resonance elastography is not associated with developing hepatocellular carcinoma in subjects with compensated cirrhosis. *Aliment Pharmacol Ther* 2011; 34:83–91
80. Nedredal GI, Yin M, McKenzie T, et al. Portal hypertension correlates with splenic stiffness as measured with MR elastography. *J Magn Reson Imaging* 2011; 34:79–87
81. Goldschmidt I, Brauch C, Poynard T, Baumann U. Spleen stiffness measurement by transient elastography to diagnose portal hypertension in children. *J Pediatr Gastroenterol Nutr* 2014; 59:197–203
82. Sharma P, Kirnake V, Tyagi P, et al. Spleen stiffness in patients with cirrhosis in predicting esophageal varices. *Am J Gastroenterol* 2013; 108:1101–1107
83. Singh S, Eaton JE, Murad MH, Tanaka H, Iijima H, Talwalkar JA. Accuracy of spleen stiffness measurement in detection of esophageal varices in patients with chronic liver disease: systematic review and meta-analysis. *Clin Gastroenterol Hepatol* 2014; 12:935e4–945e4
84. Bensamoun SF, Robert L, Leclerc GE, Debernard L, Charleux F. Stiffness imaging of the kidney and adjacent abdominal tissues measured simultaneously using magnetic resonance elastography. *Clin Imaging* 2011; 35:284–287
85. Rouvière O, Souchon R, Pagnoux G, Menager JM, Chapelon JY. Magnetic resonance elastography of the kidneys: feasibility and reproducibility in young healthy adults. *J Magn Reson Imaging* 2011; 34:880–886
86. Arani A, Da Rosa M, Ramsay E, Plewes DB, Haider MA, Chopra R. Incorporating endorectal MR elastography into multi-parametric MRI for prostate cancer imaging: initial feasibility in volunteers. *J Magn Reson Imaging* 2013; 38:1251–1260
87. Deprez JF, Brusseau E, Schmitt C, Cloutier G, Basset O. 3D estimation of soft biological tissue deformation from radio-frequency ultrasound volume acquisitions. *Med Image Anal* 2009; 13:116–127
88. Bercoff J, Sinkus R, Tanter M, Fink M. 3D ultrasound-based dynamic and transient elastography: first in vitro results. *IEEE Ultrasonics Symposium* 2004; 21:28–31
89. Weaver JB, Van Houten EE, Miga MI, Kennedy FE, Paulsen KD. Magnetic resonance elastography using 3D gradient echo measurements of steady-state motion. *Med Phys* 2001; 28:1620–1628
90. Deffieux T, Montaldo G, Tanter M, Fink M. Shear wave spectroscopy for in vivo quantification of human soft tissues visco-elasticity. *IEEE Trans Med Imaging* 2009; 28:313–322
91. Asbach P, Klatt D, Hamhaber U, et al. Assessment of liver viscoelasticity using multifrequency MR elastography. *Magn Reson Med* 2008; 60:373–379
92. Venkatesh SK, Ehman RL. Magnetic resonance elastography of liver. *Magn Reson Imaging Clin N Am* 2014; 22:433–446
93. Bamber J, Cosgrove D, Dietrich CF, et al. EFSUMB guidelines and recommendations on the clinical use of ultrasound elastography. Part 1. Basic principles and technology. *Ultraschall Med* 2013; 34:169–184
94. Hall TJ, Milkowski A, Garra B, et al. RSNA/QIBA: shear wave speed as a biomarker for liver fibrosis staging. Radiological Society of North America website. qibawiki.rsna.org/images/f/fe/IEEE2013_QIBA_2013aug9.pdf. Accessed March 7, 2015

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The reader's attention is directed to Part 1 accompanying this article, titled "Ultrasound Elastography and MR Elastography for Assessing Liver Fibrosis: Part 1, Principles and Techniques," which appears on pages 22–32 of this issue.