Pediatric MR Elastography of the Liver

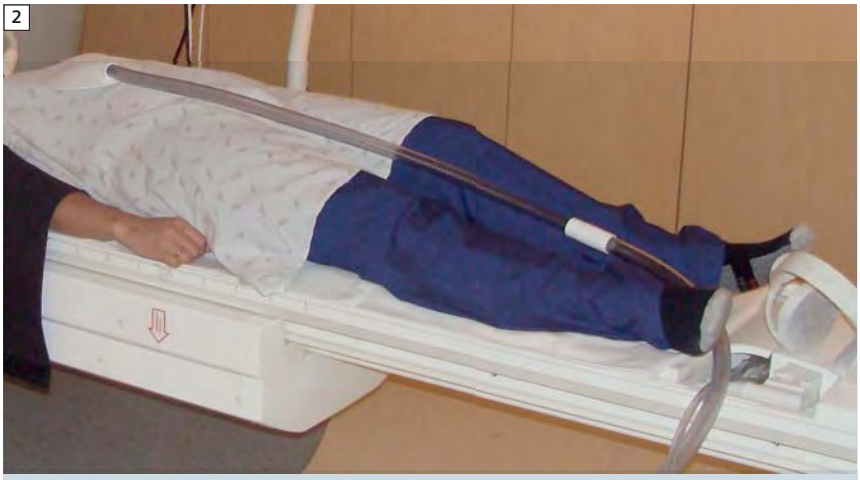
Marilyn J. Siegel, M.D.[1]; Agus Priatna, Ph.D.[2]; Bradley D. Bolster, Jr., Ph.D.[2]; John J. Kotyk, Ph.D.[1]

[1]Mallinckrodt Institute of Radiology, Washington University School of Medicine, St Louis, MO, USA
[2]R&D Collaborations, Siemens Healthcare, USA

Introduction

Hepatic cirrhosis is an increasing complication of cystic fibrosis (CF). Liver biopsy remains the gold standard for diagnosis and detection of CF, but unfortunately is prone to sampling errors. A non-invasive test that assesses the entire liver would be beneficial for both patient management and therapeutic trials. Hepatic stiffness measured with magnetic resonance elastography[$] (MRE) has shown potential as a surrogate for detecting liver disease and hepatic fibrosis [1–4]. MRE is quantifiable and can be used in patients with obesity or ascites. In conjunction with other MR scans, MRE can help differentiate fat from fibrosis. Application of MRE also spares the discomfort and risk associated with liver biopsy; it allows assessment of a large volume of the liver, decreasing sampling errors associated with sonography; and, it allows for multiple follow-up studies without risk of radiation exposure.
MRE generates images depicting the relative stiffness of liver tissue by imaging the shear wave propagation generated by an external wave generator or active acoustic driver. The mechanical excitation is conducted to the patient in the magnet pneumatically, by means of a long hose terminated with a drum-like passive driver. The driver waveform is synchronized to motion encoding gradients in the MR imaging sequence to encode tissue displacement as phase in the reconstructed images. The strength of the wave propagation in the tissue is controlled by the amplitude of the driver

1 The Resoundant acoustic driver system.



2 MR Elastography setup.

*MR scanning has not been established as safe for imaging fetuses and infants under two years of age. The responsible physician must evaluate the benefit of the MRI examination in comparison to other imaging procedures.
[$]Under development. Not for sale in the U.S.

waveform and the quality of the coupling between the passive driver and the liver.

In this study we use MRE and other MR techniques to simultaneously measure hepatic stiffness and steatosis in healthy pediatric* subjects and CF patients with cirrhosis to assess the potential value of MRE for detection of chronic liver disease. Special emphasis was placed on evaluating the methods for use on pediatric subjects where smaller body habitus markedly increases the coupling between the driver and the patient's liver. For pediatric patients it is critical to adjust the amplitude or the strength of the wave generated by the driver for both patient comfort and size, while simultaneously providing good elastography data.

Methods

The MRE data were collected on a conventional 1.5T MAGNETOM Avanto system using the MRE research application package. The MRE examination was added to a conventional MR examination of the upper abdomen and requires less than one minute of additional imaging time. After collecting T2-weighted localizer images, ten subjects with a mean age of 18.6 years (range 7–44 years) were studied. Four subjects were healthy and six of them had CF and cirrhosis documented by conventional MRI methods. Patients were imaged in the supine position with a passive pneumatic driver placed on the abdomen overlying the liver to generate mechanical waves.

MRE acquisitions were performed using a gradient-recalled echo based MR elastography sequence. A six element body matrix coil was placed anterior to the liver while six to nine elements of a spine matrix coil were positioned posteriorly. A transverse slice orientation was used with elastography motion encoding through each slice. Four acquisitions were performed per slice, each with a different phase offset between the driver and the scanner. GRAPPA parallel imaging was applied with an acceleration factor of 2, allowing data to be acquired in a single 20 second breathhold per slice. Imaging parameters were: 256 x 64 acquisition matrix, TE/TR 22/50 ms, FOV 340 or 380 mm, slice thickness 5 mm, read bandwidth 260 Hz/pixel and flip angle 25°. A 60 Hz mechanical wave was generated by the active acoustic driver (Resoundant, Mayo Clinic, Rochester, MN, USA) shown in Figure 1. The applicator of the MRE device was placed over the anterior wall of the chest adjacent to the liver as shown schematically in Figure 2. The amplitude of the driver was adjusted for pediatric patients between 10%–20% of the maximum amplitude, as opposed to the 40%–60% amplitude that was used for adult patients.

The MR wave images were generated using an offline inversion algorithm (Mayo Clinic, Rochester, MN, USA), and used to calculate elastographic images (or elastograms) that depict liver stiffness. Mean elasticity values are reported in kilopascal (kPa) by manually placing regions of interest in four regions on each cross sectional image. All patients also had intrahepatic triglyceride (IHTG) content quantified with MR spectroscopy using a Double PRESS sequence (TE 1 = 23 ms, TE 2 = 53 ms). Statistical analyses were performed using non-paired t-tests.

Results

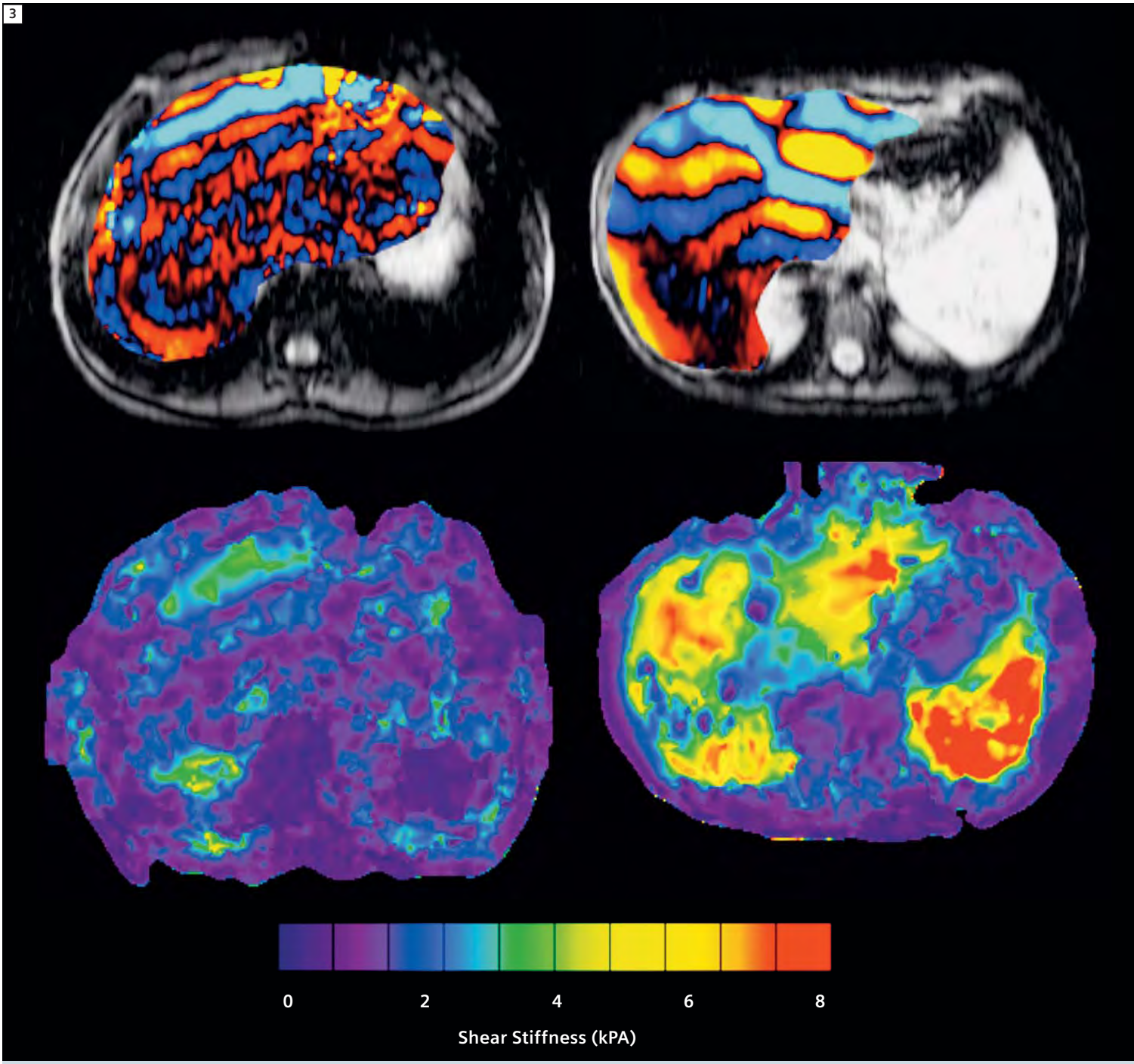
MRE was successfully accomplished in all subjects. Representative wave and MRE images of the liver from subjects with or without cirrhosis are depicted in Figure 3. The mean hepatic shear stiffness was significantly higher in subjects with cirrhosis (mean 4.84 kPa, range 4.02–6.21 kPa) than those without cirrhosis (mean 2.99 kPa, range 2.70–3.38 kPa) ($P = 0.0026$). Receiver operator characteristic analysis identified a cutoff of > 3.38 kPa as both 100% sensitive and specific for discriminating cirrhosis in this patient population.

We adjusted driver amplitude downwards roughly based on the body weight of the pediatric patients in order to avoid image artifacts due to excessive vibration amplitude. Driver amplitudes between 10%–20% provided good quality MRE data in patients ranging from 15 to 35 kg in weight. Figure 4 shows a representative case of elastograms acquired with low driver amplitudes on a 10-year-old patient. As seen in this figure, the elastograms show similar quality for both 10% and 15% amplitude.

To determine whether steatosis influenced detection of cirrhosis in CF liver disease, the IHTG content was assessed and found to be normal in four (mean 2.3%, range 1.12%–3%) and increased in six subjects (mean 6.6%, range 4.97%–8.25%) and was no different in patients with or without cirrhosis ($P = 0.27$).

Discussion and conclusions

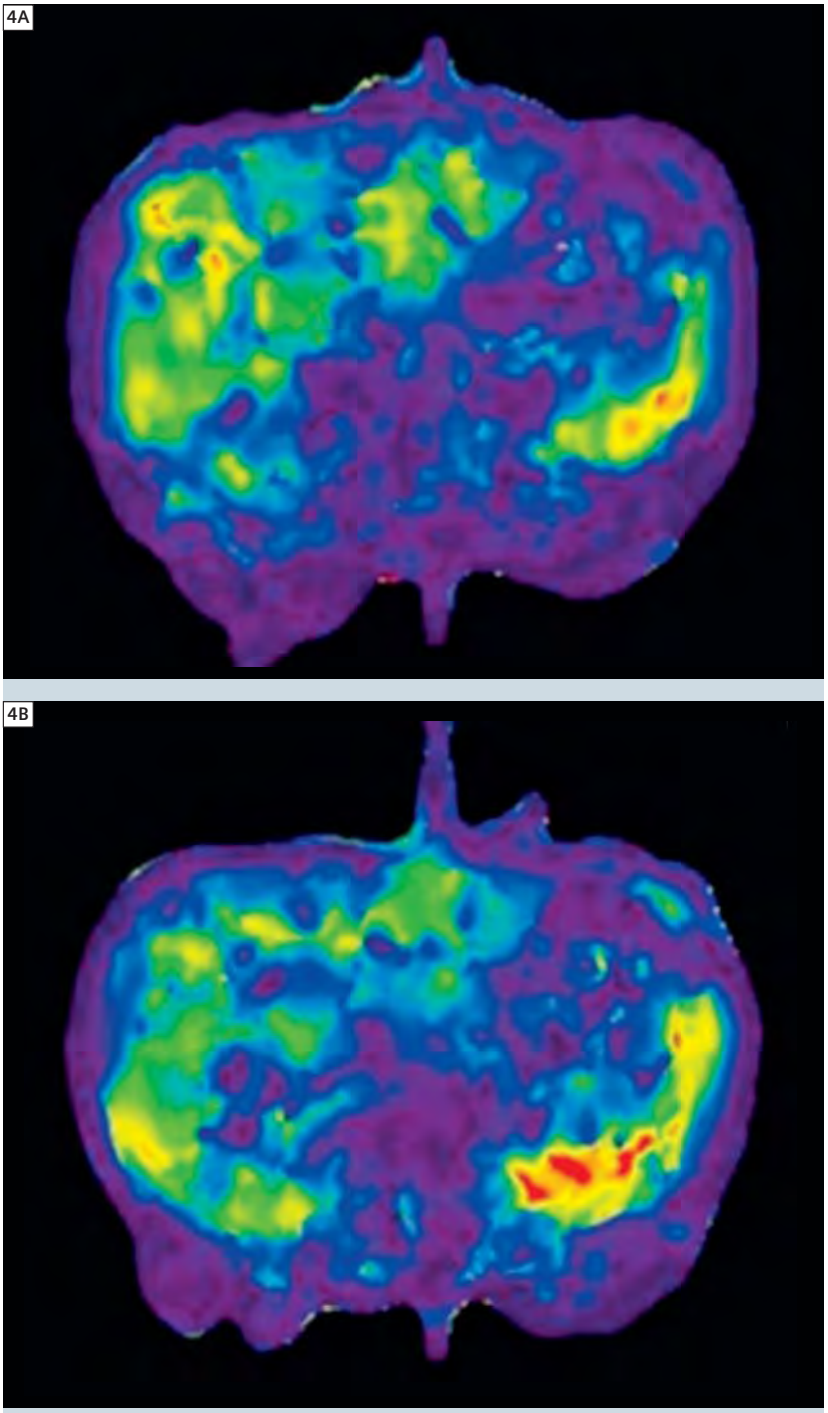
MRE can show increased liver stiffness in patients with liver disease and can be used to identify hepatic cirrhosis. Use of MRE may lead to a new quantitative method for evaluating cirrhosis in patients with CF and other chronic liver diseases. This technique has the advantages of being non-invasive, allowing assessment of a large liver area, and allowing for multiple follow up studies without risk of radiation exposure.



3 Representative wave images and elastograms in a healthy subject (left column) and a CF patient with cirrhosis (right column). In the healthy subject, the wave image (top left) shows short wavelengths consistent with normally soft liver, and the elastogram (bottom left) reveals stiffness values ranging from 0 to 3 kPa, mean 2.1 kPa. In the CF patient, the wave image (top right) shows shear waves with longer wave lengths and the elastogram (bottom right) depicts stiffness values of 4–8 kPa, mean value of 7.2 kPa.

In this study we have shown that MRE is safe and feasible when applied to a pediatric population and that it can identify increased liver stiffness in CF patients with hepatic cirrhosis. To avoid excessive signal loss due to phase dispersion, the driver amplitudes used for pediatric subjects were well below those that are used for typical adults and yet we were able to obtain good quality elastograms and wave images. Since the vibrations were well tolerated in the pediatric population, these findings provide a good starting point for future pediatric examinations.

We have demonstrated that a shear stiffness cutoff value of 3.38 kPa separates healthy patients from those with cirrhosis. Our results are similar to those in adults showing that a shear stiffness cutoff value of 2.93 kPa discriminates between healthy patients and those with chronic liver disease [1]. We also show that the presence of hepatic steatosis had no apparent effect on the liver stiffness measurements.



4 Elastograms acquired on a 10-year-old patient with **(4A)** a 10% amplitude, and **(4B)** a 15% amplitude.

References

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Contact
Marilyn J. Siegel, M.D.
Professor of Radiology and Pediatrics
Mallinckrodt Institute of Radiology
510 South Kingshighway Blvd.
St. Louis, MO 63110
USA
Phone: +1 314-454-6229
Fax: +1 314-454-2868
siegelm@mir.wustl.edu