Assessment of Liver Viscoelasticity Using Multifrequency MR Elastography

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MR elastography (MRE) allows the noninvasive assessment of the viscoelastic properties of human organs based on the organ response to oscillatory shear stress. Shear waves of a given frequency are mechanically introduced and the propagation is imaged by applying motion-sensitive gradients. An experiment was set up that introduces multifrequency shear waves combined with broadband motion sensitization to extend the dynamic range of MRE from one given frequency to, in this study, four different frequencies. With this approach, multiple wave images corresponding to the four driving frequencies are simultaneously acquired and can be evaluated with regard to the dispersion of the complex modulus over the respective frequency. A viscoelastic model based on two shear moduli and one viscosity parameter was used to reproduce the experimental wave speed and wave damping dispersion. The technique was applied in eight healthy volunteers and eight patients with biopsy-proven high-grade liver fibrosis (grade 3–4). Fibrotic liver had a significantly higher ($P < 0.01$) viscosity (14.4 ± 6.6 Pa · s) and elastic moduli (2.91 ± 0.84 kPa; 4.83 ± 1.77 kPa) than the viscosity (7.3 ± 2.3 Pa · s) and elastic moduli (1.16 ± 0.28 kPa; 1.97 ± 0.30 kPa) of normal volunteers. Multifrequency MRE is well suited for the noninvasive differentiation of normal and fibrotic liver as it allows the measurement of rheologic material properties. Magn Reson Med 60:373–379, 2008. © 2008 Wiley-Liss, Inc.

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Diffuse liver disease can be diagnosed by morphologic criteria such as size, contour, and shape of the liver. However, these findings occur late in the course of the disease, usually at a point when it has reached an irreversible stage (1–3). During a patient's clinical workup, an alteration of the size and stiffness of the liver can be subjectively detected by manual palpation.

Based on ultrasound or MR imaging a more objective approach can be selected to characterize the mechanical properties of tissues by means of elastography (4–7). In MRI, motion encoding enables the visualization of tissue-constitutive parameters by imaging harmonic shear waves propagating in organs (6). In transient ultrasound elastography, the velocity of a shock-wave impulse through liver tissue is measured for grading the stage of fibrosis (8,9). MR elastography (MRE) has recently been shown to enable the detection of liver fibrosis by using a monofrequency approach by which shear waves of one specific frequency are introduced into the liver and elastic and viscous moduli can be calculated from the respective wave images (10–13).

As demonstrated by several researchers (14–17), the wave propagation speed and the damping of shear waves in soft tissue increases with increasing harmonic driving frequency due to the dispersion of elastic waves in viscous media. Here, the dispersion of shear waves is exploited for the viscoelastic characterization of normal and fibrotic liver. Therefore, superposed tissue oscillations at multiple harmonic driving frequencies are acquired in a single MRE scan using broad-band frequency encoding (15,18–20). In the following the technical details of multifrequency MRE on human liver are introduced and appropriate data evaluation is developed. The protocol is applied in healthy volunteers and patients based on the hypothesis that normal and fibrotic liver tissue can be differentiated with high specificity and sensitivity by their elastodynamic behavior.

THEORY

In multifrequency MRE the broadband motion-encoding characteristics of a sinusoidal gradient is essential for the accumulation of a spin phase ϕ caused by harmonic vibrations at different frequencies. The efficiency ε of encoding a specific frequency component f by a sinusoidal motion encoding gradient (MEG) is the ratio between the measured phase amplitude ϕ in the images and the physical displacement amplitude u in units of radians per micrometer (μm):

$$\varepsilon = \frac{\gamma g \tau \sin(\pi N \tau f)}{\pi(1 - \tau^2 f^2)}. \qquad [1]$$

where g, τ and N denote amplitude, duration, and number of sinusoidal MEG periods, respectively; γ is the gyromagnetic ratio. Equation [1] is deduced from Ref. 20 with the extension of arbitrary N. By limiting the attention to two-dimensional (2D) wave images acquired with through-plane motion sensitization, u is henceforth given as a scalar wave field $u(x,y,t)$. A plane wave approach yields for $u(x,y,t)$ in the Fourier domain

$$U(x,y,\omega) = U_0 \exp\left[i\omega\left(\frac{\mathbf{n}\cdot\mathbf{r}}{c}\right) - \Gamma \mathbf{n}\cdot\mathbf{r} \right], \qquad [2]$$

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