

## Magnetic Resonance Elastography: A Method for the Noninvasive and Spatially Resolved Observation of Phase Transitions in Gels

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Dynamic magnetic resonance elastography (MRE) is a new imaging technique<sup>1</sup> recently developed for the noninvasive determination of biomechanical properties of biological tissue.<sup>2</sup> Compared to traditional medical palpation techniques, MRE is characterized by a high spatial resolution and a high sensitivity to the varying stiffness between healthy and pathologic tissues even in nonaccessible body regions.<sup>3</sup> Moreover, MRE also provides new information for other research fields. We report the spatially and temporally resolved observation of the sol/gel phase transition in a thermo-reversible gel. Observed wave patterns were reproduced using a model calculation based on temperature-dependent biomechanical properties of the sample.

Dynamic MRE is based on the visualization of propagating shear waves in harmonically excited samples. The shear waves are usually generated mechanically with excitation frequencies between 50 and 600 Hz.<sup>1</sup> Minimum amplitudes for particle displacement are in the order of 0.1  $\mu\text{m}$ . This enables the transmission of shear waves with low damping into the sample. The wave patterns, which depend on the local biomechanical properties of the sample, are visualized by using motion-sensitive MRI techniques.<sup>1</sup> Maps of local shear stiffness or shear moduli (elastograms) can be reconstructed from the wave images.<sup>4</sup>

The gel phantom was prepared by dissolving 22.5 g of agar (1.5%) in 1.5 L of water heated to 90 °C. The fluid gel was examined in a double-walled container open at the top. The cooling of the sample (total cooling time 5 h), monitored with a thermometer between 60 and 25 °C, showed an exponential time dependence. Shear waves with a frequency of 200 Hz were induced parallel to the  $B_0$ -field direction ( $z$ ) by a copper coil fixed to a pivoting carbon fiber rod connected with the surface of the gel. The excitation device was fixed to the standard head coil of a clinical scanner (1.5 T, Siemens, Erlangen, Germany). Data were

acquired using a modified gradient echo technique, FLASH (*Fast Low Angle Shot*,  $T_R/T_E = 40/12$  ms, field of view 160 mm, matrix  $256 \times 256$  pixel, 12 s acquisition time), sensitized to particle displacement by sinusoidal wave-encoding gradients. Motion-sensitive phase images were used for the analysis.

Representative experimental results are displayed in the first row of Figure 1. Several regions may be differentiated: (a) the solidified part (peripheral regions) with well-delineated wave patterns, (b) the transition zone, where smaller wavelengths suggest decreased stiffness, and (c) the fluid region, where no waves can be detected. Occasionally, reflected waves can be seen at the boundaries of the different compartments. With increasing time, the fluid part shrinks and the transition zone broadens until final solidification.

In a first approach wave patterns and correlating elastograms were reproduced using a model of externally driven coupled harmonic oscillators (CHO).<sup>5</sup> Adjacent volume elements were coupled horizontally and vertically by 2D arrays of coupling constants  $k(x,y,t)$ . The elements of  $k(x,y,t)$  were expressed in terms of wave propagation speeds equal to the square root of the shear stiffness of agar. The experimental data indicate that  $k(x,y,t)$  varies from a maximum coupling ( $c_{\text{max}}$ ) in the peripheral solidified parts to low values in the fluid parts. With decreasing temperature gradients the transition zone enlarges, the slope flattens, and  $k(x,y,t)$  increases to  $c_{\text{max}}$  in the central parts. As scan time is short compared to cooling time, the time dependence of  $k(x,y,t)$  may be separated. Using a coupling profile  $\mathcal{R}(x,y)$  that is fitted to an observed shear stiffness (at  $t = t_M$ )  $k(x,y,t)$  then evolves in time according to

$$k(x,y,t) = c_{\text{max}} \cdot \mathcal{R}(x,y)^{f(t)}; \quad 0 < \mathcal{R}(x,y) < 1$$

with

$$f(t) > 1 \text{ for } 0 < t < t_M, \quad f(t) = 1 \text{ for } t_M = 0, \\ \text{and } f(t) < 1 \text{ for } t > t_M$$

To fit a complete series of time-resolved MRE wave images the following parameters had to be varied: (i) maximum coupling (i.e., wave propagation speed)  $c_{\text{max}}$ , (ii)  $f(t)$  with  $t_M$ , and (iii) the form of the 2D contour function  $\mathcal{R}(x,y)$ . Best fits to experimental data were found by supervised iteration for an inverse 2-dimensional Gaussian profile  $\mathcal{R}(x,y)$  and an exponential  $f(t)$  according to

$$\mathcal{R}(x,y) = 1 - a_1 \exp[-(x-x_0)^2/\sigma_x^2 - (y-y_0)^2/\sigma_y^2]$$

$$f(t) = a_2^{-t-t_M/\Delta t}; \quad a_2 > 1$$

with a time step size  $\Delta t = 3.0$  min between each simulated wave image,  $t_M = 243$  min, off-center positions  $x_0$  and  $y_0$  at two-thirds of object size, halfwidths of 73% ( $\sigma_x$ ) and 67% ( $\sigma_y$ ) of object size, and constant factors  $a_1 = 0.9$  and  $a_2 = 1.1$ .  $c_{\text{max}}$  was found to be 2.9 m/s.  $c_{\text{max}}$  and  $\Delta t$  could be varied by  $\pm 0.2$  m/s respective  $\pm 0.5$  min without effective changes in the calculated wave patterns. From  $c_{\text{max}}$  a shear stiffness of  $5.9 \pm 0.2$  kN/m<sup>2</sup> was determined. The results of the simulated wave patterns and the corresponding coupling matrixes are displayed in Figure 1.

To reproduce the experimental conditions, the transverse excitation of the coupled oscillators occurred at the position of the shear wave excitation plate. An additional small excitation with amplitudes of one-fifth of the initial shear waves was applied

(5) (a) Sack, I.; Buntkowsky, G.; Bernarding, J.; Tolxdorff, T.; Braun, J.; *Proc. SPIE* 2001, 4320, 868–874. (b) Braun, J.; Buntkowsky, G.; Bernarding, J.; Tolxdorff, T.; Sack, I. *Magn. Reson. Imaging* 2001, 19, 703–713.

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(1) (a) Muthupillai, R.; Lomas, D. J.; Rossman, P. J.; Greenleaf, J. F.; Manduca, A.; Ehman, R. L. *Science* 1995, 269, 1854–1857. (b) Bishop, J.; Poole, G.; Leitch, M.; Plewes, D. B. *J. Magn. Reson. Imaging* 1998, 8, 1257–1265. (c) Chenevert, T. L.; Skovoroda, A. R.; O'Donnell, M.; Emelianov, S. Y. *Magn. Reson. Med.* 1998, 39, 482–490.

(2) (a) Kruse, S. A.; Smith, J. A.; Lawrence, A. J.; Dresner, M. A.; Manduca, A.; Greenleaf, J. F.; Ehman, R. L. *Phys. Med. Biol.* 2000, 45, 1579–1590. (b) Plewes, D. B.; Bishop, J.; Samani, A.; Sciarretta, J. *Phys. Med. Biol.* 2000, 45, 1591–1610. (c) Sinkus, R.; Lorenzen, J.; Schrader, D.; Lorenzen, M.; Dargatz, M.; Holz, D. *Phys. Med. Biol.* 2000, 45, 1649–1664.

(3) Sarvazyan, A. P.; Skovoroda, A. R.; Emelianov, S. Y.; Fowlkes, J. B.; Pipe, J. G.; Adler, R. S.; Buxton, R. B.; Carson, P. L. In *Acoustical Imaging*; Jones, J. P., Ed.; New York: Plenum Press, 1995; Vol. 21.

(4) (a) Manduca, A.; Oliphant, T. E.; Dresner, M. A.; Mahowald, J. L.; Kruse, S. A.; Amromin, E.; Felmlee, J. P.; Greenleaf, J. F.; Ehman, R. L. *Med. Image Anal.* 2001, in press. (b) Bishop, J.; Samani, A.; Sciarretta, J.; Plewes, D. *Phys. Med. Biol.* 2000, 45, 2081–2091. (c) Oliphant, T. E.; Manduca, A.; Ehman, R. L.; Greenleaf, J. F. *Magn. Reson. Med.* 2001, 45, 299–310. (d) Van Houten, E. E.; Paulsen, K. D.; Miga, M. I.; Kennedy, F. E.; Weaver, J. B. *Magn. Reson. Med.* 1999, 42, 779–786.