Diagnosis of liver fibrosis by multifrequency viscoelastic parameter evaluation in magnetic resonance elastography

D. Klatt[1], P. Asbach[1], U. Hamhaber[2], S. Papazoglou[1], B. Hamm[1], J. Braun[2], and I. Sack[1]

[1]Department of Radiology, Charité, Berlin, Germany, [2]Institute of Medical Informatics, Charité, Berlin, Germany

Introduction: The generation of hepatic fibrosis is associated with a structural change of liver tissue which influences its mechanical properties [1]. Viscoelastic parameters of in vivo tissues can be assessed by MR Elastography (MRE) non-invasively. This phase contrast MRI technique is based on the analysis of shear waves emanating from externally introduced tissue vibrations [2]. Recent studies report the potential of MRE to diagnose liver fibrosis [3-7].

Problem: Previous MRE studies on liver fibrosis used monofrequency mechanical excitation. Thus the viscoelastic parameters were evaluated at one specific frequency [3-7]. A more accurate characterization of tissue mechanical properties requires the analysis of wave propagation in a wider dynamic range which is feasible by multifrequency MRE [8, 9].

Objective: In this study healthy volunteers and fibrosis patients were examined by multifrequency MRE on the liver. This technique provided the simultaneous mechanical excitation, data acquisition and processing of four harmonic vibrations. The viscoelastic parameters were determined according to the springpot model [10] which accounts for both elastic and viscous behavior of tissue with the two independent parameters μ and α. This rheological model represents an interpolation between a purely elastic (α=0) and a purely viscous (α=1) material with the weighting factor α.

Methods: 18 healthy volunteers (10 females, 8 males, mean age: 34.2 ± 6.3 a) and 10 patients (4 females, 6 males, mean age: 59.7 ± 8.8 a) with histologically proven liver fibrosis (METAVIR grade 3-4) were involved in this study. Each subject was examined at least twice by multifrequency MRE. Shear waves were introduced into the liver by a rod transmitting the vibrations of a loudspeaker to the abdominal region of the subject. The excitation signal was a superposition of the frequencies 25 Hz, 37.5 Hz, 50 Hz and 62.5 Hz with an amplitude ratio of 1, 2, 4 and 8, respectively. All measurements were performed in a 1.5 T scanner using a single-shot spin-echo echo planar imaging (EPI) sequence incorporating a motion encoding gradient (MEG) in the slice-select direction (MEG frequency f_G = 50 Hz, number of MEG cycles N = 1, TR = 0.5 s). Transversal wave images were calculated by subtracting phase images acquired with reverse MEG. Temporally resolved wave propagation was captured by shifting the trigger 40 times over an 80 ms-interval. Total measurement time was 40 s which was split into two breath-holds. After Fourier-transformation the complex shear moduli $G(x,y,f)$ were calculated from the corresponding complex wave images $U(x,y,f)$ by a 2D-inversion of the Helmholtz equation. $G(x,y,f)$ was averaged spatially in regions of interest (*ROI*) as shown in fig. 1. Using the springpot model the independent viscoelastic parameters α and μ (assuming η = 1 Pa s) were fitted. Finally, a linear threshold function which maximized the sensitivity at 100% specificity was determined to separate the healthy volunteers from the patients.

Results: Fig. 1 shows multifrequency MRE experiments on the liver of a healthy volunteer and of a fibrosis patient. A visual comparison of the wave images corresponding to identical frequencies already indicates different viscoelastic properties of normal and fibrotic liver tissue. The wavelengths are enlarged and the shear waves are less damped in the fibrotic liver compared to the liver of the healthy volunteer. Mean individual viscoelastic parameters of all examined subjects are displayed in fig. 2. The volunteer and the patient from fig. 1 are symbolized by a blue square and a black asterisk, respectively. The μ-values were higher for the patients while no difference was measured in the α-values. For the separation line defined by α=–0.013μ+0.298 the sensitivity and the specificity was 80% and 100%, respectively. An ROC analysis gave an AUROC of 92.2% for differentiation between healthy volunteers and fibrosis patients.

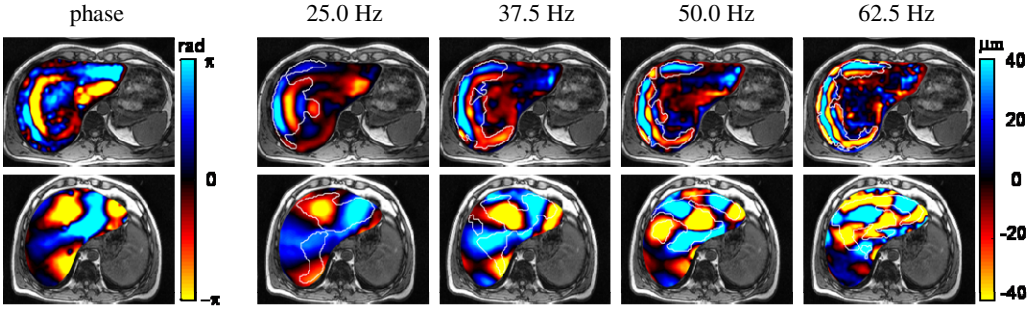

Fig. 1: Multifrequency MRE examinations of the liver in a healthy volunteer (top row) and in a fibrosis patient (bottom row). Snapshots of multifrequency wave propagation are displayed in the left column. The corresponding complex wave images $U(x,y,f)$ (real part) are illustrated in columns 2-5 for the four excitation frequencies. For obtaining real deflection values of the 37.5 Hz-, 50 Hz-, and 62.5 Hz-vibrations, the colorbar values have to be multiplied with 1/2, 1/3 and 1/4, respectively. The *ROI*s are encircled by white lines. All wave images are superposed on T1-weighted magnitude images for anatomical orientation.

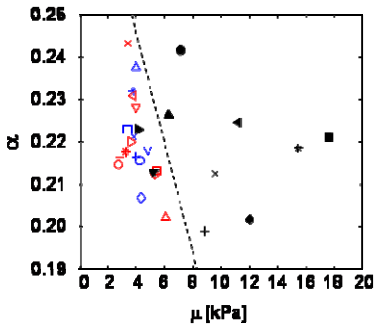

Fig. 2: Mean hepatic viscoelastic parameters according to the rheological springpot model. Patients, healthy female volunteers and healthy male volunteers are marked with black-filled, red-contoured and blue-contoured symbols, respectively. For the calculation of the separation line, see text.

Discussion and Conclusion: Mean hepatic viscoelastic parameters according to the springpot model were determined for 18 healthy volunteers and 10 patients with histologically proven liver fibrosis by a multifrequency approach. All harmonics were introduced well into the liver in all examinations. Including multifrequency data information the accuracy of MRE could be improved with regard to the monofrequency approach without additional measurement time. The AUROC of 92.2% suggests that multifrequency MRE has the potential to diagnose hepatic fibrosis non-invasively.

References: [1] Yeh WC, Ultrasound Med Biol 28(4), 467-74 (2002); [2] Muthupillai R, Science 269, 1854-57 (1995); [3] Rouviere O, Radiology 240, 440-8 (2006); [4] Huwart L, NMR Biomed. 19, 173-9 (2006); [5] Klatt D, Invest. Radiol. 41, 841-8 (2006); [6] Yin M, MRM 58(2), 346-53 (2007), [7] Salameh N, JMRI 26(4), 956-62 (2007); [8] Manduca A, ISMRM, 550 (2003); [9] Klatt D, ISMRM, 962 (2007); [10] Schiessel H, Journal of Physics 28(23), 6567-84 (1995).