MR elastography of liver transplant patients using parallel imaging techniques

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Background: Hepatitis C graft-infection after liver transplantation is seen in virtually all hepatitis-C-virus (HCV) positive patients and causes fibrosis. In magnetic resonance elastography (MRE) tissue mechanical properties are derived by analyzing externally introduced tissue vibrations using phase contrast based MRI [1]. MRE has already shown its strong potential in grading hepatic fibrosis of patients [2, 3]. Single shot multifrequency MRE [4] was specially developed for revealing viscoelastic tissue properties and frequency-independent cut-off values. In single shot MRE a short mechanical excitation burst is applied prior to the acquisition of an entire wave image which reduces patient burden due to repetitive mechanical wave excitation.
Problem: From the technical side, single shot MRE of the liver suffers from susceptibility artifacts and low SNR due to fast signal relaxation. From the clinical side, only very limited evidence on MRE of liver transplant patients is available in literature. Multiple variables (e.g. rejection treatment, cytomegalovirus disease) are associated with course and progression of fibrosis, however, prophylactic or therapeutic regimens are not established yet [5]. Liver biopsy is therefore performed frequently after liver transplantation to assess the graft for fibrosis which involves patient risk and discomfort.
Objective: The capability of MRE for assessing fibrosis in liver transplant patients within a clinically applicable measurement time is tested using a 2D parallel imaging (GRAPPA) MRE technique with multifrequency mechanical excitation. The tissue parameters are calculated from the dispersion of the complex shear modulus G^* employing the viscoelastic springpot model [6].
Methods: Multifrequency MRE was performed on 10 liver transplant patients with HCV infection (5 females, mean age: 57.0 ± 13.4 years) and on a control group of 10 healthy volunteers (3 females, mean age: 36.8 ± 7.8 years) using a 1.5T MR scanner (Magnetom Sonata, Siemens Healthcare Sector, Erlangen, Germany). A superposition of mechanical vibrations of 25 Hz, 37.5 Hz, 50 Hz and 62.5 Hz was introduced into the liver using an acoustic vibration generator [7]. 32 temporally resolved phase images of a transversal slice (thickness: 5mm) with an increment of 2.5 ms were acquired employing a spin-echo EPI sequence with parallel imaging (GRAPPA algorithm). One cycle of a 70 Hz-gradient with amplitude of 15-35 mT/m was used for motion encoding. The field of view was set to 262.5 mm x 350 mm with a spatial resolution of 2.73 mm. Acquisition parameters of the echo time and the repetition time were 41 ms and 600 ms, respectively. This resulted in 19 s total measurement time of one time-resolved 2D MRE experiment which was acquired in either 1 or 2 breath-holds depending on the capability of breath-holding. The viscoelastic parameter evaluation was performed as previously described [4]. In short, the phase images were Fourier-transformed and G^*-images corresponding to the mechanical drive frequencies were computed by applying a 2D-Helmholtz inversion to the complex wave images. The springpot model was fitted to the spatially averaged G^*-values for obtaining the frequency-independent tissue parameters α and μ. Finally, the whole procedure was repeated for 3 adjacent, transversal slices in the center of the liver and individual mean values of α and μ were calculated.
Results: Fig. 1 shows a multifrequency MRE experiment on a healthy volunteer and on two liver transplant patients. After Fourier-decomposition, stationary phase portions are filtered and mapped onto the 0 Hz-component. A visual inspection of the images at the same mechanical drive frequencies yields higher wavelengths in the liver of the patient displayed in the bottom row compared to the other two subjects which indicates an increased stiffness. In consistence, the highest μ-value was determined for this patient within the resulting viscoelastic parameter space that is displayed for all volunteers and patients in Fig. 2. While α does not vary between liver transplant patients and healthy controls, an increased μ-value was measured in some transplant patients. In four patients hepatic fibrosis reoccurred according to the μ-cut-off value of 2.84 kPa as given in [4]. The interindividual mean values ± std of the healthy volunteers (liver transplant patients) are μ = 1.98 ± 0.20 (2.79 ± 0.59) kPa and α = 0.258 ± 0.015 (0.250 ± 0.015).

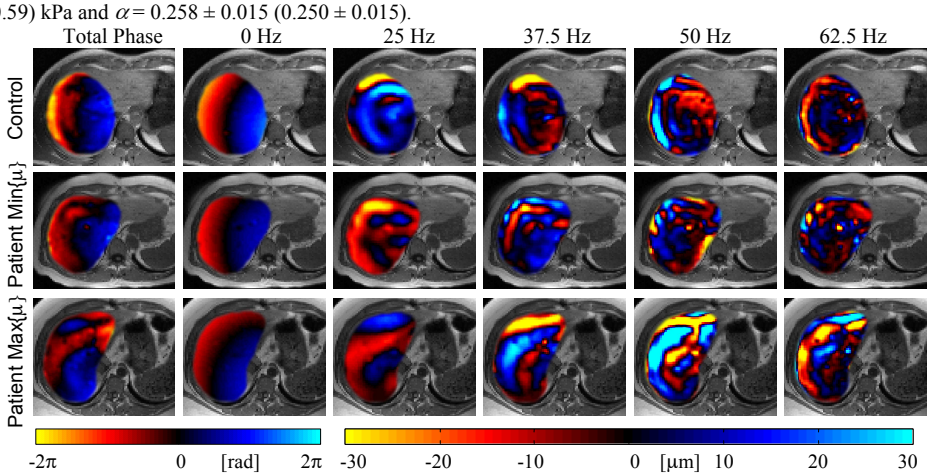

Fig. 1: 2D-Multifrequency MRE experiments on a healthy volunteer (top row) and on the liver transplant patients with the lowest (middle row) and the highest (bottom row) viscoelastic parameter μ (see fig. 2). The phase images in the left column represent a snapshot of multifrequency wave propagation. The real parts of the complex wave images with out-of-plane deflection at the respective drive frequency are illustrated in the further columns. All color-encoded images are superposed on T1-weighted images with a field of view of 200mm x 250mm for anatomical information. The color bar values have to be divided by 2, 3 and 4 in order to obtain correct deflection values of the 37.5 Hz-, 50 Hz- and 62.5 Hz-vibration, respectively.

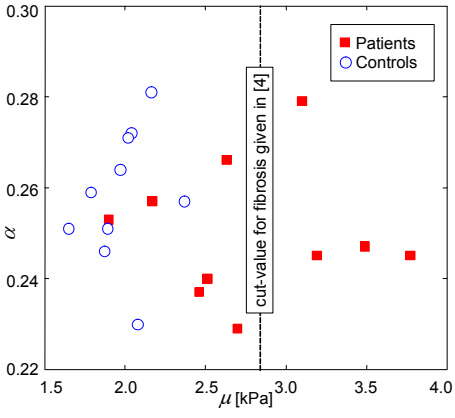

Fig. 2: Individual viscoelastic parameters according to the springpot model for all volunteers and patients. The dashed line corresponds to the μ-cut-off value for fibrosis of 2.84 kPa as given in [4].

Discussion and Conclusion: By employing a 2D GRAPPA spin-echo EPI sequence, multifrequency MRE of the liver was achieved with higher spatial resolution and less susceptibility artifacts compared to non-GRAPPA single-shot MRE [4]. This is particularly important since susceptibility artifacts and image resolution influence the accuracy of wave inversion for calculating shear modulus maps. Consequently, the new technique is potentially more accurate in discriminating between different stages of liver fibrosis. Our viscoelastic parameters deduced form the control group are consistent with data in the literature [4]. The μ-values in the patient group varied in a wide range. Four patients displayed increased hepatic elasticity associated with ≥F1 fibrosis. Because of the excellent quality of the data, this information was incorporated in the clinical treatment plan. In summary, multifrequency MRE using 2D GRAPPA spin-echo EPI was successfully applied to liver transplant patients and has the potential to monitor fibrotic changes within the grafts.
References: [1] Muthupillai et al., Science 269, 1854-1857 (1995); [2] Yin et al., Clin Gastroenterol Hepatol 5, 1207-1213 (2007) ; [3] Huwart et al., NMR Biomed 19, 173-179 (2006); [4] Asbach et al., Radiology 257, 80-86 (2010); [5] Neumann et al., Minerva Gastroenterol Dietol 50, 61-66 (2004); [6] Schiessel et al., J Physics – Math General 28, 6567-6584 (1995); [7] Klatt et al., Invest Radiol 41, 841-848 (2006).