Assessment of liver fibrosis in rats with MR imaging and elastography

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Introduction

To distinguish steatohepatosis from fibrosis or to differentiate various stages of fibrosis, clinicians mainly rely on liver biopsy [1]. In recent years, Magnetic Resonance Elastogra-phy (MRE) has been developed into a promising diagnostic tool, which determines biomechanical properties of tissues by analyzing the propagation of viscoelastic shear waves [2]. Recent studies in animal models [3] and humans [4] have shown that MRE can differentiate between different stages of liver fibrosis. In the presented study rats were fed with methionine-choline-deficient (MCD) diet in combination with a high-fat diet (HFD) to induce liver fibrosis over several weeks. Alteration in the rat liver compared to normal controls were investigated with MR Elastography, imaging (T_2, ADC), and spectroscopy. For MRE measurements a newly developed hydraulic-based actuator was used (Fig. 1) [5].

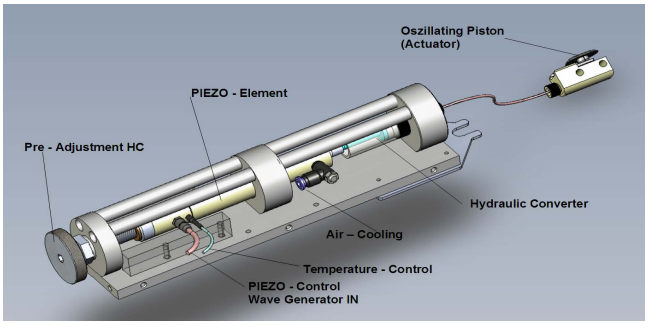

Fig. 1: *Hydraulic actuation system consisting of a piezoelectric element that drives a converter connected to an oscillating piston (actuator) via a highly rigid hydraulic tube.*

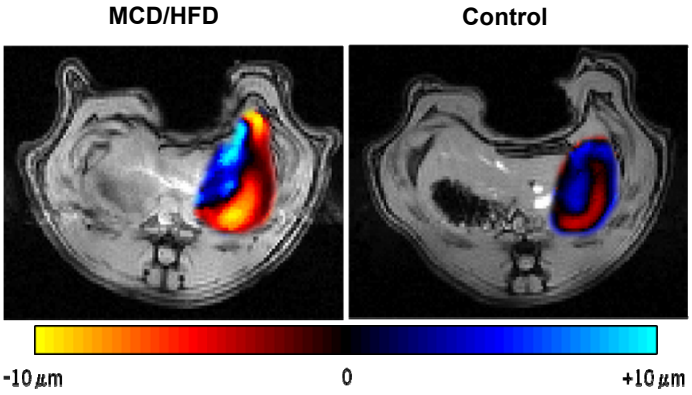

Fig. 2: *In vivo MRE examinations of the rat liver. Complex wave images (real part) are illustrated for an excitation frequency of 200 Hz. Note the longer wavelength in MCD/HFD animals.*

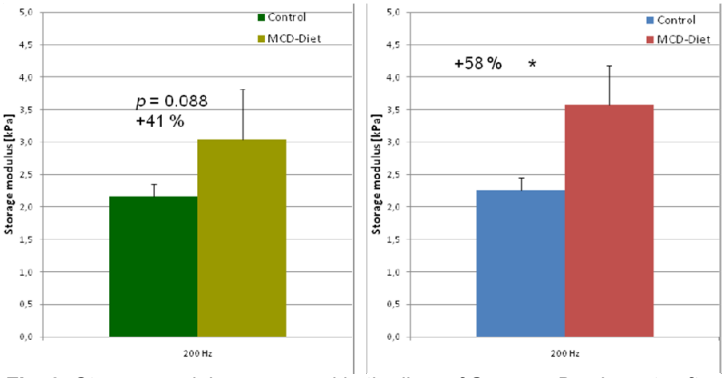

Fig. 3: *Storage modulus measured in the liver of Sprague-Dawley rats after 6 (left) and 13 weeks (right) of MCD/HFD compared to age-matched controls. Progressing fibrosis significantly alters mechanical parameters in the liver.*

Materials and Methods

Sprague-Dawley rats (weight 500-600 g) were fed with the MCD/HF-diet or chow diet for either 6 or 13 weeks. For MRI animals were anesthetized with 2% Isoflurane in O_2:N_2O (1:2) and placed on the animal bed in a supine position. All MR experiments were performed on a 4.7 T Biospec 47/40 scanner (Bruker Biospin, Ettlingen, Germany). For MRE, shear waves were induced by a hydraulic actuator (Fig. 1) with an excitation frequency of 200 Hz applied to a transversal slice through the liver. Out-of-plane motion encoding was chosen for shear waves generated by an up-down movement of the actuator head. Steady state conditions were achieved using dummy oscillations before the start of the motion encoding gradient (MEG) with frequencies identical to the mechanical excitation. Complex wave images where derived from 8 time-resolved phase-difference images by temporal Fourier transformation (Fig. 2). Complex modulus images were obtained by wave inversion and spatial averaging. Further acquisition parameters were: TR 135 ms, TE 16.2 ms, MEG cycles 2; MEG amplitude = 95 mT/m; FA 30°. The average apparent diffusion coefficient (ADC, *b*-values 200 and 500) and the average spin-spin relaxation time (T_2) were measured with a slice orientation identical to MRE. Single voxel spectroscopy of liver lipids (HepCL) was performed in the left dorsal lobe using PRESS.

Results

MRE yields significantly different storage and loss modulus in the rat liver after several weeks on MCD/HF-diet (Fig. 3). In addition to changes in mechanical properties T_2 is significantly increased while the ADC is reduced compared to control animals. However, the magnitude of the latter effects is smaller than those obtained with MRE. Liver lipid content is between 6-fold (week 6) and 10-fold (week 13) increased in MCD rats compared to controls.

References: [1] Oh et al., Aliment Pharamcol Ther 28, 503-522, [2] Muthupillai et al., Science 269, 1854-1857 (1995), [3] Salameh et al., Radiology 253, 90-7 (2009), [4] Talwalkar et al., Hepatology 47 (1), 332-342 (2008), [5] Neumaier et al., Proc. ISMRM 2009