MR elastography reveals tissue degeneration in Multiple Sclerosis patients

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INTRODUCTION: Magnetic Resonance Elastography (MRE) is a novel, non-invasive imaging technique able to directly visualize and quantitatively measure tissue elasticity. In multiple sclerosis (MS), magnetic resonance imaging (MRI) has become a gold standard in diagnosis [1]. However, conventional MRI measures such as T2 lesion load or contrast-enhancing lesions correlate only weakly with clinical symptoms and long term disease prognosis. Recently, studies comprising diffusion-weighted imaging, proton spectroscopy, or magnetization transfer provided first *in vivo* evidence of occult tissue alterations occuring in normal appearing brain matter too. In MRE, shear waves are used for measuring viscoelastic properties of diseased parenchyma [2].The shear elastic behavior of soft tissue is a sensitive indicator of pathologic tissue changes *in vivo* [3], and can thus be used for the detection and characterization of neuroinflammatory brain damage.
The feasibility of cerebral MRE as a novel disease marker in MS has not yet been studied systematically. Thus, we developed a clinically suitable cerebral MRE protocol, and subsequently investigated MS patients as well as healthy matched volunteers.

METHODS: 40 untreated MS patients (21 female; mean age 38.9±8.2 years) with relapsing-remitting disease course (mean EDSS 1.4; range 0-4) and 17 healthy volunteers (8 female; mean age 38.5±10.9 years) were investigated on a Siemens Sonata 1.5T scanner (Siemens Medical Systems, Erlangen, Germany), using a quadrature head-coil. Shear waves were introduced into the brain from the back of the head by a rocker-actuator driven by a remote loudspeaker [4]. A composite wave signal of harmonic oscillations at frequencies of 25, 37.5, 50 and 62.5 Hz was used to excite the brain mechanically. Transversal phase-difference wave images were acquired using a single-shot spin-echo EPI sequence including motion-encoding gradients of four 60-Hz-sinusoidal cycles. The temporal wave propagation was captured by shifting the trigger 80 ms in increments of 2 ms. Total measurement time was 4 minutes for a full elastographic data set. The experiment was repeated twice in each subject at different transversal image slice positions through the corpus calosum. The phase-difference data were unwrapped and Fourier-decomposed into the single frequency-components (Figure 1 top row). Corresponding wave-speed images (figure 1 bottom row) and wave-damping images (data not shown) were calculated by complex wave-image inversion. Both the wave-speed and -damping were averaged within the boundaries of the brain parenchyma including gray and white matter. The resulting dispersion data were analyzed with a viscoelastic model given by the interpolation of an elastic- and a viscous element. The so called springpot-model was used with a fixed interpolation factor *a* [5].

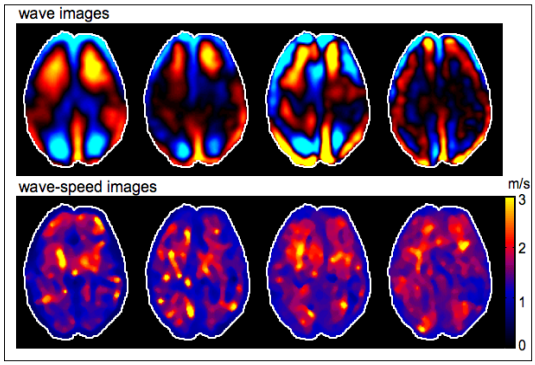

Figure 1: Wave components and resulting wave-speed maps of 25, 37.5, 50 and 62.5 Hz tissue oscillations (from left to right) measured by a multifrequency MRE-examination in a healthy volunteer.

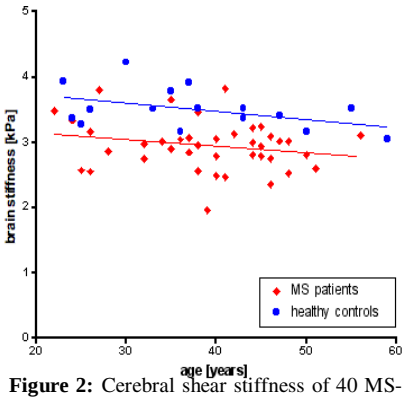

Figure 2: Cerebral shear stiffness of 40 MS-patients (red dots) and 17 matched controls (blue dots). Patients present with prominently lower brain stiffness. Visco-elasticity regresses with age in both cohorts (blue and red line).

RESULTS: The proposed setup allowed for fast acquisition of cerebral MRE data, embedded into clincial MRI routine. Figure 1 shows examplarily the wave components and corresponding wave speed maps measured in a healthy brain. The intensity in the wave-speed images increases from left to right, visualizing wave-speed dispersion as a result of the cerebral viscoelastic behavior. In the applied model, we assumed a viscosity of $a = 0.24$ in all subjects. Individual variations of the shear stiffness are presented in Figure 2. Mean stiffness values were lower in patients (2.95 ± 0.12 kPa) compared to healthy matched volunteers (3.5 ± 0.16 kPa), and thus could differentiate pathological alterations from healthy brain parenchyma with high significance ($p<0{,}0001$; student t-test) (Figure 3).

DISCUSSION: MRE detected a significant decrease of brain stiffness in MS patients, exceeding 0.5 kPa compared to matched controls. Our data indicate that chronic neuroinflammation is capable of altering the biomechanical properties of brain parenchyma. MRE provides a unique, non-invasive imaging modality that is feasable for future routine clinical applications.

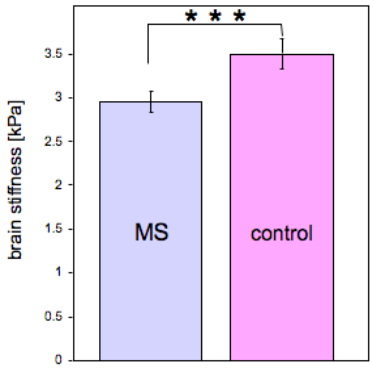

Figure 3: Mean cerebral shear stiffness in MS patients (n=40) is significantly lower (***, $p<0{,}0001$; student t-test) compared to matched controls.

CONCLUSION: MR elastography resolves *in vivo* differences of tissue elasticity between healthy and pathologically altered brain parenchyma with high sensitivity.

References: [1] Polman et al., Ann Neurol 2005;58:840-46 , [2] Muthupillai et al, Science 1995;269:1854-57 , [3] Sinkus et al ISMRM 2007;963 [4] Sack et al, NMR Biomed. 2007;epub , [5] Schiessel et al., Journal of Physics 1995;28:6567-84.