High resolution MR elastography reveals disseminated white matter degradation of brain tissue integrity in clinically isolated syndrome

Andreas Fehlner[1], Kaspar-Josche Streitberger[1,2], Friedemann Paul[3,4], Jens Würfel[3,5], Jürgen Braun[6], and Ingolf Sack[1]

[1]*Department of Radiology, Charité - Universitätsmedizin Berlin, Berlin, Germany,* [2]*Department of Neurology with experimental Neurology, Charité - Universitätsmedizin Berlin, Berlin, Germany,* [3]*NeuroCure Clinical Research Center, Charité - Universitätsmedizin Berlin, Berlin, Germany,* [4]*Clinical and Experimental Multiple Sclerosis Research Center, Department of Neurology, Charité - Universitätsmedizin Berlin, Berlin, Germany,* [5]*Institute of Neuroradiology, Universitätsmedizin Göttingen, Göttingen, Germany,* [6]*Institute of Medical Informatics, Charité - Universitätsmedizin Berlin, Berlin, Germany*

Target audience: Physicians interested in new clinical imaging markers for neuroinflammation and demyelination.

Purpose: Neuroinflammation and demyelination are associated with marked softening of brain tissue (1,2). Here we test if high resolution multifrequency MR elastography (MMRE) can detect early signatures of brain tissue degradation in multiple sclerosis by measuring the spatially resolved viscoelastic response of the brain to clinically isolated syndrome (CIS).

Methods: 17 patients with CIS (mean age 30.4 years, range 22 - 47 years, 7 females) and 33 age and sex matched controls (HC) were investigated by multifrequency magnetic resonance elastography (MMRE). The experiments were conducted on a 3T MRI system (Siemens Trio) using a single-shot EPI-based MRE sequence (3). Full 3D wave fields were acquired at 7 mechanical frequencies (25 to 60 Hz, 5 Hz increments) in 15 contiguous slices and by an image resolution of 1.9×1.9×1.9 mm^3 (FoV: 190x160 mm, TR: 2980 ms, TE: 71 ms, 8 dynamics of the wave cycle). For parameter reconstruction, multifrequency dual elasto visco (MDEV) inversion was applied as described in (1). By this method, two independent parameter maps are obtained, which represent the magnitude and the phase angle of the complex shear modulus, $|G^*|$ and φ, respectively. For comparison to previous work on MRE in MS, Helmholtz inversion (HI) was applied, followed by an automated fit of the G^*-dispersion function based on the springpot model (4) yielding shear modulus μ and viscoelastic powerlaw coefficient α. We used ANTs (5) for registering all parameter maps to standard brain atlases in order to better visualize regional effects caused by CIS.

Results: Fig. 1 shows four representative slices of group averaged parameters along with difference maps $\Delta|G^*|$ and $\Delta\varphi$, representing the relative change in viscoelasticity due to CIS. It is clearly visible that both storage and loss moduli reduce in patients and therewith cause lower $|G^*|$ values while φ remains unchanged. The disseminated reduction of $|G^*|$ is most pronounced in white matter (WM) and increases towards apical slice positions. Fig. 2 compares MRE parameters averaged in WM between groups ($|G^*|$: 2282 ± 212 Pa vs. 2023 ± 223 Pa; φ: 0.72 ± 0.06 vs. 0.70 ± 0.06) demonstrating a significant CIS-related decrease of $|G^*|$ (~11%, p = 0.001). Conventional multifrequency MRE based on HI-inversion and springpot modelling was not sensitive to CIS (μ = 3660 ± 511 Pa vs. 3355 ± 660 Pa, p = 0.08; α = 0.292 ± 0.011 vs. 0.290 ± 0.011, p = 0.562). However, as illustrated by comparison to literature values of μ and α in relapsing remitting MS (rr) and primary and secondary progressing MS (pp&sp), the current study complements previous findings on the gradual mechanical degradation of brain tissue associated with MS.

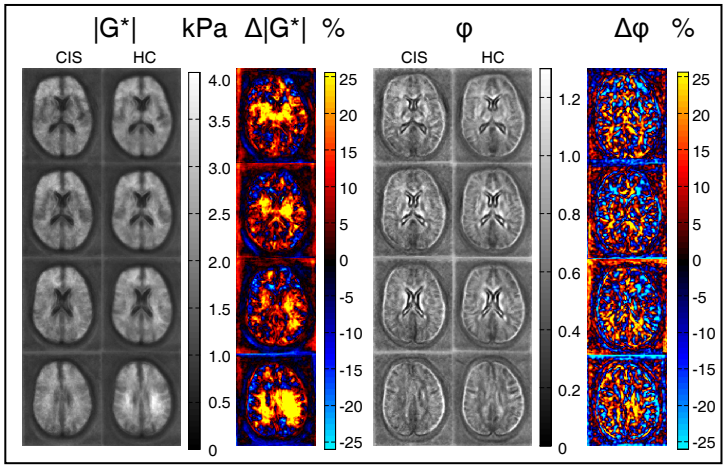

Fig. 1: Viscoelasticity changes in brain tissue due to CIS: While the magnitude modulus |G*| clearly decreases from patients to healthy controls (HC) (best represented by the relative ratio maps $\Delta|G^*|$), the phase angle φ was not sensitive to CIS. The maps illustrate group averaged values normalized to a standard brain.

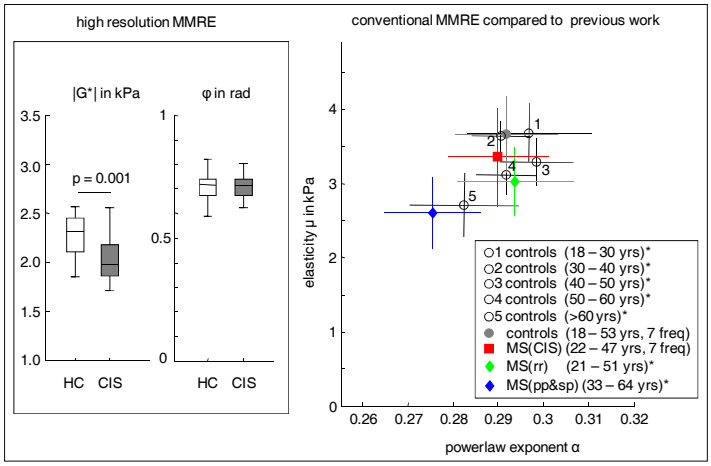

Fig. 2: Group averaged MMRE parameters of WM according to the high resolution processing pipeline (3) based on MDEV inversion (left) and conventional springpot fitting of modulus values obtained by HI on the right. *data taken from (6).

Discussion

This study demonstrates for the first time that WM viscoelasticity is significantly affected by a single neurological episode of inflammation or demyelination. Compared to the pronounced decrement of shear elasticity as observed in more progressed states of MS (4) the effect described by our study is weak as demonstrated by only a trend in μ. However, applying advanced methods for high resolution mechanical imaging such as MDEV-inversion based MMRE allows us to delineate the brain regions in which the viscoelasticity has been altered in response to autoimmune stimulation already before the manifestation of MS. Therewith high resolution MMRE may support clinical diagnosis, treatment planning and monitoring of therapy success in MS.

Literature (1) Schregel et al. PNAS 2012;109:6650-5 (2) Riek et al. Neuroimage: Clinical 2012;1:81-90 (3) Braun et al. Neuroimage, 2014;90:308-14 (4) Streitberger et al. PLoS One 2012;7(1):e29888. (5) Avants et al. Neuroimage 2011;54:2033-2044 (6) Sack et al. Soft Matter 2013;9:5672-80.