MR elastography of stroke: A feasibility study

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Background: Assessment of extent and degree of tissue damage after stroke is crucial for disease treatment and therapy planning. The characterization of neuronal tissue inside an infarcted region is still a subject of intense research. MR elastography (MRE) is capable of measuring the mechanical connectivity of soft tissue in vivo [1]. Recent applications of MRE to the brain have demonstrated its feasibility to measure diffuse CNS-degeneration by means of biomechanical parameters [2,3].
Problem: Stroke-related damage of neuronal tissue is a local effect. To date, nothing is known about the degree of variation of mechanical parameters inside a stroke region relative to healthy brain tissue. The measurement of mechanical properties of tissue requires methods insensitive to boundary conditions. MRE is based on the solution of the wave equation for the complex shear modulus. Wave inversion is mathematically ill-posed and thus inherently sensitive to boundary conditions [4].
Objective: This feasibility study aims to assess the potential of MRE for the characterization of tissue regeneration after stroke. The hypothesis is that stroke-related changes in interstitial pressure, cellular adhesion and neuronal density are directly related to local changes of biomechanical properties which are "tactual" through MRE. To prove this hypothesis, two MRE methods were applied: 1) quantitative MRE based on wave inversion in a wide range of vibration frequencies and 2) qualitative assessment of the regional changes of tissue elasticity based on variations of the amplitudes of the shear waves.

Methods: Multifrequency MRE of the brain was applied to a patient four days after occurrence of a left/right MCA territory infarction. Modest low-frequency vibrations of 25, 37.5, 50 and 62.5 Hz were induced by a head cradle connected to a remote vibration generator. 64 transverse phase images displaying the dynamics of the waves were acquired using a single-shot echo-planar imaging sequence sensitized to motion by a sinusoidal gradient in the direction of slice-selection composed of four cycles at a frequency of 60 Hz [5]. Gradient polarity was toggled on every second scan, resulting in 32 phase-difference images, which were unwrapped and processed in two different ways: 1) Helmholtz inversion was applied yielding four complex modulus images G* corresponding to the four vibration frequencies [5]. 2) Wave images were bandpass filtered to suppress both the modulation of the signal with the incident shear waves (in the low spatial frequencies) and the influence of noise. Therefore the filter function $f(k)=\exp(-1/2\cdot[k-k_0]^4/\sigma^4)$, with heuristically optimized parameters $\sigma = k_0 = 105\ m^{-1}$, was employed. The filtered waves were further decomposed into their single frequency components by temporal Fourier transform.
Results: The figure demonstrates brain MRE at 25 Hz drive frequency (data at higher frequencies are not shown). Anatomical information is shown in the outermost right figures (a, b). Real parts of complex shear waves and complex shear modulus are shown in the following two figures. The modulus map is apparently impaired by inversion-related artifacts. Nevertheless, the averaged storage modulus (G') and loss modulus (G'') in the region of stroke is significantly lower than that of healthy tissue (see table). The decrease of the complex modulus G* was observable at all drive frequencies with highest effects at 25 Hz. In contrast to the modulus map, filtered waves directly display relative changes of tissue stiffness (e). Bright image intensity reveals soft structures similar to compliance weighted MRE [6].

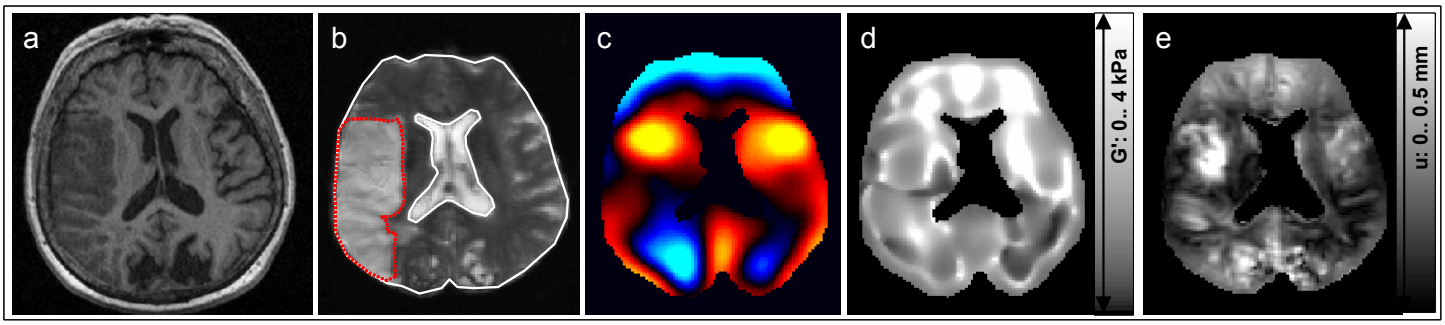

Figure: Brain MRE of stroke at 25-Hz vibration frequency. **a:** T1-weighted image for anatomical information; **b:** T2* weighted image of the same resolution as the MRE phase images. The red dotted line encompasses the infarcted region while the white solid line (excluding ventricles and stroke-region) demarcates the region of interest of healthy parenchyma. **c:** wave image (real part of 25-Hz waves after Fourier transform) with maximum amplitude of 0.8 mm. **d:** G'-map after wave inversion; **e:** bandpass-filtered wave amplitudes (u) enhancing steep changes in wave amplitudes and suppressing both noise and large wavelengths of the incident shear wave.

Discussion: Our results clearly indicate a decrease in mechanical connectivity and friction of stroke-impaired neuronal tissue. The loss of G' was in the range between 10 and 20% while an even larger effect was observed for G''. However, quantification of regional dependent elasticity changes is still a major challenge in MRE. Non-evanescent waves yield variations in G* which are not related to elasticity changes. In contrast, the analysis of wave amplitudes may provide more stability against boundary conditions since compliance weighted MRE is not based on wave inversion [6]. On the other hand, strong wave damping and amplitude nulls at wave nodes also affect this type of mechanical image contrast. In future studies lower vibration frequencies (< 25 Hz) might help to minimize wave damping while non-evanescent waves might be avoidable by changing the direction of wave encoding.
Conclusion: MRE of stroke is feasible. The results demonstrate through both a decrease in G* and an increase in wave amplitudes that tissue integrity is degraded inside the infarcted region.

Table: Averaged storage modulus (G'), loss modulus (G''), filtered wave amplitude (u) and maximum of wave amplitudes (u_{max}) inside two regions of interest (stroke region and rest of the parenchyma) as given in Figure b. Units are kPa for the moduli (G' and G'') and meters for filtered amplitudes (u and u_{max}).

	25Hz	37.5Hz	50Hz	62.5Hz	mean	SD
G' (healthy parenchyma)	1.80	1.88	1.95	2.59	2.06	0.36
G'' (healthy parenchyma)	0.83	1.01	1.08	1.14	1.02	0.13
G' (stroke region)	1.49	1.76	1.74	2.29	1.82	0.34
G'' (stroke region)	0.57	0.68	0.87	1.07	0.80	0.22
G' (ratio)	1.2	1.1	1.1	1.1	1.13	0.06
G'' (ratio)	1.5	1.5	1.2	1.1	1.31	0.20
u (healthy parenchyma)	0.181	0.042	0.019	0.011	0.063	0.080
u (stroke region)	0.204	0.060	0.023	0.013	0.075	0.088
u_{max} (stroke region)	0.701	0.174	0.088	0.042	0.251	0.305
u (ratio)	1.1	1.4	1.2	1.2	1.25	0.14
u_{max} (ratio)	3.9	4.1	4.7	4.0	4.18	0.38

Literature: [1] Muthupillai et al. Science 1995;269(5232):1854-1857. [2] Sack at al. Neuroimage 2009;46:652-657. [3] Wuerfel et al. Neuroimage. 2009 Jun 16. [Epub ahead of print]. [4] Papazoglou et al. Phys Med Biol. 2008;53:3147-3158. [5] Klatt et al. Phys Med Biol 2007;52(24):7281–7294. [6] Papazoglou et al. Phys Med Biol. 2009;54:2229-2241