An atlas of the anatomy of human brain viscoelasticity

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Target audience: Neuroradiologists, neurologists and physicists interested in fundamental properties of the brain.

Background: MR elastography (MRE) [1] is a unique modality for measuring in vivo viscoelastic constants of the human brain in a non-invasive, image-based way [2-5]. Cerebral viscoelastic constants have been reported sensitive to various pathological processes [6,7] and may provide a new diagnostic marker in neuroradiology.

Problem: To date, cerebral MRE suffers from limited spatial resolution due to artefacts related to ill-posed parameter reconstruction. As a consequence, no generalized maps of the regional variation of viscoelastic constants in the brain are available in the literature.

Objective: To introduce a novel wave field reconstruction method, to use it for analyzing 3D-MRE brain data of 23 healthy volunteers and to calculate normalized viscoelastic parameter maps capable of resolving the mechanical anatomy of the human brain.

Methods: *Subjects:* 23 healthy volunteers with no history of neurological abnormality were included in this study (11 women, age range 22 to 72 years). *Experiments*: MRE was run on a 1.5-T MRI system using a single-shot spin-echo EPI sequence with flow-compensated motion-encoding gradient (MEG) (TR / TE = 240 / 99). Motion was induced by a head-cradle connected to a non-magnetic vibration generator at the end of the patient table. Four vibration frequencies of 30, 40, 50 and 60 Hz were consecutively applied for each of which 30 adjacent transversal image slices of 8 mm^3 cubic voxels (88×96×30 matrix) were recorded along all the three motion encoding directions and at eight instances within a vibration period. Total measure time was 12 min including repetitive scans with altered frequencies. *Multifrequency dual parameter inversion*: We found that resolution and consistency of viscoelastic parameters maps can be improved by dual reconstruction, i.e. by the independent inversion of two wave equations corresponding to the complex nature of wave images in the Fourier domain. In brief, we start with representing the complex modulus by its magnitude and phase, $G^*=|G^*|(\cos\phi+i\cdot\sin\phi)$, apply this representation to the Helmholtz wave equation (see eq.(9) of [8]), and reconstruct ϕ by solving $\Delta\mathbf{x}_{mn}\cdot\mathbf{x}_{mn}=-|\Delta\mathbf{x}_{mn}||\mathbf{x}_{mn}|\cos\phi$ in a least-squares sense. $\mathbf{x}_{mn}$ is composed from real and imaginary parts of the m^{th}-component of the curl wave field at n^{th}-frequency, $c'_m(\omega_n)$ and $c''_m(\omega_n)$, respectively. ϕ is scaled by $2/\pi$ to α, the powerlaw exponent known from springpot-model based MRE [7]. As a second parameter, we reconstruct $|G^*|$ by least-squares solution of the magnitude-Helmholtz equation $|G^*||\Delta c^*_m(\omega_n)|=\rho\omega_n^2|c^*_m(\omega_n)|$. *Normalization:* T2 -weighted images (MRE magnitude images) were normalized to a template created by ANTS [9]. The template was then registered to a standard T1-atlas of the brain provided by FSL (T1w in fig.1) yielding normalized MRE magnitude images (T2w in fig.6). The deformation maps were stored and used later for the normalization of individual $|G^*|$- and α-maps.

Results: Fig.6 shows normalized MRE parameter maps which reveal details of the viscoelastic properties of various structures such as white matter (WM), cortical gray matter (GM), thalamus (TH), caudate nucleus (CN) and corpus callosum (CC). Concerning regional viscoelasticity values, we found the order of stiffness $|G^*|$ as follow (in kPa): WM (1.29±0.26), TH (1.10±0.23), CC (1.06±0.28), GM (0.96±0.32), CN (0.61±0.11); α was in the order of: TH (0.634±0.094), CC (0.573±0.066), CN (0.525±0.120), WM (0.494±0.086), GM (0.446±0.099). All regional variations were statistically significant (P < 0.01, fig.2). Furthermore we observed pronounced age-effects corroborating previous findings of brain softening [6,7].

Discussion: This is the first attempt to provide generalized maps of viscoelastic constants of the in vivo human brain. The resolution of the $|G^*|$- and α-maps is superior to published viscoelasticity maps of the brain [2-5]. On average, elasticity values represented by $|G^*|$ are slightly lower than literature values, which is a systematic bias caused by the noise in magnitude wave images and which may be accounted for in future studies. However, the novel dual reconstruction method is particularly useful for all MRE applications which rely on spatially resolved MRE parameter maps. Both $|G^*|$ and α add new information to our understanding of human brain structures. White matter fibers have a significantly higher degree of stiffness and a higher density of the viscoelastic network (given by α) than gray matter structures. Further work is required to account for anisotropic viscoelastic properties as well as to relate the regional variation in α to the underlying mechanical network structure.

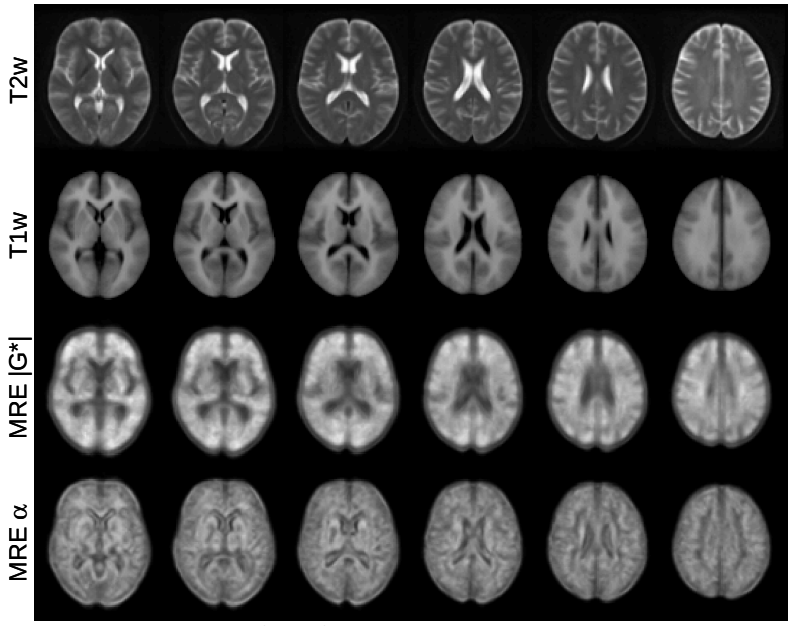

Fig.1: Example images (out of 30) of human brain viscoelasticity compared to normalized T1- and T2-weighted MRI scans.

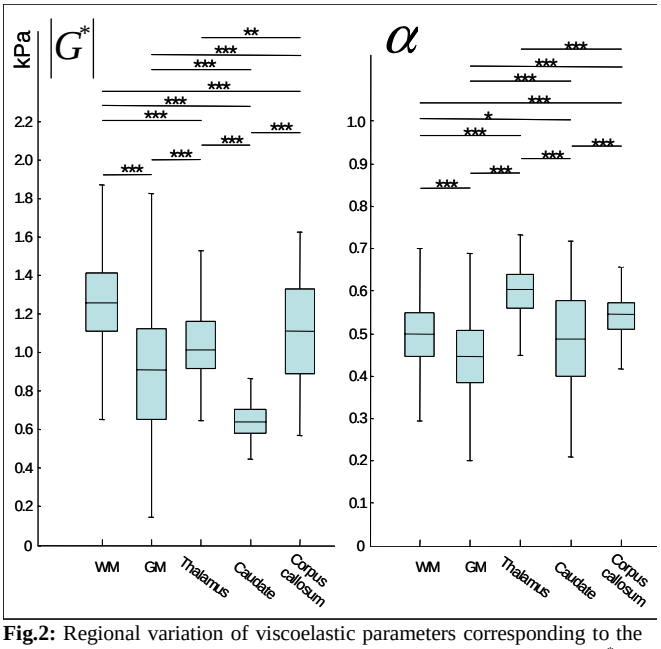

Fig.2: Regional variation of viscoelastic parameters corresponding to the dual parameter reconstruction explained in the methods section. $|G^*|$ is dominated by elastic properties while α is the viscoelastic powerlaw coefficient. *P < 0.01, **P<0.005, ***P < 0.001

Conclusion: We provide the first normalized 3D atlas of viscoelasticity of in vivo human brain.

Literature: [1] Muthupillai et al. Science 1995;269(5232):1854-1857. [2-5] Kruse et al. Neuroimage 2008;39(1):231-237. Sack at al. NMR Biomed 2008;21(3):265-271. Green at al. NMR Biomed 2008;21:755-764. [6] Murphy et al. J Magn Reson Imaging 2011;34(3):494-498. [7] Streitberger et al. PloS one 2012;7(1):e29888. [8] Papazoglou et al. Phys Med Biol 2012;57(8):2329-2346. [9] Avants et al. Neuroimage 2010;49(3):2457-2466.