MR elastography and MRI volumetry of the aging brain

K. J. Streitberger[1], D. Krefting[2], F. Paul[3], D. Klatt[1], S. Papazoglou[1], S. Hirsch[1], J. Braun[2], and I. Sack[1]
[1]Institute of Radiology, Charité - University Medicine Berlin, Berlin, Berlin, Germany, [2]Institute of Medical Informatics, Charité - University Medicine Berlin, Berlin, Berlin, Germany, [3]Neurocure, Charité - University Medicine Berlin, Berlin, Berlin, Germany

Background: Physiological aging of the brain is accompanied by ubiquitous degeneration of neurons and oligodendrocytes [1]. An alteration of the cellular matrix of an organ impacts its macroscopic viscoelastic properties, which are characterized by mechanical parameters such as stiffness and internal friction. To date Magnetic Resonance Elastography (MRE) is the only non-invasive technique for measuring the shear viscoelastic properties of living brain [2-4].
Problem: Recently, it was demonstrated that stiffness of the adult brain is continuously decreasing with years of age [5]. However, MRE is based on the solution of the inverse problem of propagating shear waves which is mathematically ill-posed and thus error prone. Changing geometrical boundary conditions as given by brain atrophy in the course of aging may therefore confound MRE-derived elasticity parameters.
Objective: In this study, the sensitivity of brain MRE to physiological aging and variations in brain volume was studied in 55 healthy volunteers ranging from 24 to 72 years of age. Aim of the study was to systematically investigate the influence of atrophy and geometrical boundary conditions in cerebral MRE.

Methods:
Experiments were run on a standard 1.5T clinical MRI scanner (Siemens, Erlangen, Germany). A custom-made head cradle was used for multifrequency head stimulation. Four transverse images slices with through-plane motion-encoding direction were chosen in a central slab through the cerebrum. 32 time-resolved phase-difference wave images, $u(x,y,t)$ were Fourier-transformed for decomposition into complex wave images at driving frequency: $U(x,y,\omega)$, ($\omega / 2\pi$ = 25, 37.5, 50 and 62.5 Hz). Complex modulus images were obtained by wave inversion ($G(x,y,\omega)=-\rho\omega^2 U/\Delta U$) and spatially averaged [6]. The resulting global modulus function was fitted by the springpot model $G=\kappa(i2\pi f)^{\alpha}$ with κ and α as variables. κ was transformed to a parameter related to shear elasticity μ taking η = 3.7 Pas as the mean viscosity of all volunteers according to [5]. Volume data were acquired by a 3D Magnetized Prepared Rapid Gradient Echo (MPRAGE) sequence (TR/TE = 2110/4.4 milliseconds, TI 1100 ms, flip angle 15°, resolution 1 mm³). Normalized volumes of the whole brain parenchyma were calculated using a method for total brain volume measurement (SIENAX software) using the default BET options (Brain Extraction Tool; part of FSL4.0 Software Library; www.fmrib.ox.ac.uk/fsl).

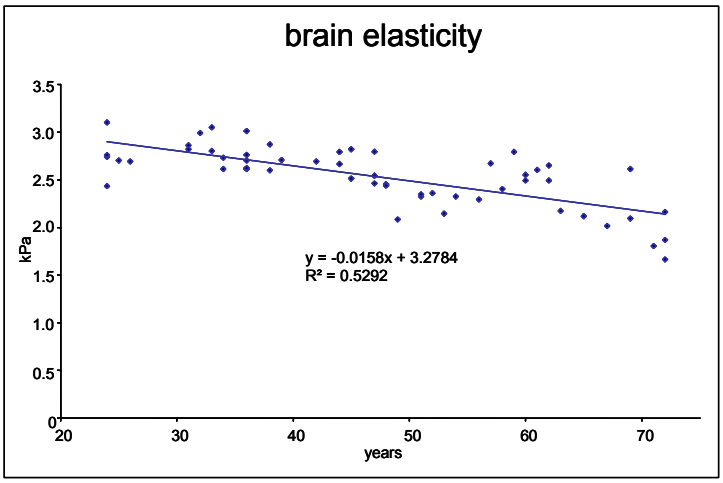

Fig.1: The shear modulus of the adult brain decreases with age. The magnitude of the relative effect per year is about 0.6% (P < 0.0001).

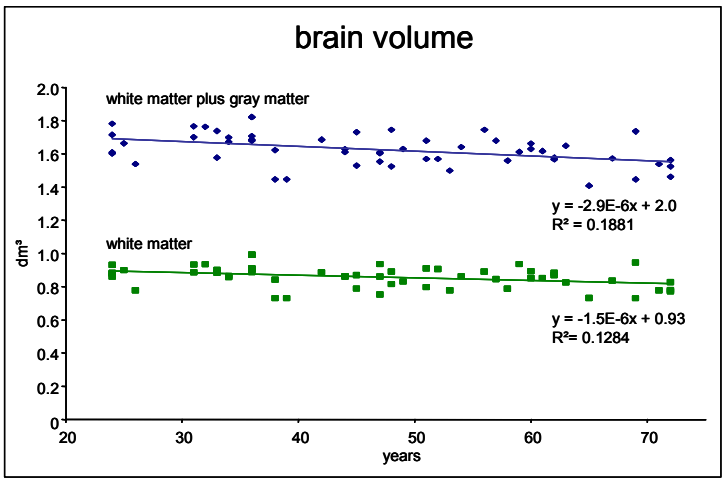

Fig.2: Volume loss of brain parenchyma during aging. The brain of adults shrinks about 0.17 % a year (P = 0.0009).

Results:
Brain MRE was successfully applied in all 55 volunteers (mean age ± SD: 47.3 ± 14.5 yrs, 28 females, 27 males). Mean shear modulus, mean brain volume and mean brain-parenchyma fraction (BPF) were 2.53 ± 0.31 kPa, 1.62 ± 0.10 dm³ and 0.975 ± 0.009, respectively. A linear decrease of the shear modulus of 16 Pa per year (-0.63%, R-square = 0.53, P < 0.0001) and a linear volume loss of 3 cm³ per year (-0.17%, R-square = 0.19, P = 0.0009) corresponding to an annual decrease of BPF of $3x10^{-4}$ (-0.03%, R-square = 0.22) were measured. A linear modulus-volume relationship of 1 Pa / cm³ (R-square = 0.20, P = 0.0006) was observed.

Discussion and conclusion:
This study represents the first systematic investigation of the relationship between brain geometry and viscoelastic constants determined by MRE. Brain geometry was quantified by standard 3D-MRI and automatic threshold-based image segmentation. The repeatability of the method was tested by several 3D MRI scans of one volunteer showing an excellent intra individual agreement. The repeatability of MRE viscoelastic parameter determination was demonstrated in [2]. The decrease of brain volume and brain-parenchymal fraction with age has been demonstrated by several groups. The decrease of brain stiffness with age was shown in [5] however without consideration of brain atrophy. Our results suggest that the main portion of the age-dependent decrease in brain stiffness is not correlated to atrophy but driven by a degradation of mechanical structure elements in brain tissue. As the annual decrease of the shear modulus is about four times more pronounced than atrophy we conclude that the maximum influence of atrophy to brain MRE does not exceed 25%. This result motivates further developments of cerebral MRE towards a clinical modality capable to quantify widespread neuronal tissue degradation occult to other neuroradiological techniques.

Literature: [1] Morrison et al, Science 1997;278:412-19 ; [2] Sack et al, NMR Biomed., 2007; [3] Kruse et al, Neuroimage 2008; 39:231-37; [4] Green et al, NMR Biomed 2008, 21: 755-64; [5] Sack et al, Neuroimage 2009; 46: 652-657; [6] Klatt et al, Phys. Med. Biol. 2007; 52: 7281-7294