# The impact of aging and gender on cerebral viscoelasticity

**I. Sack[1], B. Beierbach[1], J. Wuerfel[2], U. Hamhaber[3], D. Klatt[1], S. Papazoglou[1], P. Martus[4], and B. Juergen[3]**

[1]Department of Radiology, Charité - University Medicine Berlin, Berlin, Berlin, Germany, [2]Department of Neuroradiology, University Lübeck, Lübeck, Schleswig-Holstein, Germany, [3]Institute of Medical Informatics, Charité - University Medicine Berlin, Berlin, Berlin, Germany, [4]Institute of Biometry and Epidemiology, 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.
**Problem:** To date almost nothing is known about alterations of in vivo cerebral viscoelasticity associated with diffuse structural changes during normal aging. Although conventional MRI has become the most important neuroimaging modality, its capability to identify diffuse structural changes of the brain parenchyma is limited [2].
**Objective:** Combining MRI with acoustic waves is a promising way to measure cerebral viscoelasticity without intervention [3]. Recently, the technical feasibility of brain MR elastography was demonstrated [4-6]; A clinically applicable assay of multifrequency MRE of the brain was developed and applied to measure cerebral viscoelasticity as a function of age and sex in 55 individuals. Our hypothesis was that the viscoelasticity of the brain is sensitive to a widespread structural alteration occurring in the course of physiological aging. The results presented in this study are intended as background data for the future use of cerebral viscoelasticity as a marker of tissue integrity and diffuse degenerative processes.

## Materials and Methods

55 volunteers without overt neurological or psychiatric conditions were recruited for this study (mean age 49.35 years, SD 18.78 years, age range 18 to 88 years; 31 males, mean age 52.74 years, SD 17.61 years, age range 21 to 84 years; 24 females, mean age 44.96 years, SD 19.70 years, age range 18 to 88 years). 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. Three transverse images slices with through-plane motion-encoding direction were chosen in a central slab through the cerebrum. 40 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. The resulting global modulus function was fitted by the springpot model $G=\kappa(i2\pi f)^{\alpha}$ with $\kappa$ and $\alpha$ as variables. $\kappa$ was transformed to a parameter related to shear elasticity $\mu$ taking $\eta$ = 3.7 Pas as the mean viscosity of all volunteers derived by the three-parameter Zener model.

## Results

We observed a strong decline in brain viscoelasticity with age. Fig.1 presents two sets of wave data obtained in a young and an elderly healthy female volunteer. Stiffness differences due to senescence are immediately perceptible by comparison of the wavelengths: since large shear wavelengths correspond to a high shear modulus (stiff material), the aged brain is clearly softer than the younger one. Clear sex differences were observed with female brains being in the order of 9% stiffer than those of males ($P < 0.05$). This difference can be translated into a scale of *viscoelastic age*, according to which female brains were on average 13 years ($P < 0.05$) younger than male brains (Fig.2). Viscoelastic values are summarized in tables 1 and 2.

## Discussion

Elderly men and young women represented the minimum and the maximum in our range of brain viscoelasticities, respectively. Interestingly, this finding is not correlated to the volume of the adult brain, measured as brain parenchymal fraction, which is smallest in elderly females. We therefore conclude that brain geometry and volume only have a minor influence on our data. The parameter $\alpha$ corresponds to the ratio of elastic and viscous properties and characterizes the *structure* of the tissue (corresponding to the hypothetical alignment of springs and dashpots). In contrast, the order of magnitude of viscoelastic parameters determines the solid-fluid behavior of the material given in $\mu$ combining elastic and viscous information in the material property of *viscoelasticity*. Alteration in $\mu$ indicates a continuous phase transition on a solid-fluid scale. This tissue "liquefaction" raises the question of how neurons and glial cells may contribute to the global mechanical properties of the brain parenchyma.

## Conclusion

It was demonstrated that multifrequency MRE provides a sensitive measure of the global integrity of brain tissue. Using this new technique for the diagnosis of diffuse pathological processes, one needs to account for age- and gender related effects on viscoelastic constants of the brain.

References: Morrison et al, Science 1997;278:412-19 ; [2] Mueller et al, NMR Biomed 2006;19:655-66 ; [3] Muthupillai et al, Science 1995; 269: 1854-57 ; [4] Sack et al, NMR Biomed., 2007; [5] Kruse et al, Neuroimage 2008; 39:231-37; [6] Green et al, NMR Biomed 2008, 21: 755-64

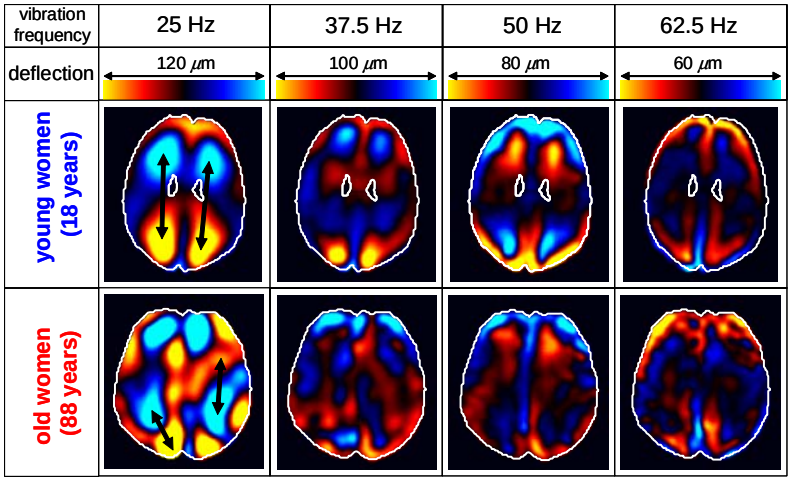


**Figure 1:** Illustration of the age dependency of wave patterns in two healthy female volunteers. Four principal harmonics corresponding to the mechanical excitation waveform were measured. Black arrows indicate the length of the shear waves as a measure of brain stiffness (the shorter arrows in the elderly volunteer indicate softening). After wave inversion and spatial averaging, four complex moduli $G(\omega)$ per volunteer are obtained whose frequency dispersion was analyzed.

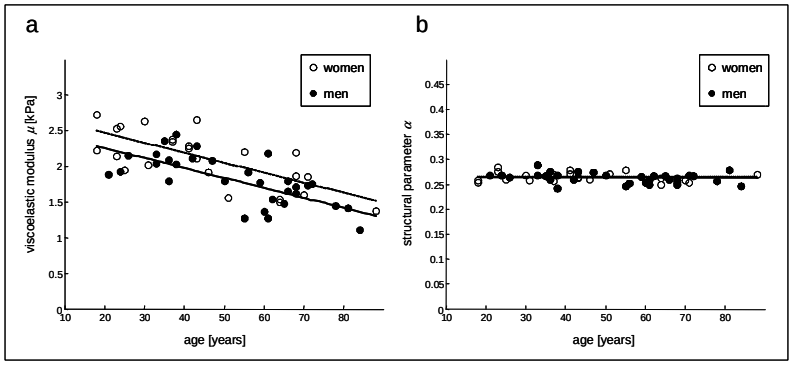


**Figure 2a:** Brain viscoelasticity parameters according to the springpot model. $\mu$ represents both elastic (stiffness) and viscous (friction) properties of brain tissue and is thus a measure of adhesion and 'connectivity' of soft tissue cells. In contrast to $\mu$, $\alpha$ does not significantly change with age and sex (**b**), indicating a relative constant geometrical alignment of structural building blocks in the healthy adult brain. Linear regression graphs were plotted separately for women (dotted line) and men (solid line).

**Table 1:** Age dependencies of complex moduli and viscoelastic parameters.

| X | *R*-square | Annual change of X | *P*-value |
|---|---|---|---|
| $\alpha$ | 0.08 | $-0.15 \times 10^{-3}$ (-0.1%) | < 0.035 |
| $\mu$ | 0.52 | -15.0 Pa (-0.8%) | < 0.001 |

**Table 2:** Gender differences of complex moduli and viscoelastic model parameters according to a linear regression model with age and sex as predictors. [1]difference of intercepts between females and males in the linear regression model. [2]quotient of the sex difference $\Delta X$ and the annual change of X

| X | $\Delta X$ females vs males[1] | Delay[2] | *P*-value |
|---|---|---|---|
| $\alpha$ | 0.001 | 3.5 years | 0.85 |
| $\mu$ | 180 Pa (9%) | 12.9 years | 0.016 |