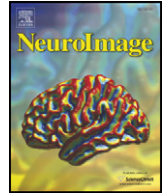




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## The impact of aging and gender on brain viscoelasticity<sup>☆</sup>

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### ABSTRACT

Viscoelasticity is a sensitive measure of the microstructural constitution of soft biological tissue and is increasingly used as a diagnostic marker, e.g. in staging liver fibrosis or characterizing breast tumors. In this study, multifrequency magnetic resonance elastography was used to investigate the in vivo viscoelasticity of healthy human brain in 55 volunteers (23 females) ranging in age from 18 to 88 years. The application of four vibration frequencies in an acoustic range from 25 to 62.5 Hz revealed for the first time how physiological aging changes the global viscosity and elasticity of the brain. Using the rheological springpot model, viscosity and elasticity are combined in a parameter  $\mu$  that describes the solid–fluid behavior of the tissue and a parameter  $\alpha$  related to the tissue's microstructure. It is shown that the healthy adult brain undergoes steady parenchymal 'liquefaction' characterized by a continuous decline in  $\mu$  of 0.8% per year ( $P < 0.001$ ), whereas  $\alpha$  remains unchanged. Furthermore, significant sex differences were found with female brains being on average 9% more solid-like than their male counterparts rendering women more than a decade 'younger' than men with respect to brain mechanics ( $P = 0.016$ ). These results set the background for using cerebral multifrequency elastography in diagnosing subtle neurodegenerative processes not detectable by other diagnostic methods.

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### Introduction

Physiological aging of the brain is accompanied by ubiquitous degeneration of neurons and oligodendrocytes (Morrison and Hof, 1997). 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 (Fung, 1993). These properties are intuitively exploited during palpation, which assesses the stiffness of soft tissue to 'feel' structural changes associated with disease. Until recently, the measurement of viscoelastic properties of the brain required an intervention (Hrapko et al., 2008), which is why there is a lack of knowledge about the mechanical behavior of the healthy brain in its intact physiological environment. To date almost nothing is known about alterations of in vivo cerebral viscoelasticity associated with diffuse structural changes during normal aging (Thibault and Margulies, 1998). Although conventional magnetic resonance imaging (MRI) has become the most important neuroimaging modality, its capability to identify diffuse structural changes of the brain parenchyma is limited (Mueller et al., 2006).

Combining MRI with acoustic waves is a new and promising way to measure cerebral viscoelasticity without intervention (McCracken et al., 2005). Recently, the technical feasibility of brain MR elastography was demonstrated; however, different and partially contradicting results were reported (Hamhaber et al., 2007; Klatt et al., 2007; Vappou et al., 2007; Xu et al., 2007; Kruse et al., 2008; Sack et al., 2008; Green et al., 2008). The disparity of data may result from a well known phenomenon in material testing: the frequency dispersion of the material's inherent complex modulus. The real part of the complex modulus ( $G'$ ) is determined by the restoration of mechanical energy due to the elastic properties of the material, while its imaginary part ( $G''$ ) is associated with loss of energy as a result of the mechanical friction inherent to the material. As former studies were conducted using single wave frequencies, the derived viscoelastic parameters are bound to specific experimental conditions and thus not generally valid. In contrast, multifrequency MRE is capable of measuring the dispersion of the complex modulus ( $G$ ) in the target tissue, thereby improving the physical significance of MRE data by utilizing higher-order viscoelastic models (Klatt et al., 2007; Asbach et al., 2008). The purpose of this study was to set up a clinically applicable assay of multifrequency MRE of the brain and 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. It

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