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# High-resolution mechanical imaging of the human brain by

- three-dimensional multifrequency magnetic resonance
- 3 elastography at 7T
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#### ABSTRACT

Magnetic resonance elastography (MRE) is capable of measuring the viscoelastic properties of brain tissue 25 in vivo. However, MRE is still limited in providing high-resolution maps of mechanical constants. We therefore 26 introduce 3D multifrequency MRE (3DMMRE) at 7T magnetic field strength combined with enhanced multifrequency dual elasto-visco (MDEV) inversion in order to achieve high-resolution elastographic maps of in vivo 28 brain tissue with  $1 \text{ mm}^3$  resolution. As demonstrated by phantom data, the new MDEV-inversion method 29 provides two high resolution parameter maps of the magnitude ( $|G^*|$ ) and the phase angle ( $\phi$ ) of the complex 30 shear modulus. MDEV inversion applied to cerebral 7T-3DMMRE data of five healthy volunteers revealed structures of brain tissue in greater anatomical details than previous work. The viscoelastic properties of cortical gray 32 matter (GM) and white matter (WM) could be differentiated by significantly lower values of  $|G^*|$  and  $\phi$  in GM 33 (21% [P < 0.01], respectively) suggesting that GM is significantly softer and less viscous than WM. 34 In conclusion, 3DMMRE at ultrahigh magnetic fields and MDEV inversion open a new window into characterizing 35 the mechanical structure of in vivo brain tissue and may aid the detection of various neurological disorders based on their effects to mechanical tissue properties.

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### Introduction

During the past few years, magnetic resonance imaging (MRI) at ultrahigh magnetic fields (UHF) of 7T and beyond has emerged as a promising imaging modality in neuroscience, providing images with better resolved anatomical details and improved signal-to-noise ratio (SNR) than conventional MRI (Duyn et al., 2007; Hu and Norris, 2004). The capability of 7T-MRI for high-resolution brain mapping has been exploited in a large variety of MRI methods such as susceptibility-weighted imaging (Deistung et al., 2008; Yao et al., 2009), diffusion-

sensitive MRI (Heidemann et al., 2010, 2012; Reischauer et al., 2012), **Q2** or functional MRI (Beisteiner et al., 2011; Poser and Norris, 2009; 53 Wacker et al., 2011).

Magnetic resonance elastography (MRE) (Muthupillai and Ehman, 55 1996) is a special MRI-based technique which promises sensitivity to 56 the microarchitecture of soft tissue due to the scaling properties of the 57 shear modulus in biological systems (Posnansky et al., 2012). MRE 58 was reported to be sensitive to subtle alterations of brain tissue associated with physiological aging (Sack et al., 2011), multiple sclerosis 60 (Wuerfel et al., 2010), Alzheimer's disease (Murphy et al., 2012a), 61 normal pressure hydrocephalus (Streitberger et al., 2011), and tumors 62 (Murphy et al., 2012b). Micro-MRE in the mouse brain revealed marked 63 softening of cerebral tissue related to demyelination, inflammation and 64 neuronal loss (Freimann et al., 2013; Riek et al., 2012; Schregel et al., 65 2012). These results show that MRE provides additional information 66 on pathologic processes that alter tissue integrity.

Previous technical developments of cerebral MRE relied either on 2D 68 MRE with multifrequency excitation (MMRE) (Latta et al., 2011; 69 Papazoglou et al., 2012; Sack et al., 2011; Streitberger et al., 2011) or 70 on 3D MRE at a single driving frequency (Green et al., 2008; Hirsch 71 et al., 2012; Johnson et al., 2013a,b; Murphy et al., 2011; Pattison et al., 72

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Abbreviations: EPI, echo planar imaging; GM, gray matter; GRAPPA, generalized autocalibrating partially parallel acquisitions; MDEV, multifrequency dual elastovisco (MDEV) inversion; MEG, motion-encoding gradient; MRE, magnetic resonance elastography; 3DMMRE, 3D MRE with multiple vibration frequency stimuli; FLASH, fast low-angle shot; FOV, field of view; UHF, ultrahigh magnetic field; ROI, region of interest; SNR, signal-to-noise ratio; WM, white matter.

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