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MR-elastography reveals degradation of tissue integrity in multiple sclerosis

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ABSTRACT

In multiple sclerosis (MS), diffuse brain parenchymal damage exceeding focal inflammation is increasingly recognized to be present from the very onset of the disease, and, although occult to conventional imaging techniques, may present a major cause of permanent neurological disability. Subtle tissue alterations significantly influence biomechanical properties given by stiffness and internal friction, that – in more accessible organs than the brain – are traditionally assessed by manual palpation during the clinical exam. The brain, however, is protected from our sense of touch, and thus our current knowledge on cerebral viscoelasticity is very limited. We developed a clinically feasible magnetic resonance elastography setup sensitive to subtle alterations of brain parenchymal biomechanical properties. Investigating 45 MS patients revealed a significant decrease (13%, $P<0.001$) of cerebral viscoelasticity compared to matched healthy volunteers, indicating a widespread tissue integrity degradation, while structure-geometry defining parameters remained unchanged. Cerebral viscoelasticity may represent a novel *in vivo* marker of neuroinflammatory and neurodegenerative pathology.

Introduction

The pathologic hallmarks of multiple sclerosis (MS) are inflammatory foci with demyelination, axonal degeneration, and reactive gliosis (Pittock and Lucchinetti, 2007). Although magnetic resonance imaging (MRI) has become the most important paraclinical tool for diagnosis and monitoring of MS, conventional MRI parameters correlate only modestly with the clinical course and neurological disability (Barkhof, 2002). Thus, new imaging modalities that provide a more specific measure of *in vivo* histopathological and cellular aspects of the disease process are needed (Miller et al., 2003). A direct measure of the tissue constitution could be based on the assessment of cell adhesion and tissue scaffold rigidity by measuring the macroscopic viscoelasticity of the brain parenchyma (Fung, 1993). Tactile measures of viscoelasticity are, for example, the stiffness or the softness of a given tissue, that can be obtained by simple palpation, as routinely employed during the physical examinations. The brain, however, is protected from our sense of touch, limiting the present knowledge on *in vivo* cerebral viscoelasticity and its relation to central nervous system pathologies. In a technical "palpation", known as magnetic resonance elastography (MRE), shear waves are applied with frequencies at the acoustic range, and a phase-sensitive MR sequence is used to detect propagating waves (Muthupillai and Ehman, 1996). Elastographic techniques have previously shown a high sensitivity for detecting subtle tissue alterations in skeletal muscle (Basford et al., 2002; Papazoglou et al., 2006), breast (McKnight et al., 2002; Sinkus et al., 2007) and liver (Asbach et al., 2008) pathologies. Cerebral MRE provides a unique tool measuring the viscoelasticity of brain parenchyma in its intact physiological environment (Kruse et al., 2008; Sack et al., 2008), circumventing the natural mechanical shielding through the skull, cerebrospinal fluid, and meninges. We recently developed a novel sensitive and highly reproducible setup that allows the calculation of global cerebral shear moduli and shear viscosities, based on a head-rocker actuator, the fast acquisition of scalar wave fields using echo planar imaging (EPI), and the analysis of complex-modulus inversion of time-resolved wave images (Sack et al., 2008). Here we investigated the potential of cerebral MRE to detect subtle diffuse parenchymal damage in mildly affected MS patients, that is not represented by macroscopically visible lesions.

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