## In Vivo Waveguide Elastography of White Matter Tracts in the Human Brain

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White matter is composed primarily of myelinated axons which form fibrous, organized structures and can act as waveguides for the anisotropic propagation of sound. The evaluation of their elastic properties requires both knowledge of the orientation of these waveguides in space, as well as knowledge of the waves propagating along and through them. Here, we present waveguide elastography for the evaluation of the elastic properties of white matter tracts in the human brain, in vivo, using a fusion of diffusion tensor imaging, magnetic resonance elastography, spatial-spectral filtering, a Helmholtz decomposition, and anisotropic inversions, and apply this method to evaluate the material parameters of the corticospinal tracts of five healthy human volunteers. We begin with an Orthotropic inversion model and demonstrate that redundancies in the solution for the nine elastic coefficients indicate that the corticospinal tracts can be approximated by a Hexagonal model (transverse isotropy) comprised of five elastic coefficients representative of a medium with fibers aligned parallel to a central axis, and provides longitudinal and transverse wave velocities on the order of 5.7 m/s and 2.1 m/s, respectively. This method is intended as a new modality to assess white matter structure and health by means of the evaluation of the anisotropic elasticity tensor of nerve fibers. Magn Reson Med 000:000-000, 2012. © 2012 Wiley Periodicals, Inc.

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The human brain has close to 100 billion neurons which are "wired" by axons and dendrites. With a total length of 63,140 miles inside the average skull, neuronal fibers determine brain morphology and account for important functional aspects associated with learning and mental health (1). Today, most information about the relationship between neuronal fiber architecture and in vivo human brain physiology is gathered by MRI-based diffusion tensor imaging (DTI) (2). DTI has become particularly important for the neuroscience community in the

study of structural connectivity and integrity of normal and diseased brain white matter. With DTI, one can also reliably visualize the brain's major white matter tracts, which is an application of DTI that is routinely implemented in the preparation and planning of neurosurgical procedures. Parameters derived from the DTI data, e.g., fractional anisotropy, have been shown to be a sensitive measure indicating microstructural damage that may not be detected with standard imaging sequences (3,4). The physical quantity behind DTI is the water diffusion coefficient. This coefficient is correlated to the displacement of diffusing water that is indirectly related to the directionality and integrity of the underlying tissue structure (5). Magnetic resonance elastography (MRE) is a more direct macroscopic measure of the inherent tissue constitution that is based on viscoelastic constants (6-8). MRE is capable of elucidating mechanical properties of the brain, in vivo, and may allow us to measure the mechanical constants of nerve fibers in their natural environment. MRE exploits the propagation characteristics of time harmonic elastic waves by analyzing wave speed and wave damping which are related to the complex moduli. Thus far, MRE of the brain (9-11) has been applied to study global changes in cerebral viscoelasticity induced by physiological aging (12), multiple sclerosis (13), hydrocephalus (14,15) and Alzheimer's disease (16). All these studies were based on the assumptions of local homogeneity and isotropy of the derived viscoelastic constants.

Here, we introduce waveguide elastography, that combines DTI, MRE, spatial-spectral filtering, a Helmholtz decomposition, and inversions for the assessment of the anisotropic elastic constants of single nerve fiber bundles in five healthy human volunteers. Therefore, we use DTI to delineate 3D-anatomy of the corticospinal tracts (CSTs) which will be shown to act as waveguides for externally induced shear waves at a 50 Hz drive frequency. 3D-vector field MRE is performed at the same spatial resolution and voxel position achieved by DTI to track the propagation of waves traveling at specific angles to the fiber directions. From the waveguide analysis (17–19) the full anisotropic elasticity tensor assuming an Orthotropic material model is accessible. DTI-MRE with waveguide elasticity inversion combines the strengths of DTI in detecting heterogeneity and structural anisotropy with the capability of MRE to deliver diagnostically meaningful constitutive parameters. It should be mentioned that the elastic coefficients we recover may only be viewed as "effective" parameters, as both the shape of the waveguides as well as boundary conditions affect the resulting vibrational behavior of waves along

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