Detection of Amyotrophic Lateral Sclerosis using In Vivo Waveguide Elastography

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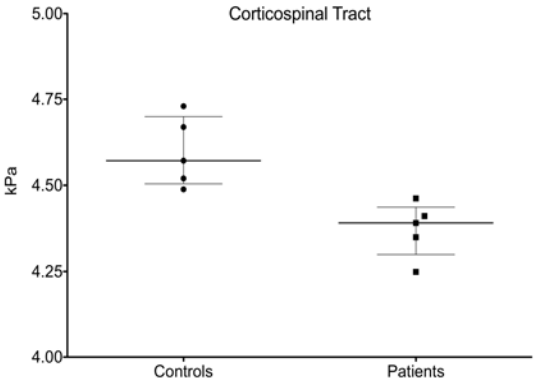
Background: The noninvasive diagnosis of brain health and pathology using MR Elastography (MRE) is a very active area of research[1-2]. Previously, we implemented a new MRE method called Waveguide Elastography (WGE) [3]. WGE combines the information from two imaging methods, i.e. MRE and DTI (Diffusion Tenor Imaging). It evaluates material parameters while taking the directionality of brain fiber tracts into account. Using WGE we recently demonstrated material parameters along the cortispinal tract (CST) of five healthy human volunteers. Here, we extend our approach and test WGE regarding sensitivity to pathologic changes. We investigated patients suffering from Amyotrophic Lateral Sclerosis (ALS), a neurodegenerative disease that primarily affects the CST and hypothesized that the stiffness values of the CSTs in ALS patients would be significantly lower than the control group. The diagnosis of ALS is still largely based on clinical signs of upper and lower motor neuron involvement that can be difficult to detect [4].

Methods: Waveguide Elastography uses information on the pathways along which elastic waves may travel, as well as a measurement of the dynamic displacements within the volume surrounding the pathways. Given the knowledge of the position vectors of a pathway, a spatial-spectral filter with a wavenumber window width from 100-200 was applied to the measured displacements to identify only those principal wave components which were traveling at particular angles to and along the fibers at every point. A further Helmholtz decomposition is implemented which separates the total field into its longitudinal and transverse components. An orthotropic inversion was then performed along the fibers to evaluate the stiffness values. By filtering along six specific directions within the local reference frame of the fiber tracts, the equations of motion decouple which allows each of the nine elastic coefficients to be solved for independently of one another. This approach enables lower order anisotropic models (such as Hexagonal or Cubic, for example) to be exposed as valid by exposing redundancies in the orthotropic coefficients.

All measurements were performed on a 1.5T clinical MRI scanner (Siemens, Erlangen, Germany). For MRE a single-shot spin-echo EPI sequence with flow-compensated motion-encoding gradient (MEG) was used (TR/TE = 240/99, 30 slices with an isotropic resolution of 2x2x2 mm^3). Motion was induced by a head-cradle connected to a non-magnetic vibration generator at the end of the patient table. Measurements were performed at 50 Hz along all three motion encoding directions and at eight time samples within a vibration period. DTI data was acquired in the same session using a single-shot EPI sequence (TR/TE-8500/96 ms, 12 non-colinear directions and one B_0 volume, b-value=1000 mm/s^2, 6 averages). Tensor calculation and tractography of the corticospinal tract was performed with tools from the FMRIB Software Library (FSL), i.e. dtifit and probtrackx.



Results: Ten subjects were included in this study with ages ranging from 51-70 years. Of these, five were healthy controls and five were patients who presented with ALS. Using WGE we found significant differences between patients and controls. The Figure to the left shows the mean values in kPa of the real component of the shear coefficient, $C_{44,}$ from our inversions on the CSTs. These results indicate that the mean stiffness of the patients was about 5% lower compared to controls ($p = 0.008$ - respecting the small sample size a Mann-Whitney-U test was used). Error bars in the Figure represent the interquartile range (i.e. the 25^{th} to the 75^{th} quartile).

In summary Waveguide Elastography, i.e. combining MRE, DTI, and anisotropic inversions, was able to detect the difference between healthy and diseased CSTs at 50 Hz. Interestingly, the use of a traditional isotropic inversion algorithm provided no significant group difference. We think this is due to the fact that the anisotropic analysis is more sensitive to myelin degradation along the waveguides.

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