Property Differences in White Matter Structures due to Distinct Wave Propagation Directions in MR Elastography

Aaron T Anderson[1], Curtis L Johnson[2], Joseph L Holtrop[2,3], Elijah EW Van Houten[4,5], Mathew DJ McGarry[5], Keith D Paulsen[5,6], Bradley P Sutton[2,3], and John G Georgiadis[1,2]

[1]Mechanical Science & Engineering, University of Illinois at Urbana-Champaign, Urbana, IL, United States, [2]Beckman Institute for Advanced Science, University of Illinois at Urbana-Champaign, Urbana, IL, United States, [3]Bioengineering, University of Illinois at Urbana-Champaign, Urbana, IL, United States, [4]Département de Génie Mécanique, Université de Sherbrooke, Sherbrooke, QC, Canada, [5]Thayer School of Engineering, Dartmouth College, Hanover, NH, United States, [6]Dartmouth-Hitchcock Medical Center, Lebanon, NH, United States

INTRODUCTION: Many of the mechanisms proposed to explain how the brain changes during normal aging (senescence) or neurodegeneration are based on advanced age or advanced stages of the disease. This involves retrospective reasoning; distinguishing cause from effect requires prospective studies. This is where the contribution of magnetic resonance elastography (MRE) is most promising. In combination with diffusion tensor imaging (DTI), MRE can provide tract-based measurements of the local mechanical properties of the tissue, which are intrinsic properties representing axon/glial matrix structural integrity. To investigate how these properties are related to brain microstructure, one needs to understand how the MRE measurement is affected by tissue mechanics. Direction-dependent shear wave propagation in white matter (WM) regions of the human brain was demonstrated by Romano et al. [1], which highlights the importance of investigating the effect of propagation direction on fiber bundles. In a typical MRE excitation arrangement, we do not have control over local wave propagation directions, and thus may be biasing the property estimates in a mechanically anisotropic material like the brain. The focus of this investigation is to quantify the effect of propagation direction on the reconstructed material properties and examine their relationship to the underlying microstructure in a well-ordered region of the brain (corpus callosum).

METHODS: Three healthy subjects aged (25-29 years old) underwent a single human brain MRE experiment with two distinct excitation directions applied along with structural imaging. A Resoundant© pneumatic forcing system was used at the anterior, for anterior-posterior excitation (A-P), and right side, for left-right excitation (L-R), at 50 Hz for each experiment. Displacement fields were acquired using a 3D multislab, multishot spiral sequence on a Siemens 3T Trio scanner with 12-channel head coil [2]. Imaging parameters included: TR/TE = 1800/73 ms; FOV = 240mm; matrix = 120x120; slices = 60 (2mm thick). The large FOV allowed for full coverage of the brain. Isotropic nonlinear inversion (NLI) [3] was employed to reconstruct maps of the viscoelastic material properties, storage modulus (G') and loss modulus (G''), for each excitation direction. Additionally, 30-direction DTI data were acquired during the same experiment over the same FOV in a co-registered fashion. Finally, a high-resolution MPRAGE acquisition was used to register a white matter tract atlas [4] to the MRE data following a previously described procedure [5].

RESULTS and DISCUSSION: Figure 1 shows an axial slice, inferior to the body of the corpus callosum, of the property reconstruction (G' and G'') for each excitation direction, structural T2, and fractional anisotropy (FA) from DTI. The differences in both the storage modulus (G') and the loss modulus (G'') for the two excitation directions highlight the significant effect of excitation modes on the highly anisotropic white matter (WM) tissue. For example, the genu and splenium of the corpus callosum (CC) are regions with highly ordered structures and the isotropic NLI reconstructions shows the largest discrepancy in G', on the order of ~2 kPa. Using the complex motion field, the wave direction was computed [6] to elucidate the local excitation modes along these well-ordered structures of interest (see Figure 2). Registration with the JHU-ICBM WM atlas [4] allowed for the extraction of the CC and other well-ordered WM structures. Figure 2 shows a scatter plot of the extracted G' versus the directional cosine between the unit dominant local fiber orientation ($\mathbf{V}_1$, obtained via DTI) and the unit wave direction for the CC ($\mathbf{u}_{wave}$). As a general trend, the storage modulus increases as the wave direction aligns with the local fiber bundle direction. This is consistent with previous experimental work [7] indicating that myelinated neurons are stiffer than the glial matrix. Further, this trend appears to agree with the hypothesis that the loss modulus is governed by the geometric organization of white matter [8], which may be determined by the integrity of the glial matrix [9].

CONCLUSION: The differences in storage modulus (G') and the loss modulus (G'') due to the different excitation directions highlight the importance of choosing an appropriate material model for the tissue so that MRE can accurately probe the microstructure. Analysis of different excitation modes shows the effect of the anisotropy of well-ordered white matter bundles on the reconstruction based on isotropic model. Clearly, the adoption of an anisotropic model is warranted.

ACKNOWLEDGEMENTS: Wave analysis code courtesy of P. Bayly [6]. Computational support provided by Calcul Quebec and UIUC-NCSA Blue Waters. Financial support by NSF grant CMMI-1437113.

REFERENCES: [1] A Romano, *et al.*, *Magn Reson Med*, 2012, 68(5):1410-1422; [2] CL Johnson, *et al.*, *Magn Reson Med*, 2014, 71(2):477-485; [3] EEW Van Houten, *et al.*, *Med Phys*, 2011, 38(4):1993-2004; [4] Mori et al., MRI Atlas of Human WM, 2005; [5] CL Johnson, *et al., NeuroImage*, 2013, 79:145-152; [6] EH Clayton, et al., J. R. Soc. Interface, 2012, 9:2899-2910; [7] YB Lu, et al., *PNAS*, 2006; 103(47):17759-17764; [8] I Sack, *et al., Soft Matter,* 2013, 9(24):5672-5680; [9] K Schregel, *et al.*, *PNAS*, 2012, 109(17):6650-6655.

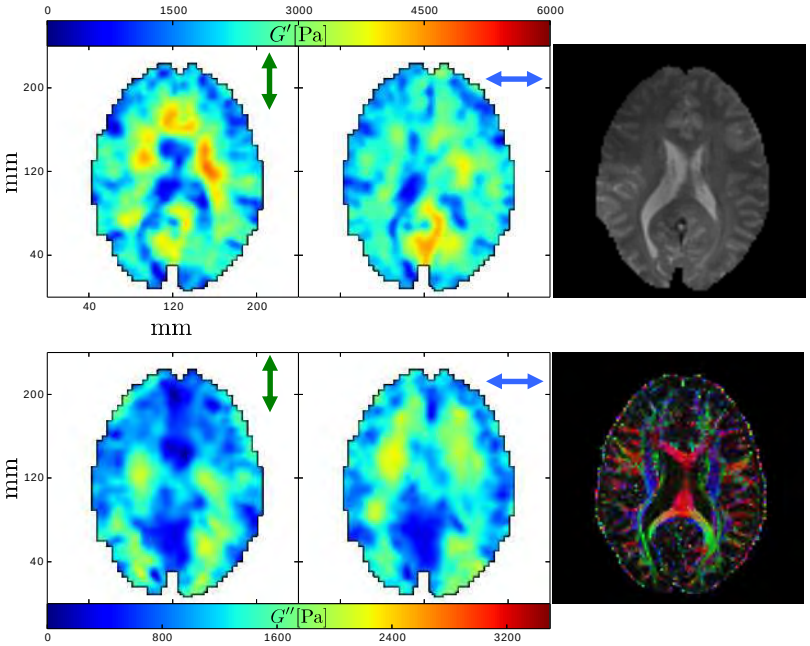

Figure 1: An axial slice of the computed storage modulus (G') and loss modulus (G'') for each excitation (↕A-P & ↔L-R); T2, and DTI fractional anisotropy (FA).

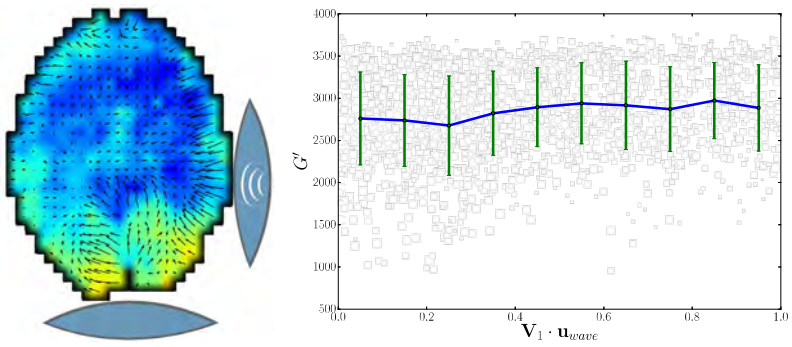

Figure 2: Wave direction for L-R excitation: vectors denote in-plane motion and color map shows out-of-plane motion (blue: down & red: up); a scatter plot of G' versus the dot product of dominant DTI vector and wave direction in the corpus callosum, points are scaled based on FA.