Observation of direction-dependent mechanical properties in the human brain with multi-excitation MR elastography

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Abstract

Magnetic resonance elastography (MRE) has shown promise in noninvasively capturing changes in mechanical properties of the human brain caused by neurodegenerative conditions. MRE involves vibrating the brain to generate shear waves, imaging those waves with MRI, and solving an inverse problem to determine mechanical properties. Despite the known anisotropic nature of brain tissue, the inverse problem in brain MRE is based on an isotropic mechanical model. In this study, distinct wave patterns are generated in the brain through the use of multiple excitation directions in order to characterize the potential impact of anisotropic tissue mechanics on isotropic inversion meth-

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ods. Isotropic inversions of two unique displacement fields result in mechanical property maps that vary locally in areas of highly aligned white matter. Investigation of the corpus callosum, corona radiata, and superior longitudinal fasciculus, three highly-ordered white matter tracts, revealed differences in estimated properties between excitations of up to 33%. Using diffusion tensor imaging to identify dominant fiber orientation of bundles, relationships between estimated isotropic properties and shear asymmetry are revealed. This study has implications for future isotropic and anisotropic MRE studies of white matter tracts in the human brain.

Keywords: magnetic resonance elastography; nonlinear inversion; anisotropic soft tissue; stiffness; human brain; white matter

1. Introduction

Neurodegeneration occurring in conditions such as Alzheimer’s disease, amyotrophic lateral sclerosis, multiple sclerosis, and normal aging affects macroscale brain tissue characteristics due to microscale tissue changes. The alteration of the neuronal and glial matrix can result in detectable changes in physical material characteristics, including mechanical properties. Magnetic resonance elastography (MRE) is a technique for noninvasively assessing tissue viscoelasticity in vivo [1]. The mechanical contrast afforded by MRE has shown great promise in diagnosing and staging a variety of conditions, most notably chronic liver disease [2, 3], and MRE of the brain has recently revealed softening in a number of neurodegenerative conditions [4, 5, 6, 7, 8, 9].

Despite the success of brain MRE, most common methodological approaches adopt an oversimplified model of the complex tissue behavior that affects the accuracy and precision of the property measures. In particular, MRE typically assumes the material is isotropic, i.e. it does not exhibit direction-dependent properties, despite the fibrous structure of brain tissue, especially white matter (WM). A number of studies on animal brains suggest the necessity of considering anisotropic tissue properties in assessing the brain with MRE [10, 11, 12, 13, 14,

15]. For instance, Velardi et al. [16] performed an ex vivo axial test of porcine WM and found that when stretched along the fiber direction stiffness appeared approximately three times greater than when stretched against the fibers. Feng et al. [10] performed shear tests on ex vivo lamb brains and found the shear modulus to be approximately 40% greater along the fiber than against. Similar behavior is expected in human brains given the shared fiber structure.

The adoption of an isotropic material model for brain MRE, in spite of the evidence supporting tissue anisotropy, is motivated by the need to maintain stability in solving the ill-posed inverse problem. Anisotropic models require additional material parameters to be estimated while enforcing isotropy reduces the burden on the inversion of noisy data. Though recent work has aimed to estimate anisotropic tissue properties with MRE [11, 12, 13, 14, 17, 18, 19, 20], including specific WM tracts in the brain [7, 15, 21, 22, 23], the effect of WM anisotropy on traditional isotropic inversion schemes has yet to be fully characterized [24].

The present study aims to explore the differences in reconstructed isotropic mechanical properties of the brain in the presence of unique mechanical excitations. We aim to use a multi-excitation MRE setup to generate distinct shear patterns in the brain, and will evaluate our hypothesis that the directionality of shear strain relative to WM fiber orientation influences mechanical property estimation. Local fiber orientation will be determined using diffusion tensor imaging (DTI) in three major WM tracts of interest: corpus callosum (CC), corona radiata (CR), and superior longitudinal fasciculus (SLF).

2. Methods

A single 28-year-old healthy male subject participated in this study approved by the University of Illinois at Urbana-Champaign Institutional Review Board after providing written informed consent. The imaging protocol consisted of two MRE scans performed using two separate actuator setups, DTI, and a high-resolution structural acquisition (MPRAGE). All scanning was performed on a

Siemens 3T Trio MRI scanner (Siemens Medical Solutions; Erlangen, Germany). Four repeats of the imaging protocol were performed on the same subject. These repeats were collected on different days, spread across four months.

2.1. MRE Acquisition

MRE displacement imaging used a 3D multislabs, multishot spiral MRE sequence for generating 3D, full vector field complex displacement data at 50 Hz with $2 \times 2 \times 2 \text{ mm}^3$ isotropic spatial resolution [25]. The specific imaging parameters for MRE include single shot in-plane spiral readout with SENSE $R = 3$; ten slabs of eight k_z sampling planes with 25% slab overlap; $TR/TE = 1800/73 \text{ ms}$; four (4) temporal phase offsets; and $FOV = 240 \times 240 \times 120 \text{ mm}$. Small strains ($\sim 10^{-5}$) in the brain were induced through whole-head vibrations using a pneumatic actuator system (Resoundant, Inc., Rochester, MN). In order to create distinct excitation patterns, two passive drivers are positioned on the patient's head inside of the head coil: a soft pillow-like pad under the posterior of the head (Figure 1(a)) and a harder pad on the right side of the head (Figure 1(b)). The soft pad is often used for head MRE experiments [26, 27] due to its slim profile allowing it to fit comfortably in the standard MRI head coil. Additionally, the position posterior to the head results in good coupling to the skull through the weight of the head. The hard pad was used for the LR experiment to achieve adequate coupling with the head through contact with both the skull and the side of the head coil. The dimensions of the head coil precluded the use of soft pad for the LR excitation case. The MRE scan was performed twice with one driver activated for the entire imaging experiment at a time. The actuator driver is switched manually through a connection on the pneumatic tube between scans without altering the head position. As expected, the two excitation directions, referred to as anterior-posterior (AP) and left-right (LR), provide distinct deformation fields in the human brain (see Figure 1). In order to ensure optimal contact and sufficiently minimize involuntary movement of the head, foam pads were placed between the head and the MR coil on the subject's left side, and the driver adjacent to the right side of the head and the

coil.

2.2. Material Property Reconstruction

Each of the individual displacement fields from MRE imaging were reconstructed into full brain material property maps using the finite element based non-linear inversion algorithm (NLI) [28, 29, 30, 31]. NLI is based on an a priori model for mechanical tissue behavior, which in this case is a heterogeneous, isotropic, viscoelastic material model. This is governed by Navier's equation of the form

$$\nabla \cdot (\mu(\nabla \tilde{\mathbf{u}} + \nabla \tilde{\mathbf{u}}^T)) + \nabla(\lambda \nabla \cdot \tilde{\mathbf{u}}) = \rho \frac{\partial^2 \tilde{\mathbf{u}}}{\partial t^2}, \quad (1)$$

where $\tilde{\mathbf{u}}$ is the 3D displacement field, λ and μ are Lamé's material constants, ρ is the density (assumed to be 1000 kg/m³), and ∇ is the gradient operator. The complex displacement field is assumed to be at a steady-state of the form $\tilde{\mathbf{u}}(x, y, z, t) = \mathbf{u}(x, y, z) \exp(i\omega t)$ (where $\mathbf{u}(x, y, z)$ is complex), and the governing equation, Eq. (1), then simplifies to

$$\nabla \cdot (\mu(\nabla \mathbf{u} + \nabla \mathbf{u}^T)) + \nabla(\lambda \nabla \cdot \mathbf{u}) = -\rho \omega^2 \mathbf{u}. \quad (2)$$

NLI employs a finite element representation of the object in order to compute an expected displacement field ($\mathbf{u}_c$) from an estimate of the material properties ($\theta = [G', G'']$). This is then compared to the measured displacement field ($\mathbf{u}_m$), and the material property estimation is iteratively updated in order to minimize a mean-squared error cost function

$$\Phi = \sum_{\Omega} \|\mathbf{u}_c(\theta) - \mathbf{u}_m\|^2 \quad (3)$$

where the summation is over the physical domain of interest, Ω . The result of the reconstruction is a spatial map of the complex shear modulus $\mu = G = G' + iG''$, where G' and G'' are the storage and loss modulus, respectively. To reduce the overall computational costs, minimization of Eq. (3) is reformatted in parallel as *subzone* subdomains of the full physical domain, Ω .

2.3. Other Imaging

DTI data was acquired in the same imaging session in a co-registered fashion with FOV and resolution matched to the MRE data. DTI parameters include: single-shot EPI with GRAPPA $R = 2$; $TR/TE = 8000/95$ ms; 30 non-collinear encoding directions; $b = 1000$ s/mm². The diffusion tensor was processed using FMRIB Diffusion Toolkit (FDT) [32] to extract the voxel-wise diffusion eigenvectors. Finally, we acquired a T_1 -weighted structural image using an MPRAGE sequence, which resulted in a $0.9 \times 0.9 \times 0.9$ mm³ isotropic resolution ($TR/TI/TE = 2000/900/2.2$ ms).

2.4. Analysis

2.4.1. Computing Strain

First the strain is calculated from MRE displacement fields to investigate the strain at each voxel to better understand how the strain state is related to the reconstructed properties from NLI between the two excitation directions. Isotropic tissue will behave the same under different shear modes; conversely, anisotropic material will respond differently in each independent property direction. The strain is computed from the MRE displacement at each temporal phase offset via

$$\varepsilon_{ij}(x_k, t_n) = \frac{1}{2} (u_{i,j} + u_{j,i})(x_k, t_n) \quad (4)$$

where x_k is the spatial coordinate and t_n is the time at point n . The strain tensor is symmetric, and thus can be written as

$$\begin{aligned} \frac{1}{2} (u_{i,j} + u_{j,i})(x_k, t_n) &= \\ &= \begin{bmatrix} u_{11} & \frac{1}{2}(u_{12} + u_{21}) & \frac{1}{2}(u_{13} + u_{31}) \\ \frac{1}{2}(u_{21} + u_{12}) & u_{22} & \frac{1}{2}(u_{23} + u_{32}) \\ \frac{1}{2}(u_{31} + u_{13}) & \frac{1}{2}(u_{32} + u_{23}) & u_{33} \end{bmatrix} (x_k, t_n) = \\ &= \begin{bmatrix} \varepsilon_{11} & \varepsilon_{12} & \varepsilon_{13} \\ \varepsilon_{12} & \varepsilon_{22} & \varepsilon_{23} \\ \varepsilon_{13} & \varepsilon_{23} & \varepsilon_{33} \end{bmatrix} (x_k, t_n), \quad (5) \end{aligned}$$

The root-mean-square (RMS),

$$\varepsilon_{rms,ij}(x_k) = \sqrt{\frac{1}{N_t} \sum_{n=1}^{N_t} [\varepsilon_{ij}(x_k, t_n)]^2}, \quad (6)$$

is computed to obtain a magnitude of the oscillatory shear and normal strains across the temporal phase offsets. Maps of the RMS values for the shear components of the strain tensor are shown in Figure 2. It is important to note the strain calculations were performed independent from NLI to reduce bias from the specific NLI formulation.

2.4.2. Fiber-Tract Reference Frame

NLI is formulated with respect to the imaging reference frame, and all inversions in this work are completed in this reference frame. However, we seek to understand how isotropic MRE reconstructions of an expected anisotropic material, and thus we want to compute the strain state relative to the direction of neuronal fiber bundles, which represent the presumed axis of symmetry in a transversely isotropic material [12, 15]. The strain tensor at each voxel, Eq. (4), can be transformed from the lab (imaging) reference frame of the MRE images, $\hat{x}^l$, into the axonal fiber-tract reference frame, $\hat{x}^f$, by constructing a transformation matrix from the DTI eigenvectors (V_j). The DTI eigenvectors, assumed to be the fiber orientation reference frame in typical DTI, are the local coordinate system of the voxel, where $\hat{x}_j^f = V_j$ and $\hat{x}_1^f$ corresponds to the principal fiber direction, while $\hat{x}_2^f$ and $\hat{x}_3^f$ correspond to the two directions perpendicular to the fiber-tracts. The transformation tensor is constructed via the cosine of the angle between the lab and fiber coordinates:

$$[T] = \cos(\hat{x}_i^l, \hat{x}_j^f). \quad (7)$$

The transformation of the strains in the lab coordinates into the fiber-tract's local orientation is then computed for each time point

$$[\varepsilon^f] = [T^T][\varepsilon^l][T] \quad (8)$$

and the RMS of strain is calculated in the same fashion as in section 2.4.1. In order to highlight the asymmetry of shear strains relative to fiber-tracts and thus the likely anisotropic response, the shear strains in planes *parallel*, ε_{12}^f and ε_{13}^f , and *perpendicular*, ε_{23}^f , to the dominant fiber direction, $\hat{x}_1^f$, are compared via

$$\varepsilon_{\parallel/\perp} = \frac{\frac{1}{2}(\varepsilon_{12}^f + \varepsilon_{13}^f)}{\varepsilon_{23}^f}. \quad (9)$$

The spatial, multiple experiment averages of Eq. (9) are computed for various regions of the brain in Table 3, with (*) indicating statistically significant differences determined by a paired *t*-test.

2.4.3. Registration

The images from a given scanning session are acquired in a co-registered fashion (both MRE scans and DTI scan). The DTI acquired during each experiment is used to register these data for identifying the WM regions of interest through an atlas [33] using the FSL TBSS tool [34]. The WM tracts investigated in this study are the corpus callosum (CC), corona radiata (CR), and superior longitudinal fasciculus (SLF). Additionally, the FAST tool in FSL [35] segmented the MPAGE to delineate the global WM region from the images for comparison with the individual tract (CC, CR, and SLF) statistics.

3. Results

An example of the differences in displacement fields for a subject undergoing two different excitations is shown in Figure 1. The displacement fields show a different displacement pattern for each excitation, particularly for the out-of-plane direction. AP excitation results in patterns with left-right symmetry, while the LR excitation exhibits anterior-posterior symmetry, as expected. The uniqueness of patterns is indicative of differentially excited shear modes, which results in distinct strain fields, and the distinct fields are necessary for investigating direction-dependent responses. Displacement fields from both AP (soft pad) and LR (hard pad) excitation were of sufficiently high quality for inversion,

with octahedral shear strain-based SNR (OSS-SNR) for all displacement fields greater than 3 [36].

Figure 2 shows the RMS strain of the displacement field for the same axial slice as in Figure 1. At the posterior of the subject’s head, both excitation directions have the strongest strain magnitudes due to the shear source at the skull and falx. However, the strain throughout the brain has voxel-wise spatial variation differing with excitation direction, especially as the shear propagates towards the center. The AP excitation shows the outline of the ventricle region in each of the strain components, which is less visible in LR excitation. The lack of definition in strain patterns for LR at the center may be due to the excitation wave passing across the long side of the ventricles.

Figure 3 presents an example of the reconstructed material property maps for the storage (G') and loss (G'') moduli at an axial slice encompassing regions adjacent to the lateral ventricles, the CC, and the CR. Note that the change of excitation orientation results in voxel-wise differences in G' and G'' of up to approximately 2 kPa. Such large differences between the AP and LR excitation appear mostly in areas with high DTI fractional anisotropy (FA): $\overline{FA}_{CC} = 0.70$, $\overline{FA}_{CR} = 0.51$, and $\overline{FA}_{SLF} = 0.50$.

A summary of the mean and standard deviation of reconstructed G' and G'' moduli across the repeated experiments for the entire brain, global WM, CC, CR, and SLF are given in Tables 1 and 2. Values are reported for each excitation and the relation between the two, with (*) indicating statistically significant differences determined by a paired t -test. The whole brain averages for G' and G'' for both excitation directions are consistent with published values and exhibit very low standard deviations across repeated experiments ($\leq 2\%$), indicating excellent reproducibility, in agreement with other brain MRE studies using NLI [26, 37]. Similarly, the global WM region exhibits consistent G' and G'' between excitations and comparable reproducibility.

Additionally, both global regions exhibit comparable and reproducible ratios of shear parallel to perpendicular with respect to dominant fiber-tracts direction,

$\varepsilon_{\parallel/\perp}^f$ (Eq. (9)), as summarized in Table 3. This is expected as the global regions do not isolate specific, ordered fiber-tracts.

The spatial mean values for G' and G'' in each WM tract for each experiment are plotted in Figure 4 against the spatial mean values for $\varepsilon_{\parallel/\perp}^f$. The CC shows the largest difference between reconstructed G' and G'' , 23% and 26% on average, for the two excitation experiments. Both G' and G'' are greater in LR excitation experiments, which corresponds to a greater $\varepsilon_{\parallel/\perp}^f$. The CR similarly exhibits greater G' and G'' in LR excitation; although, in contrast, there is a slight decrease in $\varepsilon_{\parallel/\perp}^f$. The SLF shows no discernible difference in either G' or G'' , potentially due to the variability of $\varepsilon_{\parallel/\perp}^f$ in both LR and AP excitations.

4. Discussion

The AP and LR excitations each provide distinct deformation states in the human brain, as evidenced by both the displacement fields (Figure 1) and the computed RMS shear strain fields (Figure 2). The unique strain fields are a necessary start for characterizing how MRE interprets shear strain applied to anisotropic media. The discrepancies (locally over 2kPa) in reconstructed G' and G'' (Figure 3) show the inherent limitation of the isotropic assumption used for the NLI material model when investigating anisotropic media.

The mean and standard deviation statistics (Tables 1, 2, and 3) for results in the whole brain, global WM, and individual WM regions (CC, CR, and SLF tracts) help provide initial context for the local effect of shear strain mode on the reconstructed material properties. The differences between excitation for global G' , G'' , and shear strain ($\varepsilon_{\parallel/\perp}^f$) are $< 1.5\%$ across all repeats. The findings for global WM are similar, with non-significant differences of $< 3.5\%$ between excitations.

Significant differences in reconstructed material properties occur in areas of the highest local anisotropy, as well as the greatest difference in shear strain ratio. The $\varepsilon_{\parallel/\perp}^f$ in the CC differed between the two excitations by 22.3% (normalized) and both the reconstructed G' and G'' had over 20% normalized dif-

ference, 23% and 26%, respectively. The stark difference in properties in the CC is not surprising, as the CC has a highly-aligned, well-ordered fiber structure [38] known to exhibit mechanical anisotropy [16, 39], and the two excitation fields provide sufficiently different strain states expected to illuminate direction-dependent properties in MRE. This is highlighted by Figure 4(a), where the CC properties show a linear increase in both G' and G'' with increasing $\varepsilon_{\parallel/\perp}^f$. In other words, the tissue appears stiffer when exposed to strains in planes parallel to the dominant fiber axis. This apparent relationship suggests that as the disparity in axonal shear components changes, the isotropic MRE inversion effectively “sees” a different underlying material.

The relationship between excitation mode and reconstructed MRE properties is less clear in the CR. In this case, we found a much smaller difference in shear strain ratio between excitations (8.8%). This translated in to a small, non-significant difference in G' (11%), but a large, significant difference in G'' (33%). Most interestingly, the apparent relationship between G' and G'' in the CR with $\varepsilon_{\parallel/\perp}^f$ (Figure 4(b)) is opposite from that of the CC in that G' and G'' decrease with increasing $\varepsilon_{\parallel/\perp}^f$. How the magnitude and the relationship between MRE properties and strain state in the CR differs from those in the CC may be explained by the more complex fiber structure of the CR. The CR encompasses fibers that fan in the superior-inferior direction as they approach the cortex, and also include populations of crossing fibers. The disparity in fiber structure has been previously used to understand MRE properties in the CC and CR [21], and may be underpinning the relationships reported here.

We did not observe differences in G' and G'' for the SLF, even though the SLF is also a large, well-ordered WM tract. We believe that the lack of significant differences in MRE properties between excitation is due to the strain fields themselves not being significantly different. The values for $\varepsilon_{\parallel/\perp}^f$ in the SLF exhibited higher standard deviations across repeats, even though the AP excitation had shown high reproducibility in other measures. This, in turn, resulted in poorer reproducibility of G' and G'' measures in the SLF that likely contributed to the lack of detectable significant difference. This suggests the

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9 strain fields towards the periphery of the brain generated by both excitation
10 directions are very sensitive to the excitation mode, but that they are associated
11 with consistent shear modes in the deeper WM regions.
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13 The scenario of applying unique shear modes to characterize anisotropic ma-
14 terial is similar to applying any type of mechanical tests with forcing in different
15 directions, and has previously been used in MRE experiments on phantoms to
16 characterize anisotropic effects [40, 41, 42, 43]. In these works, the shear di-
17 rection is carefully controlled and applied either along or against the known
18 directions of material symmetry. In the brain, such control over shear direc-
19 tion is not feasible due to poor mechanical transmission through the skull, and
20 also because the material anisotropy is itself spatially-varying. In this work, we
21 use two distinct excitation directions and achieved success in generating shear
22 modes sensitive to material anisotropy in two large WM tracts, the CC and the
23 CR, and not in another, the SLF. Future works could incorporate more excita-
24 tion modes to better capture the behavior of all WM regions in the brain and
25 studies to identify commonalities in WM behavior across a population.
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27 Anisotropic MRE inversion schemes may benefit from adopting a multi-
28 excitation approach. Previous anisotropic methods have aimed to reconstruct
29 direction-dependent mechanical properties from a single deformation field through
30 the incorporation of prior knowledge of material symmetry [11, 12, 14, 15, 17].
31 While the results from these methods appear promising [13, 22, 44], they may
32 suffer in characterizing the heterogeneous anisotropy of the human brain if the
33 excited shear mode is not judiciously chosen to account for material symmetries
34 and sensitive to the material complex properties. By incorporating multiple
35 excitation fields with sensitivities, anisotropic inversions may be stabilized dur-
36 ing the reconstruction of multiple material constants. For example, Tweten et
37 al. [42] and Schmidt et al. [43] performed controlled actuation studies on nu-
38 merical phantoms[42], physical phantoms, and ex vivo tissue[43]. Both studies
39 are important to anisotropic MRE because they show how a three parameter
40 incompressible transversely isotropic material model can capture more informa-
41 tion than the typical transversely isotropic model, including fiber stretch. The
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work in this study, in contrast, did not take into account the polarization of shear waves, but, as we move to higher order models, we should be careful to consider the potential effects of fiber stretching.

Finally, it is important to consider the implications of our findings on the interpretation of MRE results in WM tracts from traditional, single-frequency experiments. While we report that excitation mode and the amount of shear strain parallel and perpendicular to the plane containing the dominant fiber direction can result in significant differences in estimated mechanical properties, we, also, note that results from the AP excitation alone are very repeatable. AP excitation is the most common type of excitation used in brain MRE, generally achieved through pneumatic actuation of a soft pillow [4, 45] or a head rocker driven by remote electromechanical actuation [25, 46, 47]. LR excitation from a bite bar [48, 49, 50], lateral pneumatic actuation [51], or scanner table vibration [52] is less commonly employed. In this case, we can expect that the use of AP excitation will result in highly repeatable measurements of WM tracts, as has been reported previously [21, 47], and that these measurements should be considered less sensitive to the excitation mode.

5. Conclusions

Material testing of animal brains has shown the mechanical anisotropy of brain tissue is significant and the human brain is expected to exhibit similar anisotropic properties. However, MRE methods have typically adopted an isotropic material model for considering the brain, thus ignoring direction-dependent material properties expected to be present in WM. In this study, we performed multi-excitation MRE experiments and observed distinct differences in reconstructed isotropic material properties of well-ordered WM tracts due to excitation of unique shear modes. The differences arise from the anisotropic medium being sheared in different directions and the isotropic reconstruction “seeing” different properties depending on whether the material is sheared in planes parallel or perpendicular to the fibers. Through the use of both AP and

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9 LR excitations, we observed differences in reconstructed MRE properties, G' and
10 G'' , of up to 33% in WM tracts, while finding no difference in global properties.
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12 These findings have implications for future experiments and methodological de-
13 velopments targeting the reconstruction of anisotropic mechanical properties
14 of WM, and may provide additional contrast for elucidating microstructural
15 processes of neurodegeneration.
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Figure 1: The real component of the complex displacement fields ($\tilde{u} = \{\tilde{u}, \tilde{v}, \tilde{w}\}$) generated by excitation from two different actuator setups: (a) anterior-posterior (AP) and (b) left-right (LR). The two excitations produce distinctly different patterns, particularly for the out-of-plane direction. AP excitation results in patterns with left-right symmetry, while the LR excitation exhibits anterior-posterior symmetry, as expected.

Table 1: Summary of mean and standard deviation for the reconstructed storage modulus, G' , across experimental repeats of spatial averages of the whole brain, global WM, and selected WM regions (CC, CR, and SLF); (*) represents $p < 0.05$ for the normalized differences; $\overline{(\cdot)}$ is a two value average.

	Whole Brain	WM	CC	CR	SLF
$\overline{G'_{AP}}$	2.45 (1.1%)	2.68 (1.2%)	2.24 (1.3%)	3.03 (1.6%)	2.85 (1.9%)
$\overline{G'_{LR}}$	2.48 (1.6%)	2.74 (1.7%)	2.81 (4.2%)	3.32 (5.7%)	2.82 (5.2%)
$\frac{(\overline{G'_{AP}} - \overline{G'_{LR}})}{(\overline{G'_{AP}}, \overline{G'_{LR}})}$	-1.2%	-2.2%	-23%*	-11%	1.3%

Figure 2: The RMS shear strain components of the strain tensor from both the anterior-posterior (AP) and left-right (LR) excitations. There are similar high magnitude regions for each direction but, also, distinct differences where the excitation was applied to the subject's head.

Table 2: Summary of mean and standard deviation for the reconstructed shear modulus, G'' , across experimental repeats of spatial averages of the whole brain, global WM, and selected WM regions (CC, CR, and SLF); (*) represents $p < 0.05$ for the normalized differences; $\overline{(\)}$ is a two value average.

	Whole Brain	WM	CC	CR	SLF
$\overline{G''_{AP}}$	1.07 (2.0%)	1.22 (2.3%)	1.04 (4.6%)	1.49 (3.1%)	1.61 (5.3%)
$\overline{G''_{LR}}$	1.08 (1.8%)	1.25 (2.8%)	1.32 (6.9%)	1.84 (7.1%)	1.56 (5.1%)
$\frac{(\overline{G''_{AP}} - \overline{G''_{LR}})}{(\overline{G''_{AP}}, \overline{G''_{LR}})}$	-0.91%	-2.9%	-26%*	-33%*	4.3%

Figure 3: (a) Fractional anisotropy (FA, color intensity) from DTI (from top-left) coronal, axial and sagittal, where colors describe the fiber-tract's dominant direction: red indicates left-right, blue indicates inferior-superior, and green indicates anterior-posterior; bottom-right is a sagittal magnitude image from MRE data. The reconstructed (b) G' and (c) G'' material maps for anterior-posterior (AP, top) and left-right (LR, bottom) excitations. Significant differences in reconstructed values are easily identified.

Figure 4: Comparison of reconstructed isotropic material properties, G' and G'' , with the strain ratio of shear *parallel* to shear *perpendicular* to fibers in the fiber-tract reference frame $\bar{\epsilon}_{||/\perp}^f$ (Eq. (9)) for (a) corpus callosum, CC, (b) corona radiata, CR, and (c) superior longitudinal fasciculus, SLF. The numerical values of mean and standard deviations across experimental repeats are presented in Tables 1, 2, and 3.

Table 3: Summary of mean and standard deviation for the computed fiber-tract shear strain ratio, $\bar{\epsilon}_{||/\perp}^f$, across experimental repeats of spatial averages of the whole brain, global WM, and selected WM regions (CC, CR, and SLF); (*) represents $p < 0.05$ for the normalized differences; $\overline{(\cdot)}$ is a two value average.

	Whole Brain	WM	CC	CR	SLF
$\bar{\epsilon}_{ /\perp,AP}^f$	1.61 (0.23%)	1.62 (0.23%)	1.34 (2.3%)	1.62 (1.3%)	1.56 (8.0%)
$\bar{\epsilon}_{ /\perp,LR}^f$	1.59 (0.54%)	1.56 (0.30%)	1.66 (9.0%)	1.47 (3.3%)	1.44 (6.1%)
$\frac{(\bar{\epsilon}_{ /\perp,AP}^f - \bar{\epsilon}_{ /\perp,LR}^f)}{(\bar{\epsilon}_{ /\perp,AP}^f + \bar{\epsilon}_{ /\perp,LR}^f)}$	1.3%	3.4%	-22.3%*	8.8%*	7.5%