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Regional Correlation of Stiffness and Perfusion in the Human Brain at 7T MRI through MR Elastography and Arterial Spin Labeling Techniques

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Synopsis

Keywords: Elastography, Elastography, Arterial Spin Labeling

Motivation: We are motivated to understand the impact of **blood flow on the mechanical properties of brain tissue** for applications in neurodegenerative pathophysiology.

Goal(s): Our goal was to establish a novel postprocessing framework for correlation of structural and functional properties characterized by MR elastography (MRE) and pulsed arterial spin labeling (PASL).

Approach: We obtained MRE and PASL in 8 healthy controls, segmented the brain, and conducted regional correlation analyses of elastograms and perfusion maps.

Results: After successful data processing and validation, we found **significant inverse correlations** in the cortical gray matter, some cortex regions, as well as a similar nonsignificant trend in other regions.

Impact: These study results, which show a **perfusion–stiffness relationship** in some brain regions, point to an underlying biological mechanism relating vasculature and viscoelastic properties; however, this research direction needs further investigation, more subjects, and improved ASL techniques to strengthen regional analysis.

Introduction

The mechanical properties of the brain give us insight into disease states and open avenues for new methods of medical diagnosis[1]. It is known that brain tissue gets softer as we age[2], but it is unknown whether and how tissue property changes are related to the branched cerebral vascular system in health and disease. Research suggests that changes in perfusion may be correlated with cognitive deficits in mild cognitive impairment[3], amyloid-β deposits in Alzheimer's disease (AD)[4], and even diseased liver tissue[5]. However, there is limited research that investigates the relationship between perfusion and tissue stiffness in the healthy brain. While It is unknown how the cascade of AD-associated events contributes to its pathogenesis, amyloid-deposits, tau tangles, tissue softening, hypoperfusion, and metabolism changes are disease correlates. It has been shown in one preliminary study that perfusion, stiffness, and flux rate are connected in the brain, due to higher intravascular pressure that is present in small vessels, coupled with the constriction of vessels in non-compliant tissue[6]. This suggests that perfusion, an indicator of cell metabolic activity and blood volume, will have an impact on the measurable mechanical properties of brain tissue and can be used as a biomarker of underlying pathology. The advanced neuroimaging tools of MR elastography (MRE) and arterial spin labeling (ASL) can be utilized to quantify brain stiffness and perfusion non-invasively by voxel. First, it is necessary to develop a modular processing pipeline for the correlation of stiffness and perfusion in a healthy cohort, quantified from MRE and ASL data, to establish a baseline understanding of these two metrics for future research in Alzheimer's pathophysiology.

Methods

In this study, we obtained pulsed ASL and MRE data from 8 healthy volunteers aged 20-35 on a Siemens Magnetom 7 Tesla scanner with a 32-channel head coil. The MRE sequence was an echo-planar spin-echo 2D pulse sequence with 3D motion-encoding gradients (TE=70ms, TR=5600ms, GRAPPA=3, 1.1mm isotropic resolution)[7], and a custom pneumatic actuator applied vibrations at 50Hz[8]. The MRE phase magnitude images were masked using SPM12[9], denoised using a MP-PCA algorithm[10] and unwrapped using Segue Phase Unwrapping[11]. The resulting unwrapped displacement data was used to calculate the magnitude of the complex shear modulus (|G*|) using an iterative nonlinear viscoelastic inversion of the time-harmonic Navier's equation[12]. Also acquired at 7T, a PASL sequence was used with EPI readout (TE = 39ms, TR = 5000ms, 25 repeats, 3.5mm isotropic resolution). Arterial spins were labeled by a 10cm inversion slab proximal to the image slices, with the labeling method Q2TIPS[13]. Subtraction, Bayesian Inference, inversion of the kinetic model of label inflow, and equilibrium magnetization calculations from a proton-density (M0) image were used to acquire quantified perfusion in ml/100g tissue/min. FreeSurfer[14] segmentation was used with a custom MATLAB script to calculate the correlation coefficient of stiffness and perfusion in gray and white matter regions. Only whole brain white matter was analyzed due to its low SNR resulting from high arterial transit time and relatively low perfusion[15]. During analysis, images were visually checked and regionally evaluated based on mean, standard deviation, and voxel number to determine inconsistencies. After this process, no subjects were removed as outliers.

Results and Discussion

After both scans were coregistered to the matrix space of their respective T1 images using MRE and ASL magnitude volumes, we regionally correlated stiffness and perfusion across all 8 subjects. This analysis has shown varying strengths of inverse correlation between stiffness and perfusion in some gray matter regions of the brain. Within a cortical GM mask, stiffness and perfusion show a strong inverse correlation across subjects (p-value = 0.0121, r = -0.823). This result supports our hypothesis that increased blood flow is related to reduced stiffness due to an increase in relative size of vascular structures coupled with the constriction of vessels in non-compliant tissue[6]. This trend is also consistent with existing research showing reduced whole-brain stiffness following exercise[16] (and therefore increased perfusion[17]).

Conclusion

Our experimental results suggest that there is a measurable correlation between stiffness, a mechanical property of tissue, and perfusion, a measure of blood delivery within the tissue. Arterial spin labeling is unique in that by measuring delivery of blood to the brain tissue, it is a metric of brain health at the capillary bed level[18]. Unlike other vasculature scans, such as time of flight (TOF) angiography, ASL measures blood delivery rather than blood vessel characteristics. The establishment of correlations between stiffness and perfusion could enhance our understanding of disease pathology in Alzheimer's Disease and other neurodegenerative diseases by highlighting the interplay between tissue mechanics and metabolic and neuroinflammatory changes.

Acknowledgements

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Figures

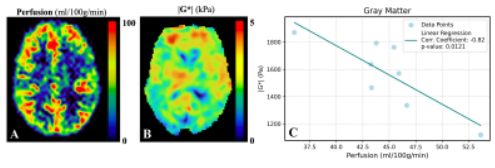

Figure 1. Preliminary results from a healthy cohort: **A)** Example perfusion map (ASL) **B)** Example elastogram (MRE) for the magnitude of the complex shear modulus, and **C)** Initial results (n=8) show a significant correlation between perfusion and shear stiffness in the gray matter.

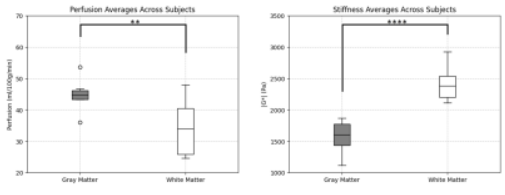

Figure 2. Averaged perfusion and shear stiffness (|G*|) across subjects. As is consistent with the literature, gray matter (GM) is softer and has higher perfusion compared with white matter (WM). Noted also is the increased variability of WM perfusion compared to GM, likely due to low SNR in WM.

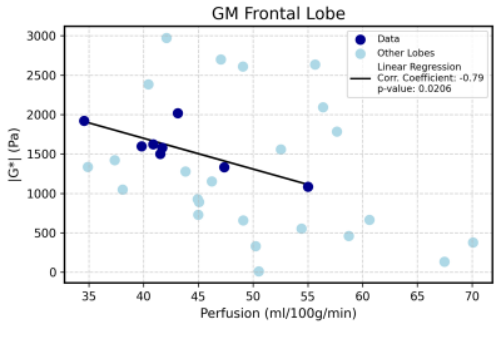

Figure 3. A significant negative correlation was observed between perfusion and stiffness in the gray matter of the frontal lobe.

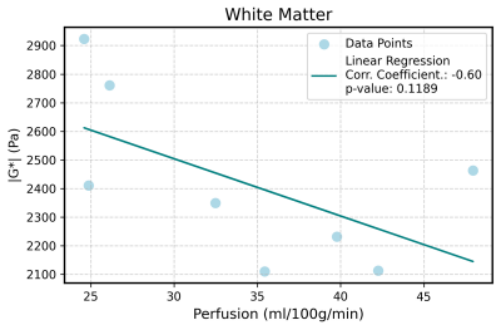

Figure 4. A nonsignificant but similar trend was observed in the white matter.

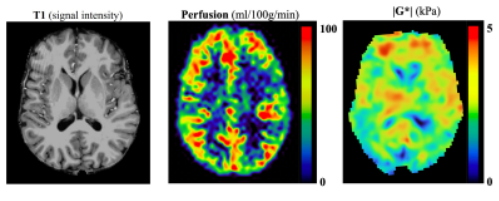

Figure 5. Example of an exemplary axial slice: T1-weighted structural signal intensity, perfusion map (ml/100g/min), and elastogram of the complex shear modulus |G*| (kPa).

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