Region-wise Correlation of Stiffness and Perfusion in the Brain at 7T Ultra-High Field MRI

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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 that tissue change is related to the branched cerebral vascular system. Existing research suggests that changes in cerebral blood flow (CBF) may be correlated with cognitive deficits in mild cognitive impairment (MCI) patients[3], amyloid-□ deposits in Alzeimer's disease[4], and even diseased liver tissue[5]. However, there is limited research that investigates the relationship between CBF and tissue stiffness in the brain. New MRI techniques allow for quantification of blood perfusion with pulsed arterial spin labeling (PASL), which may be correlated with an elastogram of the brain's stiffness calculated from magnetic resonance elastography (MRE) to determine whether, and how, these two factors are likely related.

Materials and Methods:

We obtained PASL and MRE data from 11 healthy volunteers aged 20-35 on a Siemens Magnetom 7T 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)[6], and a custom pneumatic actuator applied vibrations at 50Hz[7]. The MRE phase magnitude images were masked using SPM12[8], denoised using a MP-PCA algorithm[9] and unwrapped using Segue Phase Unwrapping[10]. Curl filtering, Fourier decomposition, and a quartic smoothing kernel were used to acquire wavefield images, before Algebraic Inversion of the Helmholtz Equation was used to calculate the magnitude of the complex shear modulus ($|G^*|$)[11]. 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 a labeling method described by Luh et. al. as Q2TIPS[12]. Subtraction, Bayesian Inference, inversion of the kinetic model of label inflow, and equilibrium magnetization calculations from an M0 image were used to acquire quantified perfusion in ml/100g tissue/min. FreeSurfer (surfer.nmr.mgh.harvard.edu) segmentation was used with a custom MATLAB script to calculate the correlation coefficient of stiffness and perfusion in gray matter regions. 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, Conclusions, Discussions:

After both scans were aligned to their respective T1 images using MRE and ASL magnitude volumes, we were able to regionally correlate stiffness and perfusion across all 11 subjects. This analysis has shown varying strengths of inverse correlation between stiffness and perfusion in some gray matter regions of the brain. Within a whole GM mask, stiffness and perfusion show a strong inverse correlation across subjects (p-value = 0.010, r = -0.732). This result supports our hypothesis that increased blood flow is related to reduced stiffness due to an increase in relative size of vascular structures. This trend is consistent with existing research showing reduced whole-brain stiffness following exercise[13] (and therefore increased perfusion[14]). There was also significant correlation found in the cuneus and insula (p-value = 0.035, r = -0.638 and p-value = 0.040, r = -0.625, respectively), two regions that are regions of interest in AD research. These experimental results suggest that there is 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[15]. 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 in a baseline healthy cohort will allow for further work in mild cognitive impairment, Alzheimer's, and other diseases with perfusion and stiffness implications.

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