

Computational Modeling of Human Cerebrovasculature for Enhancing the Capabilities to Simulate and Predict Traumatic Brain Injury

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I. INTRODUCTION

Computational human brain models have been used to study the mechanisms of traumatic brain injury (TBI), with a predominant focus on incorporating white matter fibers to understand diffuse axonal injuries. However, blood vessels remain an important component of brain tissue, yet their influence on the brain's biomechanical responses is not well understood. There is some evidence that altering vasculature mechanics via jugular compression may reduce the severity of brain deformation during an impact, and ultimately reduce injury risk [1-3]. Recent efforts have been made to elucidate blood vessel injury mechanisms by including cerebrovasculature in finite element (FE) brain models using distinct approaches [4-9]. The objective of this study was to incorporate the highly complex vasculature structure in a 3D FE brain model and investigate the influence of the vasculature on the biomechanical response of the brain at both the macro- and mesoscale.

II. METHODS

A macroscale, whole-brain vascular network was developed for incorporation into the existing CAB-20MSym brain FE model [10]. The geometry of the whole-brain vasculature was semi-automatically reconstructed using 1D beam elements from a previously published group-averaged (n=42, 20–31 years old) probabilistic brain atlas of arteries and veins [11]. Visualization of the large arteries and veins was initially acquired using time-of-flight magnetic resonance angiography (ToF-MRA) and susceptibility weighting imaging (SWI), respectively. The whole-brain cerebrovascular topology (location, direction, scale, and bifurcations) was first automatically reconstructed using a geometrical probability approach: Geodesic Minimum Spanning Trees [12]. The generated topology was then segmented and assigned vessel diameters according to a cerebrovascular atlas [13]. The network of 1D vasculature elements was morphed to match the whole-brain geometry of the CAB-20MSym model [10] and mathematically incorporated into the FE model using the embedded element method [14].

Given that the embedded technique limited the macroscale model's ability to capture the local stress and strain in the brain tissue that immediately surrounds the vasculature, a mesoscale perivascular FE model consisting of a blood vessel and surrounding brain tissue was developed to determine the change in stress distribution due to the vessel using the peripheral nodal responses from the macroscopic simulation as boundary conditions. In the mesoscopic model, the vessel wall in the 3D model consisted of three layers of hexahedral elements and was modeled with the one-term Ogden rubber material model. The wall thickness and material properties were extracted from the tensile experimental data in a passive state [17]. In the mesoscale simulation, the blood vessel was pressurized with 13 kPa, with the consideration that a pressurized blood vessel was more resistant to bending. Then, the vasculature material properties in the macroscale brain model were initially implemented using linear elastic beams informed by the stretching and bending scenarios using mesoscale models of arteries and veins.

Initial investigation into the biomechanics of incorporating cerebrovasculature in a FE brain model was performed by simulating the macroscale model using a loading condition from a previously performed *in situ* human cadaver experiment using sonomicrometry (axial rotation with 40 rad/s angular velocity and 60 ms duration) [15]. The cadaveric experiment did not show evidence of vasculature injury in this loading condition, and it was believed that vasculature injury was not likely in this condition.

III. INITIAL FINDINGS

Inclusion of blood vessels in the macroscale FE model resulted in limited changes to global deformation — with minimal reduction of the 95th percentile maximum principal strain (MPS95) from 0.393 to 0.392 — and subtly influenced the regional prediction of MPS in the brain (Fig. 1A). The 95th and 99th percentile maximum axial tensile

strains sustained by the blood vessels were 0.05 and 0.10, respectively (Fig. 1B). Experimental tests [16] reported 1.42 and 1.88 failure stretch values for pial arteries and veins, respectively, indicating this loading condition was not likely to cause vessel injury.

The inclusion of a blood vessel in the mesoscale perivascular FE model caused a non-uniform and non-linear distribution in stress, with concentrations occurring in the perivascular domain which are not captured by the macroscale model due to the spatial resolution of the whole-brain model using the embedded element method. This observation is interesting, as distinctive, localized, and progressive tau pathology of chronic traumatic encephalopathy (CTE) around neural vasculature and in depths of sulci was found in clinical post-mortem studies and is believed to be caused or triggered by mechanical disruption [17].

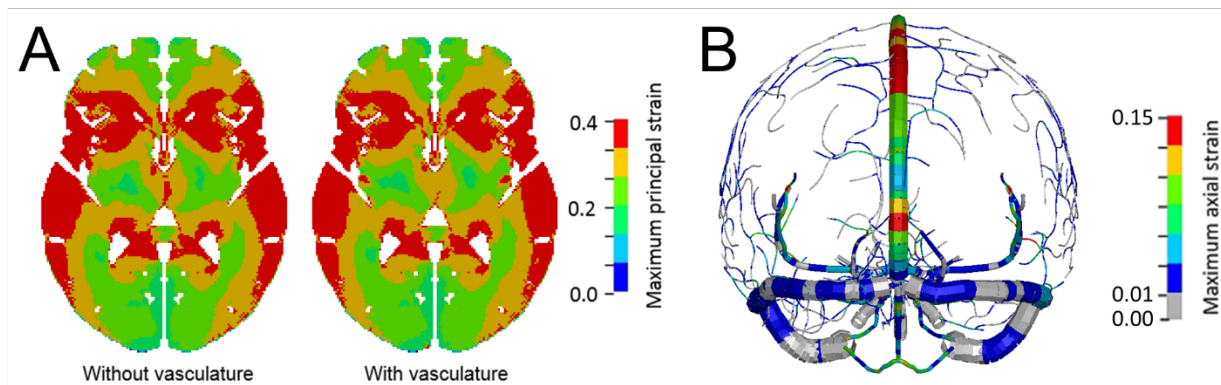


Fig. 1. (A) Influence of linear elastic cerebrovasculature on predicting the macroscale brain strain distribution during axial head rotation. (B) Maximum axial tensile strain of brain vasculature during axial head rotation.

IV. DISCUSSION

This study presented a methodology to account for the influence of cerebrovasculature in computational TBI studies that was compatible with a state-of-the-art FE model [10]. Initial findings from the macroscale simulation revealed the cerebrovasculature's minimal impact in predicted gross brain response but more pronounced effect on localized regions, which is consistent with other studies that showed that the slight global decrease in strain could be a consequence of the increased stiffness blood vessels contributed to the brain [4, 7]. The magnitude of vessel strain from a loading condition that has a high likelihood of concussion was well below the failure values reported in the literature [16] and was consistent with other FE brain models that incorporated vasculature [8].

The presented model was the initial implementation of vasculature into the CAB-20MSym model, and efforts are ongoing to improve many aspects of the fidelity of the vasculature model (e.g., material non-linearity, damage prediction, and geometric resolution). Macroscopic results are being coupled with mesoscale simulations to give insight into mechanisms associated with primary vascular injury and provide a framework to improve our understanding of secondary mechanisms associated with neurodegenerative diseases or the propensity of neuroinflammation surrounding blood vessels. This multiscale approach could also be useful in identifying correlations between the biomechanical responses and observations in clinical pathology, thus ultimately contributing to a better understanding of neurotrauma mechanisms.

V. REFERENCES

- [1] Myer, G. D., et al., *Br J Sports Med*, 2016.
- [2] Smith, D. W., et al., *Neurosurgery*, 2011.
- [3] Yuan, W., et al., *J Neurotrauma*, 2018.
- [4] Ho, J., et al., *J Biomech*, 2007.
- [5] Unnikrishnan, G., et al., *Ann Biomed Eng*, 2019.
- [6] Zhang, L., et al., *SAE*, 2002.
- [7] Zhao, W., et al., *J Biomech*, 2020.
- [8] Zhao, W., et al., *JMBBM*, 2022
- [9] Duckworth, H., et al., *Front Bioeng Biotechnol*, 2022
- [10] Giudice, J. S., et al., *Front Bioeng Biotechnol*, 2021.
- [11] Bernier, M., et al., *Hum Brain Mapp*, 2018.
- [12] Moriconi, S., et al., *IEEE Trans Med Imaging*, 2018.
- [13] Nowinski, W. L., et al., *Neuroinformatics*, 2009.
- [14] Wu, T., et al., *Ann Biomed Eng*, 2019.
- [15] Alshareef, A., et al., *J Neurotrauma*, 2018.
- [16] Monson, K. L., et al., *Dissertation*, 2001.
- [17] McKee, A., et al., *J Neuropathol Exp Neurol*, 2009.