

## Predicting the Location of Chronic Traumatic Encephalopathy Pathology

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### I. INTRODUCTION

Chronic traumatic encephalopathy (CTE) is a neurodegenerative disease linked to head impacts. Its distinctive neuropathologic feature is deposition of tau proteins in sulcal depths and in perivascular regions [1]. Previous work has investigated pathological and clinical features of CTE [1-2], and here we report our recent work [3] on exploring the link between strain and strain rate distribution within the brain and location of CTE pathology. We used a high fidelity finite element (FE) model of traumatic brain injury (TBI) to test the hypothesis that strain and strain rate produced by head impacts are greatest in sulci, where neuropathology is prominently seen in CTE. We also analysed diffusion tensor imaging (DTI) data from a large cohort of TBI patients to provide converging evidence from empirical neuroimaging data for the model's prediction.

### II. METHODS

#### *Computational Modelling*

We developed a high fidelity FE model of TBI incorporating detailed anatomy of the brain (Fig. 1), including the sulci and gyri, and nonlinear rate-dependent material models for various tissues [3]. We used the same mechanical properties for the white matter and grey matter, consistent with literature [4]. We simulated two injury cases: a helmet-to-helmet impact in an American football game with 118 g and 9.7 krad/s<sup>2</sup> peak head translational and rotational accelerations respectively and a motorcycle accident with 150 g and 10 krad/s<sup>2</sup> head accelerations [3]. The American football impact was extended over 20ms compared with the 10ms duration of the motorcycle impact. The TBI model was loaded with head accelerations and the maximum values of the first principal Green-Lagrange strain and its rate were determined for each element of the brain across the duration of the simulation. The Freesurfer software [5] was used to map the strain and strain rate at the grey matter white matter boundary, subdivided into 33 sulcal and 30 gyral anatomical regions in each hemisphere, and to evaluate the volume of the sulcal and gyral regions exceeding a 0.4 strain threshold and 150/s strain rate threshold, above which permanent brain damage is likely [6-7].

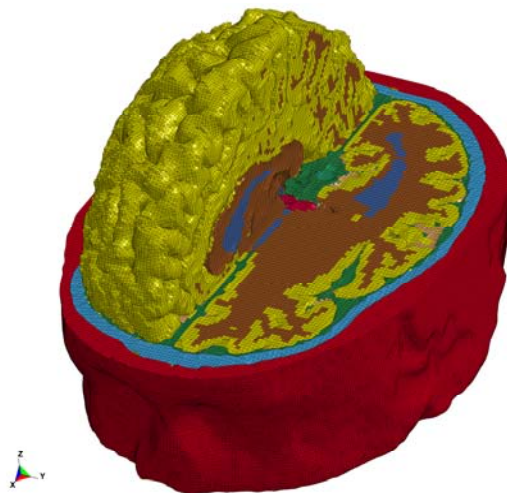


Fig. 1. Finite element mesh of the human head, showing skin (red), skull (light blue), cerebrospinal fluid (green), grey matter (yellow), white matter (brown) and ventricles (dark blue).

### III. FINDINGS

The FE model predicted a patchy distribution of strain and strain rate for both impacts, as can be seen in contour plots of Fig. 2, with their maximal values seen systematically in sulcal regions, as shown on an inflated brain image in Fig. 2 (see [3] for strain rate predictions and images of other hemispheres). Analysis of variance showed a main effect of cortical location ( $F(117) = 9.56$ ,  $P = 0.002$  for NFL impact and  $F(117) = 9.76$ ,  $P = 0.002$  for motorcycle impact), the result of larger strain in sulci than gyri. For strain rate there was a significant main effect of cortical location as well ( $F(117) = 9.92$ ,  $P = 0.002$  for NFL impact and  $F(117) = 7.60$ ,  $P = 0.007$  for motorcycle impact). The effect of impact types, i.e., NFL or motorcycle, on strain and strain rate was significantly different ( $P < 0.05$ ). American football impact had a stronger effect on strain ( $0.184 \pm 0.188$ ) than motorcycle accident ( $0.107 \pm 0.148$ ), but the motorcycle accident had a stronger effect on strain rate ( $0.246 \pm 0.273$ ) than the NFL impact ( $0.166 \pm 0.217$ ).

The empirical neuroimaging data (see [3] for details) showed larger white matter abnormalities in sulci at the white/grey matter boundary in the cohort of TBI patients with different injury causes, providing converging evidence for the maximal brain deformation in sites of CTE pathology predicted by the model.

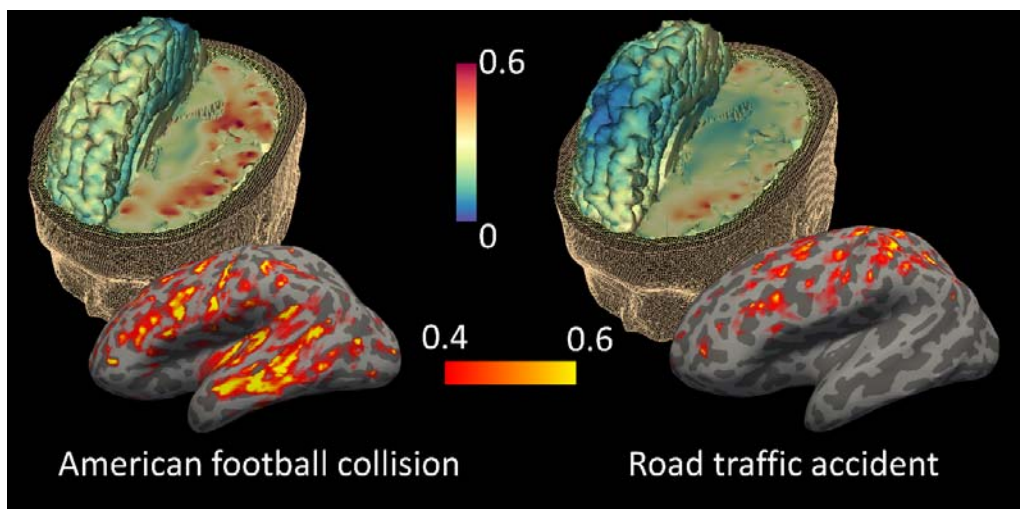


Fig. 2. Computational results showing strain contours and strain at the grey matter white matter boundary overlaid on an inflated image of brain (dark grey shows sulci and light grey shows gyri).

### IV. DISCUSSION

Our high-fidelity FE model of TBI predicts greater strain and strain rate within the sulci, the prominent location of tau pathology seen in cases of CTE and also in long-term survivors of single TBI [8]. In-vivo and in-vitro models of TBI have shown clear relationship between strain/strain rate and neurodegeneration, e.g., [6] and [7]. The analysis of diffusion MRI provides converging evidence that a similar distribution of pathology at the grey/white matter interface is seen in human imaging. This work provides a biomechanical explanation about the distribution of CTE pathology seen after head impacts, holding the promise of guiding the design of protective equipment to minimise damaging effects of brain exposure to impacts.

### V. REFERENCES

- [1] McKee AC et al, Brain, 2013.
- [2] Gavett BE et al, Clinics in Sports Medicine, 2011.
- [3] Ghajari M et al, Brain, 2017.
- [4] Kleiven S, Stapp Car Crash, 2007.
- [5] Smith S M, Hum Brain Mapp, 2002; Smith S M et al., Neuroimage, 2004.
- [6] Morrison III B et al, Stapp Car Crash, 2003.
- [7] Tang-Schomer et al, FASEB J, 2010.
- [8] Johnson et al, Brain Pathol, 2012.