Effects of sex and brain anatomy on brain strain vary across different impact severities

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I. INTRODUCTION

Brain strain is used as a biomechanical marker of brain injury [1]. Under the same head kinematics, different individuals may sustain different values of brain strain due to the differences of brain anatomy. Previous studies have analysed the effects of brain anatomy on strain using subject-specific brain models and have shown a strong relationship between intracranial volume and brain strain [2-4]. However, these studies have used a single head impact. The question is whether head kinematics of different severities has an influence on the relationship between cerebral volume and brain strain. In this preliminary study, we quantify the effect of sex and brain anatomy on brain strain by simulating multiple real-world sports impacts of different severities using a range of subject-specific finite element (FE) brain models.

II. METHODS

Subjects and subject-specific FE brain models

Magnetic Resonance Imaging (MRI) scans from a cohort of healthy human subjects (n=211) were acquired at Hammersmith Hospital, Imperial College London [5]. Each scan was processed using FreeSurfer's *recon-all* pipeline for segmentation and parcellation of brain structures [6]. Key anatomical measures, including total cerebral volume (TCV), estimated intracranial volume (eTIV), ventricular cerebrospinal fluid volume (CSFV), and mean cortical thickness (mCT), were extracted.

We identified one male and one female subject per decade from ages 10 to 80 years, resulting in a total of 14 subjects (seven males and seven females). For each subject, an FE model was generated. A segmented image was developed from MRI scans using FAST and BET segmentation of brain structures [6]. FE meshes were then created from the segmented image and smoothed to develop subject-specific models, as explained in more detail in [7].

Impact simulations and data analysis

We simulated sports impacts using real-world kinematics data collected by the validated Protecht instrumented mouthguard. These impacts were video confirmed. Impacts were selected based on the 90th percentile of maximum principal strain (MPS) in the corpus callosum, a deep brain region where strain magnitude is associated with concussive symptoms [8]. MPS used for this selection was estimated by the validated Imperial (IC) FE brain model, which was developed from the brain anatomy of an average male subject [1].

From a dataset of 1,701 elite rugby impacts, we categorised impacts into quartiles by MPS and selected the impacts at Q1, Q2, Q3, and Q4 to represent different impact severities. Given the right-skewed distribution of MPS values, we defined Q4 using the 90th percentile rather than the maximum to avoid using the potentially anomalous extreme value. These impacts were simulated using each subject-specific model. Following each simulation, the strain distribution was written into a 3D image and then registered into the standard Montreal Neurological Institute (MNI) space. MPS values were extracted for analysis using a corpus callosum binary mask.

Pearson's correlation coefficient (r) was calculated to assess the linear correlation between each brain measure and MPS for each impact. Mann-Whitney U test was performed to assess the effect of sex on MPS.

III. INITIAL FINDINGS

TABLE I MPS METRICS AND CORRELATION WITH BRAIN MEASURES ACROSS IMPACT SEVERITY LEVELS

Impact severity	*MPS (IC FE)*	*MPS mean (n=14)*	*MPS SD (n=14)*	*MPS mean (males, n=7)*	*MPS mean (females, n=7)*	*Correlation coefficient (r)*			
						TCV	**eTIV**	**CSFV**	**mCT**
Q1	0.045	0.045	0.003	0.045	0.045	0.28	0.26	-0.24	0.39
Q2	0.046	0.049	0.005	0.053	0.046	0.57*	0.63*	0.29	0.10
Q3	0.096	0.093	0.012	0.097	0.089	0.60*	0.59*	-0.25	0.34
Q4	0.129	0.143	0.028	0.155	0.129	0.83**	0.79**	-0.42	0.30

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Note: MPS on the IC FE model was used as impact selection criteria. The mean and SD of the MPS for each impact simulating on 14 subjects are shown. Pearson's *r* assessed the linear correlation of brain measures with MPS for each impact (Significance: *p<0.05, **p<0.001).

The smallest standard deviation (SD) of MPS values was observed in impact Q1, followed by Q2, Q3, and Q4, indicating that variability in MPS among subjects increased with impact severity (Table I). Of the four brain measures, CSFV and mCT showed weak correlation with MPS. In contrast, TCV and eTIV showed strong correlation with MPS, with the correlation coefficients increasing as MPS value increased (Table I and Fig. 1). Across all impact severities, female subjects sustained a lower mean MPS than male subjects. However, this sex difference was not statistically significant except for the Q2 impact (Fig. 1). The distribution of strain in CC under Q4 impact was similar between the smallest and largest brains, with the CC genu sustaining largest strain and CC body sustaining smallest strain (Fig. 1).

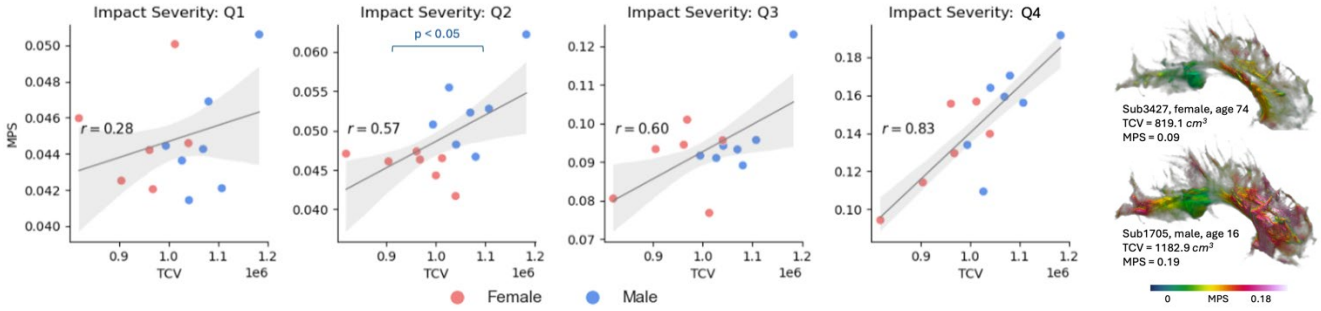

Fig. 1. The relationship between TCV and MPS across impact severities Q1 to Q4. The right panel shows the MPS in corpus callosum of the subject, with the smallest TCV (sub3427) and largest TCV (sub1705) sustained in impact Q4.

IV. DISCUSSION

We found that strain is correlated with brain volume (i.e. TCV and eTIV), which agrees with previous studies [2-4][9], but our preliminary results highlight that this correlation varies with impact severity. We simulated four real-world rugby impacts, each representing a different level of impact severity, using subject-specific brain models from a wide age range. Our results indicate that at higher impact severities, the linear correlation between brain volume and strain becomes stronger.

This finding has implications for predictive modelling. A previous study introduced scaling factors based on brain volume to improve the accuracy of machine learning models in predicting brain strain across individuals, but this was based on a single impact [2]. Our results suggest that impact severity should be incorporated into the scaling factor, as it affects the volume-strain relationship. A recent study developed separate linear regression models for the volume-strain relationship for different impacts, yielding varying slopes [9], which agrees with our findings. However, the influence of impact severity on the volume-strain relationship was not explored.

We also examined the effect of sex differences on brain strain and found that sex had a significant effect in only one of the four impacts. These preliminary results suggest that sex is not a significant factor when predicting strain for individuals with anatomical differences, which agrees with previous studies [2][4][9].

Within each impact severity, the differences in MPS between subjects were less than 0.1, and the variance in MPS was very small. However, the variance tended to increase as impact severity increased, a trend that aligns with findings from [9]. Given the small strain differences between subjects, further research is needed to assess whether these variations have implications for injury risk.

This study has limitations. While using four impacts improved upon prior studies that considered only one, all four were from the same sport. Future research should expand to other sports, as peak kinematics and strain levels vary across sports. Additionally, the subjects' TCV span is narrower than in other studies [2-4][9], which suggests that larger strain differences between subjects might be observed if a wider TCV range were included.

These preliminary results can help us better understand the effects of anatomical variations on brain strain produced in sports collisions, paving the way for utilising these models for predicting the effects of single and cumulative exposures on the brain.

V. REFERENCES

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