Traumatic Brain Injury Risk Functions Estimated Using Human and Non-Human Primate Data

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I. INTRODUCTION

Traumatic brain injury (TBI) contributes a significant portion of the injuries resulting from motor vehicle crashes, falls and sports collisions. Development of countermeasures to mitigate these injuries requires an understanding of the tolerance of the human TBI. In this study, we estimate the tissue tolerance levels for mild and severe TBI using simulations of reconstructed football impacts, volunteer data, and primate data.

II. METHODS

This work focused on simulating head impact conditions in humans and animals associated with either no injury or diffuse injury (concussion and diffuse axonal injuries). Injury risk functions (IRFs) were derived by comparing the predicted tissue-level responses with injury response.

Experimental Data

The brain injury severity levels in a comprehensive human and animal injury dataset were classified based on the Abbreviated Injury Scale (AIS) system (98 version) and organised for developing AIS2+ and AIS4+ injury risk functions. Applying this criterion, the dataset (n=466) consists of sub-injurious volunteer tests, laboratory reconstruction data of professional football, and non-human primate (NHP) tests, as briefly introduced below.

Human Data: head kinematics recorded from reconstructions of 53 National Football League (NFL) cases of helmet-to-helmet impact originally performed by Pellman *et al*. [1] and corrected by Sanchez *et al*. [2]. Concussion (AIS2 in this study) was diagnosed in 20 of the 53 cases. Head kinematics recorded from volunteer sled tests performed by the Naval Biodynamics Laboratory (NBDL) that were all non-injurious [3]. Sled tests involving 22 subjects in frontal, lateral and oblique conditions up to 16 Gs peak sled acceleration (n=335), were previously used to evaluate existing head and brain injury risk functions [4].

Animal Data: head kinematics from non-human primate (NHP) tests performed by different groups from the 1960s to the 1980s were collected. The first series of NHP experiments, conducted at the University of Pennsylvania, delivered non-impact rotational accelerations-decelerations to the head [5-6]. For this study, 56 cases of diffuse axonal injury (AIS4+) in baboon were used. The second series of NHP experiments was conducted at the Japan Automobile Research Institute, using three different apparatuses and a variety of loading conditions. For this study, only five sub-injurious macaque tests (from lateral impact conditions) were used because most other specimens were impacted multiple times. The last series of NHP experiments was conducted by the University of Michigan and used a pneumatic impacting device to deliver impacts on the heads of two different species of macaque [7-8]. From this dataset, 17 macaque tests (lateral and occipital impact conditions) were used, where there were four no injury, 8 AIS2–3 injuries, and 5 AIS4+ injury results.

Computational Models

The Global Human Body Models Consortium-owned (GHBMC) 50th percentile male detailed finite element (FE) brain model (v4.3) was used to simulate the human head impacts [9]. To reconstruct the NHP experiments, previously developed rhesus macaque (*macaca mulatta*) and baboon (*papio anubis*) brain models [10-13] were modified to harmonise numerical methods (e.g. hourglass control, mesh type, mesh density), white matter segmentation, and brain tissue constitutive models with the human brain model (Fig. 1). The same linear-viscoelastic constitutive model and brain material properties used in human brain modelling were applied to the NHP models, given that previous studies have shown a mechanical similarity between human and NHP brain properties [14]. The head impacts were simulated using species-specific FE models by applying the

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experimentally measured six degrees-of-freedom head kinematics directly to the rigid dura through the centre of gravity. For each simulated case, tissue-level strain injury metrics commonly used in the literature were assessed. These metrics included the Cumulative Strain Damage Measure (CSDM) with thresholds of 25% maximum principal strain [15], and the 95th percentile maximum principal strain (MPS95) [16].

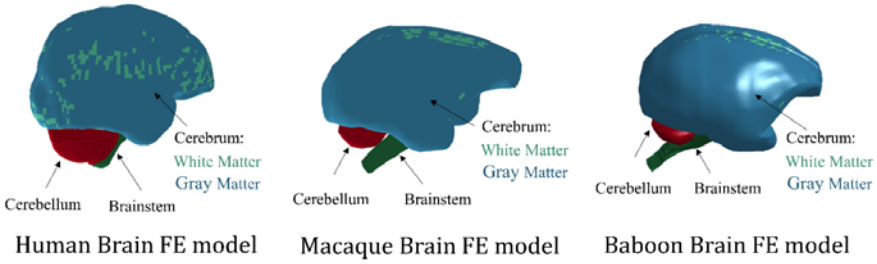

Fig. 1. FE brain models modelled with similar numbers of hex elements, anatomical detail, and constitutive models.

III. INITIAL FINDINGS

Tissue injury risk functions (IRFs) were developed using survival analysis and complied injury database (Fig. 2a) and 2b)). IRFs based on MPS metrics show better quality (narrower confidence interval) and better fit to the injury data (lower AIC values), compared to the CSDM-based IRFs. Since both the animal and human data have several mild injury cases, metrics from these cases were compared and analysed using an independent two-tailed t-test (Fig. 2c), p>0.05). MPS95 and CSDM25 were statistically indifferent for these common injury cases, thereby satisfying the hypothesis that human and NHP TBI data can be grouped for injury risk analysis.

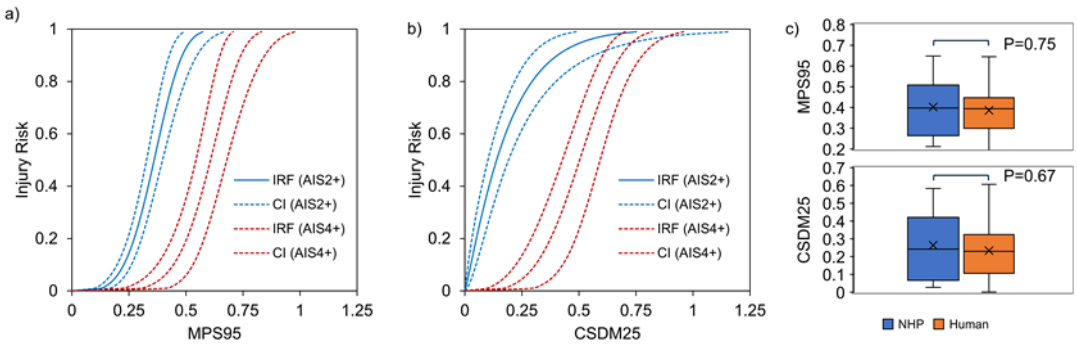

Fig. 2. Tissue-level injury risk curves developed using survival analysis based on a) MPS95 and b) CSDM25. c) Distribution of metric values for mild brain injury cases in the human and animal dataset.

DISCUSSION

This work leveraged harmonised computational models to integrate brain injury responses at the tissue level, thus providing a new method of utilising human and animal data for understanding human brain injury tolerances. Tissue-level and kinematics-based AIS2+ and AIS4+ injury risk functions were developed using an integrated dataset of sub-injurious volunteer sled tests, football reconstructions and in vivo NHP tests. Future work to improve the biofidelity of the human and animal models may improve the prediction of brain injury.

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