Tissue-level Injury Metrics in a Ferret Blast Brain Injury Model

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I. INTRODUCTION

Blast-induced traumatic brain injury (bTBI) has become a critical health concern for soldiers, especially in the context of modern warfare where blast exposures are common. Understanding and assessing the bTBI risk is crucial for ensuring soldiers' safety, therefore robust injury risk functions (IRFs) are needed. Unfortunately, collecting human exposure data with known injury outcomes is a challenge. This means animal models are essential for studying bTBI in controlled settings, using blast or shock tubes to simulate conditions. Translating animal findings to humans presents another challenge due to anatomical and physiological differences. Computational models, particularly the finite element (FE) method, have been shown to be suitable for linking animal biomechanics to human predictions to aid in future injury assessments.

In this study, a large problem space, encompassing exposures from an experimental bTBI study based on a ferret model [1], was simulated using a computational ferret head and brain model [2]. Binary injury outcomes from the ferret study were compared to predicted brain tissue metrics, and IRFs related to brain tissue response and injury outcome were developed. The developed tissue-level injury risk functions may form the foundation for future development of injury risk assessments using computational human head models.

II. METHODS

The FE ferret brain model was originally developed from computerized tomography (CT) imaging and validated for pressure and histopathological outcomes [2]. However, its isotropic brain tissue lacked detailed axonal structures, limiting its ability to capture axonal strain, which has proven critical for accurate brain injury predictions in other types of TBI [3-4]. To address this, the baseline model was upgraded with axonal structures from high-resolution diffusion tensor imaging (DTI) data [5], with anisotropic properties incorporated into the FE framework using an embedded element approach [6]. The workflow of the FE ferret model upgrade is shown in Fig. 1.

Blast simulations on the enhanced ferret brain model were performed in LS-DYNA (Ansys, Inc.) using an Arbitrary Lagrangian-Eulerian (ALE) formulation for the blast wave. Simulations were performed based on the loading conditions from a prior *in vivo* experimental study where 64 ferret specimens were subjected to a single-exposure primary blast wave generated using a compressed-gas-driven shock tube [1]. Acute injury outcomes (apnea, moderate and severe bleeding, or fatality) from the *in vivo* study, along with histological assessments, were compared to the computationally predicted brain tissue responses measured in the ferret model. The brain metrics were based on the 95th percentile values of the maximum principal strain (MPS), intracranial pressure (ICP), axonal strain (MAS), and von Mises stress (VMS). From this analysis, several tissue-level injury criteria were developed using survival analysis [7].

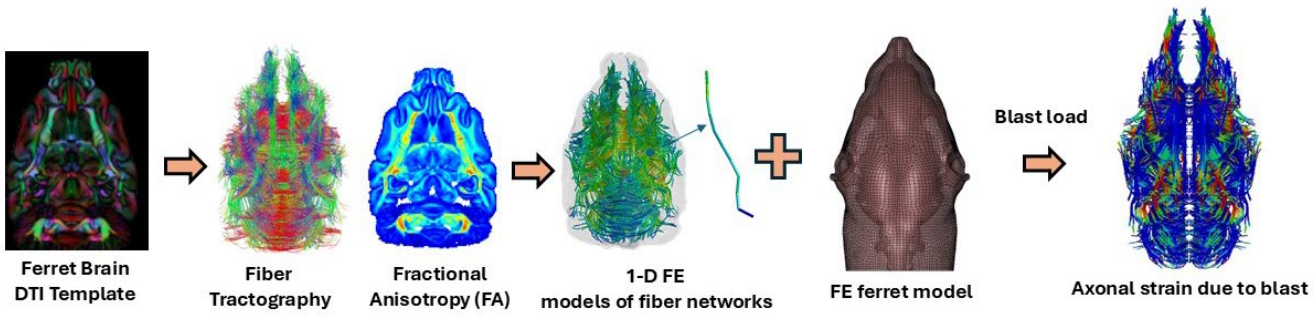

Fig. 1. FE ferret model enhancement workflow.

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III. RESULTS

The deviatoric responses of the ferret brain model (MPS, MAS, VMS) were better correlated with the injury outcome and histopathology of the *in vivo* injury models than the pressure response (ICP) (Fig. 2, left). Strains in the blasted brain were an order-of-magnitude lower than those expected to produce blunt closed-head TBI, but an order-of-magnitude higher in strain rate. These results suggest that the mechanism of neuropathology in bTBI is high-rate strain response of neural tissue, and not high pressure, as often hypothesized in the literature.

An additional 120 blast simulations were performed for exposures ranging from 100 kPa to 1000 kPa peak incident overpressure, and from 0.5 ms to 6 ms positive-phase duration. This analysis produced a dataset of tissue-level metrics that are linked to specific incident blast parameters, namely, positive peak overpressure (P_{0+}) and positive phase duration (t_p), and to a risk of injury from any of the tissue-level IRFs. This facilitated the development of exposure-risk models based on peak overpressure and duration. In general, the predicted 50% risk of injury using the computationally derived exposure-risk functions was a better fit to the injury data than the empirically derived exposure-risk functions based on a pre-defined relationship between pressure and duration (Fig. 2, right).

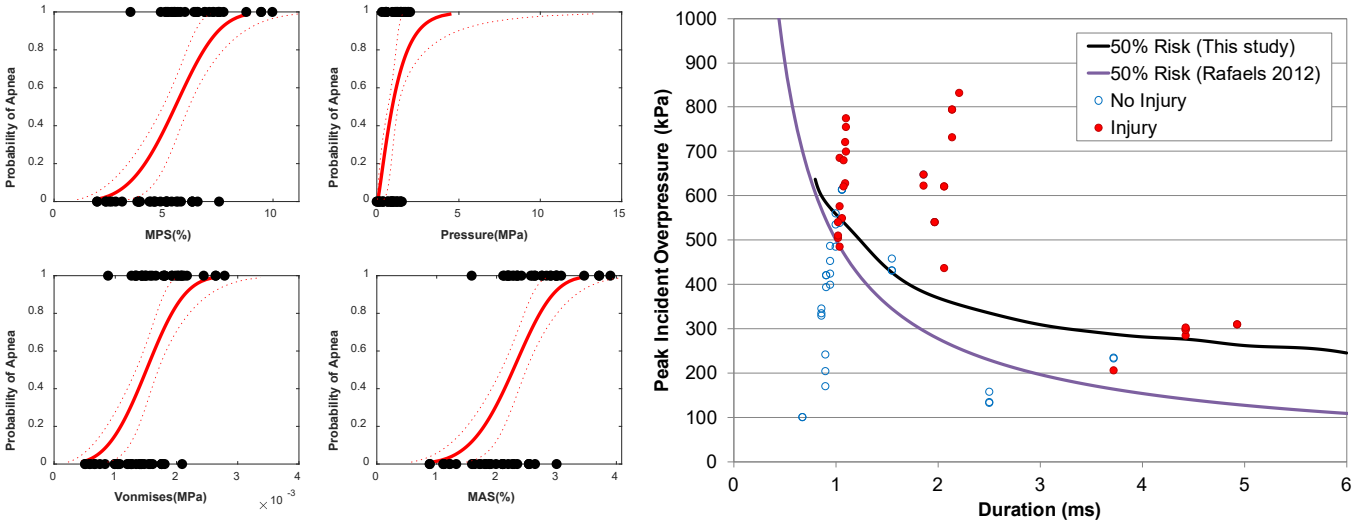

Fig. 2. *Left*: injury risk functions for apnea using tissue-level metrics. *Right*: plot of the 50% risk of ferret apnea calculated using the MPS95 function to the original test data and empirically derived 50% risk response.

IV. DISCUSSION

Correlating the local mechanics of brain tissue with injury and severity is an important step in identifying the mechanisms associated with blast neurotrauma. Combining *in vivo* test data with computational modelling is the best way to one day translate animal injury outcomes to humans, to develop a better understanding of how bTBI occurs. The results of this study suggest that high-rate deviatoric responses in brain tissue are the mechanisms associated with bTBI rather than a pressure response, and that computationally derived exposure-risk functions may provide a more accurate means to assess injury than one derived empirically when there is limited data.

Overall, this research provides a critical step towards a more accurate bTBI risk assessment framework that could one day enhance soldier safety and inform protective equipment design. However, directly applying the developed exposure-risk functions from animals to humans for blast exposures may lead to misleading conclusions without proper consideration for scaling. The current exposure-risk functions do not account for biomechanical differences between species, such as variations in head shape, skull thickness, and internal anatomy. While the application of tissue-level risk functions may account for biomechanical differences between species, there may be significant pathobiological and physiological differences not inherently modelled. Experimental data from multiple species should be used to refine and validate the tissue-level risk functions.

V. REFERENCES

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