Identifying Traumatic Brain Injury (TBI) Thresholds Using Animal and Human Finite Element Models Based on in-vivo Impact Test Data

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Abstract

Traumatic brain injuries (TBIs) cause roughly 50,000 deaths per year in America. In order to lessen the severity or prevent TBIs, accurate dummy models, simulations, and injury risk metrics must be used. Human data is ideal to develop models, but injury conditions are often complex, e.g. primary and secondary impacts, and tissue level response can often only be studied via an autopsy, but death usually only occurs as the result of severe TBI. To develop better graded injury risk metrics, animal study data must be applied to the human brain. The ultimate objective of our study was to develop a better method to scale injury data by using finite element analysis (FEA). In this study, a finite element model of a Göttingen miniature pig brain and skull was created from MRI and CT images. These pigs' brains have several characteristics in common with human brains that that make them suitable for testing such as shape and material properties. The regions of the brain were divided into white matter, gray matter, and the ventricles each with viscoelastic material properties. To validate this model, tests were conducted using Göttingen miniature pigs in a translation/rotation injury device subjecting the pig skull to a linear acceleration from 40-96 g's and an angular acceleration from 1,000-3,800 rad/s^2. Four of these pigs' brains were embedded with neutral density radio-opaque markers to track the motion of the brain with a biplanar X-ray system. Fifteen pigs were also tested without markers to allow for injury data to be taken with MRI scans and immunohistochemistry. The impact was then simulated in LS-DYNA®, and the motion of nodes closest to the marker locations was recorded and used to optimize material parameters. When used in tandem with a human model this will allow for a more accurate transfer function to scale injury data from a pig study to be relevant to humans. While the loading conditions in this study simulate a small range of possible injuries, the scaling methods involved may be applicable to a wide variety of injuries from sports injuries to blasts.

Introduction

Traumatic brain injuries contribute to roughly 30% of injury related deaths in the United States while only being present in 5% of all injury related emergency department visits[1]. Many of these injuries are preventable through better designs in vehicles or helmets. To make these improvements, injury metrics based on the kinematics of the head are used. Several kinematic metrics have been developed such as the Head Injury Criterion (HIC)[2]. HIC was developed decades ago to predict head injuries in general, and it generally relies on the probability of skull fracture, which is only present in some TBIs. This measure is a function of only the linear acceleration at the center of mass; other important variables such as the angular acceleration and location of hits are ignored. Because these variables are ignored, HIC only has a limited ability to predict brain injuries. More recently, a new injury metric was developed called the Brain Injury Criterion (BrIC) based on the angular speed, and it is intended to have greater ability to predict TBIs[3].

Both these measures as well as other measures share a weakness in that they require a large amount of injury data to be calibrated. Real life injury data is sparse since humans are

rarely instrumented during an injury event, and of the instrumented injuries, the loading conditions are often complex due to multiple impacts, blasts, etc. Real life injuries can also be reconstructed with dummy models or finite element models, but again, complicated loading and the assumptions necessary make it difficult to determine a graded risk function. Cadaver studies can be performed with simple loading conditions, but cadaver tissue might not respond biofidelically, and many injuries to the brain cannot be seen in dead tissue.

In order to fill the gaps in knowledge, animal studies are necessary. This allows for injury mechanisms to be highly controlled. Additionally, behavioral studies and histology can be performed, which is especially useful for diagnosing injuries at a lower intensity that involve no large scale yield of the material. The challenge with animal studies lies in scaling the results so that they can be applied to humans. The most common methods to scale kinematics are through a single scaling factor[4]. This factor is based on geometrical values such as characteristic length or the mass. Because the brain is a very complex organ both in its action and its geometry, intelligent animals with similar brain structure work best as a model for human brain injury. One animal model commonly used for brain injury studies is the Göttingen miniature pig. While a relatively small animal, it has a well-developed brain, so it is ideal for brain studies. The objective of this study was to develop and validate a Göttingen mini-pig brain FE model, and use this model in tandem with a human brain model.

Methods

Modeling

A Göttingen mini-pig was given an MRI and CT scans. The CT scan was used to segment the skull. Since the model is intended to be used for a low range of impacts, it was assumed that the deformation of the skull was negligible, so the skull was meshed with rigid shell elements. The brain was segmented from the MRI images. The corpus callosum, brainstem, midbrain, cerebellum, ventricles, and the cerebrum were identified. The brain was meshed with hexahedral elements, and each part was connected by shared nodes. Many material models for neural tissue have been proposed in literature[5]. In the current model, the material properties were assigned as Kelvin-Maxwell viscoelastic material models (*MAT 061) (Table 1). This material model can be easily tuned for a particular loading rate and is also computational efficient in FE simulations.

Table 1. Pig brain material properties of Kelvin/Maxwell Viscoelastic

	Density (kg/m^3)	**Bulk Modulus (MPa)**	**Short Time Modulus (MPa)**	**Long Time Modulus (MPa)**	**Time constant (1/s)**
Grey Matter	1040	2190	0.007	0.002	.01
White Matter	1050	2190	0.0104	0.0038	.01
Ventricles	1040	2190	0.00075	0.0002	.01

The skin, musculature, and other soft tissues of the head were not modeled since the loads were applied directly to the skull. Several skull-brain interface contacts were tested to simulate the layers of the meninges. The model was developed in LS-DYNA software, and the motion of the skull was applied as a prescribed boundary motion. The brain in the skull is shown in Figure 1.

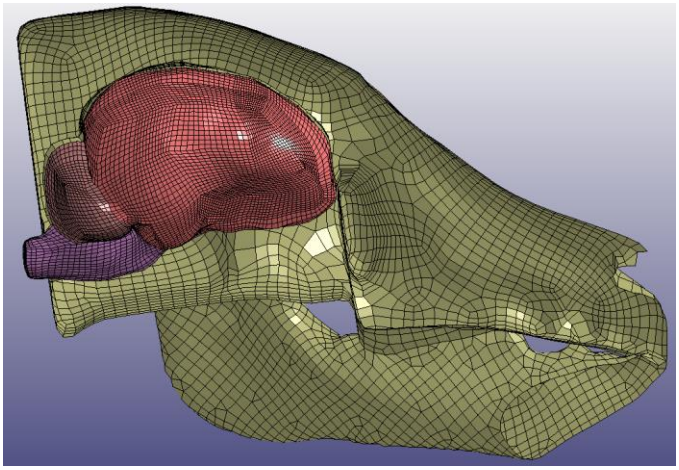


Figure 1. Pig head model with cerebrum, cerebellum, and brainstem visible.

In vivo tests

A series of *in vivo* tests were conducted on Göttingen mini-pigs[6]. The *in vivo* tests were separated into two phases. Phase one consisted of 8 tests conducted at Virginia Tech, while phase two consisted of 22 tests conducted at Wake Forest Medical Center. The test device was built with two platforms joined by a hinge (Figure 2). The animal is placed on its back so its head is at the far end of one platform, while the far end of the other platform is another hinge. The two platforms are kept from moving relative to each other prior to impact with a crushable tube. When the platforms are winched up then released, the animal swings downward and impacts a brass tube, simultaneously crushing the tube in between the platforms and allowing the animal platform to rotate. This device allows the pig brain to be subjected to both translational and rotational motion. Prior to conducting the tests, each pig was prepared surgically. Bone screws were placed in the top of the skull without penetrating the inner table, and these screws were cemented to a steel slug. This slug could then be bolted to the animal platform. Bolting the animal to the platform allows the kinematics of the skull to be measured without the damping effects of the skin and tissue around the skull. The pigs from the phase two tests conducted at Wake Forest were used to study the injuries received. Several metabolite concentrations and their changes after impact were studied with proton magnetic resonance spectroscopy (H-MRS)[7]. Additionally, histology was used to determine changes in stained pixel percentage of light and

heavy neurofilament that indicate axonal disruption. In these tests, several drop heights were tested so the brain would experience a range of impacts.

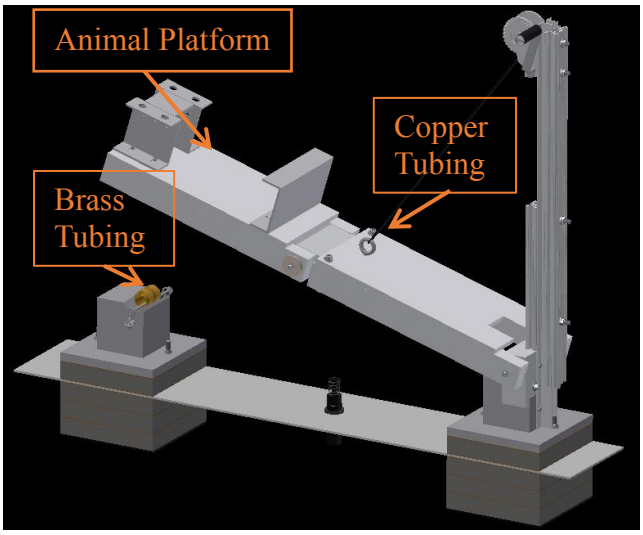


Figure 2. Translational and rotational impact injury device.

Prior to the impact, the phase one pigs were prepared with additional surgery. Neutral density targets (NDT) were implanted in the brain through trephines in the skull. During the impact, the motion of these markers was traced by x-ray motion capture. The model with the location of the nodes used for validation is shown in Figure 3. These tests were conducted to aid in computational modeling, so the drop height was held constant to verify the test repeatability.

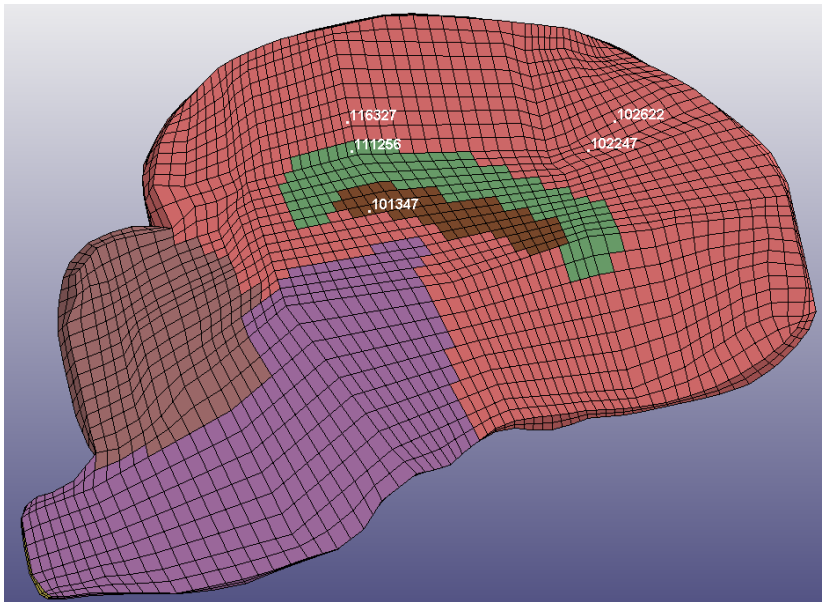


Figure 3. Half brain mesh showing locations of the nodes used for validation.

Results

Kinematics

The maximum linear speed and acceleration for the phase one tests averaged about 3.6 m/s (Fig.4) and 57 g's respectively, while the maximum angular speed change and acceleration averaged about 9 rad/s (Fig.5) and 1,484 rad/s^2. The phase two tests were conducted from varying drop heights, so there were a range of kinematics. The linear speed ranged from 2.6-4.3 m/s (Fig. 6) and acceleration from 40-96 g's. Angular speed change ranged from 7.2-10.8 rad/s

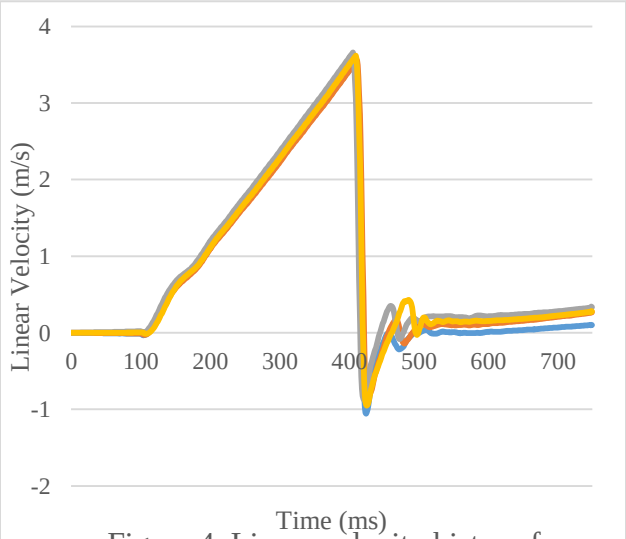


Figure 4. Linear velocity history for phase one tests.

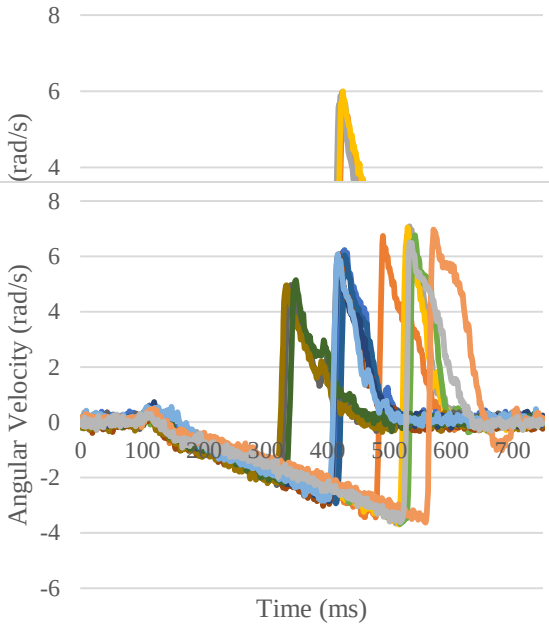


Figure 7. Angular velocity history for phase two tests.

(Fig. 7) and angular acceleration ranged from 1,015-3,815 rad/s^2.

Injuries

The pig brain injuries were quantified by the phase two tests. In total, a change in the concentration of 20 metabolites was seen with H-MRS, most notably indicating glutamate excitotoxicity. Injuries were also seen by histology staining for light and heavy neurofilament, with the stained pixel percentage increasing by 10.6% and 11.7% respectively. This indicates that the neurofilament subunits have been disconnected and dispersed, which can cause swelling or axonal disconnection or death. No significant differences in the injuries were detected throughout the range of impacts tested.

Validation

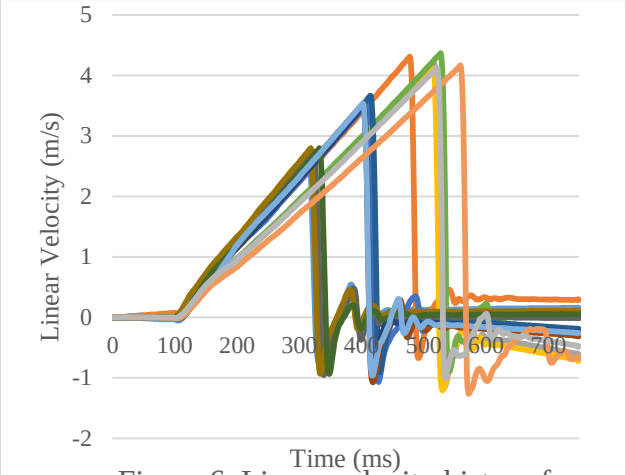


Figure 6. Linear velocity history for phase two tests.

The NDTs from the *in vivo* phase 1 tests were used to validate the FE model. The location of nodes closest to the location of each marker was recorded throughout the impact. For a model to perform well, it should match both phase and magnitude of the experimental tests. This ensures that the strains and strain rates throughout the brain are biofidelic. The magnitude of each experimental NDT and FE node is shown in Table 2. The skull-brain interface contact type that provided the best fit was a sliding contact with friction. Additionally, the range of impacts from the phase two tests were simulated to determine the difference in node motion over this range (Table 3). Even though the smallest impact was roughly 20% slower than the phase one tests and the largest impact was roughly 20% faster, the nodal displacements were very similar, which is consistent with the findings that the injury levels were seen to be consistent for all the pigs tested.

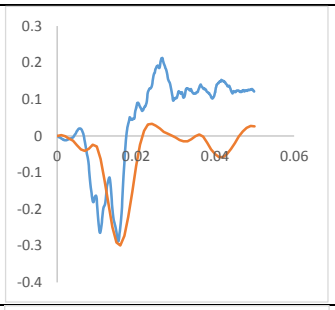
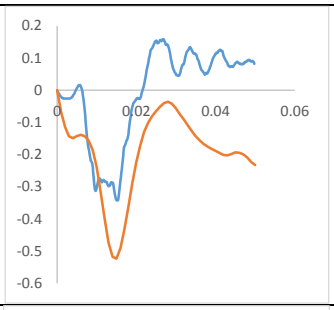
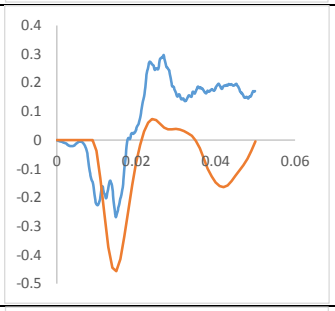
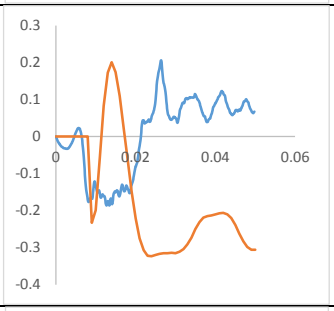
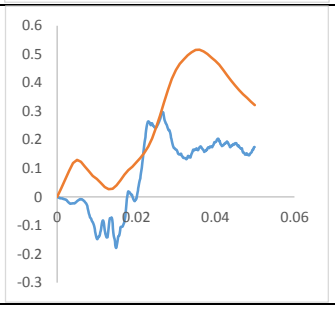
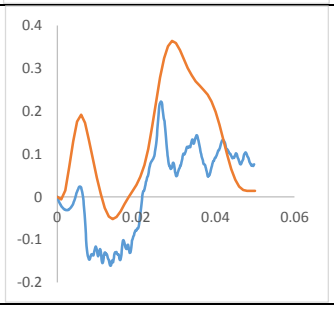
Discussion

The pig brain model produced node motion with similar magnitude and phase to the experimental marker motion. This suggests that the model will likely produce strains close to the *in vivo* tests. The injury throughout the brain can be quantified through the use of the cumulative strain damage measure (CSDM) [2]. This measure sums the percentage of elements that receive over a certain threshold for strain, and it is a correlate for diffuse axonal injury. In addition, there are other measures such as the dilatational damage measure (DDM) which is a cumulative

measure of negative pressure. While the material properties and cellular structure are very similar, it is reasonable to assume the same injury mechanisms in both human and other mammals (e.g. pig).

The risk curves of these injury metrics in human FE models were obtained from FE simulation results. The kinematic data of animal tests were scaled based the ratio of animal and human brain masses and then used as input in human FE simulations to identify the values of injury metrics. Finally, the values of injury metrics and injuries recorded in animal tests were correlated to develop the injury risk curves.

Table 2. Displacement in horizontal and vertical directions for each of the node/marker pairs.

—FE —EXP	Horizontal displacement (mm) with respect to time (s)	Vertical displacement (mm) with respect to time (s)
Node 101347		
Node 102247		
Node 102622		

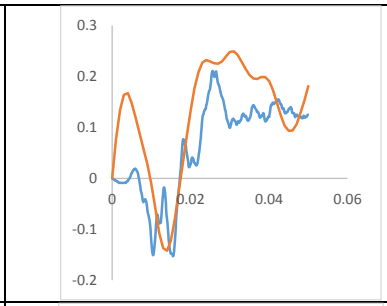
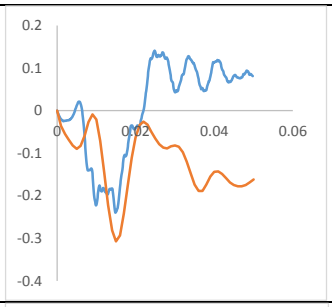
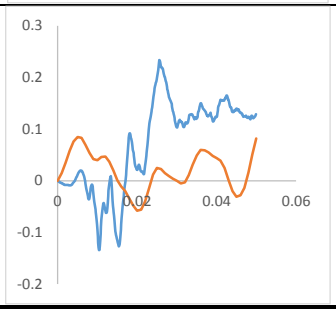
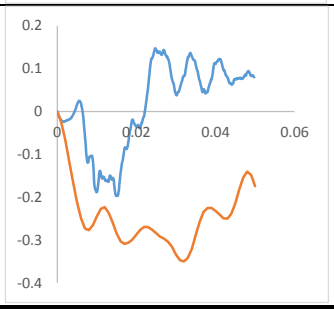
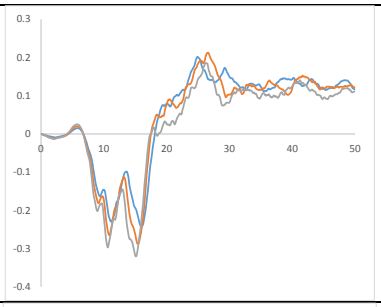
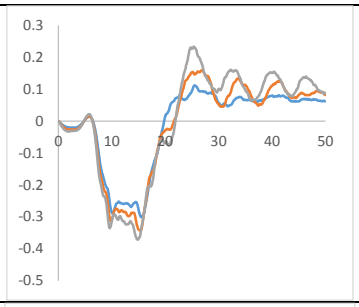
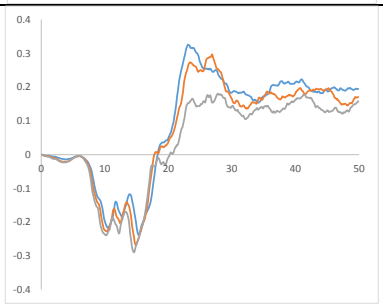
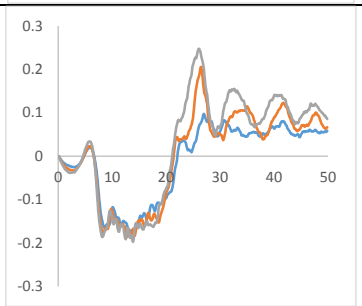
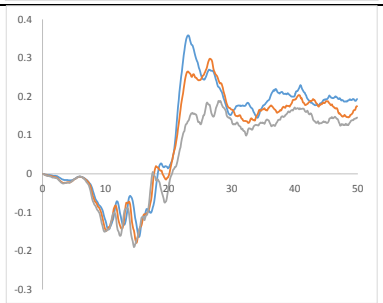
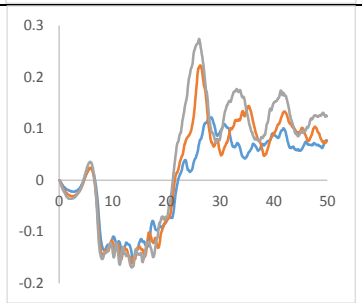
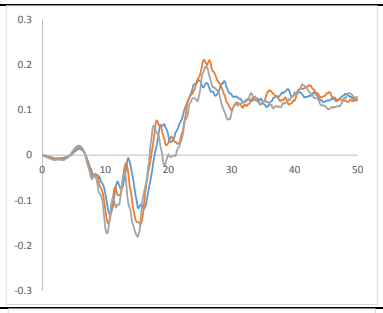
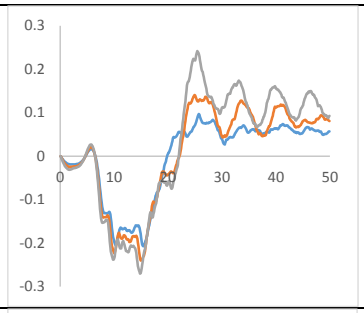
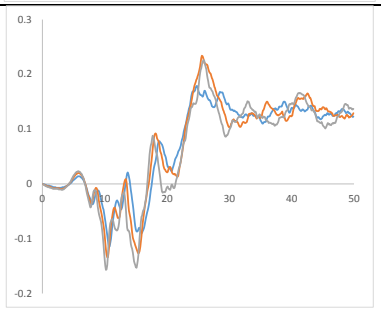
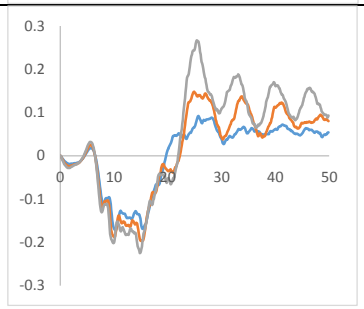
Node 111256		
Node 116327		

Table 3. Displacement in horizontal and vertical directions for each node at varying levels of impact.

Small Impact Medium Impact Large Impact	Horizontal displacement (mm) with respect to time (s)	Vertical displacement (mm) with respect to time (s)
Node 101347		
Node 102247		
Node 102622		

Node 111256		
Node 116327		

Having an accurate a pig FE model may avoid the simplistic scaling approach (e.g. based on brain masses). For example, the pig FE model could be run with the same impact conditions as pig tests to find the values of injury metrics. Then, the time histories of both linear and angular velocities could be scaled and a human FE model could be run until the model will predict the same values of injury metrics calculated by pig model. Finally, kinematic parameters of these optimized time histories will be used in the calculation of injury risk curves corresponding to human model. It is believed that these injury curves will be more biofidelic than the injury curves developed based on mass scaling and used currently in human models (e.g. Simon model).

Adopting a scaling method based on FEA has several advantages. The scaling can be developed and calibrated for a single breed of animal, which is useful when few types of animals are used for these studies. Secondly, scaling can be developed separately for different injury mechanisms. Since the geometry of an animal's brain is significantly different to a human brain, it is a reasonable assumption that a particular animal might be more or less susceptible to certain injury modes. For example, to study diffuse axonal injury, a CSDM threshold could be selected for both the human and animal model to create load scaling best suited for finding equivalent diffuse axonal injuries. FEA based scaling could lead to better graded injury risk thresholds and eventually greater prevention or mitigation of these debilitating injuries.

Acknowledgement

This work was supported by the Takata Corporation.

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