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Rapid Prediction of Brain Injury Pattern in mTBI by Combining FE Analysis With a Machine-Learning Based Approach

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ABSTRACT Mild traumatic brain injury (mTBI) is a significant issue worldwide. Public awareness of the dangers of mTBI has increased sharply in recent years, yet there is no easy-to-use tool available for early detection and post injury management. Computational models of the head impact, usually in the form of finite element analysis, are a method of choice for characterizing how mechanical impacts lead to brain damage by causing high strains in certain regions of the brain. However, those models require a prohibitively large amount of computational power as well as pre and post processing expertise, making them unrealistic to be used in clinical settings. In this study, we propose a framework that combines finite element analysis with a machine learning based approach where a large number of pre-computed FE results are used to train a statistical model. We analyzed a number of different head impact scenarios in which a football player would sustain a minor brain injury and computed brain internal strain patterns. These pre-computed strain patterns were then used to train a partial least squares regression model to be able to predict the general strain pattern and the location and magnitude of peak strains. Our models were able to predict the overall distribution pattern, including the location of the peak strain, with an average error of 3%. The peak strain magnitudes were also predicted accurately with the average error of 9% at almost real time speed (less than 10 seconds). This model may play an important role in developing a diagnostic tool for mTBI that can predict the severity of head impacts.

INDEX TERMS Diffusion tensor imaging, finite element analysis, magnetic resonance imaging, mild traumatic brain injury, partial least squares regression.

I. INTRODUCTION

Traumatic brain injury (TBI) is a growing health and socio-economical problem, and yet its mechanism is still poorly understood. Proper management of TBI is essential to avoid short-term and long-term risks ranging from brain haemorrhage to dementia. Proper quantification of the mechanism by which energy from head impacts is transferred onto the brain and its tissues, is critical for understanding mechanisms of TBI and developing effective diagnostic and treatment

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options. One of the best and probably the only way of investigating such mechanical energy transfer process is to use *in silico* models that can recapitulate the actual dynamic loading environments of head impacts. *In silico* numerical models have been in use since the 1970s by approximating the brain and head as a fluid filled spherical shell [1]. Since then models have been refined significantly to include important anatomical and mechanical details in order to improve their ability to mimic the tissue's response to mechanical loading events. A large number of high resolution finite element models of the brain exist in the literature that contain viscoelastic/hyperelastic material behaviours and internal geometries of the main anatomical substructures including the falces and ventricles [2]–[10]. Current state-of-the-art brain models can provide rich information on tissue deformation patterns after the input of the head impact data that are often obtained from wearable head sensors that measure angular and linear accelerations of the head during an impact.

A major drawback with such advancements and refinements in numerical models is that most require extremely high computational power. The early models of brain trauma had thousands of elements [3], [11], which has now increased to the order of millions [12], in order to scale for the MR voxel resolution. Such high computational cost is one of the major obstacles for computational models of head impacts to be used most commonly in clinical settings. Despite advancements in high performance computing, high fidelity finite element models can only be applied to small and limited subject numbers. However, to make an actual impact, one needs to translate computational tools to medical applications and large-scale visualisation. One possible way forward is to use population-based models [13], [14]. This is done by using large sets of pre-computed or measured data to train a model using machine learning or multivariate regression models. This concept has been demonstrated in multiple applications such as development of a surrogate knee model for predicting joint contact force [15], human femur cortical shell thickness predictions [16], shape prediction of the lower limb from a few sparse landmarks [17] and real time prediction of internal strain patterns in the human Achilles tendon during various activities [18]. In this article, we describe how this approach can be applied to the simulation of mild TBI (mTBI) as a result of a direct impact to the head, using high fidelity finite element computations customized using anatomical and structural parameters derived on a subject-specific basis.

II. METHOD

The overall workflow of our framework that combines FE analysis with statistical modelling for more efficient prediction of brain deformation pattern in TBI is described in Fig 1. Our framework is made up of two major steps – 1) subject-specific FE analysis of mTBI cases to predict brain deformation patterns after the head impact; 2) statistical model training with the results from FE analysis for rapid prediction of brain deformation patterns.

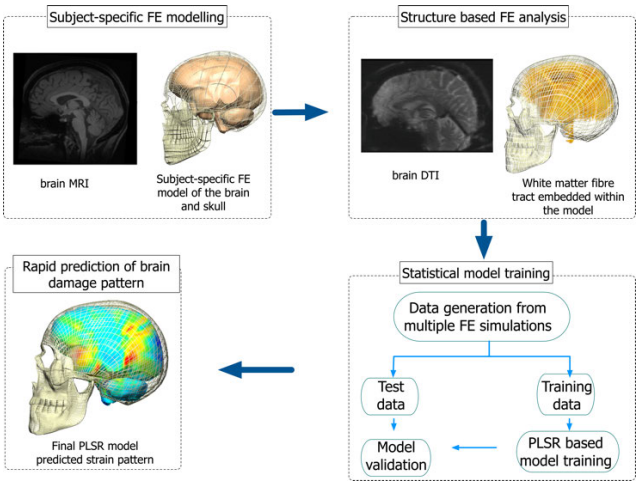

FIGURE 1. Overall framework that combines subject-specific FE analysis with a machine learning based statistical model training method for rapid prediction of brain damage pattern after TBI.

The FE modelling involves subject-specific analysis of brain deformation after mTBI. This generates spatial map of strain, which is the input to our statistical model training. Once trained, our statistical model will predict the spatial map of strain after mTBI given the spatial location and velocity of the impact only (Fig 1).

A. SUBJECT-SPECIFIC FE ANALYSIS OF THE BRAIN WITH EMBEDDED WHITE MATTER FIBRE TRACTS

A subject-specific finite element model of the human brain was generated from magnetic resonance imaging (MRI) data of our previous research [19] where a longitudinal study with male Canadian football players was performed to measure the changes in brain structure measured with MRI. Briefly, MRI data (T1 high resolution anatomical image and diffusion tensor imaging (DTI)) from football players (all male, average age $= 20.3 \pm 1.4$) was acquired longitudinally over the course of the season at three time points – 1) prior to the pre-season training camp within 2 months before the first contact practice (''PRE''); 2) post training following 14-day training camp and the first two games of the season (''PTC''); 3) post season (''POST''). We used one subject's MRI at the PRE time point – T1 imaging for the geometry extraction and DTI for the white matter fibre tract information to generate a subject-specific FE model.

The generic human brain model was obtained from the International Union of Physiological Sciences (IUPS) Physiome project [20], [21] (Fig 2). The Physiome brain model contains the scalp, skull and the brain. We then extended this to include major compartments of the brain – the cerebrum, cerebellum and the brainstem.

This generic FE model of the human brain and skull were fitted to match the geometry of the subject from T1 MRI images. This was necessary as the generic mesh came from the Visible Human dataset [22] and had a different brain shape and size from the subject's brain. We used a least

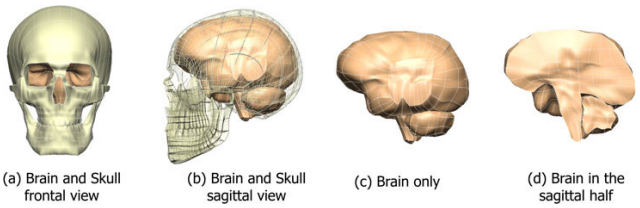

FIGURE 2. **The brain and skull model used in this study. The major structures such as cerebrum, cerebellum and brain stems are differentiated using the material mapping method as described in the text.**

squares fitting algorithm that we developed, which morphed the generic model to match the subject-specific geometry from MRI [20]. The contact between the brain and the skull was modelled using a frictional contact with friction coefficient of 0.2 [23].

The brain tissue was modelled as an anisotropic material. Especially, the white matter fibre tract orientation plays an important role as it influences the pattern of deformation along the major fibre direction [24]. This structural feature was incorporated using an orthogonal curvilinear material coordinate system (see Figure 3). Specifically, a reference material coordinate system that is both curvilinear and orthogonal was defined using the finite element coordinate system. Then the structure-based material coordinate system which is aligned to the white matter fibre tract direction from DTI results was defined. The initial FE reference material coordinate system was rotated using three sequential rotations (Cardan sequence from Euler angle) that align the reference FE coordinate system to the final DTI based material coordinate system. Since DTI vectors were available for every voxel, the Euler angles that align the reference coordinate to the final material coordinate were computed at each and every voxel. These Euler angles were then fitted as a finite element field (a node based interpolation field) as described in [25]. The fitted fibre field was used to inform the deformation of the brain. We have used this method to describe deformation patterns of various fibre based tissue structures such as cartilage [26], skin [27] and tendon [28] in our previous studies.

FIGURE 3. **Embedding the white matter fibre orientation to the FE model using the microstructurally based coordinate system.**

In terms of material properties, we adopted an anisotropic hyperelastic constitutive relation that accounts for the anisotropy and nonlinear behavior of the brain tissue due to the white matter axonal fibres [29]. Here, the strain energy function has two terms that represent ground substance matrix with embedded white matter fibre tracts.

$$W = F_1(I_1) + F_2(\lambda) \tag{1}$$

where I_1 is the first invariant of the right Cauchy stretch tensor and λ is the stretch ratio along the local fibre direction. The function F_1 describes the behaviour of the ground substance matrix and F_2 represents the behaviour of collagen fibers. The ground substance was described with the neo-Hookean material model.

$$F_1 = \frac{C_1}{2}(I_1 - 3) + \frac{C_2}{2}(I_2 - 3) \tag{2}$$

The strain energy of the white matter fibers was represented as a piecewise function that characterized their non-linear stress/strain behaviour using the following [30],

$$\begin{aligned} \lambda\frac{\partial F_2}{\partial \lambda} &= 0, \quad for\ 0 \le \lambda < 1, \\ \lambda\frac{\partial F_2}{\partial \lambda} &= C_3\left[e^{C_4(\lambda-1)} - 1\right], \quad for\ 1 \le \lambda \end{aligned} \tag{3}$$

The parameter values $C_1 \sim C_4$, were obtained from Champagne *et al.* [19] and given below (Table 1).

TABLE 1. **Material coefficients for the white matter fibre tracts included in the model.**

	Parameter	Value	Parameter	Value
Matrix	C_1	-1.034	C_2	7.809
Fibres	C_3	13.646	C_4	4.64

Other major tissues in the brain were modelled separately, which included the dura matter, falx and scalp. The subarachnoid space, which is located between the arachnoid and pia membranes and is occupied by cerebrospinal fluid (CSF) was also modelled. These materials were separately incorporated into the model using our automatic material property assignment algorithm that maps different regions in the MRI to the different elements in the FE model [31]. This method establishes mapping between the imaging modality from which the FE model was developed and by checking the location of each Gauss points within the MR imaging coordinate system, it automatically assigns the correct material value from the MRI to the model. This method allowed us to have different tissue types within our model by assigning different material values to different Gauss points. The material values used for these tissues were obtained from the literature as shown in Table 2.

Regarding the boundary condition, we used the dynamic contact mechanics algorithm developed by Champagne *et al.* [19], which allowed us to model TBI by impacting the head with an impactor as described in Zhang *et al.* [7]. We simulated both frontal and occipital impacts. In those two impact situations, the axis of the impactor was aligned with the mid-sagittal plane in the anterior-posterior direction. The rigid impactor was defined to have an initial velocity of 6.33m/sec. This loading condition closely mimics a typical head impact scenario in which a

TABLE 2. Material coefficients for other brain materials included in the model.

Tissue	Young's modulus	Density	Poisson's ratio	References
Skull bone	15 GPa	2 kg/dm^3	0.22	[32, 33]
Dura mater	31.5 MPa	1.13 kg/dm^3	0.45	[3, 33]
Scalp	16.7 MPa	1.13 kg/dm^3	0.42	[3, 33]
Falx/tentorium	31.5 MPa	1.13 kg/dm^3	0.45	[3, 33]
Subarachnoid Space	1.15 KPa	1.13 kg/dm^3	0.48	[34]

football player would sustain a minor brain injury [35], [36]. Since the impact duration was very short (∼15ms), a free boundary condition was used at the head/neck junction. We simulated both frontal and occipital impacts.

All FE simulations were performed with the open-source based computational framework developed as a part of the IUPS project. (http://physiomeproject.org/software/opencmiss).

Since we have used hyperelastic material descriptions to model the brain, we used the final strain value at the end of the simulation as the peak strain in that impact scenario. These results from 20 different impact scenarios were input to the statistical model training as described in the following section.

B. STATISTICAL MODEL TRAINING

We trained a Partial Least Squares Regression (PLSR) model by using the data obtained from FEA simulations of 20 different brain impact scenarios. For this study, the goal is to demonstrate the efficacy of our framework for one player's geometry. Hence only special location of the impact and impact velocities are required as the geometry is the same for all simulations. Specifically, we used 10 different impact velocities up to 6.33m/sec and 2 different impact locations (frontal, occipital).

PLSR is a linear regression model that predicts response variables from predictor variables [37]. The two fundamental equations in PLSR are the predictor matrix (X) and the response matrix (Y) given by

$$X_{nm} = T_{nl}P_{ml}^{T} + E, \tag{4}$$

and

$$Y_{np} = U_{nl}Q_{pl}^{T} + F, \tag{5}$$

where T and U are the projection matrices (also known as scores), and P and Q are the transposed orthogonal loading matrices (where the rows are created from eigenvectors or principal components), and E and F are the error terms. X and Y are estimated using linear regression through

$$Y = X\tilde{B} + \tilde{B}_o, \tag{6}$$

where $\tilde{B}$ is the least squares regression estimate and $\tilde{B}_o$ is the prediction error.

In our study, the predictor variables are the initial velocity and the impact location. The response variables are the stress and strain within the brain. The accuracy of model prediction was tested by doing a 'leave-one-out' analysis where one simulation from 20 was left out of the PLSR model and predicted independently, and then repeated for each scenario. Specifically, the root mean squares (RMS) errors between PLSR predictions and FE model predictions were determined by comparing the strain values from PLSR and FE models at every Gauss point within the model. We report maximum error magnitudes and locations as well as the RMS errors.

Statistical model training was done with the PLSR plugins from the Python SciPy (www.scipy.org) and scikit-learn (machine learning) modules and these methods are encapsulated in the Musculoskeletal Atlas Project, an open source toolkit for musculoskeletal model development (https://simtk.org/projects/map).

III. RESULTS

The principal strain pattern predicted by our model under different frontal and occipital impact scenarios all display heterogeneous distribution patterns, indicating that brain structures play an important role in strain distribution (Figures 4 & 5). In both frontal and occipital loading cases, the location of impact played an important role as the initial high strain was developed around the impact area – the frontal lobe for the frontal impact (Figure 4) and the occipital lobe for the occipital lobe (Figure 5). However, the subsequent strain transfer pattern followed the internal tissue structure closely as can be seen for both impact cases, especially in the coronal view of Figures 4 & 5. In particular, some areas in the brain consistently developed higher strains than others. These are most prominent in the regions of the white matter fibre tract patterns, especially the corpus callosum region as well as the sulcal region, which is in agreement with previous studies [3], [5], [38]–[42]. The magnitude of impact velocity also played an important role as the peak strain increased along with the increase in the impact velocity (Figures 4 & 5).

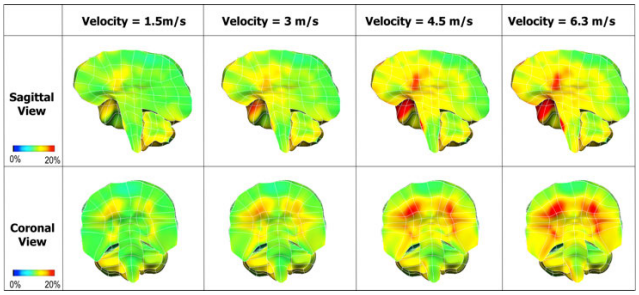

FIGURE 4. FE simulation of principal strain for frontal impact at various impact velocities. The sagittal view shows that the initial strain is developed along the location of the impact (frontal lobe). The coronal view reveals that the white matter fibre tracts, especially around the corpus callosum area are highly strained (bottom row).

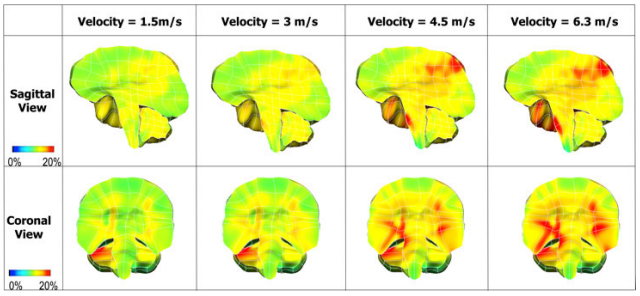

FIGURE 5. FE simulation of principal strain for occipital impact at various impact velocities. The sagittal view shows that the initial strain is developed along the location of the impact (occipital lobe). The coronal view reveals that the white matter fibre tracts, especially around the corpus callosum area are highly strained (bottom row).

Our PLSR trained model was able to predict the general principal strain distribution patterns as well as the location and magnitude of peak strains as can be seen in Figure 6. Qualitative comparisons of both frontal and sagittal plane views of the results in Figure 6 shows that the PLSR trained model was able to capture the overall strain distribution pattern including the locations of the peak strains very closely.

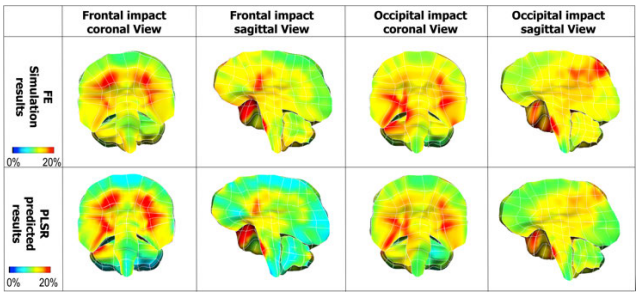

FIGURE 6. Comparison of FE simulated strain pattern and PLSR predicted strain pattern. General agreements can be seen both in the location and magnitude of maximum strains.

These results were compared more quantitatively. We used two different measures to estimate the accuracy of our PLSR model prediction. First is the average error, which was calculated by computing the difference between FE and PLSR results in all Gauss points in the models. The second measure was employed to see how well the PLSR model predict the magnitude of the maximum strain, an important measure for damage criteria in brain injuries. This was done by comparing the maximum strain values from the FE and PLSR results for all simulations performed. The results are shown in Figure 7. As can be seen, the average error between the PLSR and FE models were around 3%. When only the maximum strain magnitudes are compared, the average error between PLSR and FE models were between 7-9%, indicating that our PLSR prediction captures both the overall strain distribution pattern and the peak strains magnitude and locations well.

IV. DISCUSSIONS

In this study, we have shown that pre-computing FE simulations of head impacts during TBI can be used to train

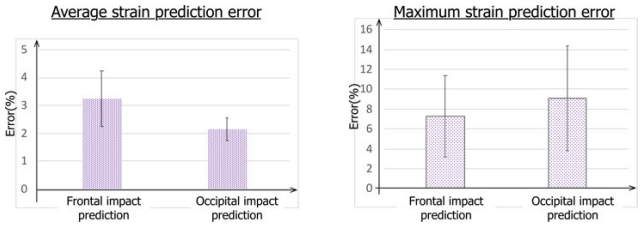

FIGURE 7. Comparison of average error between FE results and PLSR predictions as well as the comparison of maximum strain prediction.

machine learning based models, which then can serve as a surrogate model for rapid prediction of brain damage patterns after TBI. Specifically, we used the partial least squares regression (PLSR) method, which captures the pre-computed FE simulation results into a statistical look-up table. This is then used to map the FE simulation results to a surrogate model, which predicted the final strain distribution pattern with just a few parameters. In our case, we used the impact locations and impact velocity to predict the final strain distribution. And with these two parameters, we were able to predict the final strain distribution pattern, including the location of maximum strain, with the average accuracy of 3%. In terms of the magnitude of maximum strain prediction, the PLSR model prediction was within 10% of the actual maximum strain magnitude from the FE results.

Finite element analysis of the mechanical response of the brain during impact has been a popular choice of the method in traumatic brain injury research. Dozens of FE models have been developed in the past that used a variety of different types of elements, constitutive relationships, loading conditions [43]. The unique feature of our brain model against those available in the literature is that it is a structurally based model that incorporated white matter fibre directions directly into the model. Others have also recognized the importance of white matter fibre direction in brain deformation patterns and implemented the anisotropy due to the white matter fibre distribution using fractional anisotropy values in their constitutive relationships [24], [44]. Our approach differs from the previous work in that we incorporated the white matter fibre orientation as an embedded feature of the FE mesh using the microstructure based coordinate system. This allowed us to perform anisotropic FE analysis more efficiently. Another novel feature of our model is the use of our automatic material property mapping algorithm [31]. This allowed us to have a direct correspondence between numerical integration points within elements (called Gauss points) and every voxel in the MRI images, which led to the location dependent material property assignment to our model. Therefore, rather than having separate element groups for different structures in the brain, we used a holistic approach where the material properties were assigned to Gauss points according to its location within the brain – for example, Gauss points that fall into the falx/tentorium region of the brain are assigned

with the falx/tentorium material properties. This means that we can expand the material types depending on the availability of the material descriptions for different regions of the brain.

Our FE predictions show general agreements with the results reported in the literature from other mTBI studies. When comparing the results from McAllister et al[42], who reported strain distributions from 10 male football athletes with mTBI, our results match very well both quantitatively and qualitatively. Their mTBI results showed that the peak maximum principal strain occur in the corpus callosum region as in our predictions. The magnitude of the peak strain values reported by McAllister and colleagues also matched with our predictions, indicating a general agreement between our results and theirs. One major difference is the high level of strain that we predicted in the sulcal regions in the brain (Figures 4 & 5), which is not shown in the strain plots from McAllister and colleagues. However, the high strain in the sulcal region from our study is supported by another mTBI study by Ghajari *et al.* [5] who reported distinct patterns of high sulcal strains from their models of mTBI of American football players. Although our strain level is lower than what they predicted (0.2∼0.3 vs 0.4∼0.6), the peak strains in the sulcal region from their models qualitatively match the predictions from ours. This can be attributed to the modelling approach that emphasized the folding in the brain. Ghajari and colleagues explicitly modelled the major sulci and gyri of the brain. We have implicitly modelled the folded structure of the brain by using the material coordinate system which followed the direction of white matter fibre tracts, thereby creating the distinction between white and grey matters in the brain. This resulted in the high sulcal strains that are not seen in the models without this feature such as McAlister *et al.* Therefore, the predictions from our model match qualitatively with other similar mTBI cases reported in the literature.

The major contribution of our study is the incorporation of a machine learning based algorithm into our framework to enable rapid prediction of brain damage patterns. One of the biggest challenges in the management of mTBI is the lack of objective diagnostic tools. There has been a rapid growth both in terms of public awareness as well as commercial market size in concussion related diagnostic projects. However, there is still no diagnostic product that can measure the severity of mTBI in a way that offers prognostic information about the short and long-term outcomes. A sophisticated computational head injury model can estimate brain strain distribution, hence the possible damage patterns with a good degree of accuracy. But this simply takes too long (typically requiring hours on high-end workstations) to be used in a clinically meaningful way. We provide a solution to this problem by pre-computing various head impact scenarios with sophisticated FE models first and then use these results to train machine-learning based models for a rapid prediction of brain strain distribution. Specifically, we use a statistical model training based on PLSR method which was able to predict the maximum strain locations and magnitude with an accuracy of 95% and computational time of less than 10 seconds. This will be a good candidate for developing an objective diagnostic tool for brain concussion that incorporate maximum peak strain as a marker for brain damage.

While our PLSR model predicted the maximum strain with a sufficient accuracy, there are a number of limitations in our studies. First, we used hyperelastic material descriptions in our model. The method of choice for head impact FE simulation is to use hyper-viscoelastic material descriptions to incorporate time dependent material property changes after the impact. Since we have used only hyperelastic material descriptions, our model is limited to analyzing the strain behavior right after the impact and will not be suitable for quantifying damage patterns any time after that initial impact duration. However, this was good enough for our application as we are mainly interested in the maximum peak strain amplitude and locations as a damage marker. Yet, future studies will include viscoelastic material descriptions to have the time dependent strain profile as a damage marker for both chronic as well as acute injuries to the brain. Another limitation is the relatively small number of training simulations used in our PLSR method. In particular, we used the geometry from one subject only, which limited our training variables to be impact locations and velocities. More simulations may be required for different impact type and velocities as well as geometries. Furthermore, we used the FE simulations as the gold standard to train and test our results, thus the model predictions need to be interpreted with this in mind. However, the strain values and locations predicted by our FE model are in agreement with previously reported values as discussed above, which gives us confidence in our results. Moreover, we have conducted a thorough animal study with our sheep model where we impacted the sheep brain and analyzed the damage pattern by harvesting the brain damage data and performing immunohistochemistry analysis [45]. This will provide the ultimate testing dataset that can be used to train and validate our model. This result will be reported in our future publications.

In conclusion, we have developed a novel framework that combined FE simulations with a machine learning based approach that allowed us to rapidly predict brain deformation patterns with a sufficient accuracy. This framework may play an important role as a diagnostic tool for mild TBI.

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