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Using an Artificial Neural Network to Predict Traumatic Brain Injury

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Abstract

Background: Pediatric traumatic brain injury (TBI) is common, but not all injuries require hospitalization. A computational tool for ruling-in patients who will have a clinically-relevant TBI (CRTBI) would be valuable, providing an evidence-based way to safely discharge children who are at low risk for a CRTBI. We hypothesized that an Artificial Neural Network (ANN) trained on clinical and radiologist-interpreted imaging metrics could provide a tool for identifying patients likely to suffer from a CRTBI.

Methods: We used the prospectively-collected, publicly-available, multicenter Pediatric Emergency Care Applied Research Network (PECARN) TBI dataset. All patients with TBI under the age of 18 with admission head computed tomography (CT) imaging data were included. We constructed an ANN using clinical and radiologist-interpreted imaging metrics in order to predict CRTBI, as previously defined by PECARN: 1) Neurosurgical procedure, 2) Intubated > 24 hours as direct result of the head trauma, 3) Hospitalization ≥ 48 hours and evidence of TBI on CT, or 4) Death due to TBI.

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Results: Among 12,902 patients included in this study, 480 patients were diagnosed with CRTBI. Our ANN had a sensitivity of 99.73% with 98.19% precision, 97.98% accuracy, 91.23% negative predictive value, 0.0027% false negative rate, and 60.47% specificity for CRTBI. The area under the ROC curve was 0.9907.

Conclusions: We are the first to utilize artificial intelligence to predict CRTBI in a clinically meaningful manner, using radiologist-interpreted CT information, in order to identify pediatric patients likely to suffer from CRTBI. This proof-of-concept study lays the groundwork for future studies incorporating iterations of this algorithm directly into the electronic medical record for real-time, data-driven predictive assistance to physicians.

Keywords

TBI; Pediatrics; Machine Learning; Artificial Intelligence

Introduction

Traumatic brain injury (TBI) affects thousands of children in the United States every year.[34] Despite the large numbers of children who experience TBI, only a small percentage actually require hospitalization or prolonged surveillance.[31] However, identifying which patients do require monitoring versus those that can be safety discharged from the emergency department remains an important unanswered question. Thus, creation of a tool for identifying patients at risk for clinically-relevant TBI (CRTBI) could provide an evidence-based mechanism for early safe discharge and potentially reduce unnecessary healthcare expenditures.

The Pediatric Emergency Care Applied Research Network (PECARN)[1] is a consortium of 25 hospitals that developed a decision-making score based on head CT findings.[16] Numerous studies have independently published on these data in an effort to develop predictive metrics to guide treatment of children with TBI, however none have used artificial neural networks (ANN).[4,5,8,11,15–17,21,22,26,28,29] ANNs are a type of machine-learning (ML) algorithm that have been widely used in clinical medicine.[6,7,10] ANNs are often more useful than conventional statistical methods because: 1) ANNs can take any number of input variables and predict any number of outcomes 2) ANNs are capable of improving their predictive ability over time as they are exposed to new data 3) ANNs benefit from internal validation and testing and 4) ANNs tend to have stronger discriminant ability compared to conventional statistics.[2,14,32,41]

Leveraging this technology, we created a model that combines clinical and radiologist-interpreted reads to predict whether or not a pediatric patient will experience a CRTBI. We quantify the accuracy and error of this algorithm and provide an open-source software package to enable prediction generation and validation. We expand on previous PECARN predictive studies by utilizing a combination of demographic, clinical, and radiologist-interpreted CT findings to investigate CRTBI in pediatric patients using ANN. We hypothesized that we could train an ANN on clinical and radiographic data to identify which pediatric TBI patients with head CT are at risk for CRTBI.

Methods

Study population

This study utilized the prospective PECARN study of children with Clinically Relevant TBI, as described previously.[16,20] The PECARN TBI study enrolled patients under the age of 18 who experienced non-penetrating (i.e., blunt) head trauma that presented to the emergency department between 2004 and 2006, and had admission head CT imaging classification. All data analyzed in this study was de-identified and our study was approved by the Vanderbilt University Institutional Review Board. We included patients who had complete data available for all variables of interest, and thus did not impute any missing variables. 14,969 patients underwent head CT, of which 12,902 patients had complete imaging information.

Analysis and Variables Included

Descriptive statistics including Pearson correlation and t-test were used to evaluate the normally distributed cohort. Statistical significance was set *a priori* at $P < 0.05$. The input variables included in our ANN are as follows: 1) Mechanism of injury (e.g., motor vehicle collision, pedestrian struck by moving vehicle, bicycle rider struck by automobile, bicycle collision or fall from bicycle, other wheeled transport crash, fall to ground from standing/walking/running, walked or ran into stationary object, fall from an elevation, fall down stairs, sports, assault, objective struck head- accidental, and other etiology of injury); 2) Severity of injury mechanism [low (e.g., fall from ground level and walked/ran into stationary object), moderate (any other mechanism), high (e.g., motor vehicle collision with patient ejection, death of another passenger, or rollover, pediatric or bicyclist without helmet struck by motor vehicle, falls > 5 feet or patients 2 years and older, falls of > 3 feet < 2 years old)]; 3) Loss of consciousness; 4) Glasgow Coma Scale at presentation; 5) Age; and 6) Sex.

The 17 variables identified by radiologists on CT imaging included the presence or absence of the following: cerebellar hemorrhage, cerebral contusion, cerebral edema, cerebral hemorrhage/intracerebral hematoma, diastasis of the skull, epidural hematoma, extra-axial hematoma, intraventricular hemorrhage, midline shift/shift of brain structures, pneumocephalus, skull fracture (and cerebral spinal fluid leak), subarachnoid hemorrhage, subdural hematoma, traumatic infarction, diffuse axonal injury, herniation and, shear injury. Head CTs were interpreted by attending radiologists at each clinical site and a blinded pediatric radiologist made definitive interpretations on scans that were difficult to interpret.[20] Each site was responsible for ensuring the accuracy of their data reported to PECARN. In addition, a subsequent study detailed consistent inter-rater reliability in all data collected by the PECARN consortium.[23]

Our outcome of interest is “clinically-relevant TBI (CRTBI),” a composite of several variables as defined by the PECARN investigators.[20] The CRTBI variables consisted any of the following: 1) Neurosurgical procedure (e.g., dura repair for cerebrospinal fluid leak, fracture elevation, hematoma drainage, intracranial pressure monitor placement, lobectomy, tissue debridement, ventriculostomy, and “other” neurosurgical procedure) 2) Intubated > 24 hours as direct result of the head trauma 3) Hospitalization ≥ 48 hours and evidence of TBI on head CT 4) Death due to TBI.

Artificial Neural Network Analysis

We trained an ANN using offline MATLAB R2016b (9.1.0.441655) on a 64-bit MacBook Pro running OS 10.11.6. We randomly partitioned patients into three groups in order to provide holdout validation on our large dataset; 70% were for training the ANN; 15% were for validating the ANN; and 15% were for subsequent final testing of the ANN. The ANN had not been exposed to any of the final test patients until after the model was finished training and validating. A two-layer, feed-forward ANN with 11 sigmoid hidden and softmax output neurons were trained using the scaled conjugate gradient back-propagation method on the dedicated partition. We tabulated confusion tables and statistics on the testing partition, as well as for the entire dataset. We assessed the predictive ability of the model rigorously with various numerical measures of accuracy, precision, and error.

Results

In this study, we included 12,902 patients of which 63% were male and the average age was 7.99 ± 5.91 years (Table 1). Of the 12,902 patients included in these analyses, 480 suffered a CRTBI. Aside from age and gender, all other clinical and imaging variables had a univariate association with CRTBI (Table 2).

The ANN has a sensitivity of 99.73% and a negative predictive value (NPV) of 91.23% for CRTBI in the testing cohort (Table 3). When the data used for testing were combined with the remaining 85% of data, which the network was trained and validated on, the sensitivity remained very high at 99.54% and NPV of 84.38% (Table 3). Determination of specificity was much lower at 60.47% for testing and 64.17% for the entire dataset. We included other statistical measures of the ANN binary classifier (Table 3). A pictorial representation of the ANN constructed here is shown in Figure 1.

Receiver Operator Characteristic (ROC) curves for both test patients and the entire dataset are calculated and provided, as seen in Figure 2. The Area Under the ROC (AUROC) was 0.9907 for prediction of CRTBI in test patients and 0.9790 for the entire data set.

Discussion

We constructed and validated an artificial neural network (ANN), a machine-learning computational algorithm, to predict CRTBI in children using clinical and imaging data. This platform has apparent clinical utility for the inexperienced pediatric emergency care provider to assign admission for children with TBI given its very high sensitivity for CRTBI, which has small prevalence (<5%) but serious consequence, such as future intracranial procedure(s), respiratory failure, prolonged hospitalization, and/or mortality.[34] This would be the first study to our knowledge aiming at predicting TBI of any type in any patient population.

Predictive outcome and prognostication models are becoming increasingly important across medicine and surgery (e.g., CHA_2DS_2-VASc score,[12,13] Acute Physiology and Chronic Health Evaluation [APACHE],[18] Sequential Organ Failure Assessment [SOFA][40]), and modeling techniques have evolved over the years. These models have classically relied on logistic regression or conventional statistics to generate predictions, and often use fewer input variables that are manually entered. More recently, artificial neural networks (ANN) have been shown to robustly predict complications, outcomes and prognosis among numerous fields,[6,14,32,35–37] including TBI.[9,19,27,33,38,39] Thus, an ANN tool could yield predictive information for CRTBI would helpful and provide an evidence-based mechanism for treating these patients.

ANNs are computational constructs used to interpret the maximum number of combinations of data in complex systems, like making medical diagnoses, where many competing factors influence the outcome.[3] During training of the ANN, random “weights” are assigned to each input variable, compared against every variable in the model, and then used to predict the strength of correlation with the outcome of interest (Figure 1). While there is no maximum number of variables that can be included in an ANN, addition of irrelevant variables will not make the data prediction any stronger.[42] Thus, we chose to rationally design the ANN described here by only including variables which had previously been shown by univariate statistics to be significantly associated with CRTBI.

We trained an ANN on data collected from PECARN and successfully developed a very sensitive (Sensitivity= 99.73% AUC= 0.9907) tool for identifying CRTBI (NPV = 91%) in children. We optimized the ANN for sensitivity over specificity to conservatively identify patients likely to be diagnosed with CRTBI. Future iterations of this ANN with additional variables and data not available through PECARN, could be similarly leveraged to optimize specificity, thereby safely ruling out disease. However, since PECARN is a group consisting of 25 hospitals and collected data prospectively, these data most accurately reflect the epidemiological and treatment diversity seen across North America for pediatric TBI. Importantly, the number of variables included in the predictive ANN algorithm can be greatly increased compared to prior risk-calculation tools due to the overwhelmingly computational superiority of machine-learning compared to conventional statistical approaches, which are limited by degrees of freedom.[30,32,38,42] Our intent was to provide software allowing for real-world incorporation of data into a standalone application or an EMR. Future applications could self-collect this clinical data (i.e., our published algorithm depends on collected and interpreted data), and therefore would integrate all necessary input data from electronic medical record systems, and provide results for the clinician on-the-ground. Another strength of this study is its external generalizability, as we did not further divide our cohort based on any further head-injury patterns (e.g., subdural, epidural, intraparenchymal hematoma, shear) often seen in the literature, as we wanted to reflect the full-spectrum of pediatric patients with all severities and pathoanatomic types of TBI presenting to any emergency department.

In the authors’ opinion, future iterations of ANN-based predictive modeling should be center around three guiding principles: 1) prospective data collection leading to real-time updates and refinement of the algorithm, 2) directly linking ANN models to the electronic health record and 3) increase in the granularity of data available for training the ANN, for instance, using image-based processing. First, compared to traditional statistical approaches which require new analyses to be performed each time new data is added, ANNs can be constantly updated, providing real-time, up-to-date information and quantitative evidence. ANNs could be designed to be using national, regional, or even provider-specific data. Second, directly linking ANNs to the electronic health record would provide streamlined data collection and up-to-date predictive capabilities based on the most current evidence. Lastly, ANNs could be trained directly on the CT images themselves, leading to quicker diagnosis, prognosis and better utilization of hospital resources.

Although we lay the ground-work for incorporating machine-learning into evaluation of children with TBI, this study is not without limitations. First, because machine-learning algorithms are computational constructs that are not familiar to most physicians, these models can be seen as foreign and/or unproven entities.[7] However, as the importance of utilizing “big data” increases, utilizing AI and ML will inevitably be tools used going forward.[7,10,25] Second, despite the very large number of total patients, the number of patients in each individual subset of CRTBI was low. However, with additional data, we believe we can create more sophisticated models with higher specificity in the future providing even better data on who can be safely discharged without risk for readmission. Furthermore, we were not able to incorporate standardized metrics observed during the patient’s physical exam, details that are difficult to quantify and capture. Thus, while algorithm-based decision tools can be useful in guiding the physician’s decision, these constructs absolutely do not replace the information that can only be obtained by a trained physician. Third, each patient in our study obtained head CT imaging, an assumption in itself that our model is heavily dependent on, a decision that is not standardized across institutions and likely changes over time. There is an extensive literature on the utility and safety of head CT for mild TBI in children since these data’s collection.[24] These imaging data have been dichotomized without providing further quantification per covariate (e.g. degree of midline shift, quantification of hemorrhage). In reality, these CT images are interpreted by a combination of emergency medicine and/or night-hawk radiologists, such that decisions would be made way before a complex research-level interpretation could be accomplished. Lastly, we used a single-data source (PECARN) that is publicly-available and has undergone rigorous quality-improvement. However, we are limited by the clinical-practice standards of those years (2004–2006), including the rationale and threshold to obtain head-CT imaging in children. Further computational restructuring of our ANN model may also provide additional metrics for future studies that analyze the CT data directly instead of the radiologist interpretation.

We posit that in-hospital use of the model may actually increase the power of the algorithm as ANNs can be trained on new data, and has potential to be incorporated as a future online tool or packaged into the electronic medical records system (available for download in the **Supplemental Material**), but would require much of the heavy research-level classification to be performed immediately for this to be time-sensitive and clinically relevant. Currently, much of the trauma registry classifications, clinical documentation, and final imaging reads are done well-after clinical decisions are made, and often times only fully complete well after patient discharge or death.

Conclusions

Training an ANN model using data from PECARN, we have constructed a highly sensitive tool to diagnose CRTBI. Further iterations of this ANN may bring real-time, data-driven updates to the hands of pediatric emergency providers in order to provide the most accurate evidence-based care, and particularly aid mid-level and/or inexperience practitioners in small outlying or austere facilities. Immediate identification of pediatric TBI patients who are likely to require additional hospital resources allows clinical teams and hospital administrators to work synergistically to provide the best clinical care. We believe that approaches like our ANN can offer more robust and accurate predictions that can be updated prospectively in real-time.

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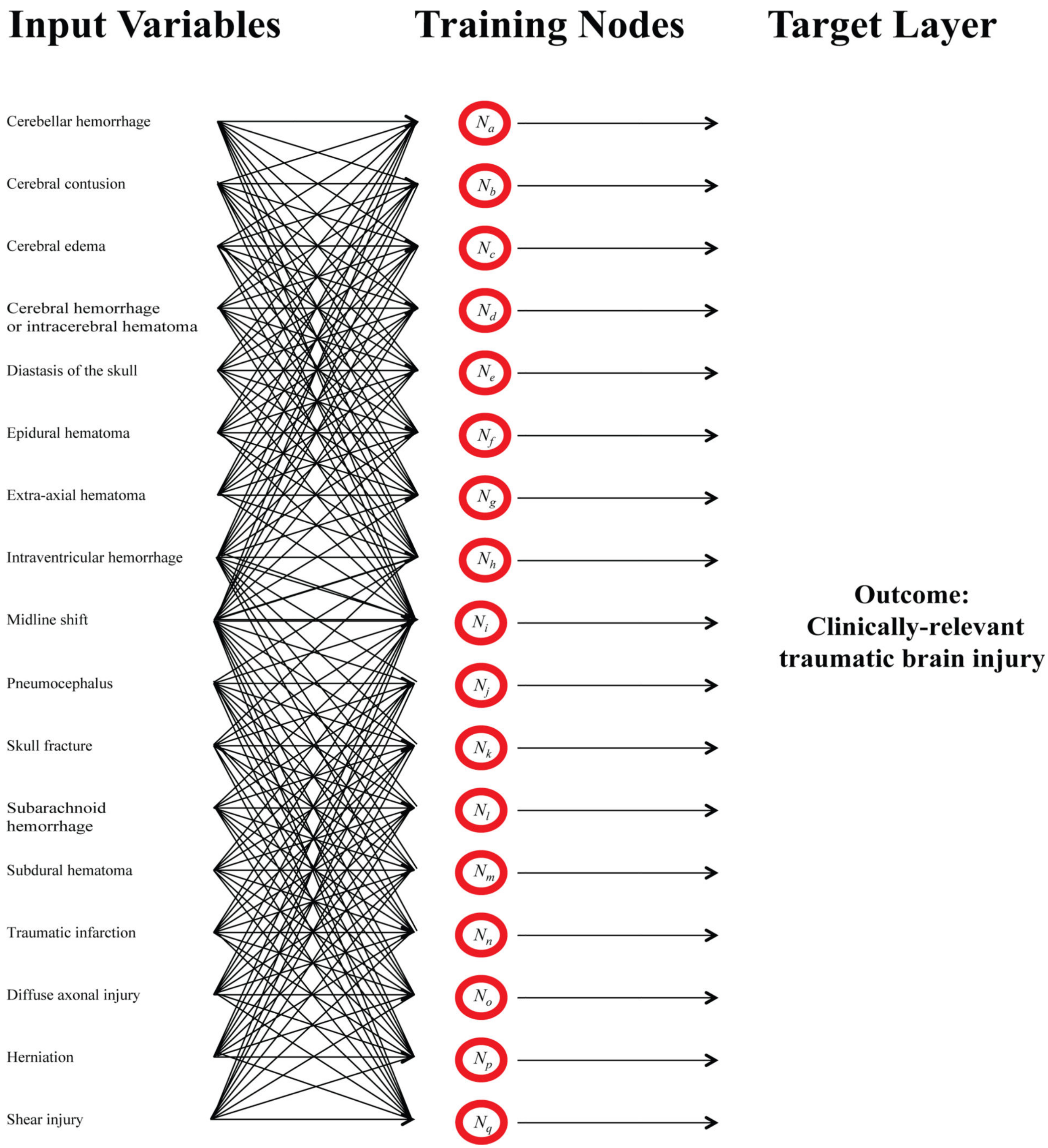

Figure 1: Schematic of the artificial neural network (ANN) constructed here.

Seventeen input variables were compared, converging on more than 100 training nodes (less training nodes were shown for simplicity). Each input variable connects, analogous to projections in neurons, to each training node. Arbitrary “weights” are then applied to each variable. Each training node is then used to determine the best “weights” of each variable to predict the outcome of interest (“target layer”).

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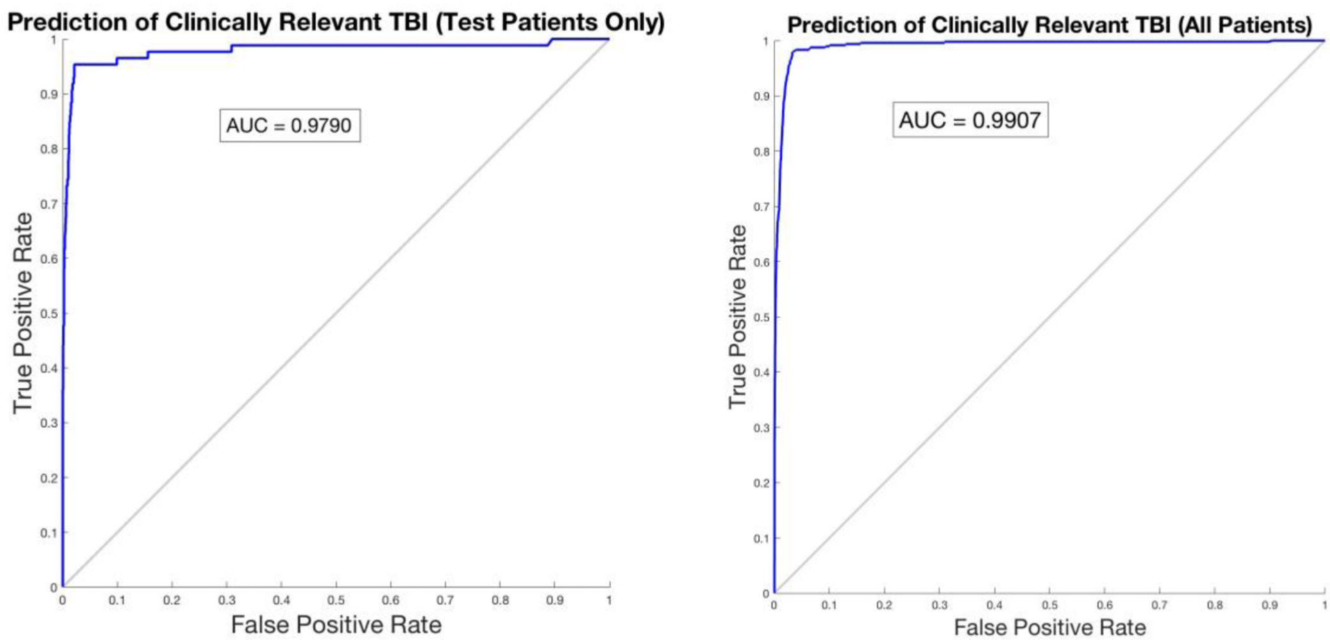

Figure 2: Receiver Operating Characteristic curve for Artificial Neural Network (ANN) predictions of clinically-relevant traumatic brain injury.

We randomly partitioned patients into three groups in order to provide holdout validation on our large dataset; 70% were for training the ANN; 15% were for validating the ANN; and 15% were for subsequent final testing of the ANN. The ANN had not been exposed to any of the test patients until after the model was finished training. The ROC for the testing set of patients (left) and the ROC for the entire dataset (right).

Table 1:

Patient Characteristics of Pediatric Traumatic Brain Injury (TBI) Patients studied using an Artificial Neural Network.

Our outcome of interest is clinically-relevant TBI, a composite of several variables as defined by the PECARN (Pediatric Emergency Care Applied Research Network) investigators. Clinically-relevant TBI included any of the following: 1) Neurosurgical procedure 2) Intubated > 24 hours as direct result of the head trauma 3) Hospitalization ≥ 48 hours, and 4) Death due to TBI.

Variable	Non-Clinically Relevant TBI (n=12,422)	Clinically Relevant TBI (n=480)	All patients (n=12,902)	P Value*
Age (Mean ± SD)	8.00 ± 5.92	7.88 ± 5.67	7.00 ± 5.91	P=0.648
Gender Ratio (M:F)	1.71	1.89	1.72	P=0.305
Severity of Injury				P <0.001
Low	1807	25	1832	
Moderate	7798	243	8041	
High	2817	212	3029	
Loss of Consciousness				P <0.001
No	7928	173	8101	
Yes	3220	239	3459	
NOS	1274	68	1342	
GCS Total	15	15	15	P <0.001

*Univariate statistical significance examined using the t-test or Pearson's chi-squared test.

List of Abbreviations:
GCS = Glasgow Coma Scale
M:F = Male:Female Ratio
n = number of patients
NOS = Not Otherwise Specified

Table 2:

Head Computed Tomography (CT) Findings of Pediatric Traumatic Brain Injury (TBI) Patients studied using an Artificial Neural Network.

Image Findings	Non-Clinically Important TBI (n=12,422)	Clinically Important TBI (n=480)	All patients (n=12,902)
Cerebellar hemorrhage			
No	12418	469	12887
Yes	4	11	15
Cerebral contusion			
No	12365	365	12730
Yes	57	115	172
Cerebral edema			
No	12415	412	12827
Yes	7	68	75
Cerebral hemorrhage or Intracerebral hematoma			
No	12384	381	12765
Yes	38	99	137
Diastasis of the skull			
No	12403	445	12848
Yes	19	34	54
Epidural hematoma			
No	12402	394	12796
Yes	20	86	106
Extra axial hematoma			
No	12358	411	12769
Yes	64	69	133
Intraventricular hemorrhage			
No	12415	456	12871
Yes	7	24	31
Midline shift of brain structures			
No	12416	401	12817
Yes	6	79	85
Pneumocephalus			
No	12361	363	12724
Yes	61	117	178
Skull fracture			
No	11828	184	12012

Image Findings	Non-Clinically Important TBI (n=12,422)	Clinically Important TBI (n=480)	All patients (n=12,902)
Yes	594	296	890
Subarachnoid hemorrhage			
No	12356	369	12725
Yes	66	111	177
Subdural hematoma			
No	12348	337	12685
Yes	74	143	217
Traumatic infarction			
No	12422	476	12898
Yes	0	4	4
Diffuse axonal injury			
No	12422	475	12897
Yes	0	5	5
Herniation			
No	12422	475	12897
Yes	0	5	5
Shear Injury			
No	12419	466	12885
Yes	3	14	17

*Univariate statistical significance examined using the t-test or Chi-squared analysis.

Table 3.

Confusion Table Statistics: Testing Results* of an Artificial Neural Network on Pediatric Traumatic Brain Injury (TBI) Patients.

We randomly partitioned patients into three groups in order to provide holdout validation on our large dataset; 70% were for training the ANN; 15% were for validating the ANN; and 15% were for subsequent final testing of the ANN. Various measures of predictive ability on the test patients, as well as test patients combined with those used for training and validation are presented as proportions.

Measure	Results (Test Group)	Results (All Patients)
Sensitivity	0.9973	0.9954
Specificity	0.6047	0.6417
Precision	0.9819	0.9863
Negative Predictive Value	0.9123	0.8438
False Positive Rate	0.3953	0.3583
False Discovery Rate	0.0181	0.0137
Accuracy	0.0027	0.0046
F1 Score	0.9798	0.9823
Matthews Correlation Coefficient	0.7337	0.7272
Area under ROC Curve	0.9907	0.9790