**BME 580.670-671 Precision Care Medicine**

**Project Title: A Computational Model to Predict Neurological Recovery Following Moderate and Severe TBI**

**Problem Statement**:

Methods are lacking to accurately predict neurological outcome following moderate and severe TBI

**Project Team:**

**Domain PIs/Mentors**

1. Dr. Robert Stevens, Associate Professor of Anesthesiology and Critical Care Medicine
2. Dr. Jose Suarez, Director, Division of Neurosciences Critical Care

**BME PIs/Mentors:**

1. Dr. Rai Winslow, Director, Institute for Computational Medicine
2. Dr. Sridevi Sarma, Associate Professor, Biomedical Engineering

**Background**:

The prediction of clinical recovery and long-term outcome following TBI is a major clinical challenge. The most widely validated TBI prediction models such as the IMPACT or CRASH scores do not discriminate outcomes with a level of accuracy that would be useful at the individual patient level (1, 2). This difficulty may reflect profound heterogeneities within TBI populations. Recent large-scale prospective studies such as CENTER-TBI (3) and TRACK-TBI (4) contain detailed data on clinical phenotypes, serum markers, brain imaging (CT and MRI) and longitudinal outcome. In a subset of patients with moderate and severe TBI admitted to the ICU, physiologic time series data are available. Our principal objective is to create high-performing prediction models by applying advanced statistical and machine learning methods to the high-resolution, multi-dimensional data available in CENTER-TBI.

**Potential Solution:**

We will leverage high-resolution data from the CENTER TBI study, a prospective multicenter observational cohort, with the aim of building novel prognostic models (3). We will integrate physiologic data from the ICU, together with neuroimaging and clinical patient data. We hypothesize that integration of features from these different modalities will yield a prediction model that will outperform current TBI prognostic models (IMPACT, CRASH) and models established utilizing each modality separately. We will also seek to identify clinically meaningful subtypes of TBI. Aims are threefold:

* **Aim 1:** Extraction and pre-processing of CENTER TBI data
* **Aim 2:** Train classifiers using different combinations of features (clinical patient data, Time series features, Imaging features) to predict neurological outcome at hospital discharge and at one year
* **Aim 3:** Identify subtypes of TBI using unsupervised clustering approaches

**Preliminary Data/Relevant Experience**:

Students will work with domain and engineering faculty to refine the study aims and hypotheses. They will build innovative models to predict TBI outcome. They will identify novel subtypes of TBI based on physiologic and demographic features, and they will link subtypes to specific clinical trajectories such as the development of coma, resolution of coma, survival, and death.

Feasibility of this work is supported by PIs Drs Stevens, Suarez and Winslow successfully mentored a Precision Care Medicine student group (2018-2019) working with another data set to build a computational prediction model in cardiac arrest patients. Results generated from that effort are in a manuscript to be submitted imminently for peer review.

**Data Set Identification**:

Data for the study will come from CENTER TBI, a large multi-center observational cohort of patients with TBI (<https://www.center-tbi.eu/>). CENTER-TBI contains high resolution data on > 5,400 patients across the severity spectrum, with approximately 1,500 identified in as moderate or severe (ICU stratum)(3, 5). Dr Stevens is an affiliate investigator on CENTER-TBI and has connections with several of the lead investigators (Drs Menon, Maas, Lingsma, van der Jagt). For model external validation purposes, we will consider the eICU and/or MIMIC-III databases. MIMIC-III contains >40,000 patient health records along with high frequency physiological time series data(6). eICU contains data on similar data on >220,000 patients admitted to over 300 ICUs in 200 hospitals across North America(7).

**References:**

1. Murray GD, Butcher I, McHugh GS, et al. Multivariable prognostic analysis in traumatic brain injury: results from the IMPACT study. J Neurotrauma 2007;24(2):329-337.

2. Collaborators MCT, Perel P, Arango M, et al. Predicting outcome after traumatic brain injury: practical prognostic models based on large cohort of international patients. BMJ 2008;336(7641):425-429.

3. Maas AI, Menon DK, Steyerberg EW, et al. Collaborative European NeuroTrauma Effectiveness Research in Traumatic Brain Injury (CENTER-TBI): a prospective longitudinal observational study. Neurosurgery 2015;76(1):67-80.

4. Nelson LD, Ranson J, Ferguson AR, et al. Validating Multidimensional Outcome Assessment Using the TBI Common Data Elements: An Analysis of the TRACK-TBI Pilot Sample. J Neurotrauma 2017.

5. Volovici V, Ercole A, Citerio G, et al. Intensive care admission criteria for traumatic brain injury patients across Europe. J Crit Care 2019;49:158-161.

6. Johnson AE, Pollard TJ, Shen L, et al. MIMIC-III, a freely accessible critical care database. Sci Data 2016;3:160035.

7. Pollard TJ, Johnson AEW, Raffa JD, et al. The eICU Collaborative Research Database, a freely available multi-center database for critical care research. Sci Data 2018;5:180178.