NEUROLOGIC EMERGENCIES: MINUTES MATTER

Innovation and Improvement in the Early Diagnosis, Treatment, and Monitoring of Neurologic Emergencies at the Michigan Center for Integrative Research in Critical Care (MCIRCC)
A neurologic emergency is a condition that is life-threatening or in which a patient is faced with poor functional recovery unless treated promptly. Acute neurologic injuries in the brain and spinal cord are among the hardest injuries to treat. Even when they aren’t fatal, the ability to recover is limited.

Each year in the United States, an estimated 2.8 million people sustain a traumatic brain injury (TBI), more than 795,000 people suffer a stroke, and approximately 17,700 sustain a spinal cord injury. That’s why the Michigan Center for Integrative Research in Critical Care (MCIRCC) is developing diagnostics, monitors and therapeutics for patients who suffer acute neurologic catastrophes such as TBI, stroke, and acute spinal cord injury (SCI).

Types of Neurologic Emergencies MCIRCC Specializes In

**Traumatic brain injury** is a disruption in the normal function of the brain that can be caused by a blow or jolt to the head, an explosive blast, or from a penetrating head injury. TBI can be lethal, result in coma, and/or leave victims with permanent severe disabilities based on the region of brain that is injured.

**Stroke** is when blood flow from an artery supplying a region of the brain is stopped due to an occlusion in the artery (Ischemic Stroke) resulting in the loss of function in areas controlled by that region of the brain. Another major type of stroke can occur when the wall of an artery in the brain breaks, causing blood to leak out of the artery and into the brain and resulting in loss of certain brain functions.

**Acute spinal cord injury** is when the spinal cord is damaged from an accident or other situation leaving it partially or permanently damaged. Depending on the level of the injury this can result in partial or complete paralysis of the limbs as well as varying degrees of respiratory difficulty.
48% of all TBI-related ED visits, hospitalizations, and deaths in the U.S. were due to falls.

Every four minutes, someone dies of stroke.

Vehicle crashes are the leading cause of SCI.

Number of years life expectancy decreases following a TBI.

Stroke is the fifth leading cause of death in the U.S., killing about 140,000 Americans each year—that’s 1 of every 20 deaths.

About 78% of new SCI cases are male.

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JOINING FORCES TO CHAMPION TBI

The Joyce and Don Massey Family Foundation

MCIRCC became intensely involved in severe TBI as a result of a partnership with the Joyce and Don Massey Family Foundation beginning in 2014. Since then, a remarkable journey to drive TBI research to a new level hit full speed. The foundation’s investment in MCIRCC and Michigan Medicine was an investment in the lives of millions of patients around the world who are impacted by TBI every year. Together, we are creating a brighter future for emergency and critical care through bold research, unparalleled education, and exceptional patient care.

Massey TBI Grand Challenge

The Grand Challenge is a powerful funding avenue for research teams comprised of medical, engineering, data, and industry experts. The competitive nature of the Challenge pushes these experts to bring their biggest and best ideas forward to receive collective, honest feedback from some of the top thought leaders in the fields of TBI, commercialization, and entrepreneurship.

The high-risk, high-reward, milestone driven proposals are selected to receive funding over a 12-month timeframe. More than 35 research teams have had projects funded resulting in their work being published in peer-reviewed journals, presenting at national conferences, and obtaining follow-up funding through other sources such as the NIH and Department of Defense. Some projects have even made it all the way to commercialization, spinning off four new companies since 2015.

Joyce Massey TBI Summit

TBI has had few advancements in diagnosis and treatment despite its high ranking amongst other injury-related deaths. Every other year the Summit brings leading TBI experts from across the country together to present their current research, discuss the future of the field and identify important barriers to improving TBI outcomes.
Partnering with the Department of Defense

Department of Defense (DoD) service members and families represent the largest U.S. population suffering from the impact of TBI. Through a collaborative partnership, the U.S. Army’s Combat Casualty Care Research Program brings expertise and resources to MCIRCC helping to accelerate the movement of translational research outputs into the field. DoD Neurotrauma leadership members form part of the Massey TBI Grand Challenge panel, assisting in reviewing proposals for funding, and providing mentoring to each of the funded teams. In addition, this partnership provides our TBI researcher community with invaluable resources and opportunities.

- Educational seminars
- Early notification of DoD funding opportunities
- Increased national awareness of U-M’s TBI research program
- User feedback to help fine-tune research
- Collaborations with leading TBI experts
- Access to DoD research database
The Michigan Center for Integrative Research in Critical Care (MCIRCC) is the innovation hub for more than 200 critical care researchers across the University of Michigan from 7 schools/colleges and 43 departments.

As one of the first comprehensive enterprises devoted to transforming critical care medicine, we foster multidisciplinary collaborations between our members—unifying scientists, clinicians, engineers and industry partners—to accelerate science and deploy cutting-edge solutions that elevate the care, outcomes, and quality of life of the critically ill and injured.

In the last four years, MCIRCC multidisciplinary teams have licensed ten new products, started 5 new companies, and received more than $30 million in funding toward innovative projects in critical care.
Leaders & Best

We Are Wolverines With A Recipe For Success.

MCIRCC is focused on leveraging our multidisciplinary model of research with our ability to integrate University of Michigan’s prestigious reputation, campus-wide talent, and supporting resources to bring university-led critical care innovations to market. Our members span many disciplines across the university, yet have the common goal of improving the lives of critical care patients and their families.
Funded and Emerging Research and Products

Below are several examples of the transformative work being accomplished by MCIRCC innovators using resources such as the Massey Grand Challenge and funding from the DoD, NIH, and other sources. While many efforts may initially be targeted for one neurologic emergency such as TBI, by recognizing the common pathophysiology shared by TBI and other neurologic injuries, most of the innovations below will find significant use in other severe neurologic conditions such as stroke, SCI, and hypoxic brain injuries caused by cardiac arrest, drowning, and others.

Barreleye

Barreleye (taken from the fish with a transparent head) collects physiological data from various monitors and calculates clinically-relevant measures such as Shock Index and Pressure Reactivity Index to gauge patient neurologic trajectory and predict potential adverse events for patients with injuries such as TBI and stroke. This non-invasive technology integrates with existing monitors and systems, and can calculate hemodynamic trends to reduce the risk of secondary brain insult.

New Intracranial Pressure Monitor

The need to invasively monitor intracranial pressure (ICP) is sometimes unavoidable after severe neurologic injuries such as TBI and hemorrhagic stroke. However, current ICP catheters have not evolved to provide any additional information. An MCIRCC team is creating a new ICP catheter that not only measures ICP but is also capable of measuring cerebral blood flow and cerebral vascular reactivity and resistance by embedding new smart materials into the catheter. By doing so, care providers will be better able to provide precision treatments to optimize cerebral health after injury.

Systolic Target Assessment Tool (STAT) for TBI Management

Timely and accurate knowledge of systolic blood pressure (SBP) aids in preventing hypotension, a major cause of secondary brain and spinal cord injury. The Systolic Target Assessment Tool is a non-invasive high-fidelity monitor that provides a near continuous indication of a critical level of a patient’s SBP, allowing first responders to keep patients at an optimal SBP to improve their chances of survival and neurologic outcome. The device combines pulse oximeter and blood pressure cuff data with a programmable algorithm for monitoring.

Valproic Acid (VPA) to Treat TBI

When an injury in the body occurs, the body tries to maintain its equilibrium by activating genes or pro-survival pathways. Some do this better than others. Valproic Acid (VPA) is FDA-approved and currently is used to treat seizures. MCIRCC researchers found that VPA activates the pro-survival pathways almost instantly when used in high doses. Pre-clinical studies demonstrate improved outcomes after severe TBI. For TBI, cardiac arrest, and potentially other neurologic injuries this improves long-term neurological recovery and healing.
Automated Optic Nerve Sheath Diameter Measurement for TBI Patients

The optic nerve is part of the central nervous system surrounded by cerebrospinal fluid (CSF) and encased in a sheath. The sheath is continuous with the lining of the brain, and its diameter changes rapidly with changing intracranial pressure. Using ultrasound to measure optic nerve sheath diameter (ONSD) has shown to be useful to track changes in intracranial pressure with high precision. However, manually assessing ONSD is cumbersome and prone to human error. An automated algorithm has been developed using image processing techniques to analyze ultrasound images to calculate ONSD. Following tests and comparison, the algorithm yielded a strong correlation between the automated method’s results and the ground truth, as well as between two manual measurements.

Automated Hematoma Segmentation for TBI Patients

Subdural hematoma (blood accumulation between the brain and skull) is one of the most common types of injuries after TBI, and its early diagnosis and removal can improve outcomes. However, its visual detection and quantitative evaluation are time consuming and prone to error. A fully automated clinical decision support system using machine learning and image processing techniques for quantitative measurement of subdural hematoma volume was created. 3D segmentation of convexity subdural hematomas is performed by analyzing textural, statistical and geometrical features from computed tomography (CT) images of the head’s intracranial region.

Point of Care Microfluidic Device for Brain Injury Blood Biomarker Detection

New science is showing the promise of measuring brain proteins and other markers in circulating blood that leak out of the brain after injury. The ability to rapidly measure these markers at the bedside and even in the field may help to significantly speed the diagnosis of neurologic injury and allow faster intervention, as well as to track the progression of injury and guide treatment. MCIRCC is developing a microfluidic testing device that will allow for the bedside detection of these blood biomarkers giving care providers a timing advantage in the diagnosis and treatment of severe neurologic injuries.

MitoLUX

Global brain injuries resulting from cardiac arrest or TBI, and severe regional brain injuries such as stroke often result in poor neurological outcomes. In each of these conditions blood flow is restricted to the brain. Upon resuscitation, blood flow is restored, which drives the generation of toxic free radicals and induces cell damage. Unique therapeutic wavelengths of infrared light (IRL) produced by the MitoLUX device directly and non-invasively modulate the mitochondrial activity and prevent generation of free radicals. The non-invasive MitoLUX protects the mitochondria and reduces stress and oxidative brain injury, improving cell survival and neurological outcomes.

Digital Extraventricular Drain Integrated ICP Monitor (DEVD)

Accurate intracranial pressure (ICP) monitoring is essential to evaluating and treating TBI and severe hemorrhagic stroke during the early hours of care. Using external ventricular drains (EVD) to monitor and treat ICP can help improve survival, yet current primitive systems are not able to take real-time digital measurements and control cerebrospinal fluid removal, and require manual adjustments by caregivers. Developed by MCIRCC researchers, DEVD aims to digitize this process so that not only would changes in pressure and flow be made automatically, but they would also be integrated with data analytics.

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CASE STUDY: SEEING THE BRAIN THROUGH THE EYES

When first responders are faced with the challenge of caring for a patient with a TBI or other severe brain injury, whether that be in the Emergency Department, in the ICU, out in the field, or on the front lines, the first two concerns are: what is the extent of their initial injury, and are there any secondary injuries underway?

Current technologies make finding those answers complex. Invasive procedures are required that involve special training and potential complications like infection or creating another injury.

The Department of Defense’s Combat Casualty Care Research Program sought development of next-generation diagnostics, monitoring, resuscitations and stabilization methods for prolonged field care (PFC) and prolonged damage control resuscitation (pDCR). Trans-Ocular Brain Impedance (TOBI) was one of the responses to this request.

To prevent secondary brain injury after a TBI and other neurologic injuries, the ability to monitor and optimize cerebrovascular autoregulation (CAR) has been one of the holy grails of neurologic care. CAR reflects the brain’s blood vessels’ ability to relax and contract to compensate for changes in blood pressure and maintain a critical level of blood flow to the brain to support its survival. If CAR is impaired, severe secondary brain injury occurs.

(Continued)

BE A VICTOR

“Severe neurologic injuries such as TBI, stroke, and SCI are perhaps the most dreaded of injuries because of our continued inability to significantly impact outcomes. Combined with the critical factor of time, the challenges to improve care have been perceived to be intractable. Transformative change is best accomplished by combining the imagination with the necessary resources to create a new reality for the victims and those who care for them.”

- Dr. Kevin Ward, MCIRCC Executive Director
The MCIRCC solution is to use non-invasive bioimpedance to evaluate changes in cerebral blood volume (CBV) to determine whether CAR is intact. Bioimpedance is an electrical property of tissues that describes the degree to which the tissues resist an externally applied electrical current and which is heavily influenced by the amount of blood that is in the tissue.

TOBI measures the tissue's resistance to an induced current, and non-invasively tracks changes in CBV from changes in cerebral blood flow and intracranial pressure to determine CAR impairment. The device can also collect additional information such as respiratory variation and heart rate, giving physicians further insight into a patient's status.

TOBI has utilized all aspects of MCIRCC—the Proposal Development Unit to secure funding awards from the DoD, the Pre-Clinical Operative and Intensive Care Unit for lab testing, the Clinical Research Unit to collect and use data from patients, Commercialization Coaching for guidance in follow-on funding and prototype development, and Data Science Services to capture and deidentify data.

The project was led by Hakam Tiba, MD, MS. His team included MCIRCC’s Executive Director, Kevin Ward, MD from the Departments of Emergency Medicine and Biomedical Engineering. Other MCIRCC members included Hasan Alam, MD (Department of Surgery), Craig Williamson, MD (Department of Neurosurgery), and Venkatakrishna Rajjee, MBBS (Department of Neurosurgery).

SAVE A LIFE - BUT FIRST, INFLUENCE SCIENCE AND DISCOVERY.

With current scattered and insufficient funding sources, high-risk research to enhance long-term survival and quality of life after a neurologic emergency seems out of reach. In order to expedite the ability to better treat patients, we are embarking on a financial model that depends upon private support from donors, investors, and entrepreneurs. The investment is great, but the return on the investment holds the promise of being a game changer. These funds will enable MCIRCC to maintain research facilities, engage our members, and enable scientists, engineers, and physicians to be disruptive and transformative in their approach to invent the solutions necessary to save lives.
For more information, contact:

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