STATE-OF-THE-HEART

Innovation and Improvement in Cardiovascular Critical Care at the Michigan Center for Integrative Research in Critical Care
Each year in the United States, approximately 400,000 patients are treated for sudden cardiac arrest. Fewer than 1 in 5 of those victims survive after an in-hospital arrest, and less than 1 in 10 out-of-hospital. Even among patients who survive, less than one third make it to hospital discharge, often dying as a result of further complications.

According to a recent statement by the American Heart Association (AHA) the demand for cardiovascular critical care has risen with the aging of the population. Between 2000 and 2005, the total number of hospital beds in the U.S. fell by 4.2%, but the number of critical care beds rose 6.5%. According to the AHA, cardiovascular medicine has lagged behind other specialties that have met the ‘critical care crisis’ with ICU-focused innovations.¹

To help meet the need for next-generation cardiovascular diagnostic tools and therapeutics, the Michigan Center for Integrative Research in Critical Care (MCIRCC) at the University of Michigan has developed a comprehensive approach to understanding the pathophysiology of cardiac arrest, cardiogenic shock, and other critical cardiovascular conditions. The fundamental challenges addressed by our program are to discover and translate new precision diagnostic and treatment strategies that are uniquely designed to provide the right treatment at the right time. This will enable the field to move away from the one-size-fits all approaches of the past to more innovative therapies of the future.

At MCIRCC, basic science researchers, clinicians, engineers, data scientists, donors, and entrepreneurs are working together to develop dozens of cutting-edge life-saving treatments and therapies. From multi-modal platforms for continuous monitoring and decision support systems to new precision treatment strategies for post-cardiac arrest brain and multi-organ injury; MCIRCC is on the forefront of innovative procedures with the same goal in mind: a better chance at patient survival, and a better quality of life during and after treatment.

¹ MedPage Today. 17 Aug 2012
Every 25 seconds an American will have a coronary event.
American Heart Association/American Stroke Association, 2012, 4/12DS5479

Victims begin experiencing brain damage within 6 minutes of cardiac arrest.
Centers for Disease Control and Prevention, 30 Apr 2015

More than 73% of sudden cardiac arrest victims in the United States die before reaching the hospital.
“Demographic and Survival Characteristics of OHCA,” CARES Summary Report, 05 Mar 2018

Cardiogenic shock (a complication of cardiac arrest, myocardial infarction, and congestive heart failure) has a mortality rate of nearly 50%.
Auxiliary Board of Northwestern Memorial Hospital
MCIRCC’s cardiovascular research and product portfolio focuses on advancing innovative therapeutics and novel diagnostics, devices, and digital health solutions to diagnose, treat and prevent severe cardiac illnesses and injuries. Our integrative approach to research plays a significant role in developing strategies that enable translational research, which includes promoting entrepreneurship and commercialization. MCIRCC has a unique commercialization program designed to create breakthrough therapies and diagnostic tests that contribute to our overall mission of reducing the burden of critical cardiovascular illness and injury. MCIRCC supports discoveries from the laboratory all the way to clinical testing, licensing and commercialization.

The projects below, and right, have been licensed to industry partners through the combined efforts of MCIRCC’s Commercialization Team and the University of Michigan Office of Tech Transfer.

**Microvascular Oximetry**
Licensed to Pendar Technologies, MCIRCC investigators developed a microvascular oximeter utilizing resonance Raman spectroscopy to non-invasively measure peripheral tissue hemoglobin oxygenation (StO2) as a real-time indicator, of reduced tissue oxygen supply from cardiac failure, shock, and other causes. The technology is portable and allows for point-of-care and continuous monitoring.

**Trans Ocular Brain Impedance (TOBI)**
TOBI is a non-invasive impedance-based, wearable monitor allowing for rapid and continuous evaluation and monitoring of cerebral autoregulation. TOBI is being developed to monitor cerebral autoregulation to improve outcomes in patients experiencing cardiac arrest or undergoing complex cardiovascular surgeries and cardiac critical care that can result in severe neurologic impairment. TOBI is licensed to New Vital Signs, Inc.
### LICENSED PRODUCTS

**Vascular Tone Monitoring System (VATMOS)**

Licensed to New Vital Signs, Inc., this Vascular Tone Monitoring System (VATMOS) detects potential cardiovascular events and hypotension much earlier than the traditional blood pressure monitoring system. This unique, wearable sensor is worn on the finger and connects to any portable device or monitor to continually measure the vascular tone and reactivity of small blood vessels.

**Rapid Oxygen**

Rapid Oxygen is a low-cost, disposable, and ultra-portable device that uses a safe chemical reaction to provide breathable oxygen support in areas where low weight requirements and lack of electrical or battery power, or the danger of using pressurized cylinders limits the use of alternative, bulkier systems. The need for alternative sources of oxygen led to the development of the Rapid Oxygen Company, LLC.

**Analytic for Hemodynamic Instability (AHI)**

The Analytic for Hemodynamic Instability (AHI) is a unique automated computer algorithm that utilizes data from a single lead of a non-invasive electrocardiogram (ECG) signal for analysis and early identification of hemodynamic decline. This non-invasive technology, licensed from MCIRCC by Fifth Eye, allows for intervention well before the development of organ injury.

**AngioAid**

AngioAid is a fully automated, computer-based platform capable of analyzing coronary angiogram videos and generating standardized assessments in real-time. The platform has the potential to identify specific areas of coronary arteries with suspected disease for more intense study and can even estimate the width of blood vessels to determine the presence and percentage of blockages.

**DRIVE**

Dynamic Respiratory Impedance Volume Evaluation (DRIVE) utilizes changes in limb blood volume produced by breathing, as measured by changes in impedance of the limb, to monitor a patient’s circulating blood volume without the risks of a more invasive treatment. Licensed by New Vital Signs, Inc., this small, wearable and wireless device provides personalized and continuous diagnostic data.

**MitoLUX**

The MitoLUX device safely delivers deeply penetrating infrared light (IRL) of a specific wavelength combination shown to prevent the formation of toxic free radicals in the brain following injury caused by acute ischemia. MitoLUX is based on collaborative discoveries at the University of Michigan and Wayne State University that have led to joint patents that are licensed to a start-up company called Mitovation, Inc.
Gastroesophageal Resuscitative Occlusion of the Aorta (GROA)
GROA is a minimally invasive means to occlude the descending aorta during cardiac arrest allowing increased coronary and cerebral blood flow during cardiopulmonary resuscitation. Occlusion is made possible using an inflatable stomach balloon that compresses the aorta between the posterior wall of the stomach and the thoracic vertebral bodies just below the level of the diaphragm. The technique may allow use of GROA by paramedics.

Therapeutic Vibration Device
MCIRCC is developing a device that delivers specific vibration frequencies to the entire body during states of shock that increase blood flow to vital organs. The device is easy to apply and has been shown in human volunteers to increase peripheral organ and brain tissue oxygenation. The device can also cause muscle contraction and increase oxygen consumption as a countermeasure to the myopathy that occurs during prolonged immobilization in the ICU after events like cardiac arrest or complex cardiovascular surgeries.

Cardiac Arrest Clinical Decision Support System
This clinical decision support system optimizes the ability of paramedics and clinicians to provide precision treatments. New signal processing and machine learning algorithms analyze the cardiac signal of patients in arrest along with other physiologic signals, such as end-tidal carbon dioxide. These help providers determine when to defibrillate, provide additional drugs, or take other measures to achieve return of spontaneous circulation. It can also predict if the victim will re-arrest.

Blood Vital Sign Platform
This unique blood vital sign platform measures important blood properties such as viscosity, red cell deformability, coagulation, and oxidative stress. The combination of these variables is extremely important in diagnosing and treating victims of cardiac emergencies such as heart failure, myocardial infarction, cardiogenic shock, and more. These indicators can help guide the use of anticoagulation medicines, blood transfusion, fluid administration, and in understanding the severity of ischemia and oxidative stress.

EROCA
Extracorporeal CPR (ECPR) is emerging as a potentially effective treatment for out-of-hospital cardiac arrest (OHCA). Using a machine outside of the body to temporarily take over the work of the heart and lungs, the Extracorporeal CPR for Out-of-Hospital Cardiac Arrest (EROCA) study, funded by the National Heart, Lung, and Blood Institute, is generating preliminary feasibility and efficacy data in human victims of cardiac arrest necessary to design a multicenter phase III clinical trial.

ECPR Preclinical Studies
Funded by the National Institutes of Health, researchers at MCIRCC and Michigan Medicine hypothesize that small blood clots and white blood cells block small blood vessels in vital organs preventing restoration of blood flow when Extracorporeal CPR (ECPR) is used to treat prolonged cardiac arrest. Using a clinically relevant large animal model will provide new fundamental knowledge about the mechanisms of no-reflow and help the team evaluate the effect of specific therapies that can then be applied to humans.

Studying Elevated Cardiac Troponin Level in the Critically Ill
Funded by a Michigan Institute for Clinical and Health Research K Award, an MCIRCC research team is creating a biorepository of patient samples to better understand the processes surrounding elevated cardiac troponins of unknown significance (ECTUS) in order to develop a potential treatment. Unlike prior research on troponin, this study treats EKTUS as a condition that may warrant specific treatment rather than a symptom of multiple organ dysfunction syndrome.

Multimodal Platform for Continuous Monitoring and Decision Support for Postoperative Cardiac Patients
This real-time clinical decision support platform analyzes patient data to predict the trajectory of patient recovery after major surgeries involving the cardiovascular system. With funding from the Department of Defense (U.S. Army Medical Research & Materiel Command), the team will train, test, and validate novel computational algorithms that analyze patient data collected from MCIRCC’s Big Data Platform.

Valproic Acid in Cardiac Arrest
In previous trials, Valproic Acid (VPA) has been shown to induce pro-survival proteomic changes in trauma, hemorrhagic shock and traumatic brain injury, and has improved survival rates and neurologic outcomes in rat cardiac arrest models. Using large animal experiments funded by the National Institutes of Health, MCIRCC researchers will employ an adaptive design model to understand how cardiac arrest and hypothermia affects the pharmacokinetics and pharmacodynamics of VPA.
MCIRCC is focused on leveraging our multidisciplinary model of research innovation with our ability to integrate the University of Michigan’s prestigious reputation, campus-wide talent, and extensive 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 critically ill and injured patients and their families.

**WHY MCIRCC?**

**WE HAVE THE RECIPE FOR SUCCESS**

The Center for Integrative Research in Critical Care is the innovation hub for more than 170 critical care researchers across the University of Michigan. 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 five new companies, and received more than $30 million in funding toward innovative projects in critical care.

**Electrocardiomatrix (ECM), ECG of the 21st Century**

ECM is software that reorganizes a 2-D electrocardiogram (ECG) into a 3-D heat-map. This makes inspection of ECG data faster and promotes unprecedented accuracy in arrhythmia detection. The MCIRCC research team that developed the ECM predicts that application of ECM in ECG analysis may lead to dramatic reduction of both false positive and false negative detection of various arrhythmias, including atrial fibrillation, and an increased ability to detect transient myocardial ischemia.

**Noninvasive Central Venous Pressure Monitoring**

MCIRCC scientists have developed and patented an impedance-based, non-invasive method to measure central venous pressure (CVP). CVP is the pressure within the right atrium (a chamber of the heart). Monitoring and optimization of CVP can improve heart function and prevent complications such as renal failure. Measurement of CVP could previously only be measured through invasive procedures, which carry risk and can only be done in special settings.

**Electrocardiomatrix (ECM), ECG of the 21st Century**

**Predicting ICU Transfer and Other Unforeseen Events (PICTURE)**

PICTURE is a powerful machine-learning algorithm based on electronic medical record (EMR). It is capable of predicting patient deterioration, which is common in patients with severe cardiac conditions. The algorithm detects patterns from common data collected in the EMR to predict that patients will develop a change in their condition that could result in death and/or the need to be transferred to the intensive care unit.
Case Study: Could Your Car Predict a Cardiac Event?

MCIRCC is one of eight institutions partnering with Toyota’s Collaborative Safety Research Center (CSRC) to study autonomous and connected vehicle technologies and their impact on broader road safety trends.

The project, led by Kayvan Najarian, PhD and Toyota’s CSRC NEXT scientists, will bring together investigators from emergency medicine, internal medicine, computational medicine & bioinformatics, and computer science.

The team is developing new technologies that could help predict cardiac events on the road and potentially prevent vehicle crashes. The research will utilize machine-learning algorithms to analyze data collected by state-of-the-art sensors to non-invasively monitor a driver’s physiology and possibly predict cardiac events.

“Autonomous and connected vehicle technologies are only just beginning to transform the transportation landscape,” said Chuck Gulash, Director of CSRC. “By working together with world-renowned institutions and making our results public, we are proud to help realize the promise of advanced mobility solutions and a safe, convenient transportation future.”

YOU CAN SAVE LIVES, INFLUENCE SCIENCE, AND SUPPORT DISCOVERY

With current scattered and insufficient funding sources discouraging high-risk research, enhancing long-term survival for cardiovascular illness and injuries requires solutions that seem almost like science fiction. So we are embarking on a unique partnership model that depends upon private support from donors, investors, and entrepreneurs. And while the investment is great, the return on the investment is even greater. These funds will enable MCIRCC teams to perform high-risk research, maintain research facilities, engage our members, and enable scientists, engineers, and clinicians to investigate problems and invent the solutions necessary to save lives.