THE HARTWELL FOUNDATION

2018 Individual Biomedical Research Award

David R. Busch, Ph.D.

Assistant Professor
Department of Anesthesiology and Pain Management

University of Texas Southwestern Medical Center

Monitoring Cerebral Blood Flow Autoregulation to Prevent Brain Injury During Extracorporeal Life Support

Extracorporeal Membrane Oxygenation (ECMO) is a lifesaving temporary intervention for critically ill children with failing hearts or lungs. It is delivered by a pump that takes over some of the work of the heart and circulates blood from the body through a parallel circuit outside the body into an artificial lung called a membrane oxygenator; an extracorporeal process that adds oxygen to the blood and removes carbon dioxide. ECMO has been used to support life in over 35,000 neonatal and pediatric patients in the United States. Unfortunately, about 1/3 of children receiving ECMO encounter neurologic complications (e.g., massive brain hemorrhage), with death an outcome in another 1/3 of cases. Most neurologic injury during ECMO is caused by either low or excess blood flow to the brain. A healthy brain can "autoregulate" to maintain sufficient but not excessive blood flow, even though blood pressure varies significantly. However, in an injured brain the pressure range for autoregulation may shift or narrow. Today, ECMO is adjusted on the basis of measures collected for crucial management of respiration and blood flow, with no technology available for real-time monitoring of risk for brain-focused neurologic injury. To maintain appropriate cerebral blood flow, the brain's changing needs require a bedside monitor to continuously identify vulnerable periods of dysregulated cerebral blood flow and guide compensatory treatments. To meet this need, I propose diffuse correlation spectroscopy (DCS), a non-invasive optical technology that measures the motion of red blood cells and provides an empirical *blood flow index*. I will also utilize time-domain diffuse optical spectroscopy (DOS) to correct the DCS signal for variations in tissue-related light scattering and absorption (e.g., swelling associated with fluid retention) and to quantify cerebral blood volume and oxygen saturation. The DCS blood flow index is directly proportional to absolute microvascular blood flow and is sensitive to changes in hematocrit and average vessel diameter, which are known to reflect changes in local microcirculation and tissue oxygen demand. The correlation between the DCS blood flow index and blood pressure provides a direct metric of cerebral autoregulation. In addition, I will use hybrid DCS+DOS to calibrate indirect metrics of cerebral autoregulation throughout ECMO support. I will use these non-invasive tools to continuously assess autoregulation in real time in 54 children during ECMO, and by comparing outcomes to post-ECMO neuroimaging will develop algorithms to predict neuroinjury. If I am successful, the translation of this technology will yield a clinical autoregulation monitor capable of identifying a blood pressure "safe zone" for the brain during ECMO, reducing morbidity and mortality in the many vulnerable children receiving this lifesaving support.