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Vivonics' Technology Can Improve Recovery after Traumatic Brain Injury

By Jennifer Reisch

According to a Defense and Veterans Brain Injury Center (DVBIC) analysis of surveillance data released by the Department of Defense (DoD), 375,519 U.S. military personnel were diagnosed with a traumatic brain injury (TBI) between 2000 and 2017. DoD personnel are at an increased risk of TBI in both wartime and peacetime training incidents. Post-injury swelling (edema) is a common physiological complication of TBI which can result in added physical damage to the brain, increasing the risk of mortality, brain damage, and long-term disability in personnel suffering TBI. According to Ryan Myers, Ph.D., lead engineer and director of technology and business development at Vivonics, Inc., studies have demonstrated that rapidly lowering brain temperature can reduce the incidence and severity of cerebral edema as well as mortality and complications during treatment and recovery in animals and humans.

Vivonics has been developing a portable system to provide a level of cooled airflow shown to lower pig brain temperatures to both normothermic and therapeutic hypothermic temperatures under Department of Navy (DoN) Phase II contract M67854-19-C-6502. The portable device being developed is the Intranasal Cooler for Encephalopathy Prevention in Combat Casualties (ICEPICC), which will enable a combat medic or paramedic to perform intranasal cooling by affixing a nasal cannula and temperature probe to the patient and setting the desired brain temperature on a simple user interface.

Courtesy of Vivonics, Inc.

Conceptual rendering of unit

Brain cooling can prevent encephalopathy during events including traumatic brain injury, stroke, cardiac arrest, and respiratory failure, where blood oxygen availability is low, swelling is prevalent, and intracranial pressure is high. Cooling of the vessels within the nasal cavity as well as the barrier between the nasal cavity and the brain is a minimally invasive technique used to reduce brain temperature back to normal (normothermia) or even below normal body temperature (therapeutic hypothermia) without requiring cranial access, Myers explained.

Several treatments, including cooling caps, blankets, cuffs, evaporative cooling elements, water cooling nasal cannulas and even direct cold saline injection into the carotid artery, have been

shown to reduce brain temperatures to 33 to 35 degrees Celsius, which is in the therapeutic hypothermia range. However, none of the existing technologies are particularly well suited for military implementation; therefore, the DoN currently does not attempt to cool the brain after TBI despite the significant potential in lessening the degree and impact of TBI.

The concept design for the ICEPICC system is a compact device that provides convective and conductive cooling of the brain. It can provide immediate rapid prophylactic cooling and longer-term therapeutic cooling without dehydrating tissues in the nasal passages. ICEPICC combines the ease of use, ruggedness, size, weight, and power (SWaP) required of military medical equipment to ensure that cooling can be applied as soon as possible, Myers said.

Conceptual rendering of unit

The patented thermoelectric cooler (TEC) based system does not require a pressurized air source, specialized reactant, or circulating liquid; it can be powered by a battery or via an outlet. The system is designed for unit level care through hospitalization, including en route care.

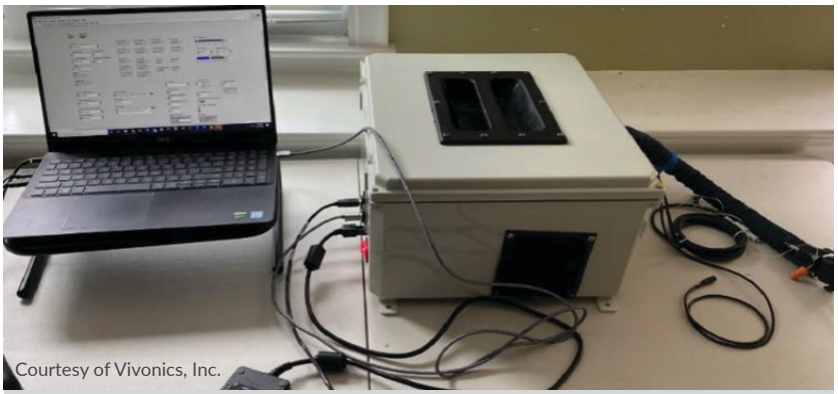
Vivonics has completed the animal studies necessary before human studies of the system can be performed. In the animal study, ICEPICC was found to be safe and effective at lowering brain temperature in healthy pigs. The team is currently preparing three scientific peer reviewed manuscripts about the animal studies. The company's submission has been accepted for distinguished poster by the Neurocritical Care Society (NCS) for its annual meeting, held in October 2021. An article will also be submitted to the NCS companion journal.

Myers said, "We had a hypothesis that we could cool the brain through intranasal cooling, ultimately for traumatic brain injury or trauma patients. To assure safety before testing on humans, the first stage is to evaluate a procedure on animals."

Pigs were chosen for the study because pig noses are similar to human noses in tissue composition. According to Myers, it's important to try to mimic a human as much as possible in an animal model. One of the worries with intranasal cooling was that it would dry out the back of the naval cavity and create more trauma or increase cranial pressure because of the air flow.

"The pig is the model of choice for this type of study because of the closeness in physiology of their nasal cavities, their tissue membranes and their consistent body temperature. Also, their temperature is about 1.5 degrees Celsius higher than ours. They run around 38-39 degrees Celsius and that allows us to show that we can reduce the 'fever' to normothermia by bringing brain temperature down 1.7 degrees Celsius, which is what we ended up showing. That's about a fever of 101 degrees Fahrenheit reduced back to normal. The benefit to testing an animal with elevated temperatures compared to a human is that we can actually show the reduction as opposed to starting at normal baseline and then going hypothermic, which is not the goal."

Before starting the animal studies Vivonics did a literature review of similar previous studies. "We then went to our collaborator, Dr. Jonathan Morrison at the University of Maryland, who is an expert in large animal models and who ultimately led the performance of the studies. There are clinicians on the team who are thinking four steps ahead about what potential outcomes should be measured during the animal studies so that they can be compared to the planned outcome measures in future human studies. Once we had the model designed with the University of Maryland we went to the Food and Drug Administration to make sure that this was the type of study they would want to see in order to reach the indications we are going for. We spent time upfront so that we wouldn't have to repeat the animal studies later on, which is a real risk when considering the FDA approval process. The FDA did suggest a few things and we heeded their advice, expanding the animal study just a little bit," Myers explained. Ultimately the animal study was run at the University of Maryland over several months.



Animal studey setup

Vivonics is ready to enter into a pilot study with brain injured adults. The company is preparing documents to present to the FDA which will show the results of the animal study and how those results suggest a human study is appropriate. The documents will also describe the proposed studies in humans to get feedback from the FDA on that study. Vivonics is also applying widely for funding for human testing as their current funding will only cover the initial pilot portion of this testing.

Once approved, ICEPICC has potential application to several medical conditions in the commercial medical market as well as the DoD. According to the Centers for Disease Control and Prevention, in 2010, about 2.5 million emergency department (ED) visits, hospitalizations, or deaths were associated with TBI—either alone or in combination with other injuries—in the United States. TBI contributed to the deaths of more than 50,000 people and was a diagnosis in more than 280,000 hospitalizations and 2.2 million ED visits. The ICEPICC has the potential for both prophylactic cooling and therapeutic cooling to improve outcomes for these patients.

In addition to TBI, tens of thousands of patients die each year in the United States due to neurological complications after cardiac arrest, and targeted brain temperature management has been shown to improve outcomes and neurological recovery after cardiac arrest.

Vivonics' mission is to improve human health and performance outside traditional healthcare settings. For more information, visit the company website at https://www.vivonics.com/.

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