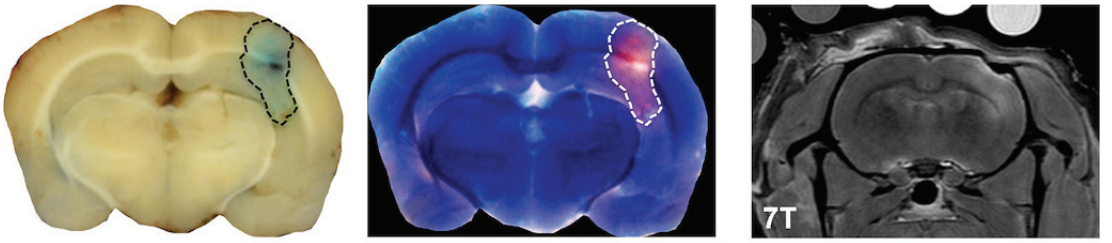
World Scientific

ICP Imperial College Press

PRESS RELEASE

Focal blood-brain-barrier disruption with high-frequency pulsed electric fields

July 15, 2014 — Novel method uses bursts of nanosecond duration electric pulses to open the blood-brain-barrier as a potential therapy for brain cancer and neurological disorders.



Pathologic and MRI evidence of blood-brain-barrier (BBB) disruption induced by the VEIN (Vascular Enabled Integrated Nanosecond) pulse generation system. Two, minimally invasive needle electrodes with 1 mm active length were spaced 4.0 mm apart and inserted into the right cerebral hemisphere 1.5 mm beneath the surface of the dura. A burst of 200, 500 ns duration square pulses of alternating polarity with a voltage-to-distance ratio of 250 V/cm were applied through the electrodes. In the case shown above, bursts were repeated once per second for 10 min. The extent of BBB disruption is shown by the dotted line surrounding Evans blue-albumin complex uptake on the gross brain slice preparation (left) and the corresponding fluorescent image (middle). Additionally, areas of BBB disruption appear as hyperintense (white) on the T1-weighted MRI exam, due to the uptake of a gadolinium-Evans blue tracer. Scale bar represents 5 mm. (Credit: John H. Rossmeisl Jr., Neurology and Neurosurgery, Virginia-Maryland Regional College of Veterinary Medicine and Virginia Tech-Wake Forest University School of Biomedical Engineering and Sciences).

A team of researchers from the Virginia Tech-Wake Forest University School of Biomedical Engineering and Sciences have developed a new way of using electricity to open the blood-brain-barrier (BBB). The Vascular Enabled Integrated Nanosecond pulse (VEIN pulse) procedure consists of inserting minimally invasive needle electrodes into the diseased tissue and applying multiple bursts of nanosecond pulses with alternating polarity. It is thought that the bursts disrupt tight junction proteins responsible for maintaining the integrity of the BBB without causing damage to the surrounding tissue. This technique is being developed for the treatment of brain cancer and neurological disorders, such as Parkinson's disease, and is set to appear in the upcoming issue of the journal TECHNOLOGY.

The BBB is a network of tight junctions that normally acts to protect the brain from foreign substances by preventing them from leaking out of blood vessels. However, it also limits the effectiveness of drugs to treat brain disease. Temporarily opening the BBB is a way to ensure that drugs can still be effective.

For the treatment of brain cancer, "VEIN pulses could be applied at the same time as biopsy or through the same track as the biopsy probe in order to mitigate damage to the healthy tissue by limiting the number of needle insertions," says Rafael V. Davalos, Ph.D., director of the Bioelectromechanical Systems Laboratory at Virginia Tech.

Additionally, the group shows that VEIN pulses can be applied without causing muscle contractions, which may dislodge the electrodes and require the use of a neuroblocker and general anesthesia. According to Christopher B. Arena, Ph.D., co-lead author on the paper with Paulo A. Garcia, Ph.D. and Michael B. Sano, Ph.D., "the fact that the pulses alternate in polarity helps to avoid unwanted, electrically induced movement. Therefore, it could be possible to perform this procedure without using a neuroblocker and with patients under conscious sedation. This is similar to how deep brain stimulation is implemented clinically to treat Parkinson's disease."

The team now plans to translate the technology into clinical applications through a university spin-out company, VoltMed, Inc.

Additional co-authors of the TECHNOLOGY paper are John D. Olson from the Center for Biomolecular Imaging at Wake Forest, and Thomas Rogers-Cotrone and John H. Rossmeisl Jr. from the Neurology and Neurosurgery department at the Virginia-Maryland Regional College of Veterinary Medicine.

This research was supported in part by grants from the National Science Foundation (CBET 1055913 and I-Corps 1265105), the Golfers Against Cancer, and the Center for Biomolecular Imaging in the Wake Forest School of Medicine.

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