Tiny bubbles offer sound solution for drug delivery

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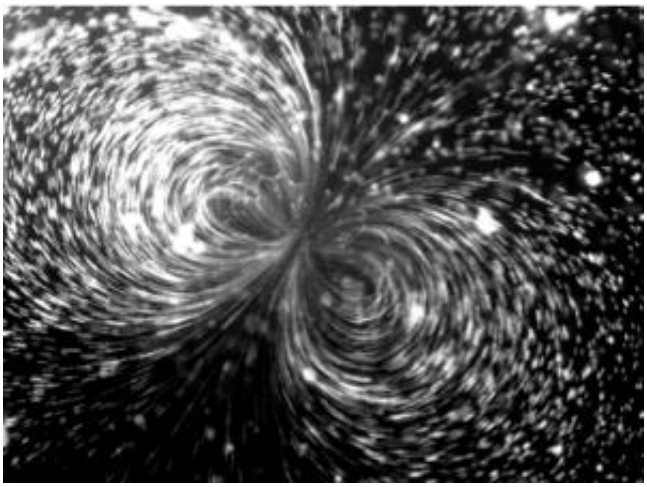

Cavitation microstreaming generated by a SonoVue microbubble and marked by fluorescent beads. Under ultrasound exposure, microbubbles can produce streaming flows which may contribute to blood-brain barrier opening and will be investigated directly using our in vitro platform. Credit: Miles M. Aron, courtesy of BUBBL, University of Oxford, England

Your brain is armored. It lives in a box made of bones with a security system of vessels. These vessels protect the brain and central nervous system from harmful chemicals circulating in the blood. Yet this protection system—known as the blood-brain barrier—also prevents delivery of drugs that could help treat patients with brain cancers and brain diseases such as Alzheimer's disease. The heavily guarded brain has long frustrated physicians tending patients in need of brain

treatments without surgery.

With recent advances in technology, the blood-brain barrier can now be opened safely, noninvasively and in a targeted manner using ultrasound. One of the newest approaches aiming to advance this research will be presented during Acoustics '17 Boston, the third joint meeting of the Acoustical Society of America and the European Acoustics Association being held June 25-29, in Boston, Massachusetts.

Investigators at the University of Oxford in the United Kingdom, collaborating with colleagues at the University of Twente in the Netherlands, have produced a promising in vitro experimental platform to investigate relationships between the way the blood-brain barrier opens, how long it takes to recover, and the sounds emitted during blood-brain barrier opening. Think of it as a blood-brain barrier on-a-chip using cultured cells rather than animal or human models.

"The key advantage of our system is that it uses three modalities—involving light, sound, and electrical fields—to simultaneously monitor acoustic emissions, blood-brain barrier disruption and recovery, and the biological response of blood-brain barrier cells in real-time," said Miles M. Aron at the University of Oxford.

Researchers have tried to open the blood-brain barrier using ultrasound since the 1950s. The breakthrough for safely opening the blood-brain barrier was to use tiny bubbles that interact with the ultrasound field known as "cavitation agents." Several cavitation agents are already approved for enhancing contrast in ultrasound imaging by the U.S. Food and Drug Administration. Cavitation agents work by oscillating rapidly or "singing" when exposed to ultrasound.

"The treatment can be monitored externally by 'listening' to the re-

radiated sound from the cavitation agents interacting with the ultrasound field. These acoustic emissions provide information regarding the energy of cavitation within the blood vessels and are already being used to adjust ultrasound parameters in real-time to reduce the likelihood of damaging healthy cells during treatment," Aron said.

The team monitors acoustic emissions and the integrity of the blood-brain barrier in real-time throughout the treatment, an improvement compared to other approaches that generally involve blood-brain barrier assessment only after the treatment is completed, Aron said.

In addition, the team uses fluorescent probes to monitor either changes in the cells during treatment, or mechanical and chemical effects from the cavitation agents as they are exposed to ultrasound in real-time.

"By analyzing multiple sources of data during ultrasound exposure and throughout BBB recovery, we aim to better understand this promising new treatment," Aron said. "With the Oxford Centre for Drug Delivery Devices, OxCD3, we are currently working on a non-invasive method to detect and treat brain metastases before they become deadly. Our in vitro system will play a critical role in the development of this and other next-generation approaches to ultrasound-mediated blood brain barrier opening."

More information: Main meeting website: acousticalsociety.org/content/acoustics-17-boston

Provided by Acoustical Society of America

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