

Focused Ultrasound *and the Blood-brain Barrier*

Overview

Focused ultrasound (FUS) is an innovative, noninvasive therapeutic technology that has the potential to improve the quality of life and decrease the cost of care for patients with neurological disorders, including brain tumors, neurodegenerative diseases, and psychiatric disorders. FUS utilizes beams of ultrasound energy focused on precise targets in the brain to create a variety of biological effects without damaging surrounding healthy tissue. The therapeutic effects of FUS are achieved without incisions or the use of radiation.

The blood-brain barrier (BBB) is a protective layer of tightly joined cells that lines the blood vessels in the brain and prevents harmful substances, such as toxins and infectious agents, from diffusing into the surrounding brain tissue. Unfortunately, the BBB also limits the amount of medication that can reach disease targets in the brain. A safe, temporary opening of this barrier may enable delivery of therapeutic concentrations of drugs to the brain and allow treatment of a wide range of neurologic conditions, including brain tumors, Alzheimer's disease, Parkinson's disease, ALS, epilepsy, and other neurodegenerative diseases and psychiatric disorders.

Focused ultrasound has been shown to open the BBB in a noninvasive, safe, and targeted manner. It is capable of reliably producing a therapeutic window of up to four hours immediately after treatment. FUS for BBB opening is performed in conjunction with intravenous administration of ultrasound contrast agents – also known as microbubbles. These microbubbles oscillate within the blood vessels in response to the applied ultrasound waves, putting localized pressure on the endothelial cells lining the vessels and forcing apart the tight junctions.

State of the Field

Safe, reliable, temporary, and repetitive opening of the BBB has been an unmet critical medical need for the delivery of therapeutics to the brain and the treatment of a range of neurological disorders. The current methods of getting through this barrier – either via direct brain injections or using mannitol – are far from ideal, and FUS may offer a safer, more controllable, and more effective option.

Currently, robust preclinical work is ongoing at several sites throughout the world using FUS in conjunction with microbubbles to open the BBB and deliver large molecules including drugs, DNA-loaded nanoparticles, gene-carrying viral vectors, and antibodies in models of Alzheimer's, Parkinson's, and gliomas. Clinical trials are also under way to assess the safety and feasibility of FUS to open the BBB in patients with gliomas and Alzheimer's disease.

The Foundation

In November 2017, the Focused Ultrasound Foundation held a workshop to determine the best path to advance ultrasound-mediated BBB opening, either alone or combined with drug delivery approaches (e.g., antibodies, viral vectors, or nanoparticles) for targeted treatment of a variety of neurological disorders. The Foundation convened a multidisciplinary group of thought leaders including ultrasound experts, neuroscientists, neurologists, neuroradiologists, and representatives from the FDA, the NIH, and industry. The [report arising from that workshop](#) serves as our roadmap for future studies.