Focused ultrasound

Physics

 1. Ultrasound Basics

Ultrasound = sound waves above 20,000 Hz (beyond human hearing).

FUS typically uses frequencies between 200 kHz to several MHz.

Ultrasound travels as longitudinal pressure waves through tissues, causing oscillations in the particles of the medium.

2. Focusing the Ultrasound

Just like light can be focused with a lens, ultrasound waves can be focused using:

Concave transducers (geometrical focusing)

Phased arrays (electronic focusing via time delays)

This concentrates the energy in a small focal zone (millimeter-sized), enabling precise targeting.

3. Mechanisms of Action

There are thermal and mechanical effects depending on intensity and duration:

 Thermal Effects (High-Intensity FUS) Absorption of ultrasound energy leads to tissue heating.

If temp > 60°C, it causes coagulative necrosis (e.g., in tumor ablation).

Mechanical Effects

Acoustic cavitation: formation and collapse of microbubbles (in liquids or tissues with gas), which can:

Increase BBB permeability

Causes microstreaming and shear stress

Radiation force: ultrasound can push or displace tissue, used in neuromodulation or drug delivery.

4. Applications in Neuroscience

MRgFUS (MRI-guided focused ultrasound) is used for:

Thalamotomy for essential tremor

Reversible BBB opening (for chemo delivery in glioblastoma)

Neuromodulation without thermal damage (low-intensity FUS)

5. Key Physical Parameters

Parameter Description

Frequency (f) Affects penetration and resolution Intensity (I) Power per unit area, determines heating/mechanics Focal length Distance from transducer to focus Beam width Size of focal zone, smaller = higher precision Duty cycle % of time the ultrasound is “on” Pulse repetition Relevant in pulsed FUS (for non-thermal effects)

CNS Anatomical Targets & Indications 1. Thalamus Target: Ventral intermediate nucleus (Vim) of the thalamus

Application:

Essential tremor

Parkinsonian tremor

Mechanism: High-intensity focused ultrasound (HIFU) causes thermocoagulative lesioning for tremor suppression.

Guidance: MRI-guided (MRgFUS)

2. Globus Pallidus Internus (GPi) Application:

Parkinson’s disease (dyskinesia, rigidity)

Dystonia

Mechanism: Lesioning via thermal ablation

3. Subthalamic Nucleus (STN) Application:

Advanced Parkinson’s disease

Note: Currently less used than Vim or GPi due to anatomical complexity and potential for side effects.

4. Anterior Limb of the Internal Capsule (ALIC) Application:

 Obsessive-compulsive disorder (OCD)

 Major depressive disorder (MDD)

Mechanism: Capsulotomy using FUS as a non-invasive psychiatric neurosurgical intervention.

5. Hippocampus Application:

 Experimental seizure control in temporal lobe epilepsy

Mechanism: Lesioning or neuromodulation (research phase)

6. Brain Tumors & Metastases Targets: Variable — glioblastoma, meningioma, metastases

Application:

 BBB opening for chemotherapy delivery

 Thermal ablation of tumors (in selected cases)

Mechanism:

Reversible blood-brain barrier (BBB) disruption using microbubble-enhanced low-intensity FUS

Experimental direct ablation (only in accessible areas)

7. Brainstem / Pons / Cerebellum Application: Mostly experimental

 Neuromodulation

 Pain control (e.g., central post-stroke pain)

Challenge: Proximity to critical structures → requires very precise targeting

8. Spinal Cord (experimental) Research into neuromodulation of the dorsal columns or motor tracts

Challenging due to acoustic shadowing by vertebral bone and narrow intervertebral windows

 Non-CNS Targets Prostate: Ablation for prostate cancer or BPH

Uterus: Fibroid treatment

Liver, kidney, pancreas: Tumor ablation

Bone metastases: Pain palliation

 Summary Table Target Area FUS Application Mechanism Vim (Thalamus) Essential tremor, Parkinsonian tremor Lesioning GPi Parkinson’s, Dystonia Lesioning ALIC OCD, Depression Capsulotomy Tumor areas BBB opening, Ablation Cavitation / Thermal Hippocampus Epilepsy (research) Lesion / Modulation Spinal Cord Neuromodulation (research) Modulation

see MRgFUS

see High Intensity focused ultrasound.

Focused ultrasound is a unique noninvasive technique that can transiently disrupt the blood-brain barrier (BBB) and increase accumulation of drugs within targeted areas of the brain.

Arsiwala et al. summarized the current understanding of different types of targeted ultrasound mediated BBB/BTB disruption techniques. We also discuss influence of the tumor microenvironment on BBB opening, as well as the role of immunological response following disruption. Lastly, we highlight the gaps between evaluation of the parameters governing opening of the BBB/BTB. A deeper understanding of physical opening of the BBB/BTB and the biological effects following disruption can potentially enhance treatment strategies for patients with brain tumors [1].

1)
Arsiwala TA, Sprowls SA, Blethen KE, Adkins CE, Saralkar PA, Fladeland RA, Pentz W, Gabriele A, Kielkowski B, Mehta RI, Wang P, Carpenter JS, Ranjan M, Najib U, Rezai AR, Lockman PR. Ultrasound-mediated disruption of the blood tumor barrier for improved therapeutic delivery. Neoplasia. 2021 Jun 14;23(7):676-691. doi: 10.1016/j.neo.2021.04.005. Epub ahead of print. PMID: 34139452.