# Histotripsy

Histotripsy is the first noninvasive, non-ionizing, and non-thermal ablation technology guided by real-time imaging. Using focused ultrasound delivered from outside the body, histotripsy mechanically destroys tissue through cavitation, rendering the target into acellular debris.

## Histotripsy in neurosurgery

- Overcoming the Blood-Brain Barrier: Focused Ultrasound in Glioblastoma Treatment
- Acoustic Cavitation Emissions Predict Near-complete/complete Histotripsy Treatment in Soft Tissues
- A pre-clinical MRI-guided all-in-one focused ultrasound system for murine brain studies
- Rescue Stenting for Failed Mechanical Thrombectomy in Acute Basilar Artery Occlusions: Analysis of the PC-SEARCH Registry
- State of Practice on Transcranial MR-Guided Focused Ultrasound: A Report from the ASNR Standards and Guidelines Committee and ACR Commission on Neuroradiology Workgroup
- Treatment envelope of transcranial histotripsy: challenges and strategies to maximize the treatment location profile
- Boiling Histotripsy in Ex Vivo Human Brain: Proof-of-concept
- Future Directions of MR-guided Focused Ultrasound

A in vitro study investigated the effects of ultrasound frequency and focal spacing on blood clot liquefaction via transcranial histotripsy. Histotripsy pulses were delivered using two 256-element hemispherical transducers of different frequency (250 and 500 kHz) with 30-cm aperture diameters. A 4-cm diameter spherical volume of in vitro blood clot was treated through 3 excised human skullcaps by electronically steering the focus with frequency proportional focal spacing: λ/2, 2 λ/3 and λ with 50 pulses per location. The pulse repetition frequency across the volume was 200 Hz, corresponding to a duty cycle of 0.08% (250 kHz) and 0.04% (500 kHz) for each focal location. Skull heating during treatment was monitored. Liquefied clot was drained via catheter and syringe in the range of 6-59 mL in 0.9-42.4 min. The fastest rate was 16.6 mL/min. The best parameter combination was λ spacing at 500 kHz, which produced large liquefaction through 3 skullcaps (23.1 ± 4.0, 37.1 ± 16.9 and 25.4 ± 16.9 mL) with the fast rates (3.2 ± 0.6, 5.1 ± 2.3 and 3.5 ± 0.4 mL/min). The temperature rise through the 3 skullcaps remained below 4°C [1)]

## Dosages

Duclos et al. studied the effect of various histotripsy dosages on tumor cell kill and associated bleeding in a murine glioma model (glioma [Gl261] and lung metastasis [LL/2-Luc2]).

GL261 or LL/2-Luc2 cells were cultured and implanted into the brains of C57BL/6 mice. Histotripsy (1-cycle pulses, 5 Hz PRF, 30 MPa-P) was performed using a 1 MHz transducer for five different dosages for each cell line: 5, 20 or 200 pulses per location (PPL) at a single treatment point, or 5 or 10-20 PPL at multiple treatment points. MRI, bioluminescence imaging and histology were used to assess tumor ablation and treatment effects within 4-6 h post-treatment.

All treatment groups resulted in a reduction of BLI intensity for the LL/2-Luc2 tumors, with significant signal reductions for the multi-point groups. The average pre-/post-treatment BLI flux (photons/s, ×108) for the different treatment groups were: 4.39/2.19 (5 PPL single-point), 5.49/1.80 (20 PPL single-point), 3.86/1.73 (200 PPL single-point), 2.44/1.11 (5 PPL multi-point) and 5.85/0.80 (10 PPL multi-point). MRI and H&E staining showed increased tumor damage and hemorrhagic effects with increasing histotripsy dose for both GL261 and LL/2-Luc2 tumors, but the increase in tumor damage was diminished beyond 10-20 PPL for single-point treatments and outweighed by increased hemorrhage. In general, hemorrhage was confined to be within 1 mm of the treatment boundary for all groups [2)]

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